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(54) Title: COMPOSITIONS AND METHODS FOR IMMUNOONCOLOGY

(57) Abstract: The present invention is directed to genome editing systems, reagents and methods for immunooncology.

COMPOSITIONS AND METHODS FOR IMMUNOONCOLOGY

RELATED APPLICATIONS

This application claims priority to U.S. Provisional patent application number 62/263169, filed December 4, 2015, U.S. Provisional patent application number 62/316784, filed April 1, 2016, and U.S. Provisional patent application number 62/394290, filed September 14, 2016. The entire contents of these applications are incorporated herein by reference.

BACKGROUND

CRISPRs (Clustered Regularly Interspaced Short Palindromic Repeats) evolved in bacteria as an adaptive immune system to defend against viral attack. Upon exposure to a virus, short segments of viral DNA are integrated into the CRISPR locus of the bacterial genome. RNA is transcribed from a portion of the CRISPR locus that includes the viral sequence. That RNA, which contains sequence complimentary to the viral genome, mediates targeting of a Cas9 protein to the sequence in the viral genome. The Cas9 protein cleaves and thereby silences the viral target.

Recently, the CRISPR/Cas system has been adapted for genome editing in eukaryotic cells. The introduction of site-specific single (SSBs) or double strand breaks (DSBs) allows for target sequence alteration through, for example, non-homologous end-joining (NHEJ) or homology-directed repair (HDR).

SUMMARY OF THE INVENTION

The inventions described herein relate to compositions and methods for immunooncology, for example, cells modified at specific target sequences in their genome, including as modified by introduction of CRISPR systems that include gRNA molecules which target said target sequences, and methods of making and using therefore. For example, the present disclosure relates to gRNA molecules, CRISPR systems, cells, and methods useful for genome editing of cells, e.g., T cells, e.g., T-cells further engineered to express a chimeric antigen receptor, and useful for treating diseases such as cancers.

In a first aspect, the invention provides a gRNA molecule including a tracr and crRNA, wherein the crRNA includes a targeting domain that is complementary with a target sequence of an allogeneic T-cell

target selected from B2M, CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, TRBC2, HLA-A, HLA-B, HLA-C, DCK, CD52, FKBP1A, CIITA, NLRC5, RFXANK, RFX5, RFXAP, or NR3C1.

In embodiments of the gRNA molecule:

2(a) the allogeneic T-cell target is B2M, and the targeting domain includes any one of SEQ ID NO: 1 to SEQ ID NO: 83 or SEQ ID NO: 5492 to SEQ ID NO: 5527;

2(b) the allogeneic T-cell target is TRAC, and the targeting domain includes any one of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965;

2(c) the allogeneic T-cell target is TRBC1, and the targeting domain includes any one of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097;

2(d) the allogeneic T-cell target is TRBC2, and the targeting domain includes any one of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226;

2(e) the allogeneic T-cell target is CD247, and the targeting domain includes any one of SEQ ID NO: 84 to SEQ ID NO: 392;

2(f) the allogeneic T-cell target is CD3D, and the targeting domain includes any one of SEQ ID NO: 393 to SEQ ID NO: 532 or SEQ ID NO: 10780 to SEQ ID NO: 10794;

2(g) the allogeneic T-cell target is CD3E, and the targeting domain includes any one of SEQ ID NO: 533 to SEQ ID NO: 839 or SEQ ID NO: 10677 to SEQ ID NO: 10764;

2(h) the allogeneic T-cell target is CD3G, and the targeting domain includes any one of SEQ ID NO: 840 to SEQ ID NO: 968 or SEQ ID NO: 10765 to SEQ ID NO: 10779;

2(i) the allogeneic T-cell target is HLA-A, and the targeting domain includes any one of SEQ ID NO: 969 to SEQ ID NO: 1345;

2(j) the allogeneic T-cell target is HLA-B, and the targeting domain includes any one of SEQ ID NO: 1346 to SEQ ID NO: 1698;

2(k) the allogeneic T-cell target is HLA-C, and the targeting domain includes any one of SEQ ID NO: 1699 to SEQ ID NO: 2068;

2(l) the allogeneic T-cell target is DCK, and the targeting domain includes any one of SEQ ID NO: 5278 to SEQ ID NO: 5491;

2(m) the allogeneic T-cell target is CD52, and the targeting domain includes any one of SEQ ID NO: 6227 to SEQ ID NO: 6324;

2(n) the allogeneic T-cell target is FKBP1A, and the targeting domain includes any one of SEQ ID NO: 6325 to SEQ ID NO: 6583 or SEQ ID NO: 6662 to SEQ ID NO: 6749;

2(o) the allogeneic T-cell target is NR3C1, and the targeting domain includes any one of SEQ ID NO: 2069 to SEQ ID NO: 2941;

2(p) the allogeneic T-cell target is CIITA, and the targeting domain includes any one of SEQ ID NO: 6750 to SEQ ID NO: 7716 or SEQ ID NO: 7717 to SEQ ID NO: 7804; or

2(q) the allogeneic T-cell target is NLRC5, and the targeting domain includes any one of SEQ ID NO: 8622 to SEQ ID NO: 10089.

In embodiments of the gRNA molecule, the allogeneic T-cell target is TRAC, and the targeting domain includes SEQ ID NO: 5569, SEQ ID NO: 5585, SEQ ID NO: 5587, SEQ ID NO: 5592, SEQ ID NO: 5601, SEQ ID NO: 5589, SEQ ID NO: 5600, SEQ ID NO: 5594, SEQ ID NO: 5571, SEQ ID NO: 5593, SEQ ID NO: 5574,SEQ ID NO: 5598, SEQ ID NO: 5586, SEQ ID NO: 5599, SEQ ID NO: 5591, SEQ ID NO: 5610, SEQ ID NO: 5608, SEQ ID NO: 5617, SEQ ID NO: 5619, or SEQ ID NO: 5620., for example, the targeting domain includes SEQ ID NO: 5569, SEQ ID NO: 5586, SEQ ID NO: 5587, SEQ ID NO: 5592, SEQ ID NO: 5599, or SEQ ID NO: 5600, for example, targeting domain includes SEQ ID NO: 5569, SEQ ID NO: 5587, SEQ ID NO: 5592 or SEQ ID NO: 5586, for example, the targeting domain includes SEQ ID NO: 5569.

In embodiments of the gRNA molecule, the allogeneic T-cell target is TRBC2, and the targeting domain includes SEQ ID NO: 5719, SEQ ID NO: 5694, SEQ ID NO: 5706, SEQ ID NO: 5696, SEQ ID NO: 5711, SEQ ID NO: 5708, SEQ ID NO: 5709, SEQ ID NO: 5712, SEQ ID NO: 5703, SEQ ID NO: 5707, SEQ ID NO: 5687, SEQ ID NO: 5705, SEQ ID NO: 5713, SEQ ID NO: 5715, or SEQ ID NO: 5710.

In embodiments of the gRNA molecule, the allogeneic T-cell target is B2M, and the targeting domain includes SEQ ID NO: 5519, SEQ ID NO: 5497, SEQ ID NO: 5499, SEQ ID NO: 5498, SEQ ID NO: 5503, SEQ ID NO: 5496, SEQ ID NO: 5507, SEQ ID NO: 5515, SEQ ID NO: 5493, SEQ ID NO: 5506, SEQ ID NO: 5509, SEQ ID NO: 5517, SEQ ID NO: 5521, SEQ ID NO: 5520, SEQ ID NO: 5500, SEQ ID NO: 5494, SEQ ID NO: 5508, SEQ ID NO: 5514, or SEQ ID NO: 5492, for example, the targeting domain includes SEQ ID NO: 5496, SEQ ID NO: 5498, or SEQ ID NO: 5509.

In embodiments of the gRNA molecule, the allogeneic T-cell target is CIITA, and the targeting domain includes SEQ ID NO: 7771, SEQ ID NO: 7769, SEQ ID NO: 7773, SEQ ID NO: 7726, SEQ ID NO: 7758, SEQ ID NO: 7739, SEQ ID NO: 7779, SEQ ID NO: 7770, SEQ ID NO: 7749, SEQ ID NO: 7754, SEQ ID NO: 7745, SEQ ID NO: 7785, SEQ ID NO: 7731, SEQ ID NO: 7772, SEQ ID NO: 7743, or SEQ ID NO: 7750, for example, the targeting domain includes SEQ ID NO: 7769, SEQ ID NO: 7771, SEQ ID NO: 7739, or SEQ ID NO: 7785.

In embodiments of the gRNA molecule, the allogeneic T-cell target is CD3E, and the targeting domain includes SEQ ID NO: 10729, SEQ ID NO: 10719, SEQ ID NO: 10764, SEQ ID NO: 10789, SEQ ID NO: 10701, SEQ ID NO: 10700, or SEQ ID NO: 10722.

In embodiments of the gRNA molecule, the allogeneic T-cell target is FKBP1A, and the targeting domain includes SEQ ID NO: 6693, SEQ ID NO: 6705, SEQ ID NO: 6694, SEQ ID NO: 6708, or SEQ ID NO: 6699.

In a second aspect, the invention provides a gRNA molecule including a tracr and crRNA, wherein the crRNA includes a targeting domain that is complementary with a target sequence of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule selected from CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, or PTPN11.

In embodiments of the gRNA molecule:

15(a) the inhibitory molecule is CD274 (PD-L1), and the targeting domain includes any one of SEQ ID NO: 2942 to SEQ ID NO: 3270;

15(b) the inhibitory molecule is HAVCR2 (TIM3), and the targeting domain includes any one of SEQ ID NO: 3271 to SEQ ID NO: 3541;

15(c) the inhibitory molecule is LAG3, and the targeting domain includes any one of SEQ ID NO: 3542 to SEQ ID NO: 4032;

15(d) the inhibitory molecule is PDCD1 (PD-1), and the targeting domain includes any one of SEQ ID NO: 4033 to SEQ ID NO: 4589 or SEQ ID NO: 5720 to SEQ ID NO: 5815; or

15(e) the downstream effector of signaling through an inhibitory molecule is PTPN1, and the targeting domain includes any one of SEQ ID NO: 4590 to SEQ ID NO: 5277.

In embodiments of the gRNA molecule, the inhibitory molecule is PDCD1, and the targeting domain includes SEQ ID NO: 5743, SEQ ID NO: 5798, SEQ ID NO: 5748, SEQ ID NO: 5722, SEQ ID NO: 5800, SEQ ID NO: 5735, SEQ ID NO: 5724, SEQ ID NO: 5731, SEQ ID NO: 5725, SEQ ID NO: 5775, SEQ ID NO: 5766, SEQ ID NO: 5727, SEQ ID NO: 5744, SEQ ID NO: 5751, or SEQ ID NO: 5734, for example, the targeting domain includes SEQ ID NO: 5775.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the targeting domain includes 17, 18, 19, 20, 21 (if present in the reference sequence), 22 (if present in the reference sequence), 23 (if present in the reference sequence), 24 (if present in the reference sequence), or 25 (if present in the reference sequence) consecutive nucleic acids of any one of the recited targeting domain sequences. In other embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the targeting domain consists of 17, 18, 19, 20, 21 (if present in the reference sequence), 22 (if present in the reference sequence), 23 (if present in the reference sequence), or 24 (if present in the reference sequence), or 25 (if present in the reference sequence) consecutive nucleic acids of any one of the recited targeting domain sequences. In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the 17, 18, 19, 20, 21 (if present in the reference sequence), 22 (if present in the reference sequence), 23 (if present in the reference sequence), or 24 (if present in the reference sequence), or 25 (if present in the reference sequence) consecutive nucleic acids of any one of the recited targeting domain sequences are the 17, 18, 19, 20, 21 (if present in the reference sequence), 22 (if present in the reference sequence), 23 (if present in the reference sequence), or 24 (if present in the reference sequence), or 25 (if present in the reference sequence) consecutive nucleic acids disposed at the 3' end of the recited targeting domain sequence. In other embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the 17, 18, 19, 20, 21 (if present in the reference sequence), 22 (if present in the reference sequence), 23 (if present in the reference sequence), or 24 (if present in the reference sequence), or 25 (if present in the reference sequence) consecutive nucleic acids of any one of the recited targeting domain sequences are the 17, 18, 19, 20, 21 (if present in the reference sequence), 22 (if present in the reference sequence), 23 (if present in the reference sequence), or 24 (if present in the reference sequence), or 25 (if present in the reference sequence) consecutive nucleic acids disposed at the 5' end of the recited targeting domain sequence. In other embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the 17, 18, 19, 20, 21 (if present in the reference sequence), 22 (if present in the reference sequence), 23 (if present in the reference sequence), or 24 (if present in the reference

sequence), or 25 (if present in the reference sequence) consecutive nucleic acids of any one of the recited targeting domain sequences do not include either the 5' or 3' nucleic acid of the recited targeting domain sequence.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the targeting domain consists of the recited targeting domain sequence.

The following general aspects of the gRNA molecule may be combined, alone or in combination, with any of the gRNAs comprising a targeting domain described herein, for example, a targeting domain recited in any of the aforementioned aspects and embodiments.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, a portion of the crRNA and a portion of the tracr hybridize to form a flagpole including SEQ ID NO: 6584 or SEQ ID NO: 6585. In other embodiments, the flagpole further includes a first flagpole extension, located 3' to the crRNA portion of the flagpole, wherein said first flagpole extension includes SEQ ID NO: 6586. In other embodiments, the flagpole further includes a second flagpole extension located 3' to the crRNA portion of the flagpole and, if present, the first flagpole extension, wherein said second flagpole extension includes SEQ ID NO: 6587.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the tracr includes, for example, consists of:

(a) SEQ ID NO: 7820, optionally further including, at the 3' end, an additional 1, 2, 3, 4, 5, 6, or 7 uracil (U) nucleotides;

(b) SEQ ID NO: 6660; or

(c) SEQ ID NO: 6661. In such embodiments, the crRNA portion of the flagpole includes SEQ ID NO: 6607 or SEQ ID NO: 6608.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the tracr includes SEQ ID NO: 6589 or SEQ ID NO: 6590, and optionally, if a first flagpole extension is present, a first tracr extension, disposed 5' to SEQ ID NO: 6589 or SEQ ID NO: 6590, said first tracr extension including SEQ ID NO: 6591.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the targeting domain and the tracr are disposed on separate nucleic acid molecules.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the crRNA includes (for example, consists of), from 5' to 3', [targeting domain]-:

a) SEQ ID NO: 6584;

b) SEQ ID NO: 6585;

c) SEQ ID NO: 6605;

d) SEQ ID NO: 6606;

e) SEQ ID NO: 6607;

f) SEQ ID NO: 6608; or

g) SEQ ID NO: 7806.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the tracr includes (for example, consists of), from 5' to 3':

a) SEQ ID NO: 6589;

b) SEQ ID NO: 6590;

c) SEQ ID NO: 6609;

d) SEQ ID NO: 6610;

e) SEQ ID NO: 6660;

f) SEQ ID NO: 6661;

g) SEQ ID NO: 7820;

h) SEQ ID NO: 7807;

i) SEQ ID NO: 7808;

j) SEQ ID NO: 7809;

k) any of a) to j), above, further including, at the 3' end, at least 1, 2, 3, 4, 5, 6 or 7 uracil (U) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 uracil (U) nucleotides;

l) any of a) to k), above, further including, at the 3' end, at least 1, 2, 3, 4, 5, 6 or 7 adenine (A) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 adenine (A) nucleotides; or

m) any of a) to l), above, further including, at the 5' end (e.g., at the 5' terminus), at least 1, 2, 3, 4, 5, 6 or 7 adenine (A) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 adenine (A) nucleotides.

In preferred embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the targeting domain and the tracr are disposed on separate nucleic acid molecules, and the nucleic acid molecule including the targeting domain includes SEQ ID NO: 6607, optionally disposed immediately 3' to the targeting domain, and the nucleic acid molecule including the tracr includes, e.g., consists of, SEQ ID NO: 6660.

In other embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the targeting domain and the tracr are disposed on a single nucleic acid molecule, and wherein the tracr is disposed 3' to the targeting domain. In such embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the gRNA molecule further includes a loop, disposed 3' to the targeting domain and 5' to the tracr, for example, a loop that includes (for example, consists of) SEQ ID NO: 6588.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the gRNA molecule includes (for example, consists of), from 5' to 3', [targeting domain]-:

(a) SEQ ID NO: 6601;

(b) SEQ ID NO: 6602;

(c) SEQ ID NO: 6603;

(d) SEQ ID NO: 6604;

(e) SEQ ID NO: 7811; or

(f) any of (a) to (e), above, further including, at the 3' end, 1, 2, 3, 4, 5, 6 or 7 uracil (U) nucleotides.

In preferred embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the targeting domain and the tracr are disposed on a single nucleic acid molecule, and wherein said nucleic acid molecule includes, e.g., consists of, said targeting domain and SEQ ID NO: 6601, optionally disposed immediately 3' to said targeting domain.

In preferred embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, the targeting domain and the tracr are disposed on a single nucleic acid molecule, and

wherein said nucleic acid molecule includes, e.g., consists of, said targeting domain and SEQ ID NO: 7811, optionally disposed immediately 3' to said targeting domain.

In embodiments, the gRNA molecule consists of unmodified RNA nucleotides and nucleic acid bonds. In other embodiments, the gRNA molecule contains one or more modifications, for example as described herein. In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, one, or optionally more than one, of the nucleic acid molecules of the gRNA molecule includes:

a) a, e.g., three, phosphorothioate modification(s) at the 3' end of said nucleic acid molecule or molecules;

b) a, e.g., three, phosphorothioate modification(s) at the 5' end of said nucleic acid molecule or molecules;

c) a, e.g., three, 2'-O-methyl modification(s) at the 3' end of said nucleic acid molecule or molecules;

d) a, e.g., three, 2'-O-methyl modification(s) at the 5' end of said nucleic acid molecule or molecules;

e) a 2' O-methyl modification at each of the 4^{th}-to-terminal, 3^{rd}-to-terminal, and 2^{nd}-to-terminal 3' residues of said nucleic acid molecule or molecules; or

f) any combination thereof.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, when a CRISPR system (e.g., an RNP as described herein, e.g., an RNP that includes a Cas9 molecule, for example as described herein) including the gRNA molecule (e.g., as described herein) is introduced into a cell, an indel is formed at or near the target sequence complementary to the targeting domain of the gRNA molecule. In embodiments, the indel is a frameshift mutation. In embodiments, the indel is an indel listed in any of Figure 34A, Figure 34B, Figure 36, Figure 38, Figure 41, Figure 44, Figure 48, Figure 49, Figure 50 or Figure 53.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, when a CRISPR system (e.g., an RNP as described herein, e.g., an RNP that includes a Cas9 molecule, for example as described herein) including the gRNA molecule (e.g., as described herein) is introduced into a population of cells, an indel is formed at or near the target sequence complementary to the targeting domain of the gRNA molecule in at least about 40%, e.g., at least about 50%, e.g., at least about 60%, e.g., at least about 70%, e.g., at least about 80%, e.g., at least about 90%, e.g., at least about

95%, e.g., at least about 96%, e.g., at least about 97%, e.g., at least about 98%, e.g., at least about 99%, of the cells of the population. In embodiments, an indel that is a frameshift mutation is formed at or near the target sequence complementary to the targeting domain of the gRNA molecule in at least about 20%, e.g., at least about 30%, e.g., at least about 35%, e.g., at least about 40%, e.g., at least about 45%, e.g., at least about 50%, e.g., at least about 55%, e.g., at least about 60%, e.g., at least about 65%, e.g., at least about 70%, e.g., at least about 75%, e.g., at least about 80%, e.g., at least about 85%, e.g., at least about 90%, e.g., at least about 95%, e.g., at least about 99%, of the cells of the population. In embodiments, in at least about 30%, e.g., least about 40%, e.g., at least about 50%, e.g., at least about 60%, e.g., at least about 70%, e.g., at least about 80%, e.g., at least about 90%, e.g., at least about 95%, e.g., at least about 96%, e.g., at least about 97%, e.g., at least about 98%, e.g., at least about 99%, of the cells of the population, the indel is an indel listed in any of Figure 34A, Figure 34B, Figure 36, Figure 38, Figure 41, Figure 44, Figure 48, Figure 49, Figure 50 or Figure 53. In embodiments, the five most frequently detected indels in said population of cells include three or more, e.g., four, e.g., five, of the indels associated with any gRNA listed in any of Figure 34A, Figure 34B, Figure 36, Figure 38, Figure 41, Figure 44, Figure 48, Figure 49, Figure 50 or Figure 53. The indel or indel pattern is as measured and/or quantitated by, for example, next generation sequencing (NGS).

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, when a CRISPR system (e.g., an RNP as described herein, e.g., an RNP that includes a Cas9 molecule, for example as described herein) including the gRNA molecule (e.g., as described herein) is introduced into a cell (or population of cells) as described herein, expression of the gene including the target sequence complementary to the targeting domain of the gRNA molecule is reduced or eliminated in said cell. In embodiments, expression of said gene is reduced or eliminated in at least about 40%, e.g., at least about 50%, e.g., at least about 60%, e.g., at least about 70%, e.g., at least about 80%, e.g., at least about 90%, e.g., at least about 95%, e.g., at least about 96%, e.g., at least about 97%, e.g., at least about 98%, e.g., at least about 99%, of the cells of the population. In embodiments, the reduced or eliminated expression is measured by flow cytometry. In other embodiments, for example, in the case of FKBP1A, reduced or eliminated expression is measured by a functional assay, for example as described herein.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, when a CRISPR system (e.g., an RNP as described herein, e.g., an RNP that includes a Cas9 molecule, for example as described herein) including the gRNA molecule (e.g., as described herein) is introduced into a cell as described herein, no off-target indels are formed in said cell, e.g., as detectible by next generation sequencing and/or a nucleotide insertional assay, for example as described herein.

In embodiments of the gRNA molecule, including in any of the aforementioned aspects and embodiments, when a CRISPR system (e.g., an RNP as described herein, e.g., an RNP that includes a Cas9 molecule, for example as described herein) including the gRNA molecule (e.g., as described herein) is introduced into a population of cells as described herein, an off-target indel is detected in no more than about 5%, e.g., no more than about 1%, e.g., no more than about 0.1%, e.g., no more than about 0.01%, of the cells of the population of cells e.g., as detectible by next generation sequencing and/or a nucleotide insertional assay.

In any of the aforementioned aspects and embodiments reciting a cell, the cell is (or population of cells includes) a mammalian, primate, or human cell, e.g., is a human cell. In any of the aforementioned aspects and embodiments reciting a cell, the cell is (or population of cells includes) an immune effector cell, for example, a T cell or NK cell, e.g., is a T cell, for example, a CD4+ T cell, a CD8+ T cell, or a combination thereof.

In any of the aforementioned aspects and embodiments reciting a cell, the cell (or population of cells) has been, or will be, engineered to express a chimeric antigen receptor (CAR). In embodiments, the CAR is:

(a) a CD19 CAR; or

(b) a BCMA CAR. In embodiments:

(a) the CAR is a CD19 CAR including an antigen binding domain including any one of SEQ ID NO: 7883 to SEQ ID NO: 7898;

(b) the CAR is a CD19 CAR including SEQ ID NO: 7909 or SEQ ID NO: 7920;

(c) the CAR is a BCMA CAR including an antigen binding domain including any one of SEQ ID NO: 7939 to SEQ ID NO: 8112, e.g., including an antigen binding domain of SEQ ID NO: 7949; or

(d) the CAR is a BCMA CAR including any one of SEQ ID NO: 8549 to SEQ ID NO: 8621, e.g., including SEQ ID NO: 8559.

In any of the aforementioned aspects and embodiments reciting a cell, the cell is allogeneic with respect to a patient to be administered said cell. In other embodiments, the cell is autologous with respect to a patient to be administered said cell.

In another aspect, the invention provides a composition including a first gRNA molecule of any of the previous aspects and embodiments, further including a Cas9 molecule. In embodiments, the Cas9 molecule includes, e.g., consists of, any one of SEQ ID NO: 6611 or SEQ ID NO: 7821 to SEQ ID NO:

7831. In embodiments, the Cas9 molecule is an active or inactive *s. pyogenes* Cas9. In preferred embodiments, the first gRNA molecule and Cas9 molecule are present in a ribonuclear protein complex (RNP).

In aspects, the composition may include more than one gRNA molecule, for example, more than one gRNA molecule, each of which is complexed with a Cas9 molecule described herein. For example, in embodiments, the composition further includes a second gRNA molecule; a second gRNA molecule and a third gRNA molecule; or a second gRNA molecule, a third gRNA molecule, and a fourth gRNA molecule, wherein the second gRNA molecule, the third gRNA molecule (if present), and the fourth gRNA molecule (if present) are a gRNA molecule as described herein, for example, a gRNA molecule of any of the previous aspects and embodiments, and wherein each gRNA molecule of the composition is complementary to a different target sequence (i.e., comprises a different targeting domain). In embodiments, the first gRNA molecule, the second gRNA molecule, the third gRNA molecule (if present), and the fourth gRNA molecule (if present) are complementary to target sequences within the same gene. In such embodiments, the first gRNA molecule, the second gRNA molecule, the third gRNA molecule (if present), and the fourth gRNA molecule (if present) are complementary to target sequences not more than 20000 nucleotides, not more than 10000 nucleotides, not more than 6000, not more than 5000 nucleotides, not more than 4000, not more than 1000 nucleotides, not more than 500 nucleotides, not more than 400 nucleotides, not more than 300 nucleotides, not more than 200 nucleotides, not more than 100 nucleotides, not more than 90 nucleotides, not more than 80 nucleotides, not more than 70 nucleotides, not more than 60 nucleotides, not more than 50 nucleotides, not more than 40 nucleotides, not more than 30 nucleotides, not more than 20 nucleotides or not more than 10 nucleotides apart. In other embodiments the first gRNA molecule, the second gRNA molecule, the third gRNA molecule (if present), and the fourth gRNA molecule (if present) are complementary to target sequence within different genes or loci, for example, different genes as described herein.

In embodiments, the first gRNA molecule is the gRNA molecule of any of 2(b), 2(c), 2(d), 2(d), 2(e), 2(f), 2(g) or 2(h); and the second gRNA molecule is the gRNA molecule of any of 2(a), 2(i), 2(j), 2(k) or 2(q); and the third gRNA molecule is the gRNA molecule of any of 15(a), 15(b), 15(c), 15(d), or 15(e). In other embodiments, the first gRNA molecule is the gRNA molecule of any of 2(b), 2(c), 2(d), 2(d), 2(e), 2(f), 2(g) or 2(h); and the second gRNA molecule is the gRNA molecule of any of 2(l), 2(m), 2(n), or 2(o); and the third gRNA molecule is the gRNA molecule of any of 15(a), 15(b), 15(c), 15(d), or 15(e). In other embodiments, the first gRNA molecule is the gRNA molecule of any of 2(b), 2(c), 2(d), 2(d), 2(e), 2(f), 2(g) or 2(h); and the second gRNA molecule is the gRNA molecule of any of 2(l), 2(m), 2(n), or 2(o). In other embodiments, the first gRNA molecule is the gRNA molecule of any of 2(b), 2(c),

2(d), 2(d), 2(e), 2(f), 2(g) or 2(h); and the second gRNA molecule is the gRNA molecule of any of 2(a), 2(i), 2(j), or 2(k). In other embodiments, the first gRNA molecule is the gRNA molecule of any of 2(b), 2(c), 2(d), 2(d), 2(e), 2(f), 2(g) or 2(h); and the second gRNA molecule is the gRNA molecule of any of 15(a), 15(b), 15(c), 15(d), or 15(e). In other embodiments, first gRNA molecule is the gRNA molecule of any of 15(a), 15(b), 15(c), 15(d), or 7(e); and the second gRNA molecule is the gRNA molecule of any of 15(a), 15(b), 15(c), 15(d), or 15(e). In embodiments of any of the aforementioned embodiments, a third gRNA is present, and the third gRNA molecule is a gRNA molecule of any of 15(a), 15(b), 15(c), 15(d), or 15(e). In embodiments, the composition consists of two gRNA molecules of any of the aforementioned gRNA molecule aspects and embodiments. In embodiments, the composition consists of three gRNA molecules of any of the aforementioned gRNA molecule aspects and embodiments. In embodiments, the composition consists of a first gRNA molecule of any of the aforementioned aspects and embodiments, wherein the targeting domain of said first gRNA molecule is a targeting domain of any of 2(a), 2(i), 2(j), or 2(k); and a second gRNA molecule of any of the aforementioned gRNA molecule aspects and embodiments, wherein the targeting domain of said second gRNA molecule is a targeting domain of any of 2(b), 2(c), 2(d), 2(f), 2(g), 2(h), or 2(i).

In embodiments, the composition includes two gRNA molecules, and the targeting domain of said first gRNA molecule includes, for example, consists of, SEQ ID NO: 5519, SEQ ID NO: 5497, SEQ ID NO: 5499, SEQ ID NO: 5498, SEQ ID NO: 5503, SEQ ID NO: 5496, SEQ ID NO: 5507, SEQ ID NO: 5515, SEQ ID NO: 5493, SEQ ID NO: 5506, SEQ ID NO: 5509, SEQ ID NO: 5517, SEQ ID NO: 5521, SEQ ID NO: 5520, SEQ ID NO: 5500, SEQ ID NO: 5494, SEQ ID NO: 5508, SEQ ID NO: 5514, or SEQ ID NO: 5492; and the targeting domain of said second gRNA molecule includes, for example, consists of, SEQ ID NO: 5569, SEQ ID NO: 5585, SEQ ID NO: 5587, SEQ ID NO: 5592, SEQ ID NO: 5601, SEQ ID NO: 5589, SEQ ID NO: 5600, SEQ ID NO: 5594, SEQ ID NO: 5571, SEQ ID NO: 5593, SEQ ID NO: 5574,SEQ ID NO: 5598, SEQ ID NO: 5586, SEQ ID NO: 5599, SEQ ID NO: 5591, SEQ ID NO: 5610, SEQ ID NO: 5608, SEQ ID NO: 5617, SEQ ID NO: 5619, or SEQ ID NO: 5620..

In embodiments, the composition includes two gRNA molecules, and the targeting domain of said first gRNA molecule includes, for example, consists of, SEQ ID NO: 5496, SEQ ID NO: 5498, or SEQ ID NO: 5509; and the targeting domain of said second gRNA molecule includes, for example, consists of, SEQ ID NO: 5569, SEQ ID NO: 5586, SEQ ID NO: 5587, SEQ ID NO: 5592, SEQ ID NO: 5599, or SEQ ID NO: 5600.

In embodiments, the composition includes two gRNA molecules, and the targeting domain of said first gRNA molecule includes, for example, consists of, SEQ ID NO: 5496, SEQ ID NO: 5498, or SEQ ID

NO: 5509; and the targeting domain of said second gRNA molecule includes, for example, consists of, SEQ ID NO: 5569.

In embodiments, the composition includes two gRNA molecules, and the targeting domain of said first gRNA molecule includes, for example, consists of, SEQ ID NO: 5496, SEQ ID NO: 5498, or SEQ ID NO: 5509; and the targeting domain of said second gRNA molecule includes, for example, consists of, SEQ ID NO: 10729, SEQ ID NO: 10719, SEQ ID NO: 10764, SEQ ID NO: 10789, SEQ ID NO: 10701, SEQ ID NO: 10700, or SEQ ID NO: 10722.

In embodiments, including in any of the aforementioned aspects and embodiments, the composition further includes a third gRNA molecule described herein, for example, in any of the aforementioned gRNA molecule aspects and embodiments, wherein the targeting domain of said third gRNA molecule is a targeting domain of any of 2(n) or 2(q). In embodiments, the targeting domain of said third gRNA molecule includes, for example, consists of, SEQ ID NO: 7771, SEQ ID NO: 7769, SEQ ID NO: 7773, SEQ ID NO: 7726, SEQ ID NO: 7758, SEQ ID NO: 7739, SEQ ID NO: 7779, SEQ ID NO: 7770, SEQ ID NO: 7749, SEQ ID NO: 7754, SEQ ID NO: 7745, SEQ ID NO: 7785, SEQ ID NO: 7731, SEQ ID NO: 7772, SEQ ID NO: 7743, or SEQ ID NO: 7750; for example, includes (for example consists of) SEQ ID NO: 7769, SEQ ID NO: 7771, SEQ ID NO: 7739, or SEQ ID NO: 7785.

In embodiments, including in any of the aforementioned aspects and embodiments, the composition further includes a fourth gRNA molecule described herein, for example, in any of the aforementioned gRNA molecule aspects and embodiments, wherein the targeting domain of said fourth gRNA molecule is complementary to a target sequence of a target of an NK inhibitory molecule, for example, LILRB1. In embodiments, the targeting domain of said fourth gRNA molecule includes, e.g., consists of:

a) any one of SEQ ID NO: 10090 to SEQ ID NO: 10673;
b) 17, 18, 19, 20, 21, 22, 23, or 24 consecutive nucleotides, preferably 20 consecutive nucleotides, of any one of SEQ ID NO: 10090 to SEQ ID NO: 10673.
c) The 5' 17, 18, 19, 20, 21, 22, 23 or 24 nucleotides, preferably 20 nucleotides, of any one of SEQ ID NO: 10090 to SEQ ID NO: 10673; or
d) The 3' 17, 18, 19, 20, 21, 22, 23 or 24 nucleotides, preferably 20 nucleotides, of any one of SEQ ID NO: 10090 to SEQ ID NO: 10673.

In embodiments of the composition (including in any of the aforementioned aspects and embodiments), the targeting domain of the first gRNA molecule (as described herein), the targeting domain of the second

gRNA molecule (as described herein), and, if present, the targeting domain of the third gRNA molecule (as described herein), include, e.g., consist of, the sequences of any of:

a) Combination A1 to combination A72 of Table 33;
b) Combination B1 to combination B84 of Table 34;
c) Combination C1 to combination C42 of Table 35;
d) Combination D1 to combination D36 of Table 36;
e) Combination E1 to combination E30 of Table 37; or
f) Combination F1 to combination F60 of Table 38.

In any of the aforementioned aspects and embodiments, each of said gRNA molecules is in a ribonuclear protein complex (RNP) with a Cas9 molecule described herein.

In embodiments, the gRNA molecule or composition is formulated in a medium suitable for electroporation.

In embodiments wherein each of said gRNA molecules is in a RNP with a Cas9 molecule described herein, each of said RNP complexes is at a concentration of less than about 10uM, e.g., less than about 3uM, e.g., less than about 1uM, e.g., less than about 0.5uM, e.g., less than about 0.3uM, e.g., less than about 0.1uM.

In embodiments, the composition further includes a cell, e.g., a population of cells, e.g., an immune effector cell, e.g., a CAR-expressing immune effector cell, e.g., described herein.

In another aspect, the invention provides a nucleic acid that encodes a gRNA molecule of any of the previous gRNA molecule aspects or embodiments, or a (for example, all) component(s) of a composition of any of the aforementioned composition aspects and embodiments. In embodiments, the nucleic acid includes a promoter operably linked to the sequence that encodes the gRNA molecule. In embodiments, the promoter is a promoter recognized by an RNA polymerase II or RNA polymerase III. In other embodiments, the promoter is a U6 promoter or an HI promoter. In embodiments, the nucleic acid further encodes a Cas9 molecule. In embodiments, the nucleic acid includes a promoter operably linked to the sequence that encodes a Cas9 molecule, for example, an EF-1 promoter, a CMV IE gene promoter, an EF-1α promoter, an ubiquitin C promoter, or a phosphoglycerate kinase (PGK) promoter.

In another aspect, the invention provides a vector that includes the nucleic acid of any of any of the aforementioned nucleic acid aspects and embodiments. In embodiments, the vector is selected from the

group consisting of a lentiviral vector, an adenoviral vector, an adeno-associated viral (AAV) vector, a herpes simplex virus (HSV) vector, a plasmid, a minicircle, a nanoplasmid, and an RNA vector.

In another aspect, the invention provides a composition that includes a gRNA molecule of any the aforementioned gRNA molecule aspects and embodiments, and nucleic acid encoding a Cas9 molecule, for example, as described herein.

In another aspect, the invention provides a composition that includes a nucleic acid encoding a gRNA molecule of any the aforementioned gRNA molecule aspects and embodiments, and a Cas9 molecule, for example, as described herein.

In embodiments of any of the compositions of the invention, the composition further includes a template nucleic acid. In embodiments, the template nucleic acid includes a nucleotide that corresponds to a nucleotide of a target sequence of the gRNA molecule. In embodiments, the template nucleic acid includes nucleic acid encoding a chimeric antigen receptor (CAR), for example, as described herein. In embodiments, the CAR is (a) a CD19 CAR, e.g., as described in WO2012/079000 or WO2014/153270; or (b) a BCMA CAR, e.g., as described herein, e.g., a BCMA CAR including SEQ ID NO: 8559. In embodiments, the template nucleic acid includes nucleic acid encoding an NK inhibitory molecule, for example, as described herein.

In another aspect, the invention provides a method of altering e.g., altering the structure, e.g., sequence of, a target sequence of a cell, including contacting said cell with a) a gRNA molecule, e.g., more than one gRNA molecule, of any of the previous gRNA molecule aspects and embodiments, and a Cas9 molecule, for example, as described herein; b) a gRNA molecule, e.g., more than one gRNA molecule, of any of the previous gRNA molecule aspects and embodiments and nucleic acid encoding a Cas9 molecule, for example, as described herein; c) nucleic acid encoding a gRNA molecule, e.g., more than one gRNA molecule, of any of the previous gRNA molecule aspects and embodiments and a Cas9 molecule, for example, as described herein; d) nucleic acid encoding a gRNA molecule, e.g., more than one gRNA molecule, of any of the previous gRNA molecule aspects and embodiments and nucleic acid encoding a Cas9 molecule, for example, as described herein; e) any of a) to d), above, and a template nucleic acid; f) any of a) to d) above, and nucleic acid including sequence encoding a template nucleic acid; g) a composition of any of the previous composition aspects and embodiments; or h) a vector of any of the previous vector aspects and embodiments. In embodiments, the gRNA molecule or nucleic acid encoding the gRNA molecule, and the Cas9 molecule or nucleic acid encoding the Cas9 molecule, are formulated in a single composition. In other embodiments, the gRNA molecule or nucleic acid encoding the gRNA molecule, and the Cas9 molecule or nucleic acid encoding the Cas9 molecule, are formulated in more

than one composition. In embodiments, the more than one composition are delivered, for example, delivered to a cell described herein, simultaneously or sequentially. In embodiments, the cell is an animal cell, for example, a mammalian, primate, or human cell. In embodiments, the cell is an immune effector cell (e.g., a population of immune effector cells), for example, a T cell or NK cell, for example, T cell, for example, a CD4+ T cell, a CD8+ T cell, or a combination thereof. In embodiments, the cell has been, or will be, engineered to express a chimeric antigen receptor (CAR), for example, as described herein. In embodiments, the cell includes, or will include a chimeric antigen receptor (CAR), for example, as described herein. In embodiments, the cell includes, or will include nucleic acid encoding a chimeric antigen receptor (CAR), for example, as described herein. In embodiments, the CAR is (a) a CD19 CAR; or (b) a BCMA CAR. In embodiments, the CAR is a CD19 CAR including an antigen binding domain including any one of SEQ ID NO: 7883 to SEQ ID NO: 7898. In embodiments, the CAR is a CD19 CAR and includes any one of SEQ ID NO: 7908 to SEQ ID NO: 7920. In embodiments, the CAR is a BCMA CAR including an antigen binding domain including any one of SEQ ID NO: 7939 to SEQ ID NO: 8112. In embodiments, the CAR is a BCMA CAR and includes any one of SEQ ID NO: 8549 to SEQ ID NO: 8621, e.g., includes SEQ ID NO: 8559. In embodiments the cell is allogeneic with respect to a patient to be administered said cell. In embodiments, the cell is isolated from a healthy human donor. In embodiments the cell is autologous with respect to a patient to be administered said cell.

In another aspect, the invention provides a cell, altered by a method of any of the aforementioned method aspects and embodiments, for example, altered by a method described herein. In another aspect, the invention provides a cell that includes a first gRNA molecule of any of the aforementioned gRNA molecule aspects and embodiments, or a composition of any of the aforementioned composition aspects and embodiments, a nucleic acid of any of the aforementioned nucleic acid aspects and embodiments, or a vector of any of the aforementioned vector aspects and embodiments. In embodiments, the gRNA molecule, composition, nucleic acid or vector is introduced into said cell ex vivo. In other embodiments, the gRNA molecule, composition, nucleic acid or vector is introduced into said cell in vivo. In embodiments, the cell is an animal cell, for example, a mammalian, primate, or human cell. In embodiments, the cell is an immune effector cell (e.g., a population of immune effector cells), for example, a T cell or NK cell, for example, T cell, for example, a CD4+ T cell, a CD8+ T cell, or a combination thereof. In embodiments, the cell has been, or will be, engineered to express a chimeric antigen receptor (CAR), for example, as described herein. In embodiments, the cell includes, or will include a chimeric antigen receptor (CAR), for example, as described herein. In embodiments, the cell includes, or will include nucleic acid encoding a chimeric antigen receptor (CAR), for example, as described herein. In embodiments, the CAR is (a) a CD19 CAR; or (b) a BCMA CAR. In embodiments,

the CAR is a CD19 CAR including an antigen binding domain including any one of SEQ ID NO: 7883 to SEQ ID NO: 7898. In embodiments, the CAR is a CD19 CAR and includes any one of SEQ ID NO: 7908 to SEQ ID NO: 7920. In embodiments, the CAR is a BCMA CAR including an antigen binding domain including any one of SEQ ID NO: 7939 to SEQ ID NO: 8112. In embodiments, the CAR is a BCMA CAR and includes any one of SEQ ID NO: 8549 to SEQ ID NO: 8621, e.g., includes SEQ ID NO: 8559. In embodiments the cell is allogeneic with respect to a patient to be administered said cell. In embodiments, the cell is isolated from a healthy human donor. In embodiments the cell is autologous with respect to a patient to be administered said cell. In embodiments, the cell includes, has included, or will include a second gRNA molecule of any of claims 1-60, or a nucleic acid encoding the second gRNA molecule of any of the aforementioned gRNA molecule aspects and embodiments, wherein the first gRNA molecule and second gRNA molecule include nonidentical targeting domains. In embodiments, the first gRNA molecule includes a targeting domain complementary with a target sequence of an allogeneic T-cell target (e.g., a targeting domain described in Tables 1, 3, 4 or 5), and the second gRNA molecule includes a targeting domain complementary with a target sequence of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule (e.g., includes a targeting domain described in Table 2 or Table 6). In embodiments, the inhibitory molecule or downstream effector of signaling through an inhibitory molecule is CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, or PTPN11. In embodiments, the first gRNA molecule includes a targeting domain complementary with a target sequence of TRAC, TRBC1, TRBC2, CD247, CD3D, CD3E, or CD3G, and the second gRNA molecule includes a targeting domain complementary with a target sequence of NLRC5, e.g., includes a targeting domain including (e.g., consisting of) any one of SEQ ID NO: 8622 to SEQ ID NO: 10089. In embodiments, the first gRNA molecule includes a targeting domain complementary with a target sequence of TRAC, TRBC1, TRBC2, CD247, CD3D, CD3E, or CD3G, and the second gRNA molecule includes a targeting domain complementary with a target sequence of B2M, HLA-A, HLA-B or HLA-C. In embodiments, the cell further includes, has included, or will include a third gRNA molecule of any of the aforementioned gRNA molecule aspects and embodiments, or a nucleic acid encoding the third gRNA molecule of any of the aforementioned gRNA molecule aspects and embodiments, wherein the first gRNA molecule, the second gRNA molecule and the third gRNA molecule include nonidentical targeting domains. In embodiments, the third gRNA molecule includes a targeting domain complementary with a target sequence of CIITA, RFXANK, RFX5, or RFXAP, e.g., CIITA, e.g., includes a targeting domain including, e.g., consisting of, any one of SEQ ID NO: 7717 to SEQ ID NO: 7804, e.g., includes a targeting domain including, e.g.,

consisting of, any one of SEQ ID NO: 7769, SEQ ID NO: 7771, or SEQ ID NO: 7785. In embodiments, the cell includes three gRNA molecules, and the first gRNA molecule includes a targeting domain complementary with a target sequence of TRAC; the second gRNA molecule includes a targeting domain complementary with a target sequence of B2M; and the third gRNA molecule includes a targeting domain complementary with a target sequence of CIITA. In embodiments, the cell includes three gRNA molecules, and the first gRNA molecule includes a targeting domain complementary with a target sequence of TRAC; the second gRNA molecule includes a targeting domain complementary with a target sequence of NLRC5; and the third gRNA molecule includes a targeting domain complementary with a target sequence of CIITA. In embodiments, the cell includes two gRNA molecules, and the first gRNA molecule includes a targeting domain complementary with a target sequence of TRAC, TRBC1, TRBC2, CD247, CD3D, CD3E, or CD3G, and the second gRNA molecule includes a targeting domain complementary with a target sequence of NR3C1, DCK, CD52 or FKBP1A.

In embodiments of the cell which includes a gRNA molecule (e.g., more than one gRNA molecule described herein):

(1) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(2) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(3) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(4) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(5) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(6) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(7) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(8) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(9) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(10) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(11) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(12) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide

RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(13) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(14) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(15) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(16) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(17) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(18) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(19) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(20) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(21) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(22) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(23) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(24) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(25) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(26) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(27) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(28) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(29) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(30) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(31) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(32) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(33) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(34) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(35) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(36) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(37) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(38) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(39) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(40) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(41) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(42) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(43) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(44) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(45) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(46) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(47) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(48) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(49) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(50) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(51) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(52) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(53) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(54) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(55) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324; or

(56) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583.

In embodiments, including in any of the aforementioned cell aspects and embodiments, the cell further includes a third gRNA molecule including a targeting domain complementary with a target sequence of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule, wherein the inhibitory molecule or downstream effector of signaling through an inhibitory molecule is CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, or PTPN11, for example, the third gRNA molecule is comprises a targeting domain of any of 15(a) to 15(e).

In embodiments of the cell which includes a gRNA molecule (e.g., more than one gRNA molecule described herein):

(1) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(2) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(3) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(4) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(5) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(6) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(7) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(8) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(9) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(10) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(11) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide

RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(12) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(13) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(14) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(15) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(16) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(17) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(18) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(19) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain

selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(20) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(21) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(22) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(23) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(24) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(25) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(26) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(27) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(28) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(29) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(30) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(31) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(32) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(33) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(34) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815; or

(35) the first gRNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule includes a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277.

In embodiments of the cell, the targeting domain of the first gRNA molecule, the targeting domain of the second gRNA molecule, and, if present, the targeting domain of the third gRNA molecule, include, e.g., consist of, the sequences of any of:

g) Combination A1 to combination A72 of Table 33;
h) Combination B1 to combination B84 of Table 34;
i) Combination C1 to combination C42 of Table 35;
j) Combination D1 to combination D36 of Table 36;
k) Combination E1 to combination E30 of Table 37; or
l) Combination F1 to combination F60 of Table 38.

In embodiments of the cell, the first gRNA molecule includes a targeting domain including SEQ ID NO: 5569, SEQ ID NO: 5592, or SEQ ID NO: 5586, and the second gRNA molecule includes a targeting domain including SEQ ID NO: 5775.

In any of the aforementioned cell aspects and embodiments, a gene including a target sequence complementary to the targeting domain of the first gRNA molecule, and, optionally, a gene including a target sequence complementary to the targeting domain of the second gRNA molecule and/or a gene including a target sequence complementary to the targeting domain of the third gRNA molecule, has been altered such that expression of a functional product of the gene including a target sequence complementary to the targeting domain of the first gRNA molecule, and, optionally, the gene including a target sequence complementary to the targeting domain of the second gRNA molecule and/or a functional product of a gene including a target sequence complementary to the targeting domain of the third gRNA molecule, has been reduced or eliminated.

In another aspect, the invention provides a method of providing an anti-tumor immunity in a subject, the method including administering to the subject an effective amount of a cell as described herein, for example, a cell of any of the aforementioned cell aspects and embodiments.

In another aspect, the invention provides a method of treating cancer in a subject, the method including administering to the subject an effective amount of a cell as described herein, for example, a cell of any of the aforementioned cell aspects and embodiments.

In another aspect, the invention provides a method of treating a subject having a disease associated with expression of a tumor antigen, e.g., a proliferative disease, a precancerous condition, a cancer, and a non-cancer related indication associated with expression of the tumor antigen, the method including administering to the subject an effective amount of a cell as described herein, for example, a cell of any of the aforementioned cell aspects and embodiments. In embodiments, the disease associated with expression of a tumor antigen is cancer or a non-cancer related indication. In embodiments, Th disease is cancer selected from colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell

carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers, combinations of said cancers, and metastatic lesions of said cancers. In embodiments, the cancer is a hematologic cancer selected from the group consisting of chronic lymphocytic leukemia (CLL), acute leukemias, acute lymphoid leukemia (ALL), B-cell acute lymphoid leukemia (B-ALL), T-cell acute lymphoid leukemia (T-ALL), chronic myelogenous leukemia (CML), acute myeloid leukemia (AML), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin’s lymphoma, Hodgkin’s lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and pre-leukemia.

In embodiments of any of the aforementioned methods, the method further includes administering a chemotherapeutic agent, for example, cyclophosphamide, fludarabine, or cyclophosphamide and fludarabine. In embodiments of the methods, the method includes administering a lymphodepleting agent or immunosuppressant prior to administering to the subject an effective amount of the cell as described herein, for example, a cell of any of the aforementioned cell aspects and embodiments.

In another aspect, the invention provides a method of preparing cells (e.g., a population of cells) for immunotherapy, the method including: (a) modifying cells by reducing or eliminating expression of a component of a T-cell receptor (TCR), for example, by introducing into said cells a gRNA molecule (as described herein), e.g., more than one gRNA molecule, of any of 2b to 2h, e.g., a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 3, 4, 5, 10, 11 or 12; (b) modifying cells by reducing or eliminating expression of an HLA (e.g., HLA-A, HLA-B, and/or HLA-C) or B2M, for example, by introducing into said cells a gRNA molecule (as described herein), e.g., more than one gRNA molecule, of any of 2a, 2i, 2j or 2k, e.g., a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 6

or 7; and (c) expanding said cells. In embodiments, the method further includes modifying said cells by reducing or eliminating expression of CIITA, for example, by introducing into said cells a gRNA molecule (as described herein), e.g., more than one gRNA molecule, of 2p, e.g., a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 8 or 9, wherein said modifying optionally takes place before the step of expanding said cells.

In another aspect, the invention provides a method of preparing cells (e.g., a population of cells) for immunotherapy including: (a) modifying cells by reducing or eliminating expression of a component of a T-cell receptor (TCR), for example, by introducing into said cells a gRNA molecule (as described herein), e.g., more than one gRNA molecule, of any of 2b to 2h, e.g., a gRNA molecule (as described herein), e.g., more than one gRNA molecule, of any of claims 3, 4, 5, 10, 11 or 12; (b) modifying cells by reducing or eliminating expression of a target for an immunosuppressant, for example, by introducing into said cells a gRNA molecule (as described herein), e.g., more than one gRNA molecule (as described herein), of any of 2l, 2m, 2n or 2o, e.g., a gRNA molecule (as described herein), e.g., more than one gRNA molecule, of claim 13; and (c) expanding said cells.

In embodiments of any of the aforementioned methods of preparing cells, the method further includes (d) modifying cells by reducing or eliminating expression of a first inhibitory molecule or downstream effector of signaling through an inhibitory molecule, for example, introducing into said cells a gRNA molecule (as described herein), e.g., more than one gRNA molecule, of claim 14 or 15; wherein said modifying optionally takes place before the step of expanding said cells.

In another aspect, the invention provides a method of preparing cells (e.g., a population of cells) for immunotherapy including: (a) modifying cells by reducing or eliminating expression of a first inhibitory molecule or downstream effector of signaling through an inhibitory molecule, for example, by introducing into said cells a gRNA molecule (as described herein), e.g., more than one gRNA molecule, of claim 14, e.g., a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 15-17; and (c) expanding said cells.

In embodiments of any of the aforementioned methods of preparing cells, the method further includes (e) modifying cells by reducing or eliminating expression of a second inhibitory molecule or downstream effector of signaling through an inhibitory molecule, for example, by introducing into said cells a gRNA molecule, e.g., more than one gRNA molecule, of claim 14 or 15, wherein the first inhibitory molecule or downstream effector of signaling through an inhibitory molecule and second inhibitory molecule or downstream effector of signaling through an inhibitory molecule are different.

In embodiments of any of the aforementioned methods of preparing cells, the introduction of each of the gRNA molecules is simultaneous or sequential. In embodiments, the introduction of each of the gRNA molecules is sequential, and separated by a period of at least 24 hours, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days or 10 days.

In embodiments of any of the aforementioned methods of preparing cells, the method further includes introducing into the cells nucleic acid encoding a chimeric antigen receptor (CAR), e.g., described herein. In embodiments, the nucleic acid encoding a CAR is disposed on a template nucleic acid. In embodiments, the nucleic acid encoding a CAR is disposed on a RNA vector. In embodiments, the nucleic acid encoding a CAR is disposed on a lentiviral vector.

In embodiments of any of the aforementioned methods of preparing cells, the method further includes isolating cells which are negative for TCR expression. In embodiments, the isolating results in a population of cells in which greater than about 75%, for example, greater than about 80%, 85%, 90%, 91%, 92%, 93, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% of the cells are negative for TCR expression. In embodiments, the step of isolating cells which are negative for TCR expression includes contacting the cell population with a composition including an antibody specific for a component of a T cell receptor (TCR), optionally bound to a solid support or detectable label, and isolating the cells which do not bind to said antibody. In embodiments, the cells are immune effector cells, for example, T cells or NK cells, for example, T cells. In embodiments, the cells are allogeneic with respect to a subject to which they are to be administered, for example, the cells are isolated from a healthy donor, e.g., a donor which does not suffer from a condition associated with expression of a tumor antigen. In embodiments, the cells are autologous with respect to a subject to which they are to be administered. In embodiments of any of the aforementioned methods of preparing cells, steps (a) and/or (b) are performed ex vivo. In embodiments, step (c) is performed ex vivo. In embodiments, the expansion of step (c) is performed for a period of at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 days, or for a period of 2-15, 2-14, 2-13, 2-12, 2-11, 2-10, 3-10, 2-9, 3-9, 2-8, 3-8, 2-7, 3-7, 2-6, 3-6, 2-5, or 3-5 days.

In embodiments of any of the aforementioned methods of preparing cells, the gRNA molecules are gRNA molecules described herein, and the targeting domains of each of the gRNA molecules (for example, used in combination) include, for example, consist of, the sequences of any of the combinations listed in Table 33, Table 34, Table 35, Table 36, Table 37 or Table 38. In embodiments the targeting domains of each of the gRNA molecules include, for example, consist, of the sequences of any of:

a) Combination A1 to combination A72 of Table 33, for example, combination A1 to A4, combination A5 to A8, combination A37 to A40, or combination A41 to A44;

b) Combination B1 to combination B84 of Table 34;
c) Combination C1 to combination C42 of Table 35;
d) Combination D1 to combination D36 of Table 36, for example, combination D2, combination D4, combination D20, or combination D22;
e) Combination E1 to combination E30 of Table 37, for example, combination E2, combination E4, combination E8, or combination E10; or
f) Combination F1 to combination F60 of Table 38, for example, any of combination F1 to F4, combination F5 to F8, combination F13 to F16, or combination F17 to F20.

In another aspect, the invention provides a method of treating a subject in need thereof that includes administering cells (e.g., population of cells) prepared by a method of preparing cells described herein, for example, a method of any of the aforementioned aspects and embodiments of methods of preparing cells. In embodiments, particularly in embodiments that include a gRNA molecule which binds to a target sequence of a target for an immunosuppressant, the method further includes administering an immunosuppressive agent, for example, rapamycin, a rapalog or mTor inhibitor, e.g., RAD001. In embodiments, the subject has a disease associated with expression of a tumor antigen, e.g., a proliferative disease, a precancerous condition, a cancer, and a non-cancer related indication associated with expression of the tumor antigen, wherein said administration treats said disease associated with expression of a tumor antigen. In embodiments, the disease associated with expression of a tumor antigen is cancer or a non-cancer related indication. In embodiments, the disease is cancer selected from colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers, combinations of said cancers, and metastatic lesions of said cancers. In embodiments, the cancer is a hematologic cancer selected from the group consisting of chronic lymphocytic leukemia (CLL), acute leukemias, acute lymphoid leukemia (ALL), B-cell acute lymphoid leukemia (B-ALL), T-cell acute

lymphoid leukemia (T-ALL), chronic myelogenous leukemia (CML), acute myeloid leukemia (AML), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and pre-leukemia.

In another aspect, the invention provides method of treating a patient suffering from a disease including:

(a) providing a population of cells from an allogeneic donor;

(b) introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) including a first gRNA molecule (or nucleic acid encoding said gRNA molecule) including a targeting domain complementary to a target sequence in a gene selected from CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, and TRBC2;

(c) optionally, selecting those cells in which expression of functional TCR has been reduced or eliminated;

(d) transducing the cells with nucleic acid encoding a CAR; and

(e) administering the cells to a patient in need thereof, e.g., a patient who has a disease associated with expression of an antigen recognized by the CAR. In embodiments, the first gRNA molecule to CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, or TRBC2 is a gRNA molecule of any of 2(b)-2(h), e.g., is a gRNA molecule of any of claims 3, 4, 5, 10, 11 or 12.

In embodiments, the method of treating a patient suffering from a disease further includes introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) including a second gRNA molecule (or nucleic acid encoding said gRNA molecule) including a targeting domain complementary to a target sequence in a gene selected from B2M, HLA-A, HLA-B or HLA-C. In embodiments, the second gRNA to B2M, HLA-A, HLA-B or HLA-C is a gRNA molecule of any of 2(a) or 2(i)-2(k), e.g., is a gRNA molecule of any of claims 6 or 7. In embodiments, the method further includes introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) including a third gRNA molecule (or nucleic acid encoding said gRNA molecule) including a targeting domain complementary to a target sequence in a gene selected from CIITA, RFXANK, RFXAP, RFX5, HLA-DM, HLA-DO, HLA-DR, HLA-DQ and HLA-DP. In embodiments, the third gRNA molecule is a gRNA molecule of any of 2(a) or 2(i)-2(k), e.g., is a gRNA molecule of any of claims 6 or 7.

In other embodiments, the method of treating a patient suffering from a disease further includes introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) including a second gRNA molecule (or nucleic acid encoding said gRNA molecule) including a targeting domain complementary to a target sequence in a gene selected from DCK, CD52, FKBP1A or NR3C1. In embodiments, the second gRNA molecule to DCK, CD52, FKBP1A or NR3C1 is a second gRNA molecule of any of 2(l)-2(o), e.g., is a second gRNA molecule of claim 13. In embodiments where the second gRNA is to DCK, the method further including administering a nucleoside analog-based drug to said patient, for example, the nucleoside analog-based drug is cytarabine or gemcitabine. In embodiments, where the second gRNA is to CD52, the method further including administering an anti-CD52 antibody or antigen-binding fragment thereof to said patient, for example, the anti-CD52 antibody or antigen-binding fragment thereof is alemtuzumab (CAMPATH®). In embodiments where the second gRNA is to FKBP1A, the method further including administering FK506, cyclosporine, rapamycin or rapalog, or mTor inhibitor such as RAD001, to said patient. In embodiments where the second gRNA is to NR3C1, the method further including administering a corticosteroid to said patient, for example, the corticosteroid is dexamethasone.

In embodiments of any of the aforementioned methods of treating a patient suffering from a disease, the gRNA molecules are gRNA molecules described herein, and the targeting domains of each of the gRNA molecules (for example, used in combination) include, for example, consist of, the sequences of any of the combinations listed in Table 33, Table 34, Table 35, Table 36, Table 37 or Table 38. In embodiments the targeting domains of each of the gRNA molecules include, for example, consist, of the sequences of any of:

a) Combination A1 to combination A72 of Table 33, for example, combination A1 to A4, combination A5 to A8, combination A37 to A40, or combination A41 to A44;
b) Combination B1 to combination B84 of Table 34;
c) Combination C1 to combination C42 of Table 35;
d) Combination D1 to combination D36 of Table 36, for example, combination D2, combination D4, combination D20, or combination D22;
e) Combination E1 to combination E30 of Table 37, for example, combination E2, combination E4, combination E8, or combination E10; or
f) Combination F1 to combination F60 of Table 38, for example, any of combination F1 to F4, combination F5 to F8, combination F13 to F16, or combination F17 to F20.

In embodiments of any of the aforementioned methods of treating a patient suffering from a disease, the method further includes introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR

system) including a fourth gRNA molecule (or nucleic acid encoding said gRNA molecule) including a targeting domain complementary to a target sequence in a gene selected from CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, or PTPN11, for example, a fourth gRNA molecule is to CD274, HAVCR2, LAG3, PDCD1 or PTPN11, for example, a gRNA molecule of any of 15(a)-(e), e.g., a gRNA molecule of any of claims 16-17.

In another aspect, the invention provides a method of treating a patient suffering from a disease including:

(a) providing a population of cells (as described herein), for example, immune effector cells;

(b) introducing into the population of cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) including a first gRNA molecule (or nucleic acid encoding said gRNA molecule) including a targeting domain complementary to a target sequence in a gene selected from CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, and TRBC2;

(c) introducing into the population of cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) including a second gRNA molecule (or nucleic acid encoding said gRNA molecule) including a targeting domain complementary to a target sequence in a gene selected from B2M, HLA-A, HLA-B and HLA-C;

(d) optionally, selecting those cells in which expression of functional TCR, functional B2M, or both functional TCR and B2M has been reduced or eliminated;

(d) introducing into the population of cells a nucleic acid encoding a CAR; and

(e) administering the population of cells to a patient in need thereof, e.g., a patient who has a disease associated with expression of an antigen recognized by the CAR. In embodiments of the method, the method further comprises (f) introducing into the population of cells a CRISPR System (e.g., an S. pyogenes Cas9 CRISPR system) including a third gRNA molecule (or nucleic acid encoding said gRNA molecule) including a targeting domain complementary to a target sequence in a gene selected from CIITA, RFXANK, RFX5, and RFXAP. In embodiments, the first gRNA molecule includes a targeting domain complementary to a target sequence in a gene selected from TRAC, TRBC1 and TRBC2, for example, as described herein, for example, TRAC, for example, includes (for example consists of) a targeting domain selected from SEQ ID NO: 5569, SEQ ID NO: 5585, SEQ ID NO: 5592, SEQ ID NO: 5601, SEQ ID NO: 5589, SEQ ID NO: 5600, SEQ ID NO: 5594, SEQ ID NO: 5571, SEQ ID NO: 5593, SEQ ID NO: 5574,SEQ ID NO: 5598, SEQ ID NO: 5586, SEQ ID NO: 5599, SEQ ID NO: 5591, SEQ ID NO: 5610, SEQ ID NO: 5608, SEQ ID NO: 5617, SEQ ID NO: 5619, and SEQ ID NO: 5620, for example, selected from SEQ ID NO: 5569, SEQ ID NO: 5592, SEQ ID NO: 5587, SEQ ID NO: 5599,

SEQ ID NO: 5600, and SEQ ID NO: 5586, e.g., selected from SEQ ID NO: 5569, SEQ ID NO: 5586, and SEQ ID NO: 5592. In other embodiments, the first gRNA molecule includes a targeting domain complementary to a target sequence in a gene selected from CD3E, CD3G and CD3D, for example, as described herein. In embodiments, the second gRNA molecule includes a targeting domain complementary to a target sequence in a B2M gene, for example, as described herein, for example, including (for example consisting of) a targeting domain selected from SEQ ID NO: 5519, SEQ ID NO: 5497, SEQ ID NO: 5499, SEQ ID NO: 5498, SEQ ID NO: 5503, SEQ ID NO: 5496, SEQ ID NO: 5507, SEQ ID NO: 5515, SEQ ID NO: 5493, SEQ ID NO: 5506, SEQ ID NO: 5509, SEQ ID NO: 5517, SEQ ID NO: 5521, SEQ ID NO: 5520, SEQ ID NO: 5500, SEQ ID NO: 5494, SEQ ID NO: 5508, SEQ ID NO: 5514, and SEQ ID NO: 5492, for example, selected from SEQ ID NO: 5496, SEQ ID NO: 5498 and SEQ ID NO: 5509. In embodiments, the third gRNA molecule includes a targeting domain complementary to a target sequence in a CIITA gene, for example, as described herein, for example, including (for example consisting of) a targeting domain selected from SEQ ID NO: 7771, SEQ ID NO: 7769, SEQ ID NO: 7773, SEQ ID NO: 7726, SEQ ID NO: 7758, SEQ ID NO: 7739, SEQ ID NO: 7779, SEQ ID NO: 7770, SEQ ID NO: 7749, SEQ ID NO: 7754, SEQ ID NO: 7745, SEQ ID NO: 7785, SEQ ID NO: 7731, SEQ ID NO: 7772, SEQ ID NO: 7743, or SEQ ID NO: 7750, for example, selected from SEQ ID NO: 7769, SEQ ID NO: 7771, SEQ ID NO: 7739 or SEQ ID NO: 7785. In preferred embodiments, the targeting domains of each of the gRNA molecules (for example, used in combination) include, for example, consist of, the sequences of any of the combinations listed in Table 33, Table 34, or Table 38. In embodiments the targeting domains of each of the gRNA molecules include, for example, consist, of the sequences of any of:

a) Combination A1 to combination A72 of Table 33, for example, combination A1 to A4, combination A5 to A8, combination A37 to A40, or combination A41 to A44;
b) Combination B1 to combination B84 of Table 34; or
c) Combination F1 to combination F60 of Table 38, for example, any of combination F1 to F4, combination F5 to F8, combination F13 to F16, or combination F17 to F20.

In embodiments of the method of treating a patient suffering from a disease, the method further includes introducing into said cells a nucleic acid molecule encoding an NK inhibitory molecule (e.g., as described herein), e.g., a nucleic acid molecule encoding an HLA-G:B2M fusion, e.g., a nucleic acid molecule encoding SEQ ID NO: 10674. In embodiments of the method of treating a patient suffering from a disease the cell (or population of cells) is an immune effector cell (or population of immune effector cells), for example, a T cell (or population of T cells). In embodiments, the cell (or population of cells) is allogeneic relative to the patient, for example, is isolated from a healthy human donor. In other

embodiments, the cell (or population of cells) is autologous relative to the patient. In embodiments, the CAR is a CD19 CAR (for example, described herein), for example, a CD19 CAR including an antigen binding domain including any one of SEQ ID NO: 7883 to SEQ ID NO: 7898. In other embodiments, the CAR is a BCMA CAR, for example, including an antigen recognition domain including any one of SEQ ID NO: 7939 to SEQ ID NO: 8112 or SEQ ID NO: 8155 to SEQ ID NO: 8166, e.g., includes an antigen recognition domain including, e.g., consisting of, SEQ ID NO: 7949, for example, including any one of SEQ ID NO: 8549 to SEQ ID NO: 8621, e.g., including, e.g., consisting of, SEQ ID NO: 8559.

In another aspect, the invention provides a modified cell, which has reduced or eliminated expression of: a) a component of the T cell receptor; b) B2M; and/or c) CIITA, relative to an unmodified cell of the same type. In embodiments, the component of the T cell receptor is a TCR alpha chain or a TCR beta chain, for example, the TCR alpha chain. In other embodiments, the component of the TCR is CD3 delta, CD3 epsilon, or CD3 gamma, e.g., is CD3 epsilon. In embodiments, the modified cell (or population of cells) has reduced or eliminated expression of a component of the T cell receptor, B2M and CIITA.

In another aspect, the invention provides a modified cell, including an insertion or deletion of a base pair, e.g., more than one base pair, at or near: a) a gene encoding a component of the T cell receptor; b) B2M; and/or c) CIITA; relative to an unmodified cell of the same type. In embodiments, each of said insertions or deletions is an indel. In embodiments, each of said insertion or deletion is a frameshift mutation. In embodiments, the modified cell (or population of cells) an insertion or deletion of a base pair, e.g., more than one base pair, at or near a gene encoding a component of the T cell receptor, B2M and CIITA.

In another aspect, the invention provides a population of cells including the modified cell of any the aforementioned cell (e.g., modified cell) aspects and embodiments, wherein in at least about 30% of the cells, at least one said insertion or deletion is a frameshift mutation, e.g., as measured by NGS.

In another aspect, the invention provides a cell including (e.g., a population of cells including a cell, e.g., more than one cell, including):

(a) Nucleic acid sequence encoding a CAR, e.g., as described herein;
(b) Optionally, nucleic acid sequence encoding an NK inhibitory molecule, e.g., as described herein, e.g., nucleic acid encoding an HLA-G or HLA-G:B2M fusion as described herein;
(c) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3E, CD3D or CD3G, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA including a targeting domain to a component of a TCR (e.g., TRAC,

TRBC1, TRBC2, CD3E, CD3D, or CD3G e.g. TRAC), e.g., including a targeting domain listed in Table 1, Table 4, Table 5, Table 6e, Table 6f, or Table 6g;

(d) An indel at or near a sequence of the gene encoding B2M or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA including a targeting domain to B2M, e.g., including a targeting domain listed in Table 1 or Table 3;

(e) Optionally, an indel at or near a sequence of the gene encoding CIITA or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA including a targeting domain to CIITA, e.g., including a targeting domain listed in Table 1 or Table 6c; and

(f) Optionally, an indel at or near a sequence of the gene encoding LILRB1 or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA including a targeting domain to LILRB1, e.g., including a targeting domain listed in Table 6d;

Wherein the cell (or population of cells including said cell) expresses the CAR and, optionally, the NK inhibitory molecule, and exhibits reduced or eliminated expression and/or function of one or more of: i) a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), ii) B2M, iii) CIITA, and/or iv) LILRB1. In embodiments the targeting domain sequences of the gRNA molecules (as described herein) to a component of a TCR, B2M and CIITA include, for example, consist of the targeting domains listed in any combination listed in Table 33, Table 34 or Table 38, for example,

a) Combination A1 to combination A72 of Table 33, for example, combination A1 to A4, combination A5 to A8, combination A37 to A40, or combination A41 to A44;

b) Combination B1 to combination B84 of Table 34; or

c) Combination F1 to combination F60 of Table 38, for example, any of combination F1 to F4, combination F5 to F8, combination F13 to F16, or combination F17 to F20.

In another aspect, the invention provides a cell including (e.g., a population of cells including a cell, e.g., more than one cell, including):

(a) Nucleic acid sequence encoding a CAR, e.g., as described herein;

(b) Optionally, nucleic acid sequence encoding an NK inhibitory molecule, e.g., as described herein, e.g., nucleic acid encoding an HLA-G as described herein;

(c) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA including a targeting domain to a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), e.g., including a targeting domain listed in Table 1, Table 4, Table 5, Table 6e, Table 6f, or Table 6g;

(d) An indel at or near a sequence of the gene encoding NLRC5 or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA including a targeting domain to NLRC5, e.g., including a targeting domain listed in Table 1;

(e) Optionally, an indel at or near a sequence of the gene encoding CIITA or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA including a targeting domain to CIITA, e.g., including a targeting domain listed in Table 1 or Table 6c; and

(f) Optionally, an indel at or near a sequence of the gene encoding LILRB1 or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA including a targeting domain to LILRB1, e.g., including a targeting domain listed in Table 6d;

Wherein the cell (or population of cells including one or more of said cells) expresses the CAR and, optionally, the NK inhibitory molecule, and exhibits reduced or eliminated expression and/or function of one or more of: i) a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), ii) B2M, iii) NLRC5, and/or iv) LILRB1.

In another aspect, the invention provides a cell including (e.g., a population of cells including a cell, e.g., more than one cell, including):

(a) Nucleic acid sequence encoding a CAR, e.g., as described herein;

(b) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA including a targeting domain to a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), e.g., including a targeting domain listed in Table 1, Table 4, Table 5, Table 6e, Table 6f, or Table 6g; and

(c) An indel at or near a sequence of the gene encoding FKBP1A or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA including a targeting domain to FKBP1A, e.g., including a targeting domain listed in Table 1 or Table 6b;

Wherein the cell (or population of cells including a cell, e.g., more than one cell, including) expresses the CAR, and exhibits reduced or eliminated expression and/or function of one or more of: i) a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), and/or ii) FKBP12. In embodiments the targeting domain sequences of the gRNA molecules (as described herein) to a component of a TCR and FKBP1A include, for example, consist of the targeting domains listed in any combination listed in Table 35, Table 36 or Table 37, for example

a) Combination C1 to combination C42 of Table 35;

b) Combination D1 to combination D36 of Table 36, for example, combination D2, combination D4, combination D20, or combination D22; or

c) Combination E1 to combination E30 of Table 37, for example, combination E2, combination E4, combination E8, or combination E10.

In another aspect, the invention provides a cell including (e.g., a population of cells including a cell, e.g., more than one cell, including):

(a) Nucleic acid sequence encoding a CAR, e.g., as described herein;

(b) Nucleic acid sequence encoding a rapamycin-resistant mTor, e.g., as described herein, e.g., nucleic acid sequence encoding an mTor including a S2035 mutation, e.g., an S2035I mutation; and;

(c) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA including a targeting domain to a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), e.g., including a targeting domain listed in Table 1, Table 4, Table 5, Table 6e, Table 6f, or Table 6g;

Wherein the cell (or population of cells including said cell, e.g., more than one of said cell,) expresses the CAR and the rapamycin-resistant mTor, and exhibits reduced or eliminated expression and/or function of a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC).

In embodiments, that include an indel at or near a gene encoding a component of the TCR, B2M and CIITA, the targeting domain of the gRNA molecule to a component of the TCR, the targeting domain of the gRNA molecule to B2M, and the targeting domain of the gRNA molecule to CIIRA comprise, e.g., consists of, respectively: a) the targeting domain sequences for said gRNA molecules listed in any combination of A1 to A72 in Table 33; b) the targeting domain sequences for said gRNA molecules listed in any combination of F1 to F60 in Table 38; or c) the targeting domain sequence for each gRNA molecule listed in any combination of B1 to B84 in Table 34.

In embodiments, that include an indel at or near a gene encoding a component of the TCR and FKBP1A, the targeting domain of the gRNA molecule to a component of the TCR, and the targeting domain of the gRNA molecule(s) to FKBP1A comprise, e.g., consists of, respectively, a) the targeting domain sequences for said gRNA molecules listed in any combination of C1 to C42 in Table 35; b) the targeting domain sequences for said gRNA molecules listed in any combination of D1 to D36 in Table 36; or c) the targeting domain sequences for said gRNA molecules listed in any combination of E1 to E30 in Table 37.

In embodiments of any of the cell aspects and embodiments described above, each of said indels in said cell is made by introducing into said cell a gRNA molecule, e.g., more than one gRNA molecule, (e.g., a CRISPR system, e.g., more than one CRISPR system, including said gRNA molecule, e.g., each of said more than one gRNA molecules), each including a targeting domain which is complementary to a target sequence at or near each of said indels.

In another aspect, the invention provides a population of cells, wherein at least about 30%, for example, at least about 50%, for example, at least about 75%, for example, at least about 90% of the cells of the population are a cell of any of the aforementioned cell aspects or embodiments. In embodiments, in at least about 30% of said cells (e.g., in at least about 40%, e.g., in at least about 50%, e.g., in at least about 60%, e.g., in at least about 70%, e.g., in at least about 80%, e.g., in at least about 90%, e.g., in at least about 95%, e.g., in at least about 99% of said cells), each of said indels is a frameshift mutation. In embodiments, including in any of the aforementioned cell aspects and embodiments, the invention provides a cell (or population of cells) that includes an indel listed in Figure 34A, Figure 34B or Figure 49. In embodiments, including in any of the aforementioned cell aspects and embodiments, the invention provides a cell (or population of cells) that includes an indel listed in Figure 36 or Figure 48. In embodiments, including in any of the aforementioned cell aspects and embodiments, the invention provides a cell (or population of cells) that includes an indel listed in Figure 38, Figure 41, Figure 44 or Figure 50. In embodiments, including in any of the aforementioned cell aspects and embodiments, the invention provides a cell (or population of cells) that includes an indel listed in Figure 53.

In another aspect, the invention provides a population of cells that include a cell of any of the aforementioned cell aspects and embodiments. In embodiments, at least about 20% of the cells of the population of cells is a cell of any of the aforementioned cell aspects and embodiments. In embodiments, at least about 50% of the cells of the population of cells is a cell of any of the aforementioned cell aspects and embodiments. In embodiments, less than about 5%, e.g., less than about 1%, e.g., less than about 0.01%, of the cells of the population of cells includes an off-target indel. In embodiments, the cell of the population of cells is engineered to express a chimeric antigen receptor (CAR). In embodiments, the CAR is a CD19 CAR (for example, described herein), for example, a CD19 CAR including an antigen binding domain including any one of SEQ ID NO: 7883 to SEQ ID NO: 7898, or includes the sequence of SEQ ID NO: 7909 or SEQ ID NO: 7920. In other embodiments, the CAR is a BCMA CAR, for example, including an antigen recognition domain including any one of SEQ ID NO: 7939 to SEQ ID NO: 8112 or SEQ ID NO: 8155 to SEQ ID NO: 8166, e.g., including an antigen recognition domain

including, e.g., consisting of, SEQ ID NO: 7949, for example, including any one of SEQ ID NO: 8549 to SEQ ID NO: 8621, e.g., including, e.g., consisting of, SEQ ID NO: 8559. In embodiments, the cell is an animal cell, for example, a mammalian, primate, or human cell, e.g., a human cell. In embodiments, the cell is an immune effector cell (e.g., a population of immune effector cells), for example, a T cell or NK cell, for example, a T cell, for example, a CD4+ T cell, a CD8+ T cell, or a combination thereof. In embodiments, the cell is allogeneic relative to a patient to be administered said cell, for example, the cell is isolated from a healthy human subject. In other embodiments, the cell is autologous relative to a patient to be administered said cell.

In another aspect, the invention provides a method of treating a disease, e.g., a cancer, in a patient in need thereof, including administering the cell of any of the aforementioned cell aspects and embodiments. In embodiments, particularly in embodiments in which expression or function of a target for an immunosuppressant has been reduced or eliminated, the method further includes administering an immunosuppressant, e.g., RAD001.

In another aspect, the invention provides a gRNA molecule as described herein (for example in any of the aforementioned gRNA molecule aspects and embodiments), a composition as described herein (for example in any of the aforementioned composition aspects and embodiments), a nucleic acid as described herein (for example in any of the aforementioned nucleic acid aspects and embodiments), a vector as described herein (for example in any of the aforementioned vector aspects and embodiments), or a cell (or population of cells) as described herein (for example in any of the aforementioned cell (e.g., modified cell) or population of cells aspects and embodiments), for use as a medicament.

In another aspect, the invention provides a gRNA molecule as described herein (for example in any of the aforementioned gRNA molecule aspects and embodiments), a composition as described herein (for example in any of the aforementioned composition aspects and embodiments), a nucleic acid as described herein (for example in any of the aforementioned nucleic acid aspects and embodiments), a vector as described herein (for example in any of the aforementioned vector aspects and embodiments), or a cell (or population of cells) as described herein (for example in any of the aforementioned cell (e.g., modified cell) or population of cells aspects and embodiments), for use in the manufacture of a medicament.

In another aspect, the invention provides a gRNA molecule as described herein (for example in any of the aforementioned gRNA molecule aspects and embodiments), a composition as described herein (for example in any of the aforementioned composition aspects and embodiments), a nucleic acid as described herein (for example in any of the aforementioned nucleic acid aspects and embodiments), a vector as described herein (for example in any of the aforementioned vector aspects and embodiments), or a cell (or

population of cells) as described herein (for example in any of the aforementioned cell (e.g., modified cell) or population of cells aspects and embodiments), for use in the treatment of a disease.

In another aspect, the invention provides a gRNA molecule as described herein (for example in any of the aforementioned gRNA molecule aspects and embodiments), a composition as described herein (for example in any of the aforementioned composition aspects and embodiments), a nucleic acid as described herein (for example in any of the aforementioned nucleic acid aspects and embodiments), a vector as described herein (for example in any of the aforementioned vector aspects and embodiments), or a cell (or population of cells) as described herein (for example in any of the aforementioned cell (e.g., modified cell) or population of cells aspects and embodiments), for use in the treatment of a disease, wherein the disease is a disease associated with expression of a tumor antigen, e.g., a proliferative disease, a precancerous condition, a cancer, and a non-cancer related indication associated with expression of the tumor antigen.

In another aspect, the invention provides a gRNA molecule as described herein (for example in any of the aforementioned gRNA molecule aspects and embodiments), a composition as described herein (for example in any of the aforementioned composition aspects and embodiments), a nucleic acid as described herein (for example in any of the aforementioned nucleic acid aspects and embodiments), a vector as described herein (for example in any of the aforementioned vector aspects and embodiments), or a cell (or population of cells) as described herein (for example in any of the aforementioned cell (e.g., modified cell) or population of cells aspects and embodiments), for use in the treatment of a cancer, wherein the cancer is a hematologic cancer selected from the group consisting of chronic lymphocytic leukemia (CLL), acute leukemias, acute lymphoid leukemia (ALL), B-cell acute lymphoid leukemia (B-ALL), T-cell acute lymphoid leukemia (T-ALL), chronic myelogenous leukemia (CML), acute myeloid leukemia (AML), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin’s lymphoma, Hodgkin’s lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and pre-leukemia.

In another aspect, the invention provides a gRNA molecule as described herein (for example in any of the aforementioned gRNA molecule aspects and embodiments), a composition as described herein (for example in any of the aforementioned composition aspects and embodiments), a nucleic acid as described herein (for example in any of the aforementioned nucleic acid aspects and embodiments), a vector as

described herein (for example in any of the aforementioned vector aspects and embodiments), or a cell (or population of cells) as described herein (for example in any of the aforementioned cell (e.g., modified cell) or population of cells aspects and embodiments), for use in the treatment of a cancer, e.g., wherein the cancer is selected from the group consisting of mesothelioma, adenocarcinoma, glioblastoma, colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers, combinations of said cancers, and metastatic lesions of said cancers.

In addition to the specific features of the invention described above, it is contemplated that the following general features of gRNA molecules, Cas9 molecules and cells are applicable to any aspect and embodiment of the invention described herein, including those aspects and embodiments described above.

In any of the aspects and embodiments disclosed herein, the gRNA molecule (e.g., the gRNA molecule, or combination of gRNA molecules, including a targeting domain described herein) may include one or more of the following features:

In certain embodiments, the gRNA molecule (e.g., the gRNA molecule, or one or more gRNA molecules of a combination of gRNA molecules, including a targeting domain described herein) is a dgRNA molecule, wherein the targeting domain and the tracr are disposed on separate nucleic acid molecules. In embodiments, the crRNA includes, from 5' to 3', [targeting domain]-:

a) SEQ ID NO: 6584;

b) SEQ ID NO: 6585;

c) SEQ ID NO: 6605;

d) SEQ ID NO: 6606;

e) SEQ ID NO: 6607;

f) SEQ ID NO: 6608; or

g) SEQ ID NO: 7806. In a preferred embodiment, the crRNA includes, from 5' to 3', [targeting domain]-[SEQ ID NO: 6607]. In embodiments, the tracr includes more than 15, e.g., 20 or more, 30 or more, 40 or more, 50 or more, 60 or more, 70 or more, or 80 or more, nucleotides of the *S. Pyogenes* tracr sequence (GUUGGAACCAUUCAAAACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGC). In embodiments, the tracr additionally includes 1 or more, e.g., 1, 2, 3, 4, 5, 6, or 7, e.g., preferably 4 or 7, U nucleotides at the 3' end. In preferred dgRNA embodiments, the tracr includes SEQ ID NO: 7820. In embodiments, the tracr additionally includes 1 or more, e.g., 1, 2, 3, 4, 5, 6, or 7, e.g., preferably 4 or 7, U nucleotides at the 3' end. In preferred dgRNA embodiments, the tracr includes, e.g., consists of, SEQ ID NO: 6660. In preferred dgRNA embodiments, the crRNA includes, e.g., consists of, [targeting domain]-SEQ ID NO: 6607, and the tracr includes SEQ ID NO: 7820, e.g., includes, e.g., consists of, SEQ ID NO: 6660.

In other embodiments, the gRNA molecule (e.g., the gRNA molecule, or one or more gRNA molecules of a combination of gRNA molecules, including a targeting domain described herein) is a sgRNA molecule, wherein the targeting domain and the tracr are disposed a single nucleic acid molecule. In embodiments, the sgRNA molecule includes, e.g., consists of: [targeting domain]-

(a) SEQ ID NO: 6601;

(b) SEQ ID NO: 6602;

(c) SEQ ID NO: 6603;

(d) SEQ ID NO: 6604; or

(e) any of (a) to (d), above, further including, at the 3' end, 1, 2, 3, 4, 5, 6 or 7 uracil (U) nucleotides. In a preferred embodiment, the sgRNA molecule includes [targeting domain]-SEQ ID NO: 6601. In a preferred embodiment, the sgRNA molecule includes, e.g., consists of, [targeting domain]-SEQ ID NO: 7811.

In embodiments, including in any of the aforementioned aspects and embodiments, one or more of the nucleic acid molecules of the gRNA molecule described herein, e.g., all of the nucleic acid molecules of the gRNA molecule described herein, do not include a modification to a nucleotide or internucleotide bond. In other embodiments, including in any of the aforementioned aspects and embodiments, one or

more of the nucleic acid molecules of the gRNA molecule described herein include one or more modifications to a nucleotide or internucleotide bond, e.g. as described herein. In embodiments, said modification includes a 2' O-methyl modification. In embodiments, said modification includes a phosphorothioate modification. In embodiments, said modification includes a 2' O-methyl modification at each of the 1, 2, 3 or more, e.g., 3, 3' nucleotides of the nucleic acid of the gRNA molecule. In embodiments, said modification includes a 2' O-methyl modification at each of the 4th-to-terminal, 3rd-to-terminal, and 2nd-to-terminal 3'nucleotides of the nucleic acid of the gRNA molecule. In embodiments, said modification includes a 2' O-methyl modification at each of the 1, 2, 3 or more, e.g., 3, 5' nucleotides of the nucleic acid of the gRNA molecule. In embodiments, said modification includes a 2' O-methyl modification at each of the 4th-to-terminal, 3rd-to-terminal, and 2nd-to-terminal 3'nucleotides of the nucleic acid of the gRNA molecule, and a 2' O-methyl modification at each of the 1, 2, 3 or more, e.g., 3, 5' nucleotides of the nucleic acid of the gRNA molecule. In embodiments, said modification includes one or more, e.g., 1, 2, 3, or more, e.g., 3, phosphorothioate bonds at the 3' end of the nucleic acid molecule of the gRNA. In embodiments, said modification includes one or more, e.g., 1, 2, 3, or more, e.g., 3, phosphorothioate bonds at the 5' end of the nucleic acid molecule of the gRNA. In embodiments, said modification includes one or more, e.g., 1, 2, 3, or more, e.g., 3, phosphorothioate bonds at the 3' end and at the 5' end of the nucleic acid molecule of the gRNA. In embodiments involving a dgRNA molecule, both the molecule including the tracr and the molecule including the crRNA are modified as described herein. In other embodiments involving a dgRNA molecule, the molecule including the tracr is unmodified, and the molecule including the crRNA is modified as described herein. In other embodiments involving a dgRNA molecule, the molecule including the crRNA is unmodified, and the molecule including the tracr is modified as described herein.

In aspects of the invention that include more than one gRNA molecule, each gRNA molecule can independently be a dgRNA molecule or a sgRNA molecule, e.g., as described herein. In embodiments, all of the gRNA molecules of a combination described herein are dgRNA molecules. In embodiments, all of the gRNA molecules of a combination described herein are sgRNA molecules. In embodiments, one or more of the gRNA molecules of a combination described herein are dgRNA molecules, and one or more of the other gRNA molecules of a combination described herein are sgRNA molecules.

In embodiments, the gRNA molecule of the invention is a gRNA molecule that produces an indel at or near the target sequence of the gRNA when introduced into a cell described herein. In embodiments, the gRNA molecule of the invention is a gRNA molecule that produces an indel in at least about 70%, e.g., at least about 80%, e.g., at least about 90%, e.g., at least about 95%, e.g., at least about 96%, e.g., at least about 97%, e.g., at least about 98%, e.g., at least about 99%, or more, of the cells, e.g., as described

herein, of a population of cells to which the gRNA molecule is introduced. In embodiments, the indel frequency is measured by NGS, e.g., as described herein. In embodiments, said indel or indels are or include frameshift mutations. In embodiments, the gRNA molecule of the invention is a gRNA molecule that produces a frameshift mutation in at least about 30%, e.g., at least about 40%, e.g., at least about 50%, e.g., at least about 60%, e.g., at least about 70%, e.g., at least about 75%, e.g., at least about 80%, e.g., at least about 85%, e.g., at least about 90%, e.g., at least about 95%, or more, of the cells, e.g., as described herein, of a population of cells to which the gRNA molecule is introduced. In embodiments, the frameshift mutation frequency is measured by NGS, e.g., as described herein. In embodiments, said indel, indel frequency, frameshift mutation and/or frameshift mutation frequency is measured in the cell (or population or cells) after introduction of the gRNA molecule as an RNP with a Cas9 molecule described herein. In embodiments, said indel, indel frequency, frameshift mutation and/or frameshift mutation frequency is measured in the cell (or population or cells) after introduction of the gRNA molecule by electroporation.

In embodiments, the gRNA molecule of the invention is a gRNA molecule that produces an indel at an off-target site with at least a 50-fold, e.g., at least 100-fold, e.g., at least 1000-fold, lower frequency than at or near the target sequence of the gRNA, when introduced into a cell or population of cells described herein. In preferred embodiments, the gRNA does not produce a detectable indel at any off-target site when introduced into a cell or population of cells described herein. In embodiments, the off-target indel analysis is measured by targeted off-target sequencing of predicted off-target binding sites, e.g., as described herein. In embodiments, off-target indel analysis is measured by nucleotide insertional analysis, e.g., as described herein. In embodiments, the off-target analysis is measured in the cell (or population or cells) after introduction of the gRNA molecule as an RNP with a Cas9 molecule described herein. In embodiments, the off-target analysis is measured in the cell (or population or cells) after introduction of the gRNA molecule by electroporation.

In embodiments, the RNP or combination of RNPs is delivered to the cells by a single electroporation. In embodiments the cells of the invention are subjected to only a single electroporation step.

In aspects and embodiments of the invention that include a combination of gRNA molecules, each of the gRNA molecules of the combination can independently include any of the aforementioned features.

In any of the aspects and embodiments disclosed herein, the Cas9 molecule may include one or more of the following features:

In aspects the Cas9 molecule is an S. Pyogenes Cas9, e.g., a modified or unmodified S. Pyogenes Cas9 molecule as described herein. In embodiments, the Cas9 molecule includes SEQ ID NO: 6611. In other embodiments, the Cas9 molecule includes, e.g., consists of, SEQ ID NO: 7821. In other embodiments, the Cas9 molecule includes, e.g., consists of, SEQ ID NO: 7822. In other embodiments, the Cas9 molecule includes, e.g., consists of, SEQ ID NO: 7823. In other embodiments, the Cas9 molecule includes, e.g., consists of, SEQ ID NO: 7824. In other embodiments, the Cas9 molecule includes, e.g., consists of, SEQ ID NO: 7825. In other embodiments, the Cas9 molecule includes, e.g., consists of, SEQ ID NO: 7826. In other embodiments, the Cas9 molecule includes, e.g., consists of, SEQ ID NO: 7827. In other embodiments, the Cas9 molecule includes, e.g., consists of, SEQ ID NO: 7828. In other embodiments, the Cas9 molecule includes, e.g., consists of, SEQ ID NO: 7829. In other embodiments, the Cas9 molecule includes, e.g., consists of, SEQ ID NO: 7830. In other embodiments, the Cas9 molecule includes, e.g., consists of, SEQ ID NO: 7831. Preferred Cas9 molecules are Cas9 molecules that include, e.g., consist of, SEQ ID NO: 7821, SEQ ID NO: 7822, SEQ ID NO: 7825 and SEQ ID NO: 7828.

In aspects and embodiments that include one or more RNP complexes, e.g., one or more RNP complexes that include a Cas9 molecule described herein, each of said RNP complexes is at a concentration of less than about 10uM, e.g., less than about 3uM, e.g., less than about 1uM, e.g., less than about 0.5uM, e.g., less than about 0.3uM, e.g., less than about 0.1uM. In embodiments, said concentration is the concentration of the RNP complex in the composition including the cell (e.g., population of cells), e.g., as described herein, to which the RNP is to be introduced, e.g., as described herein, e.g., by electroporation. In embodiments, the media of the composition is suitable for electroporation.

In aspects and embodiments of the invention that include a combination of gRNA molecules, for example a combination of RNPs that include different gRNA molecules, each of the Cas9 molecules of the combination can independently include any of the aforementioned features.

In any of the aspects and embodiments disclosed herein, the cell (e.g., population of cells) may include one or more of the following features:

In aspects, the cell (e.g., population of cells) includes one or more cells that have reduced or eliminated expression of a component of the T-cell receptor (TCR). In embodiments, the reduced or eliminated expression of a component of the T-cell receptor (TCR) includes reduced or eliminated expression of TRAC. In embodiments, the reduced or eliminated expression of a component of the T-cell receptor (TCR) includes reduced or eliminated expression of TRBC1. In embodiments, the reduced or eliminated expression of a component of the T-cell receptor (TCR) includes reduced or eliminated expression of

TRBC2. In embodiments, the reduced or eliminated expression of a component of the T-cell receptor (TCR) includes reduced or eliminated expression of CD3G. In embodiments, the reduced or eliminated expression of a component of the T-cell receptor (TCR) includes reduced or eliminated expression of CD3D. In embodiments, the reduced or eliminated expression of a component of the T-cell receptor (TCR) includes reduced or eliminated expression of CD3E. In embodiments, said reduced or eliminated expression of said component of the TCR is the result of introduction of one or more, e.g., one or two, e.g., one gRNA molecule described herein to said component of the TCR into said cell. In embodiments, the cell includes an indel, e.g., a frameshift mutation, e.g., as described herein, at or near the target sequence of a targeting domain of a gRNA molecule to said component of the TCR. In embodiments, the population of cells includes at least about 50%, e.g., at least about 60%, e.g., at least about 70%, e.g., at least about 80%, e.g., at least about 90% or more cells (as described herein) which exhibit reduced or eliminated expression of a component of the TCR. In embodiments, said reduced or eliminated expression of a component of the TCR is as measured by flow cytometry, e.g., as described herein.

In aspects, (including either alternatively, or in addition to, the reduced or eliminated expression of a component of the TCR) the cell (e.g., population of cells) includes one or more cells that have reduced or eliminated expression of beta-2 microglobulin (B2M). In embodiments, said reduced or eliminated expression of said B2M is the result of introduction of one or more, e.g., one or two, e.g., one gRNA molecule described herein to B2M into said cell. In embodiments, the cell includes an indel, e.g., a frameshift mutation, e.g., as described herein, at or near the target sequence of a targeting domain of a gRNA molecule to said B2M. In embodiments, the population of cells includes at least about 50%, e.g., at least about 60%, e.g., at least about 70%, e.g., at least about 80%, e.g., at least about 90% or more cells (as described herein) which exhibit reduced or eliminated expression of B2M. In embodiments, said reduced or eliminated expression of B2M is as measured by flow cytometry, e.g., as described herein.

In aspects, (including either alternatively, or in addition to, the reduced or eliminated expression of a component of the TCR and/or B2M) the cell (e.g., population of cells) includes one or more cells that have reduced or eliminated expression of CIITA. In embodiments, said reduced or eliminated expression of said CIITA is the result of introduction of one or more, e.g., one or two, e.g., one gRNA molecule to said CIITA described herein into said cell. In embodiments, the cell includes an indel, e.g., a frameshift mutation, e.g., as described herein, at or near the target sequence of a targeting domain of a gRNA molecule to said CIITA. In embodiments, the population of cells includes at least about 50%, e.g., at least about 60%, e.g., at least about 70%, e.g., at least about 80%, e.g., at least about 90% or more cells (as described herein) which exhibit reduced or eliminated expression of CIITA. In embodiments, said reduced or eliminated expression of B2M is as measured by flow cytometry, e.g., as described herein.

In aspects, (including either alternatively, or in addition to, the reduced or eliminated expression of a component of the TCR) the cell (e.g., population of cells) includes one or more cells that have reduced or eliminated expression of a target of an immunosuppressant, e.g., FKBP1A. In embodiments, said reduced or eliminated expression of said FKBP1A is the result of introduction of one or more, e.g., one or two, e.g., one, gRNA molecule described herein to said FKBP1A into said cell. In embodiments, the cell includes an indel, e.g., a frameshift mutation, e.g., as described herein, at or near the target sequence of a targeting domain of a gRNA molecule to said FKBP1A. In embodiments, the population of cells includes at least about 50%, e.g., at least about 60%, e.g., at least about 70%, e.g., at least about 80%, e.g., at least about 90% or more cells (as described herein) which exhibit reduced or eliminated expression of FKBP1A. In embodiments, said reduced or eliminated expression of FKBP1A is as measured by flow cytometry, e.g., as described herein.

In some aspects, it is desired that the cell exhibits reduced or eliminated expression of more than one gene. In an aspect, the cell exhibits reduced or eliminated expression of a component of the TCR (e.g., TRAC, TRBC1, TRBC2, CD3E, CD3G, and/or CD3D), reduced or eliminated expression of B2M, and reduced or eliminated expression of CIITA. In embodiments, the reduced or eliminated expression results from introduction into the cell a combination of gRNA molecules, wherein the gRNA molecules of the combination include the targeting domain sequences listed in any of combinations A1 to A72. In embodiments, the reduced or eliminated expression results from introduction into the cell a combination of gRNA molecules, wherein the gRNA molecules of the combination include the targeting domain sequences listed in any of combinations B1 to B84. In embodiments, said cell includes an indel, e.g., a frameshift mutation, at or near the target sequences of each of the gRNA molecule targeting domains listed in Table 33, Table 34 or Table 38 (e.g., the gRNA molecules in any of combinations A1 to A72, B1 to B84, or F1 to F60).

In some aspects, it is desired that the cell exhibits reduced or eliminated expression of more than one gene. In an aspect, the cell exhibits reduced or eliminated expression of a component of the TCR (e.g., TRAC, TRBC1, TRBC2, CD3E, CD3G, and/or CD3D), and reduced or eliminated expression of a target of an immunosuppressant, e.g., FKBP1A. In embodiments, the reduced or eliminated expression results from introduction into the cell a combination of gRNA molecules, wherein the gRNA molecules of the combination include the targeting domain sequences listed in any of combinations C1 to C42. In embodiments, the reduced or eliminated expression results from introduction into the cell a combination of gRNA molecules, wherein the gRNA molecules of the combination include the targeting domain sequences listed in any of combinations D1 to D36. In embodiments, said cell includes an indel, e.g., a frameshift mutation, at or near the target sequences of each of the gRNA molecule targeting domains

listed in Table 35, Table 36 or Table 37 (e.g., the gRNA molecules in any of combinations C1 to C42, D1 to D36, or E1 to E30).

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRAC, and B2M (including embodiments when expression or function of an additional target, e.g., more than one additional target, e.g., CIITA, is also reduced or eliminated), the gRNA molecule which targets TRAC is selected from SEQ ID NO: 7833, SEQ ID NO: 7834, SEQ ID NO: 7835, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7836 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7837 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7836 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7837 and SEQ ID NO: 10798, and the gRNA molecule which targets B2M is selected from SEQ ID NO: 7853, SEQ ID NO: 7854, SEQ ID NO: 7855, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7856 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7857 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7856 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7857 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRAC, and B2M (including embodiments when expression or function of an additional target, e.g., more than one additional target, e.g., CIITA, is also reduced or eliminated), the gRNA molecule which targets TRAC is selected from SEQ ID NO: 7833, SEQ ID NO: 7834, SEQ ID NO: 7835, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7836 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7837 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7836 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7837 and SEQ ID NO: 10798, and the gRNA molecule which targets B2M is selected from SEQ ID NO: 7858, SEQ ID NO: 7859, SEQ ID NO: 7860, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7861 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7862 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7861 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7862 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRAC, and B2M (including embodiments when expression or function of an

additional target, e.g., more than one additional target, e.g., CIITA, is also reduced or eliminated), the gRNA molecule which targets TRAC is selected from SEQ ID NO: 7838, SEQ ID NO: 7839, SEQ ID NO: 7840, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7841 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7842 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7841 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7842 and SEQ ID NO: 10798, and the gRNA molecule which targets B2M is selected from SEQ ID NO: 7853, SEQ ID NO: 7854, SEQ ID NO: 7855, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7856 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7857 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7856 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7857 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRAC, and B2M (including embodiments when expression or function of an additional target, e.g., more than one additional target, e.g., CIITA, is also reduced or eliminated), the gRNA molecule which targets TRAC is selected from SEQ ID NO: 7838, SEQ ID NO: 7839, SEQ ID NO: 7840, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7841 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7842 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7841 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7842 and SEQ ID NO: 10798, and the gRNA molecule which targets B2M is selected from SEQ ID NO: 7858, SEQ ID NO: 7859, SEQ ID NO: 7860, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7861 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7862 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7861 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7862 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRBC, and B2M (including embodiments when expression or function of an additional target, e.g., more than one additional target, e.g., CIITA, is also reduced or eliminated), the gRNA molecule which targets TRBC is selected from SEQ ID NO: 7843, SEQ ID NO: 7844, SEQ ID NO: 7845, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7846 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7847 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7846 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of,

SEQ ID NO: 7847 and SEQ ID NO: 10798, and the gRNA molecule which targets B2M is selected from SEQ ID NO: 7853, SEQ ID NO: 7854, SEQ ID NO: 7855, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7856 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7857 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7856 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7857 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRBC, and B2M (including embodiments when expression or function of an additional target, e.g., more than one additional target, e.g., CIITA, is also reduced or eliminated), the gRNA molecule which targets TRBC is selected from SEQ ID NO: 7843, SEQ ID NO: 7844, SEQ ID NO: 7845, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7846 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7847 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7846 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7847 and SEQ ID NO: 10798, and the gRNA molecule which targets B2M is selected from SEQ ID NO: 7858, SEQ ID NO: 7859, SEQ ID NO: 7860, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7861 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7862 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7861 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7862 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRBC, and B2M (including embodiments when expression or function of an additional target, e.g., more than one additional target, e.g., CIITA, is also reduced or eliminated), the gRNA molecule which targets TRBC is selected from SEQ ID NO: 7848, SEQ ID NO: 7849, SEQ ID NO: 7850, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7851 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7852 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7851 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7852 and SEQ ID NO: 10798, and the gRNA molecule which targets B2M is selected from SEQ ID NO: 7853, SEQ ID NO: 7854, SEQ ID NO: 7855, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7856 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7857 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7856 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7857 and SEQ ID NO: 10798. As described

herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRBC, and B2M (including embodiments when expression or function of an additional target, e.g., more than one additional target, e.g., CIITA, is also reduced or eliminated), the gRNA molecule which targets TRBC is selected from SEQ ID NO: 7848, SEQ ID NO: 7849, SEQ ID NO: 7850, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7851 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7852 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7851 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7852 and SEQ ID NO: 10798, and the gRNA molecule which targets B2M is selected from SEQ ID NO: 7858, SEQ ID NO: 7859, SEQ ID NO: 7860, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7861 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7862 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7861 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7862 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRAC, and FKBP1A (including embodiments when expression or function of an additional target, e.g., more than one additional target, is also reduced or eliminated), the gRNA molecule which targets TRAC is selected from SEQ ID NO: 7833, SEQ ID NO: 7834, SEQ ID NO: 7835, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7836 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7837 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7836 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7837 and SEQ ID NO: 10798, and the gRNA molecule which targets FKBP1A is selected from SEQ ID NO: 7863, SEQ ID NO: 7864, SEQ ID NO: 7865, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7866 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7867 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7866 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7867 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRAC, and FKBP1A (including embodiments when expression or function of

an additional target, e.g., more than one additional target, is also reduced or eliminated), the gRNA molecule which targets TRAC is selected from SEQ ID NO: 7833, SEQ ID NO: 7834, SEQ ID NO: 7835, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7836 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7837 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7836 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7837 and SEQ ID NO: 10798, and the gRNA molecule which targets FKBP1A is selected from SEQ ID NO: 7868, SEQ ID NO: 7869, SEQ ID NO: 7870, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7871 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7872 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7871 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7872 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRAC, and FKBP1A (including embodiments when expression or function of an additional target, e.g., more than one additional target, is also reduced or eliminated), the gRNA molecule which targets TRAC is selected from SEQ ID NO: 7838, SEQ ID NO: 7839, SEQ ID NO: 7840, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7841 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7842 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7841 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7842 and SEQ ID NO: 10798, and the gRNA molecule which targets FKBP1A is selected from SEQ ID NO: 7863, SEQ ID NO: 7864, SEQ ID NO: 7865, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7866 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7867 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7866 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7867 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRAC, and FKBP1A (including embodiments when expression or function of an additional target, e.g., more than one additional target, is also reduced or eliminated), the gRNA molecule which targets TRAC is selected from SEQ ID NO: 7838, SEQ ID NO: 7839, SEQ ID NO: 7840, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7841 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7842 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7841 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of,

SEQ ID NO: 7842 and SEQ ID NO: 10798, and the gRNA molecule which targets FKBP1A is selected from SEQ ID NO: 7868, SEQ ID NO: 7869, SEQ ID NO: 7870, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7871 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7872 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7871 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7872 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRBC, and FKBP1A (including embodiments when expression or function of an additional target, e.g., more than one additional target, is also reduced or eliminated), the gRNA molecule which targets TRBC is selected from SEQ ID NO: 7843, SEQ ID NO: 7844, SEQ ID NO: 7845, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7846 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7847 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7846 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7847 and SEQ ID NO: 10798, and the gRNA molecule which targets FKBP1A is selected from SEQ ID NO: 7863, SEQ ID NO: 7864, SEQ ID NO: 7865, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7866 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7867 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7866 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7867 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRBC, and FKBP1A (including embodiments when expression or function of an additional target, e.g., more than one additional target, is also reduced or eliminated), the gRNA molecule which targets TRBC is selected from SEQ ID NO: 7843, SEQ ID NO: 7844, SEQ ID NO: 7845, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7846 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7847 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7846 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7847 and SEQ ID NO: 10798, and the gRNA molecule which targets FKBP1A is selected from SEQ ID NO: 7868, SEQ ID NO: 7869, SEQ ID NO: 7870, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7871 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7872 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7871 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7872 and SEQ ID NO: 10798. As

described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRBC, and FKBP1A (including embodiments when expression or function of an additional target, e.g., more than one additional target, is also reduced or eliminated), the gRNA molecule which targets TRBC is selected from SEQ ID NO: 7848, SEQ ID NO: 7849, SEQ ID NO: 7850, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7851 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7852 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7851 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7852 and SEQ ID NO: 10798, and the gRNA molecule which targets FKBP1A is selected from SEQ ID NO: 7863, SEQ ID NO: 7864, SEQ ID NO: 7865, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7866 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7867 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7866 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7867 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In preferred embodiments in which it is intended to reduce or eliminate expression of both a component of the T cell receptor, e.g., TRBC, and FKBP1A (including embodiments when expression or function of an additional target, e.g., more than one additional target, is also reduced or eliminated), the gRNA molecule which targets TRBC is selected from SEQ ID NO: 7848, SEQ ID NO: 7849, SEQ ID NO: 7850, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7851 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7852 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7851 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7852 and SEQ ID NO: 10798, and the gRNA molecule which targets FKBP1A is selected from SEQ ID NO: 7868, SEQ ID NO: 7869, SEQ ID NO: 7870, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7871 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7872 and SEQ ID NO: 6660, a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7871 and SEQ ID NO: 10798, and a dgRNA comprising, e.g., consisting of, SEQ ID NO: 7872 and SEQ ID NO: 10798. As described herein, in embodiments of any of the combinations, each of said gRNA molecules is provided as an RNP with a Cas9 molecule, e.g., a Cas9 molecule described herein.

In one aspect, the cell exhibits reduced or eliminated expression of only one component of the TCR (though it may exhibit reduced or eliminated expression of one or more other targets which are not a

component of the TCR). In embodiments, the cell comprises an indel at or near a target sequence within only a single gene (or its regulatory elements) that is a component of the TCR (though the cell may comprise an indel at or near a target sequence within one or more additional genes (or its regulatory elements) which are not a component of the TCR). Thus, in embodiments, the cell does not comprise an indel within more than one gene that is a component of a TCR. In embodimetns, the cell does not comprise an indel within TRAC and within a gene encoding a second component of the TCR, e.g., TRBC1 or TRBC2.

In one aspect, the cell does not exhibit reduced or eliminated expression of a gene comprising a target sequence of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule (though it may exhibit reduced or eliminated expression of one or more other genes). In embodiments, the cell does not include an indel at or near a target sequence in a gene (or its regulatory elements) of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule (though it may include an indel at one or more other genes (or its regulatory elements)). In embodimetns, the cell does not comprise an indel within PDCD1 or its regulatory elements.

In aspects, the cell is an animal cell, for example, a mammalian, primate, or human cell, e.g., a human cell. In aspects, the cell is an immune effector cell (e.g., a population of cells including one or more immune effector cells), for example, a T cell or NK cell, for example a T cell, for example a CD4+ T cell, a CD8+ T cell, or a combination thereof.

In aspects, the cell the cell is autologous with respect to a patient to be administered said cell. In other aspects, the cell is allogeneic with respect to a patient to be administered said cell. In embodiments, the cell is allogeneic with respect to a patient to be administered said cell, and is an induced pluripotent stem cell or is a cell derived therefrom. In embodiments, the cell is allogeneic with respect to a patient to be administered said cell, and is an immune effector cell, e.g., a T cell, isolated from a healthy human donor.

In aspects, a cell (or population of cells), e.g., as described herein, e.g., a CAR-expressing cell as described herein, is modified and/or altered, e.g., by the methods described herein, ex vivo. In other aspects, a cell (or population of cells), e.g., as described herein, e.g., a CAR-expressing cell as described herein, is modified and/or altered, e.g., by the methods described herein, in vivo. In aspects, the CRISPR systems, gRNA molecules (including in an RNP complex with a Cas9 molecule as described herein) and/or compositions (e.g., compositions comprising more than one gRNA molecule of the invention) of the invention are introduced into a cell, e.g., as described herein, e.g., a CAR-expressing cell as described herein, ex vivo. In other aspects, the CRISPR systems, gRNA molecules (including in an RNP complex with a Cas9 molecule as described herein) and/or compositions (e.g., compositions comprising more than

one gRNA molecule of the invention) of the invention are introduced into a cell, e.g., as described herein, e.g., a CAR-expressing cell as described herein, in vivo.

In aspects, the cell has been, is, or will be, engineered to express a chimeric antigen receptor (CAR), as described herein (for example, the cell includes, or will include, nucleic acid sequence encoding a CAR). In embodiments, the CAR recognizes an antigen selected from: CD19; CD123; CD22; CD30; CD171; CS-1 (also referred to as CD2 subset 1, CRACC, SLAMF7, CD319, and 19A24); C-type lectin-like molecule-1 (CLL-1 or CLECL1); CD33; epidermal growth factor receptor variant III (EGFRvIII); ganglioside G2 (GD2); ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); TNF receptor family member B cell maturation (BCMA); Tn antigen ((Tn Ag) or (GalNAcα-Ser/Thr)); prostate-specific membrane antigen (PSMA); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Fms-Like Tyrosine Kinase 3 (FLT3); Tumor-associated glycoprotein 72 (TAG72); CD38; CD44v6; Carcinoembryonic antigen (CEA); Epithelial cell adhesion molecule (EPCAM); B7H3 (CD276); KIT (CD117); Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Mesothelin; Interleukin 11 receptor alpha (IL-11Ra); prostate stem cell antigen (PSCA); Protease Serine 21 (Testisin or PRSS21); vascular endothelial growth factor receptor 2 (VEGFR2); Lewis(Y) antigen; CD24; Platelet-derived growth factor receptor beta (PDGFR-beta); Stage-specific embryonic antigen-4 (SSEA-4); CD20; Folate receptor alpha; Receptor tyrosine-protein kinase ERBB2 (Her2/neu); Mucin 1, cell surface associated (MUC1); epidermal growth factor receptor (EGFR); neural cell adhesion molecule (NCAM); Prostase; prostatic acid phosphatase (PAP); elongation factor 2 mutated (ELF2M); Ephrin B2; fibroblast activation protein alpha (FAP); insulin-like growth factor 1 receptor (IGF-I receptor), carbonic anhydrase IX (CAIX); Proteasome (Prosome, Macropain) Subunit, Beta Type, 9 (LMP2); glycoprotein 100 (gp100); oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); tyrosinase; ephrin type-A receptor 2 (EphA2); Fucosyl GM1; sialyl Lewis adhesion molecule (sLe); ganglioside GM3 (aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); transglutaminase 5 (TGS5); high molecular weight-melanoma-associated antigen (HMWMAA); o-acetyl-GD2 ganglioside (OAcGD2); Folate receptor beta; tumor endothelial marker 1 (TEM1/CD248); tumor endothelial marker 7-related (TEM7R); claudin 6 (CLDN6); thyroid stimulating hormone receptor (TSHR); G protein-coupled receptor class C group 5, member D (GPRC5D); chromosome X open reading frame 61 (CXORF61); CD97; CD179a; anaplastic lymphoma kinase (ALK); Polysialic acid; placenta-specific 1 (PLAC1); hexasaccharide portion of globoH glycoceramide (GloboH); mammary gland differentiation antigen (NY-BR-1); uroplakin 2 (UPK2); Hepatitis A virus cellular receptor 1 (HAVCR1); adrenoceptor beta 3 (ADRB3); pannexin 3 (PANX3); G protein-coupled receptor 20 (GPR20); lymphocyte antigen 6 complex, locus K 9 (LY6K); Olfactory receptor 51E2 (OR51E2); TCR

Gamma Alternate Reading Frame Protein (TARP); Wilms tumor protein (WT1); Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Melanoma-associated antigen 1 (MAGE-A1); ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML); sperm protein 17 (SPA17); X Antigen Family, Member 1A (XAGE1); angiopoietin-binding cell surface receptor 2 (Tie 2); melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2); Fos-related antigen 1; tumor protein p53 (p53); p53 mutant; prostein; surviving; telomerase; prostate carcinoma tumor antigen-1 (PCTA-1 or Galectin 8), melanoma antigen recognized by T cells 1 (MelanA or MART1); Rat sarcoma (Ras) mutant; human Telomerase reverse transcriptase (hTERT); sarcoma translocation breakpoints; melanoma inhibitor of apoptosis (ML-IAP); ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene); N-Acetyl glucosaminyl-transferase V (NA17); paired box protein Pax-3 (PAX3); Androgen receptor; Cyclin B1; v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Ras Homolog Family Member C (RhoC); Tyrosinase-related protein 2 (TRP-2); Cytochrome P450 1B1 (CYP1B1); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites), Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Paired box protein Pax-5 (PAX5); proacrosin binding protein sp32 (OY-TES1); lymphocyte-specific protein tyrosine kinase (LCK); A kinase anchor protein 4 (AKAP-4); synovial sarcoma, X breakpoint 2 (SSX2); Receptor for Advanced Glycation Endproducts (RAGE-1); renal ubiquitous 1 (RU1); renal ubiquitous 2 (RU2); legumain; human papilloma virus E6 (HPV E6); human papilloma virus E7 (HPV E7); intestinal carboxyl esterase; heat shock protein 70-2 mutated (mut hsp70-2); CD79a; CD79b; CD72; Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Fc fragment of IgA receptor (FCAR or CD89); Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); CD300 molecule-like family member f (CD300LF); C-type lectin domain family 12 member A (CLEC12A); bone marrow stromal cell antigen 2 (BST2); EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2); lymphocyte antigen 75 (LY75); Glypican-3 (GPC3); Fc receptor-like 5 (FCRL5); and immunoglobulin lambda-like polypeptide 1 (IGLL1), e.g., as described herein.

In embodiments, the CAR includes an antigen recognition domain that binds CD19, e.g., as described herein. In embodiments, the CAR includes an anti-CD19 binding domain that includes, e.g., consists of, SEQ ID NO: 7895. In embodiments, the CAR includes an anti-CD19 binding domain that includes, e.g., consists of, SEQ ID NO: 7884.

In embodiments, the CAR includes an antigen recognition domain that binds BCMA, e.g., as described herein. In embodiments, the CAR includes an anti-BCMA binding domain that includes, e.g., consists of, SEQ ID NO: 7949.

In embodiments, the CAR includes an antigen binding domain, a transmembrane domain, and an intracellular signaling domain. In embodiments the transmembrane domain includes the sequence of SEQ ID NO: 6644. In embodiments, the intracellular signaling domain includes a primary signaling domain and/or a costimulatory signaling domain. In embodiments, the primary signaling domain includes, e.g., consists of, the sequence of SEQ ID NO: 6648 or SEQ ID NO: 6650. In embodiments, the costimulatory signaling domain includes, e.g., consists of, the sequence of SEQ ID NO: 6646 or SEQ ID NO: 6636, e.g., includes, e.g., consists of, the sequence of SEQ ID NO: 6646. In other embodiments, the costimulatory signaling domain includes sequence from the intracellular signaling domain of CD28.

In embodiments, the CAR is a CD19 CAR, and includes, e.g., consists of, the sequence of SEQ ID NO: 7920. In embodiments, the CAR is a CD19 CAR, and includes, e.g., consists of, the sequence of SEQ ID NO: 7909. In embodiments, the cell, e.g., described herein, includes nucleic acid sequence encoding a CD19 CAR described herein, e.g., a CD19 CAR that includes the sequence of SEQ ID NO: 7920 or SEQ ID NO: 7909.

In embodiments, the CAR is a BCMA CAR, and includes, e.g., consists of, the sequence of SEQ ID NO: 8559. In embodiments, the cell, e.g., described herein, includes nucleic acid sequence encoding a BCMA CAR described herein, e.g., a BCMA CAR that includes SEQ ID NO: 8559. In embodiments, the nucleic acid sequence encoding the BCMA CAR includes, e.g., consists of, SEQ ID NO: 8574.

In aspects, the cell of the invention (e.g., the population of the cells of the invention), e.g., described herein, further include nucleic acid sequence encoding an NK inhibitory molecule. Such cells are preferred when the cells exhibit reduced or eliminated expression of one or more major histocompatibility class I (MHC I) molecules (e.g., via reduced or eliminated expression of B2M, e.g., achieved by the methods described herein) and/or reduced or eliminated expression of one or more major histocompatibility class II (MHC II) molecules (e.g., via reduced or eliminated expression of CIITA, e.g., achieved by the methods described herein). In embodiments, the NK inhibitory molecule is an HLA-G molecule, e.g., an HLA-G molecule that does not require B2M, e.g., HLA-G2, HLA-G3, HLA-G4. In other embodiments, the NK inhibitory molecule is an HLA-G:B2M fusion molecule. An exemplary HLA-G:B2M fusion molecule is SEQ ID NO: 10674. An exemplary nucleic acid sequence encoding said HLA-G:B2M fusion is SEQ ID NO: 10675.

In embodiments, the cell (e.g., population of cells), exhibits reduced or eliminated expression of a target of an NK inhibitory molecule, e.g., reduced or eliminated expression of LILRB1.

In embodiments, a CAR-expressing cell of the invention (e.g., the cell wherein expression or function of one or more proteins has been reduced or eliminated, e.g., by the methods described herein), maintains

the ability to proliferate in response to stimulation, for example, binding of the CAR to its target antigen. In embodiments, the proliferation occurs ex vivo. In embodiments, the proliferation occurs in vivo. In embodiments, the proliferation occurs both ex vivo and in vivo. In embodiments, the level of proliferation is substantially the same as the level of proliferation exhibited by the same cell type (e.g., a CAR-expressing cell of the same type) but which has not had expression or function of one or more proteins reduced or eliminated, e.g., by the methods described herein. In embodiments, the level of proliferation is at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or more of the level of proliferation exhibited by the same cell type (e.g., a CAR-expressing cell of the same type) but which has not had expression or function of one or more proteins reduced or eliminated, e.g., by the methods described herein.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting. Headings, sub-headings or numbered or lettered elements, e.g., (a), (b), (i) etc, are presented merely for ease of reading. The use of headings or numbered or lettered elements in this document does not require the steps or elements be performed in alphabetical order or that the steps or elements are necessarily discrete from one another. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1: Cas9 editing of the B2M locus. Fraction of editing detected by NGS in HEK-293 Cas9GFP 24h post-delivery of crRNA targeting the B2M locus and trRNA by lipofection. Each dot indicates a different crRNA, the trRNA was held constant. Genomic coordinates indicate location on Chromosome 15. (n=3).

Figure 2: Histogram for TCR expression after editing with gRNA molecules comprising targeting domains to TCR-alpha, as listed in table 1. Shown is the %mCherry+TCR- cells after 7 days in Jurkat cells, using three different concentrations of lentivirus.

Figure 3: Shown is the %TCR- primary T cells 6 and 12 days after introduction of lentivirus encoding the gRNA shown and Cas9/mCherry. Data represents %mCherry+TCR- edited cells.

Figure 4: Shown is the %PD1- primary T cells in the mCherry+ gated population 3 days post restimulation (with CD3/CD28 beads) and 8 days post activation, in cells transfected with lentivirus encoding the gRNA indicated and Cas9/mCherry.

Figure 5A and 5B: Shown is expression of TCR on day 7 of culture using TRAC-8 gRNA (Fig. 5A) and PD-1 on day 8 of culture using PD1-6 gRNA (Fig. 5B) histograms.

Figure 6: Expression profiles of primary T cells engineered to express a CD19 CAR and treated with RNP comprising gRNA targeting TCR alpha. Pre-enrichment shows the cell populations that are CAR+/- and TCR+/- following 11 days in culture. Post-enrichment shows >98% TCR- T cells after isolation using a CD3 microbead negative selection step.

Figure 7: Shown is the cytotoxic activity of CD19 CAR transduced T-cells against a target positive (Nalm6-luc) and target negative (K562-luc) cell line. "T1" and "T8" refer to gRNA TRAC-1 and TRAC-8 respectively. Shown are lentivirus or RNP-introduced Cas9/gRNA, and the results for both unsorted and TCR- sorted ("sorted") T cell populations

Figure 8: Excision within the B2M gene employing CRISPR systems comprising two gRNA molecules. In each experiment, cells were exposed to gRNA with the targeting domain of CR00442 and a second gRNA molecule, as indicated. Shown is the predicted excision product size.

Figure 9: Results of gRNA pair exposure to B2M gene with expected excision products of less than 100. * indicates expected excision product seen (green arrow); ? = expected excision product could not be resolved from the assay. Yellow arrow indicates wild type fragment.

Figure 10: Results of gRNA pair exposure to B2M gene with expected excision products ~4000 base pairs. Red * indicates expected excision product seen (green box); Purple * = less than 10% editing efficiency. Orange boxes indicate wild type fragment.

Figure 11: Results of gRNA pair exposure to B2M gene with expected excision products ~6000 base pairs. Red * indicates expected excision product seen (green box); Purple * = less than 10% editing efficiency. Orange boxes indicate wild type fragment.

Figure 12: Mean ($n \geq 3$) editing of CRISPR systems with dgRNAs as indicated to TRAC in HEK cells (stably expressing Cas9) or primary human CD3+ T cells (delivery of dgRNA:Cas9 RNP by electroporation). Also shown is % of cells exhibiting loss of TCR as determined by flow cytometry using an anti-TCRa/b antibody.

Figure 13: Mean (n≥3) editing of CRISPR systems with dgRNAs as indicated to coding regions of TRBC1 and TRBC2 in HEK cells (stably expressing Cas9). Also shown is % of T cells exhibiting loss of TCR as determined by flow cytometry using an anti-TCR a/b antibody.

Figure 14: Mean (n≥3) editing of CRISPR systems with dgRNAs as indicated to B2M in HEK cells (stably expressing Cas9), in CD34+ primary human hematopoietic stem cells, and % loss of B2M in primary CD3+ T cells as measured by flow cytometry. NGS assays were run 24 hours after introduction of the CRISPR systems to the indicated cells; Flow cytometry assay was run 3-5 days after introduction of the CRISPR systems to the CD3+ T cells.

Figure 15: Editing as measured by loss of TCR (flow cytometry) of CRISPR systems comprising the indicated gRNA molecule in primary human CD3+ T cells from three different donors. For each gRNA, left bar = donor #1; middle bar = donor #2; right bar = donor #3.

Figure 16: Mean (n≥3) editing of CRISPR systems with dgRNAs as indicated to PDCD1 in HEK cells (stably expressing Cas9) as measured by NGS, and in primary human CD3+ cells (RNP electroporation) as measured by loss of PD-1 (flow cytometry using anti-PD-1 antibody).

Figure 17A: Flow Cytometry expression of TCR and/or B2M after electroporation of gRNA to TRAC and/or B2M at the indicated ratios.

Figure 17B: % of cells negative for both B2M and TCR at the indicated gRNA ratios.

Figure 17C: editing of either B2M or TCR as measured by flow cytometry.

Figure 17D: Viability of cells 24 hours after electroporation.

Figure 18: % Editing using dgRNAs containing targeting domains to PDCD1 (the targeting domain of the CRxxxx sequence indicated) in primary CD3+ T cells as measured by NGS (yellow bars) or loss of PD-1 by flow cytometry (using anti-PD-1 antibody). NGS sequencing was performed 24 hours post-RNP delivery; flow cytometry performed at day 5 post-RNP delivery.

Figure 19: % Editing (n>=3) using dgRNAs containing targeting domains to PDCD1 (the targeting domain of the CRxxxx sequence indicated) in primary CD3+ T cells as measured by loss of PD-1 by flow cytometry (using anti-PD-1 antibody) across three different donors (donor #4, left-most bar; donor $5, middle bar; donor #6, right-most bar). Systems with targeting domains to some targets show > 50% loss of PD-1, with consistent results across multiple donors. gRNAs including the targeting domain of

CR00852, CR00828, CR00870, CR00848, CR00855 and CR00838 show greater than 50% editing across at least 2 donors.

Figure 20: % Editing (n>=3) using dgRNAs containing targeting domains to B2M (the targeting domain of the CRxxxx sequence indicated) in primary CD3+ T cells as measured by loss of B2M by flow cytometry across three different donors (donor #1, left-most bar; donor #4, middle bar; donor #5, right-most bar). Systems with targeting domains to some target sequences show > 40% loss of B2M, with consistent results across multiple donors. gRNAs including the targeting domain of CR00442, CR00444 and CR00455 show greater than 40% editing across at least 2 donors.

Figure 21: % editing (N=3) as measured by NGS in HEK293 cells stably expressing Cas9 using dgRNAs that include the targeting domain to FKBP1A as indicated (each unlabeled bar uses the targeting domain of the odd-numbered CRxxxx that falls between the labeled numbers. For example, the data for the dgRNA that includes the targeting domain of CR002073 is reported at the bar falling between that labeled CR002072 and CR002074).

Figure 22: % editing (N=3) and % Frameshift edit (FS) as measured by NGS in HEK293 cells stably expressing Cas9 using dgRNAs that include the targeting domain to FKBP1A as indicated.

Figure 23: % editing (N=3) and % Frameshift edit (FS) as measured by NGS in HEK293 cells stably expressing Cas9 using dgRNAs that include the targeting domain to FKBP1A as indicated.

Figure 24: % editing (N=3) and % Frameshift edit (FS edit) as measured by NGS in CD3+ T cells using RNPs that include dgRNAs that include the targeting domain to FKBP1A indicated.

Figure 25: % of CD3+ T cells that are B2M-, TCR- (as measured by anti-CD3 Ab), or B2M-/TCR- (double negative) as measured by FACS (at day 4 following first electroporation) following either sequential electroporation of RNPs comprising gRNAs to the targets, or simultaneous electroporation of RNPs comprising gRNAs to the targets.

Figure 26: % of CD3+ T cells that are B2M-, TCR- (as measured by anti-CD3 Ab), or B2M-/TCR- (double negative) as measured by NGS (48 hours following first electroporation) following either single electroporation, sequential electroporation of RNPs comprising gRNAs to the targets, or simultaneous ("Simult") electroporation of RNPs comprising gRNAs to the targets (B2M and TRAC).

Figure 27: Schematic for preparation of gene edited TCR-/B2M- BCMA CAR transduced T cells.

Figure 28: Surface expression of TCR (using anti-CD3-PercpCy5.5) and B2M (using anti-B2M-APC) five days post (RNP) electroporation. T-cells transduced with RNPs containing gRNA to B2M labeled "B2M"; T-cells transduced with RNPs containing gRNA to TRAC labeled "TCR". T-cells transduced with BCMA CAR are indicated as "CAR". Untransduced cells are indicated as "UTD". Cells electroporated with Cas9 but no guide RNA are indicated as "no guide". CD4 staining using anti-CD4-V450 is shown in the lower panel to verify that the loss of CD3 staining is due to loss of the TCR and not due to loss of T-cells.

Figure 29: Surface expression of TCR and B2M compared in total T cells versus CAR+ T cells from each population. "CAR" indicates CAR transduction; "No Guide" indicates Cas9 electroporation with no gRNA; "B2M" indicates electroporation with RNP containing gRNA specific for B2M; "TCR" indicates electroporation with RNP containing gRNA specific for TRAC.

Figure 30: CAR expression levels in cells electroporated with RNPs containing gRNAs specific for B2M ("B2M") and TRAC ("TCR") or electroporated with Cas9 wihtout grNA ("No guide").

Figure 31: Evaluation of T-cell proliferation in response to tumor cell lines expressing a high level of BCMA (KMS11), a low level of BCMA (RPMI8226) or which are BCMA- (Nalm6). T cells are either electroporated with cas9 with no gRNA ("No guide") or electroporated with RNP containing gRNAs to B2M and TRAC ("B2M + TCR"); and/or either transduced with lentiviral vector encoding a BCMA CAR ("BCMA CAR") or untransduced ("UTD"), as indicated.

Figure 32: Proliferation of CAR+ CD4+ and/or CD8+ T cells in response to tumor cell lines expressing a high level of BCMA (KMS11), a low level of BCMA (RPMI8226) or which are BCMA- (Nalm6). Cells are either electroporated with cas9 with no gRNA ("No guide") or electroporated with RNP containing gRNAs to B2M and TRAC ("B2M + TCR"); and/or either transduced with lentiviral vector encoding a BCMA CAR ("BCMA CAR") or untransduced ("UTD"), as indicated.

Figure 33A and 33B: Evaluation of TRAC targeting gRNAs for effects on cell surface TCR expression. 33A shows loss of CD3 staining is shown for RNPs containing guides CR000961 (961), CR000978 (978), CR000984 (984), CR000992 (992), CR000985 (985), and CR000960 (gRNA1) and CR000979 (gRNA8). 33B shows loss of CD3 staining is shown for RNPs containing guides CR000991 (991), CR000992 (992), CR000993 (993), and CR000978 (978). 991 and 992 are nearly superimposable.

Figure 33C: Genomic editing of the TRAC locus resulting from human primary T cell electroporation with RNP containing the indicated gRNA targeting the TRAC locus is shown. The frequency of

insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence is shown (%frameshift edits).

Figure 34A and 34B: The top 5 most frequently observed sequence changes are shown in detail for each TRAC targeting gRNA used for primary human T cell editing. Figures 34A and 34B are the outcome from 2 independently performed electroporation experiments. Wild type (wt) unmodified bases are shown in uppercase letters. Deletions relative to wt sequence are shown by "-"; insertions relative to wt sequence are shown by lowercase letters. Data for each experiment are the average from triplicate PCR products. Figure 34A to 34B disclose SEQ ID NOS 10845-10899, respectively, in order of appearance.

Figure 35: Evaluation of B2M targeting gRNAs for effects on cell surface B2M expression. Guide numbers indicate CR00xxx identifier of targeting domain.

Figure 36: Genomic editing of the B2M locus resulting from human primary T cell electroporation with RNP containing the indicated gRNA targeting the B2M locus. The frequency of insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence is shown (%frameshift edits) in the top panel. The top 10 most frequently observed sequence changes are shown in the bottom panel in detail for each B2M targeting gRNA used for primary human T cell editing. Wild type (wt) unmodified bases are shown in uppercase letters. Deletions relative to wt sequence are shown by "-"; insertions relative to wt sequence are shown by lowercase letters. Data are the average from triplicate PCR products. Figure 36 discloses SEQ ID NOS 10900-10919, respectively, in order of appearance.

Figure 37: % editing at Day 3 post electroporation (Day 5 of cell culture) in primary human T cells by RNPs that include the indicated dgRNA to CIITA (number indicates CRxxxxx identifier of targeting domain) at the indicated concentration, as measured by flow cytometry using an anti-HLA-DR reagent.

Figure 38: Genomic editing of the CIITA locus resulting from human primary T cell electroporation with RNP containing the indicated gRNA targeting the CIITA locus is shown. The frequency of insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence is shown (%frameshift edits). The top 5 most frequently observed sequence changes are shown in detail in the bottom panel. Wild type (wt) unmodified bases are shown in uppercase letters. Deletions relative to wt sequence are shown by "-"; insertions relative to wt sequence are shown by lowercase letters. Data are the average from triplicate PCR products. Figure 38 discloses SEQ ID NOS 10920-10939, respectively, in order of appearance.

Figure 39: % editing at Day 3 post electroporation in primary human T cells by RNPs that include the indicated dgRNA to CIITA (number indicates CR00xxxx identifier of targeting domain) at the indicated concentration, as measured by flow cytometry using an anti-HLA-DR reagent. % editing represents the expression of HLA-DR at the cell surface in cells electroporated with CIITA guide relative to the expression in cells electroporated without guide RNA.

Figure 40: Genomic editing of the CIITA locus resulting from human primary T cell electroporation with RNP containing the indicated gRNA targeting the CIITA locus is shown. The frequency of insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence is shown (%frameshift edits).

Figure 41: The top 5 most frequently observed sequence changes (indels) for each CIITA targeting gRNA used for primary human T cell editing. Data are the average from triplicate PCR products. Wild type (wt) unmodified bases are shown in uppercase letters. Deletions relative to wt sequence are shown by "-"; insertions relative to wt sequence are shown by lowercase letters. Figure 41 discloses SEQ ID NOS 10940-10974, respectively, in order of appearance.

Figure 42: % editing at Day 3 post electroporation in primary human T cells by RNPs that include the indicated dgRNA to CIITA (number indicates CR00xxxx identifier of targeting domain) at the indicated concentration, as measured by flow cytometry using an anti-HLA-DR reagent. % editing represents the expression of HLA-DR at the cell surface in cells electroporated with CIITA guide relative to the expression in cells electroporated without guide RNA.

Figure 43: Genomic editing of the CIITA locus resulting from human primary T cell electroporation with RNP containing the indicated gRNA targeting the CIITA locus is shown. The frequency of insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence is shown (%frameshift edits).

Figure 44. The top 5 most frequently observed sequence changes for each CIITA targeting gRNA used for primary human T cell editing. Data are the average from triplicate PCR products. Wild type (wt) unmodified bases are shown in uppercase letters. Deletions relative to wt sequence are shown by "-"; insertions relative to wt sequence are shown by lowercase letters. Figure 44 discloses SEQ ID NOS 10975-11014, respectively, in order of appearance.

Figure 45: Schematic protocol for preparation of primary human T cells edited at the B2M, TRAC, and CIITA loci (triple edited cells).

Figure 46: Evaluation of editing of TRAC, B2M, and CIITA by testing cell surface expression of CD3 epsilon, B2M, and HLA-DR, respectively, by flow cytometry. Cell surface expression was tested in cells that had been electroporated with a single targeting RNP (B2M 442 single, TRAC 961 single, or CIITA 991 single) or with 3 RNPs simultaneously (Triple 1, Triple 2, Triple 3, Triple 4; according to the details in Figure 45). Cells without electroporation are indicated as "No EP". Cells electroporated with Cas9 but no guide RNA are indicated as "No Guide".

Figure 47: Genomic editing of the B2M, TRAC, and CIITA loci resulting from human primary T cell simultaneous electroporation with 3 RNPs containing gRNAs targeting the B2M, TRAC, and CIITA loci. The frequency of insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence is shown in parentheses.

Figure 48: The top 10 most frequently observed sequence changes at the B2M locus in primary human T cells for the B2M targeting gRNA CR00442 in the context of simultaneous editing of 3 loci (triple editing) with different concentrations of each RNP as shown in the schematic in figure 45. Wild type (wt) unmodified bases are shown in uppercase letters. Deletions relative to wt sequence are shown by "-"; insertions relative to wt sequence are shown by lowercase letters. Data are the average from triplicate PCR products. Figure 48 discloses SEQ ID NOS 11015-11054, respectively, in order of appearance.

Figure 49: The top 10 most frequently observed sequence changes at the TRAC locus in primary human T cells for the TRAC targeting gRNA CR000961 in the context of simultaneous editing of 3 loci (triple editing) with different concentrations of each RNP as shown in the schematic in figure 45. Wild type (wt) unmodified bases are shown in uppercase letters. Deletions relative to wt sequence are shown by "-"; insertions relative to wt sequence are shown by lowercase letters. Data are the average from triplicate PCR products. Figure 49 discloses SEQ ID NOS 11055-11094, respectively, in order of appearance.

Figure 50: The top 10 most frequently observed sequence changes at the CIITA locus in primary human T cells for the CIITA targeting gRNA CR002991 in the context of simultaneous editing of 3 loci (triple editing) with different concentrations of each RNP as shown in the schematic in figure 45. Wild type (wt) unmodified bases are shown in uppercase letters. Deletions relative to wt sequence are shown by "-";

insertions relative to wt sequence are shown by lowercase letters. Data are the average from triplicate PCR products. Figure 50 discloses SEQ ID NOS 11095-11134, respectively, in order of appearance.

Figure 51: The format of the guide RNA was evaluated for efficiency of editing. Guide RNAs against TRAC (CR000961; upper panel) or B2M (CR00442; lower panel) were synthesized in the single guide or dual guide format with or without the indicated chemical modifications (PS or OMePS). RNPs were electroporated into human primary T cells at the indicated concentrations. Editing efficiency was evaluated by analysis of cell surface staining of CD3 epsilon for TRAC editing (upper) and B2M protein for B2M editing (lower) by flow cytometry.

Figure 52: Genomic editing of the FKBP1A locus resulting from human primary T cell electroporation with RNPs containing the indicated gRNAs targeting FKBP1A. The frequency of insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence is shown.

Figure 53: The top 5 most frequently observed sequence changes for each FKBP1A targeting gRNA used for primary human T cell editing are shown. Wild type (wt) unmodified bases are shown in uppercase letters. Deletions relative to wt sequence are shown by "-"; insertions relative to wt sequence are shown by lowercase letters. Data are the average from triplicate PCR products. Figure 53 discloses SEQ ID NOS 11135-11159, respectively, in order of appearance.

Figure 54: T cells were edited with RNPs containing gRNAs comprising targeting domains to FKBP1A (CR002086, CR002097, CR002122; indicated as 2086, 2097, and 2112, respectively) or with negative controls: 442 (an irrelevant guide CR00442 targeting B2M); Cas9 (Cas9 alone with no trRNA or crRNA); trRNA (tracer RNA, but no crRNA or Cas9 protein); Cas9+trRNA (Cas9 and tracer RNA but no crRNA); EP (cells only with electroporation); no EP (cells only with no electroporation). After electroporation cells were treated with 2.5 nM RAD001 (upper panel) or left untreated (lower panel) and the impact on mTOR pathway inhibition was evaluated by analyzing S6 phosphorylation (pS6) by flow cytometry. The Y-axis indicates forward scatter (FSC) and the X-axis indicates the level of pS6. Positive staining for pS6 (shown in the gating trace) was determined by gating above the fluorescence level seen in a control stained with isotype antibody (not shown). Quantitation of S6 phosphorylation from the flow cytometry data is shown in the graph in the lower panel.

Figure 55A and 55B: Cytokine production by edited CART cells in response to antigen exposure. Gene editing was performed on CART cells using the CR000961 guide to target the TRAC locus and/or the CR002097 and CR002086 guides to target the FKBP1A locus (as indicated by cr961, 2097, and 2086, respectively). CART cells electroporated with an RNP containing no guide RNA were prepared as a negative control. CART cells expressing either CART-CD19, CART-BCMA-10, or untransduced (UTD) (as indicated) were mixed with the indicated cancer cell (KMS11 (BCMA positive), Nalm6 (CD19 positive), or RPMI8226 (BCMA positive)) at an effector to target ratio of either 1:1 or 1:2.5 (as indicated). Cell culture supernatants were collected and interferon gamma was measured (Figure A) or IL-2 was measured (Figure B).

Figure 56: Killing of antigen positive cancer cell lines by edited CART cells. Gene editing was performed on CART cells using the CR000961 guide to target the TRAC locus and/or the CR002097 and CR002086 guides to target the FKBP1A locus (as indicated by cr961, 2097, and 2086, respectively). CART cells electroporated with an RNP containing no guide RNA were prepared as a negative control. CART cells expressing either CART-CD19, CART-BCMA-10, or untransduced (UTD) (as indicated) were mixed with the indicated cancer cell lines that stable express the luciferase reporter (KMS11 (BCMA positive), Nalm6 (CD19 positive), or RPMI8226 (BCMA positive)) at an effector to target ratio of 1:1. Luciferase signal was measured and cell killing was determined as a loss of luciferase activity.

Figure 57: Proliferation of edited CART cells in response to antigen exposure. Gene editing was performed on CART cells using the CR000961 guide to target the TRAC locus and/or the CR002097 and CR002086 guides to target the FKBP1A locus (as indicated by 961, 2097, and 2086, respectively). CART cells electroporated with an RNP containing no guide RNA were prepared as a negative control. CART cells expressing either CART-CD19 (labeled CD19CAR), CART-BCMA-10 (labeled BCMA10CAR), or untransduced (UTD) (as indicated) were mixed with the indicated cancer cell lines (KMS11 (BCMA positive), Nalm6 (CD19 positive), or RPMI8226 (BCMA positive)) at an effector to target ratio of 1:1. Proliferation was measured by counting the sum of CD4+ and CD8+ cells that are CAR+ relative to a fixed number of counting beads.

Figure 58: Sensitivity to gene edited (TRAC and/or FKBP1A) CART cells to RAD001. CART cells were prepared expressing the BCMA10 CAR (A), the CD19 CAR (B), or no CAR (C; UTD). Gene editing was performed on CART cells or UTD cells using the CR000961 guide to target the TRAC locus and/or the CR002097 and CR002086 guides to target the FKBP1A locus (as indicated by 961, 2097, and 2086, respectively). CART cells electroporated with an RNP containing no guide RNA were prepared as a

negative control. After RNP electroporation cells were treated with 2.5 nM RAD001 (upper panel, indicated at +RAD001) or left untreated (lower panel, indicated as –RAD001) and the impact on mTOR pathway inhibition was evaluated by analyzing S6 phosphorylation (pS6) by flow cytometry. The Y-axis indicates side scatter (SSC) and the X-axis indicates the level of phosphorylated S6 protein (pS6). Positive staining for pS6, shown in the lower right quadrant of the FACS plots, was determined by gating above the fluorescence level seen in a control stained with isotype antibody (not shown). The percentage of cells with phosphorylation of S6 is shown with histograms (upper panels) and graphically (lower panel).

Figure 59: Expression of HLA-G/B2M fusion protein in SupT1 cells, as detected by HLA-G flow cytometry. The light gray histogram indicates the background fluorescence in the PE channel in untransduced cells. The dark gray histogram indicates fluorescence in the PE channel from cells transduced with HLA-G/B2M.

Figure 60: Editing efficiency at targeted B2M locus in CD34+ hematopoietic stem cells by different Cas9 variants, as evaluated by NGS and Flow cytometry. NLS = SV40 NLS; His6 (SEQ ID NO: 10795) or His8 (SEQ ID NO: 10796) refers to 6 or 8 histidine residues, respectively; TEV = tobacco etch virus cleavage site; Cas9 = wild type S. pyogenes Cas9 – mutations or variants are as indicated).

Figure 61: Editing efficiency at targeted B2M locus in primary human T cells by different Cas9 variants and a range of concentrations, as measured by flow cytometry.

Figure 62: Editing efficiency of two different Cas9 variants, at various concentrations, in primary human T cells using two different gRNAs targeting either B2M (left panel) or TRAC (right panel). Editing efficiency (% editing) was measured by flow cytometry by measuring the loss of cell surface expression of B2M (left panel) or TCR (right panel).

Figure 63: Off-target activity for TRAC and B2M guides was assessed using an dsDNA oligo-insertion method in Cas9 overexpressing HEK-293 cells. The on-target site (triangle) and the potential off-target sites (circles) detected are indicated; y-axis indicates frequency of detection. All gRNAs were tested in dgRNA format with the targeting domain indicated by the CRxxxxx identifier. Where indicated, each gRNA was modified such that the 5' three internucleotide bonds and the 3' three internucleotide bonds are phosphorotioate bonds ("PS").

Figure 64: Off-target activity for CIITA-, FKBP1A-, PDCD1-, TRAC- and TRBC2-targeting guide RNA molecules was assessed using an dsDNA oligo-insertion method in Cas9 overexpressing HEK-293 cells. The on-target site (triangle) and the potential off-target sites (circles) detected are indicated; y-axis indicates frequency of detection. All gRNAs were tested in dgRNA format with the targeting domain indicated by the CRxxxxx identifier.

Figure 65: % editing in primary human CD3+ T cells as measured by loss of surface expression of CD3 (as measured by flow cytometry) 72 hours after introduction of CRISPR systems targeting CD3 delta (dgRNA comprising the indicated targeting domain). Each % CD3-negative cells is the average of three independent experiments (SD= standard deviation).

Figure 66: % editing in primary human CD3+ T cells as measured by loss of surface expression of CD3 (as measured by flow cytometry) 72 hours after introduction of CRISPR systems targeting CD3 gamma (dgRNA comprising the indicated targeting domain). Each % CD3-negative cells mean value is the average of three independent experiments (SD= standard deviation).

DEFINITIONS

The terms “CRISPR system,” “Cas system” or “CRISPR/Cas system” refer to a set of molecules comprising an RNA-guided nuclease or other effector molecule and a gRNA molecule that together are necessary and sufficient to direct and effect modification of nucleic acid at a target sequence by the RNA-guided nuclease or other effector molecule. In one embodiment, a CRISPR system comprises a gRNA and a Cas protein, e.g., a Cas9 protein. Such systems comprising a Cas9 or modified Cas9 molecule are referred to herein as “Cas9 systems” or “CRISPR/Cas9 systems.” In one example, the gRNA molecule and Cas molecule may be complexed, to form a ribonuclear protein (RNP) complex.

The terms “guide RNA,” “guide RNA molecule,” “gRNA molecule” or “gRNA” are used interchangeably, and refer to a set of nucleic acid molecules that promote the specific directing of a RNA-guided nuclease or other effector molecule (typically in complex with the gRNA molecule) to a target sequence. In some embodiments, said directing is accomplished through hybridization of a portion of the gRNA to DNA (e.g., through the gRNA targeting domain), and by binding of a portion of the gRNA molecule to the RNA-guided nuclease or other effector molecule (e.g., through at least the gRNA tracr). In embodiments, a gRNA molecule consists of a single contiguous polynucleotide molecule, referred to herein as a “single guide RNA” or “sgRNA” and the like. In other embodiments, a gRNA molecule consists of a plurality, usually two, polynucleotide molecules, which are themselves capable of

association, usually through hybridization, referred to herein as a "dual guide RNA" or "dgRNA," and the like. gRNA molecules are described in more detail below, but generally include a targeting domain and a tracr. In embodiments the targeting domain and tracr are disposed on a single polynucleotide. In other embodiments, the targeting domain and tracr are disposed on separate polynucleotides.

The term "targeting domain" as the term is used in connection with a gRNA, is the portion of the gRNA molecule that recognizes, e.g., is complementary to, a target sequence, e.g., a target sequence within the nucleic acid of a cell, e.g., within a gene.

The term "crRNA" as the term is used in connection with a gRNA molecule, is a portion of the gRNA molecule that comprises a targeting domain and a region that interacts with a tracr to form a flagpole region.

The term "target sequence" refers to a sequence of nucleic acids complimentary, for example fully complementary, to a gRNA targeting domain. In embodiments, the target sequence is disposed on genomic DNA. In an embodiment the target sequence is adjacent to (either on the same strand or on the complementary strand of DNA) a protospacer adjacent motif (PAM) sequence recognized by a protein having nuclease or other effector activity, e.g., a PAM sequence recognized by Cas9. In embodiments, the target sequence is a target sequence of an allogeneic T cell target. In embodiments, the target sequence is a target sequence of an inhibitory molecule. In embodiments, the target sequence is a target sequence of a downstream effector of an inhibitory molecule.

The term "flagpole" as used herein in connection with a gRNA molecule, refers to the portion of the gRNA where the crRNA and the tracr bind to, or hybridize to, one another..

The term "tracr" as used herein in connection with a gRNA molecule, refers to the portion of the gRNA that binds to a nuclease or other effector molecule. In embodiements, the tracr comprises nucleic acid sequence that binds specifically to Cas9. In embodiments, the tracr comprises nucleic acid sequence that forms part of the flagpole.

The terms "Cas9" or "Cas9 molecule" refer to an enzyme from bacterial Type II CRISPR/Cas system responsible for DNA cleavage. Cas9 also includes wild-type protein as well as functional and non-functinal mutants thereof.

The term "complementary" as used in connection with nucleic acid, refers to the pairing of bases, A with T or U, and G with C. The term complementary refers to nucleic acid molecules that are completely

complementary, that is, form A to T or U pairs and G to C pairs across the entire reference sequence, as well as molecules that are at least 80%, 85%, 90%, 95%, 99% complementary.

"Template Nucleic Acid" as used in connection with homology-directed repair or homologous recombination, refers to nucleic acid to be inserted at the site of modification by the CRISPR system donor sequence for gene repair (insertion) at site of cutting. In one aspect, the template nucleic acid comprises nucleic acid sequence encoding a chimeric antigen receptor (CAR), e.g., as described herein. In one aspect, the template nucleic acid comprises a vector comprising nucleic acid sequence encoding a chimeric antigen receptor (CAR), e.g., as described herein.

An "indel," as the term is used herein, refers to a nucleic acid comprising one or more insertions of nucleotides, one or more deletions of nucleotides, or a combination of insertions and delections of nucleotides, relative to a reference nucleic acid, that results after being exposed to a composition comprising a gRNA molecule, for example a CRISPR system. Indels can be determined by sequencing nucleic acid after being exposed to a composition comprising a gRNA molecule, for example, by NGS. With respect to the site of an indel, an indel is said to be "at or near" a reference site (e.g., a site complementary to a targeting domain of a gRNA molecule) if it comprises at least one insertion or deletion within about 10, 9 , 8, 7, 6, 5, 4, 3, 2, or 1 nucleotide(s) of the reference site, or is overlapping with part or all of said refrence site (e.g., comprises at least one insertion or deletion overlapping with, or within 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 nucelotides of a site complementary to the targeting domain of a gRNA molecule, e.g., a gRNA molecule described herein).

An "indel pattern," as the term is used herein, refers to a set of indels that results after exposure to a composition comprising a gRNA molecule. In an embodiment, the indel pattern consists of the top three indels, by frequency of appearance. In an embodiment, the indel pattern consists of the top five indels, by frequency of appearance. In an embodiment, the indel pattern consists of the indels which are present at greater than about 5% frequency relative to all sequencing reads. In an embodiment, the indel pattern consists of the indels which are present at greater than about 10% frequency relative to to total number of indel sequencing reads (i.e., those reads that do not consist of the unmodified reference nucleic acid sequence). In an embodiment, the indel pattern includes of any 3 of the top five most frequently observed indels. The indel pattern may be determined, for example, by sequencing cells of a population of cells which were exposed to the gRNA molecule.

An "off-target indel," as the term I used herein, refers to an indel at or near a site other than the target sequence of the targeting domain of the gRNA molecule. Such sites may comprise, for example, 1, 2, 3, 4, 5 or more mismatch nucleotides relative to the sequence of the targeting domain of the gRNA. In

exemplary embodiments, such sites are detected using targeted sequencing of in silico predicted off-target sites, or by an insertional method known in the art.

The term "inhibitory molecule" refers to a molecule, which when activated, causes or contributes to an inhibition of cell survival, activation, proliferation and/or function; and the gene encoding said molecule and its associated regulatory elements, e.g., promoters. In embodiments, an inhibitory molecule is a molecule expressed on an immune effector cell, e.g., on a T cell. Non-limiting examples of inhibitory molecules are PD-1, PD-L1, PD-L2, CTLA4, TIM3, LAG3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta. It will be understood that the term inhibitory molecule refers to the gene (and its associated regulatory elements) encoding an inhibitory molecule protein when it is used in connection with a target sequence or gRNA molecule. In an embodiment, gene encoding the inhibitory molecule is *CD274*. In an embodiment, the gene encoding the inhibitory molecule is *HAVCR2*. In an embodiment, the gene encoding the inhibitory molecule is *LAG3*. In an embodiment, the gene encoding the inhibitory molecule is *PDCD1*.

The term "downstream effector of signaling through an inhibitory molecule" refers to a molecule that mediates the inhibitory effect of an inhibitory molecule; and the gene encoding said molecule and its associated regulatory elements, e.g., promoters. It will be understood that the term downstream effector of signaling through an inhibitory molecule refers to the gene (and its associated regulatory elements) encoding a downstream effector of signaling through an inhibitory molecule protein when it is used in connection with a target sequence or gRNA molecule. In an embodiment, the gene encoding the downstream effector of signaling through an inhibitory molecule is *PTPN11*.

The terms "allogeneic T cell target" and "allogeneic T-cell target" are used interchangeably herein, and refer to a protein that mediates or contributes to a host versus graft response, mediates or contributes to a graft versus host response, or is a target for an immunosuppressant; and the gene encoding said molecule and its associated regulatory elements, e.g., promoters. It will be understood that the term allogeneic T cell target refers to the gene (and its associated regulatory elements) encoding an allogeneic T cell target protein when it is used in connection with a target sequence or gRNA molecule. Without being bound by theory, inhibition or elimination of one or more allogeneic T cell targets, e.g., by the methods and compositions disclosed herein, may improve the efficacy, survival, function and/or viability of an allogeneic cell, e.g., an allogeneic T cell, for example, by reducing or eliminating undesirable immunogenicity (such as a host versus graft response or a graft versus host response).

In a non-limiting example, the protein that mediates or contributes to a graft versus host response or host versus graft response is one or more components of the T cell receptor. In an embodiment, the component of the T cell receptor is the T cell receptor alpha, for example the constant domain of the TCR alpha. In an embodiment, the component of the T cell receptor is the T cell receptor beta chain, for example the constant domain 1 or constant domain 2 of the TCR beta. In an embodiment, the component of the T cell receptor is the T cell receptor delta chain. In an embodiment, the component of the T cell receptor is the T cell receptor epsilon chain. In an embodiment, the component of the T cell receptor is the T cell receptor zeta chain. In an embodiment, the component of the T cell receptor is the T cell receptor gamma chain. Thus, in embodiments where the protein encoded by the allogeneic T cell target is a component of the TCR, the gene encoding the allogeneic T cell target may be, for example, *TRAC, TRBC1, TRBC2, CD3D, CD3E, CD3G or CD247*, and combinations thereof.

In a non-limiting example, the protein that mediates or contributes to a graft versus host response or host versus graft response is an HLA protein or B2M. Examples of HLA proteins include HLA-A, HLA-B and HLA-C. Thus, in embodiments where the allogeneic T cell target protein is a HLA or B2M protein, the gene encoding the allogeneic T cell target may be, for example, *HLA-A, HLA-B, HLA-C* or *B2M*, and combinations thereof. In other embodiments, the allogeneic T cell target protin is NLRC5, and the gene encoding the allogeneic T cell target may be, for example, *NLRC5*.

In a non-limiting example, the protein that mediates or contributes to a graft versus host response or host versus graft response is a major histocompatibility complex class II (MHC II) molecule (e.g., HLA-Dx (where x refers to a letter of a MHC II protein, e.g., HLA-DM, HLA-DO, HLA-DR, HLA-DQ and/or HLA-DP)), or a regulatory factor for expression of a MHC II, and combinations thereof. A non-limiting example is CIITA (also referred to herein as C2TA). Thus, in embodiments where the allogeneic T cell target protein is a CIITA, the gene encoding the allogeneic T cell target may be, for example, *CIITA*. In another non-limiting example, the protein that mediates or contributes to a graft versus host response or host versus graft response is RFXANK. In another non-limiting example, the protein that mediates or contributes to a graft versus host response or host versus graft response is RFXAP. In another non-limiting example, the protein that mediates or contributes to a graft versus host response or host versus graft response is RFX5.

The term "target for an immunosuppressant" as used herein refers to a molecular target, for example a receptor or other protein, for an immunosuppressant agent (the terms, "immunosuppressant" and "immunosuppressive" are used interchangably herein in connection with an agent, or target for an agent). An immunosuppressant agent is an agent that suppresses immune function by one of several mechanisms

of action. In other words, an immunosuppressive agent is a role played by a compound which is exhibited by a capability to diminish the extent and/or voracity of an immune response. One example of a type of activity exhibited by an immunosuppressant agent is the activity of eliminating T-cells, for example, activated T-cells. Antoher example of a type of activity exhibited by an immunosuppressant agent is the activity of reducing the activity or activation level of T-cells. As a non-limiting example, an immunosuppressive agent can be a calcineurin inhibitor, a target of rapamycin, an interleukin-2 a-chain blocker, an inhibitor of inosine monophosphate dehydrogenase, an inhibitor of dihydrofolic acid reductase, a corticosteroid, cyclosporine, or an immunosuppressive antimetabolite. Classical cytotoxic immunosuppressants act by inhibiting DNA synthesis. Others may act through activation of T-cells or by inhibiting the activation of helper cells. As non limiting examples, targets for immunosuppressive agent can be a receptor for an immunosuppressive agent such as: Deoxycytidine kinase, CD52, glucocorticoid receptor (GR), a FKBP family gene member, e.g., FKBP12, and a cyclophilin family gene member. In an embodiment, the target for an immunosuppressant is deoxycytidine kinase (DCK), and the immunosuppressant is a nucleoside analog-based drug such as cytarabine (cytosine arabinoside) or gemcitabine. In an embodiment, the target for an immunosuppressant is GR, and the immunosuppressant is a corticosteroid such as dexamethasone. In an embodiment, the target for an immunosuppressant is CD52, and the immunosuppressant is an anti-CD52 antibody or antigen-binding fragment thereof such as alemtuzumab (CAMPATH®). In an embodiment, the target for an immunosuppressant is FKBP12, and the immunosuppressant is FK506 (or analog or FKBP12-binding fragment thereof), cyclosporine, rapamycin or rapalog, or mTor inhibitor such as RAD001. Thus, in embodiments where the allogeneic T cell target is a target for an immunosuppressant protein, the gene encoding the allogeneic T cell target may be, for example, *NR3C1, FKBP1A, CD52,* or *DCK*, and combinations thereof.

The term "rapamycin-resistant mTor" refers to an mTor protein (and the gene encoding said mTor protein) which has reduced or eliminated binding to FKBP12 (including in the presence of rapamycin, FK506, a rapalog, cyclosporin and/or other mTor inhibitor such as RAD001). In exemplary embodiments, the rapamycin-resistant mTor comprises one or more mutations to the FRB domain. In an exemplary embodiment, the rapamycin resistant mTor comprises, e.g., consists of, a mutation to S2035, e.g., comprises, e.g., consists of, an S2035I mutation.

The term "a" and "an" refers to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

The term "about" when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass variations of ±20% or in some instances ±10%, or in some instances ±5%, or

in some instances ±1%, or in some instances ±0.1% from the specified value, as such variations are appropriate to perform the disclosed methods.

The term "Chimeric Antigen Receptor" or alternatively a "CAR" refers to a set of polypeptides, typically two in the simplest embodiments, which when in an immune effector cell, provides the cell with specificity for a target cell, typically a cancer cell, and with intracellular signal generation. In some embodiments, a CAR comprises at least an extracellular antigen binding domain, a transmembrane domain and a cytoplasmic signaling domain (also referred to herein as "an intracellular signaling domain") comprising a functional signaling domain derived from a stimulatory molecule and/or costimulatory molecule as defined below. In some aspects, the set of polypeptides are contiguous with eachother. In some embodiments, the set of polypeptides include a dimerization switch that, upon the presence of a dimerization molecule, can couple the polypeptides to one another, e.g., can couple an antigen binding domain to an intracellular signaling domain. In one aspect, the stimulatory molecule is the zeta chain associated with the T cell receptor complex. In one aspect, the cytoplasmic signaling domain further comprises one or more functional signaling domains derived from at least one costimulatory molecule as defined below. In one aspect, the costimulatory molecule is chosen from the costimulatory molecules described herein, e.g., 4 1BB (i.e., CD137), CD27 and/or CD28. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen binding domain, a transmembrane domain and an intracellular signaling domain comprising a functional signaling domain derived from a stimulatory molecule. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen binding domain, a transmembrane domain and an intracellular signaling domain comprising a functional signaling domain derived from a costimulatory molecule and a functional signaling domain derived from a stimulatory molecule. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen binding domain, a transmembrane domain and an intracellular signaling domain comprising two functional signaling domains derived from one or more costimulatory molecule(s) and a functional signaling domain derived from a stimulatory molecule. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen binding domain, a transmembrane domain and an intracellular signaling domain comprising at least two functional signaling domains derived from one or more costimulatory molecule(s) and a functional signaling domain derived from a stimulatory molecule. In one aspect the CAR comprises an optional leader sequence at the amino-terminus (N-ter) of the CAR fusion protein. In one aspect, the CAR further comprises a leader sequence at the N-terminus of the extracellular antigen binding domain, wherein the leader sequence is optionally cleaved from the antigen binding domain (e.g., a scFv) during cellular processing and localization of the CAR to the cellular membrane.

A CAR that comprises an antigen binding domain (e.g., a scFv, or TCR) that targets a specific tumor marker X, such as those described herein, is also referred to as XCAR. For example, a CAR that comprises an antigen binding domain that targets CD19 is referred to as CD19CAR. As another example, a CAR that comprises an antigen binding domain that targets BCMA is referred to as a BCMA CAR.

The term "signaling domain" refers to the functional portion of a protein which acts by transmitting information within the cell to regulate cellular activity via defined signaling pathways by generating second messengers or functioning as effectors by responding to such messengers.

The term "antibody," as used herein, refers to a protein, or polypeptide sequence derived from an immunoglobulin molecule which specifically binds with an antigen. Antibodies can be polyclonal or monoclonal, multiple or single chain, or intact immunoglobulins, and may be derived from natural sources or from recombinant sources. Antibodies can be tetramers of immunoglobulin molecules.

The term "antibody fragment" refers to at least one portion of an antibody, that retains the ability to specifically interact with (e.g., by binding, steric hinderance, stabilizing/destabilizing, spatial distribution) an epitope of an antigen. Examples of antibody fragments include, but are not limited to, Fab, Fab', F(ab')2, Fv fragments, scFv antibody fragments, disulfide-linked Fvs (sdFv), a Fd fragment consisting of the VH and CH1 domains, linear antibodies, single domain antibodies such as sdAb (either VL or VH), camelid VHH domains, multi-specific antibodies formed from antibody fragments such as a bivalent fragment comprising two Fab fragments linked by a disulfide brudge at the hinge region, and an isolated CDR or other epitope binding fragments of an antibody. An antigen binding fragment can also be incorporated into single domain antibodies, maxibodies, minibodies, nanobodies, intrabodies, diabodies, triabodies, tetrabodies, v-NAR and bis-scFv (see, e.g., Hollinger and Hudson, Nature Biotechnology 23:1126-1136, 2005). Antigen binding fragments can also be grafted into scaffolds based on polypeptides such as a fibronectin type III (Fn3)(see U.S. Patent No.: 6,703,199, which describes fibronectin polypeptide minibodies).

The term "scFv" refers to a fusion protein comprising at least one antibody fragment comprising a variable region of a light chain and at least one antibody fragment comprising a variable region of a heavy chain, wherein the light and heavy chain variable regions are contiguously linked, e.g., via a synthetic linker, e.g., a short flexible polypeptide linker, and capable of being expressed as a single chain polypeptide, and wherein the scFv retains the specificity of the intact antibody from which it is derived. Unless specified, as used herein an scFv may have the VL and VH variable regions in either order, e.g., with respect to the N-terminal and C-terminal ends of the polypeptide, the scFv may comprise VL-linker-VH or may comprise VH-linker-VL.

The portion of the CAR of the invention comprising an antibody or antibody fragment thereof may exist in a variety of forms where the antigen binding domain is expressed as part of a contiguous polypeptide chain including, for example, a single domain antibody fragment (sdAb), a single chain antibody (scFv), a humanized antibody or bispecific antibody (Harlow et al., 1999, In: Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, NY; Harlow et al., 1989, In: Antibodies: A Laboratory Manual, Cold Spring Harbor, New York; Houston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; Bird et al., 1988, Science 242:423-426). In one aspect, the antigen binding domain of a CAR composition of the invention comprises an antibody fragment. In a further aspect, the CAR comprises an antibody fragment that comprises a scFv. The precise amino acid sequence boundaries of a given CDR can be determined using any of a number of well-known schemes, including those described by Kabat et al. (1991), "Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD ("Kabat" numbering scheme), Al-Lazikani et al., (1997) JMB 273,927-948 ("Chothia" numbering scheme), or a combination thereof.

As used herein, the term "binding domain" or "antibody molecule" refers to a protein, e.g., an immunoglobulin chain or fragment thereof, comprising at least one immunoglobulin variable domain sequence. The term "binding domain" or "antibody molecule" encompasses antibodies and antibody fragments. In an embodiment, an antibody molecule is a multispecific antibody molecule, e.g., it comprises a plurality of immunoglobulin variable domain sequences, wherein a first immunoglobulin variable domain sequence of the plurality has binding specificity for a first epitope and a second immunoglobulin variable domain sequence of the plurality has binding specificity for a second epitope. In an embodiment, a multispecific antibody molecule is a bispecific antibody molecule. A bispecific antibody has specificity for no more than two antigens. A bispecific antibody molecule is characterized by a first immunoglobulin variable domain sequence which has binding specificity for a first epitope and a second immunoglobulin variable domain sequence that has binding specificity for a second epitope.

The portion of the CAR of the invention comprising an antibody or antibody fragment thereof may exist in a variety of forms where the antigen binding domain is expressed as part of a contiguous polypeptide chain including, for example, a single domain antibody fragment (sdAb), a single chain antibody (scFv), a humanized antibody, or bispecific antibody (Harlow et al., 1999, In: Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, NY; Harlow et al., 1989, In: Antibodies: A Laboratory Manual, Cold Spring Harbor, New York; Houston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; Bird et al., 1988, Science 242:423-426). In one aspect, the antigen binding domain of a CAR composition of the invention comprises an antibody fragment. In a further aspect, the CAR comprises an antibody fragment that comprises a scFv.

The term “antibody heavy chain,” refers to the larger of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations, and which normally determines the class to which the antibody belongs.

The term “antibody light chain,” refers to the smaller of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations. Kappa (□) and lambda (□) light chains refer to the two major antibody light chain isotypes.

The term “recombinant antibody” refers to an antibody which is generated using recombinant DNA technology, such as, for example, an antibody expressed by a bacteriophage or yeast expression system. The term should also be construed to mean an antibody which has been generated by the synthesis of a DNA molecule encoding the antibody and which DNA molecule expresses an antibody protein, or an amino acid sequence specifying the antibody, wherein the DNA or amino acid sequence has been obtained using recombinant DNA or amino acid sequence technology which is available and well known in the art.

The term “antigen” or “Ag” refers to a molecule that provokes an immune response. This immune response may involve either antibody production, or the activation of specific immunologically-competent cells, or both. The skilled artisan will understand that any macromolecule, including virtually all proteins or peptides, can serve as an antigen. Furthermore, antigens can be derived from recombinant or genomic DNA. A skilled artisan will understand that any DNA, which comprises a nucleotide sequences or a partial nucleotide sequence encoding a protein that elicits an immune response therefore encodes an “antigen” as that term is used herein. Furthermore, one skilled in the art will understand that an antigen need not be encoded solely by a full length nucleotide sequence of a gene. It is readily apparent that the present invention includes, but is not limited to, the use of partial nucleotide sequences of more than one gene and that these nucleotide sequences are arranged in various combinations to encode polypeptides that elicit the desired immune response. Moreover, a skilled artisan will understand that an antigen need not be encoded by a “gene” at all. It is readily apparent that an antigen can be generated synthesized or can be derived from a biological sample, or might be macromolecule besides a polypeptide. Such a biological sample can include, but is not limited to a tissue sample, a tumor sample, a cell or a fluid with other biological components.

The term “anti-cancer effect” refers to a biological effect which can be manifested by various means, including but not limited to, e.g., a decrease in tumor volume, a decrease in the number of cancer cells, a decrease in the number of metastases, an increase in life expectancy, decrease in cancer cell proliferation, decrease in cancer cell survival, or amelioration of various physiological symptoms associated with the

cancerous condition. An "anti-cancer effect" can also be manifested by the ability of the peptides, polynucleotides, cells and antibodies in prevention of the occurrence of cancer in the first place. The term "anti-tumor effect" refers to a biological effect which can be manifested by various means, including but not limited to, e.g., a decrease in tumor volume, a decrease in the number of tumor cells, a decrease in tumor cell proliferation, or a decrease in tumor cell survival.

The term "autologous" refers to any material derived from the same individual into whom it is later to be re-introduced.

The term "allogeneic" refers to any material derived from a different animal of the same species as the individual to whom the material is introduced. Two or more individuals are said to be allogeneic to one another when the genes at one or more loci are not identical. In some aspects, allogeneic material from individuals of the same species may be sufficiently unlike genetically to interact antigenically

The term "xenogeneic" refers to a graft derived from an animal of a different species.

The term "cancer" refers to a disease characterized by the uncontrolled growth of aberrant cells. Cancer cells can spread locally or through the bloodstream and lymphatic system to other parts of the body. Examples of various cancers are described herein and include but are not limited to, breast cancer, prostate cancer, ovarian cancer, cervical cancer, skin cancer, pancreatic cancer, colorectal cancer, renal cancer, liver cancer, brain cancer, lymphoma, leukemia, lung cancer and the like. The terms "tumor" and "cancer" are used interchangeably herein, e.g., both terms encompass solid and liquid, e.g., diffuse or circulating, tumors. As used herein, the term "cancer" or "tumor" includes premalignant, as well as malignant cancers and tumors.

"Derived from" as that term is used herein, indicates a relationship between a first and a second molecule. It generally refers to structural similarity between the first molecule and a second molecule and does not connotate or include a process or source limitation on a first molecule that is derived from a second molecule. For example, in the case of an intracellular signaling domain that is derived from a CD3zeta molecule, the intracellular signaling domain retains sufficient CD3zeta structure such that is has the required function, namely, the ability to generate a signal under the appropriate conditions. It does not connotate or include a limitation to a particular process of producing the intracellular signaling domain, e.g., it does not mean that, to provide the intracellular signaling domain, one must start with a CD3zeta sequence and delete unwanted sequence, or impose mutations, to arrive at the intracellular signaling domain.

The phrase "disease associated with expression of a tumor antigen as described herein" includes, but is not limited to, a disease associated with expression of a tumor antigen as described herein or condition associated with cells which express a tumor antigen as described herein including, e.g., proliferative diseases such as a cancer or malignancy or a precancerous condition such as a myelodysplasia, a myelodysplastic syndrome or a preleukemia; or a noncancer related indication associated with cells which express a tumor antigen as described herein. In one aspect, a cancer associated with expression of a tumor antigen as described herein is a hematological cancer. In one aspect, a cancer associated with expression of a tumor antigen as described herein is a solid cancer. Further diseases associated with expression of a tumor antigen described herein include, but not limited to, e.g., atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases associated with expression of a tumor antigen as described herein. Non-cancer related indications associated with expression of a tumor antigen as described herein include, but are not limited to, e.g., autoimmune disease, (e.g., lupus), inflammatory disorders (allergy and asthma) and transplantation. In some embodiments, the tumor antigen-expressing cells express, or at any time expressed, mRNA encoding the tumor antigen. In an embodiment, the tumor antigen -expressing cells produce the tumor antigen protein (e.g., wild-type or mutant), and the tumor antigen protein may be present at normal levels or reduced levels. In an embodiment, the tumor antigen -expressing cells produced detectable levels of a tumor antigen protein at one point, and subsequently produced substantially no detectable tumor antigen protein.

The term "conservative sequence modifications" refers to amino acid modifications that do not significantly affect or alter the binding characteristics of the antibody or antibody fragment containing the amino acid sequence. Such conservative modifications include amino acid substitutions, additions and deletions. Modifications can be introduced into an antibody or antibody fragment of the invention by standard techniques known in the art, such as site-directed mutagenesis and PCR-mediated mutagenesis. Conservative amino acid substitutions are ones in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine, tryptophan), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, one or more amino acid residues within a CAR of the invention can be replaced with other amino acid residues from the same side chain family and the altered CAR can be tested using the functional assays described herein.

The term "stimulation," refers to a primary response induced by binding of a stimulatory molecule (e.g., a TCR/CD3 complex or CAR) with its cognate ligand (or tumor antigen in the case of a CAR) thereby mediating a signal transduction event, such as, but not limited to, signal transduction via the TCR/CD3 complex or signal transduction via the appropriate NK receptor or signaling domains of the CAR. Stimulation can mediate altered expression of certain molecules.

The term "stimulatory molecule," refers to a molecule expressed by an immune cell (e.g., T cell, NK cell, B cell) that provides the cytoplasmic signaling sequence(s) that regulate activation of the immune cell in a stimulatory way for at least some aspect of the immune cell signaling pathway. In one aspect, the signal is a primary signal that is initiated by, for instance, binding of a TCR/CD3 complex with an MHC molecule loaded with peptide, and which leads to mediation of a T cell response, including, but not limited to, proliferation, activation, differentiation, and the like. A primary cytoplasmic signaling sequence (also referred to as a "primary signaling domain") that acts in a stimulatory manner may contain a signaling motif which is known as immunoreceptor tyrosine-based activation motif or ITAM. Examples of an ITAM containing cytoplasmic signaling sequence that is of particular use in the invention includes, but is not limited to, those derived from CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and DAP12. In a specific CAR of the invention, the intracellular signaling domain in any one or more CARS of the invention comprises an intracellular signaling sequence, e.g., a primary signaling sequence of CD3-zeta. In a specific CAR of the invention, the primary signaling sequence of CD3-zeta is the sequence provided as SEQ ID NO:18, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like. In a specific CAR of the invention, the primary signaling sequence of CD3-zeta is the sequence as provided in SEQ ID NO:20, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like.

The term "antigen presenting cell" or "APC" refers to an immune system cell such as an accessory cell (e.g., a B-cell, a dendritic cell, and the like) that displays a foreign antigen complexed with major histocompatibility complexes (MHC's) on its surface. T-cells may recognize these complexes using their T-cell receptors (TCRs). APCs process antigens and present them to T-cells.

An "intracellular signaling domain," as the term is used herein, refers to an intracellular portion of a molecule. The intracellular signaling domain generates a signal that promotes an immune effector function of the CAR containing cell, e.g., a CART cell. Examples of immune effector function, e.g., in a CART cell, include cytolytic activity and helper activity, including the secretion of cytokines.

In an embodiment, the intracellular signaling domain can comprise a primary intracellular signaling domain. Exemplary primary intracellular signaling domains include those derived from the molecules responsible for primary stimulation, or antigen dependent simulation. In an embodiment, the intracellular signaling domain can comprise a costimulatory intracellular domain. Exemplary costimulatory intracellular signaling domains include those derived from molecules responsible for costimulatory signals, or antigen independent stimulation. For example, in the case of a CART, a primary intracellular signaling domain can comprise a cytoplasmic sequence of a T cell receptor, and a costimulatory intracellular signaling domain can comprise cytoplasmic sequence from co-receptor or costimulatory molecule.

A primary intracellular signaling domain can comprise a signaling motif which is known as an immunoreceptor tyrosine-based activation motif or ITAM. Examples of ITAM containing primary cytoplasmic signaling sequences include, but are not limited to, those derived from CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and DAP12.

The term "zeta" or alternatively "zeta chain", "CD3-zeta" or "TCR-zeta" is defined as the protein provided as GenBan Acc. No. BAG36664.1, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like, and a "zeta stimulatory domain" or alternatively a "CD3-zeta stimulatory domain" or a "TCR-zeta stimulatory domain" is defined as the amino acid residues from the cytoplasmic domain of the zeta chain, or functional derivatives thereof, that are sufficient to functionally transmit an initial signal necessary for T cell activation. In one aspect the cytoplasmic domain of zeta comprises residues 52 through 164 of GenBank Acc. No. BAG36664.1 or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like, that are functional orthologs thereof. In one aspect, the "zeta stimulatory domain" or a "CD3-zeta stimulatory domain" is the sequence provided as SEQ ID NO:18. In one aspect, the "zeta stimulatory domain" or a "CD3-zeta stimulatory domain" is the sequence provided as SEQ ID NO:20.

The term a "costimulatory molecule" refers to a cognate binding partner on a T cell that specifically binds with a costimulatory ligand, thereby mediating a costimulatory response by the T cell, such as, but not limited to, proliferation. Costimulatory molecules are cell surface molecules other than antigen receptors or their ligands that are contribute to an efficient immune response. Costimulatory molecules include, but are not limited to an MHC class I molecule, BTLA and a Toll ligand receptor, as well as OX40, CD27, CD28, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), and 4-1BB (CD137). Further examples of such costimulatory molecules include CDS, ICAM-1, GITR, BAFFR, HVEM (LIGHTR), SLAMF7,

NKp80 (KLRF1), NKp44, NKp30, NKp46, CD160, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, and a ligand that specifically binds with CD83.

A costimulatory intracellular signaling domain can be the intracellular portion of a costimulatory molecule. A costimulatory molecule can be represented in the following protein families: TNF receptor proteins, Immunoglobulin-like proteins, cytokine receptors, integrins, signaling lymphocytic activation molecules (SLAM proteins), and activating NK cell receptors. Examples of such molecules include CD27, CD28, 4-1BB (CD137), OX40, GITR, CD30, CD40, ICOS, BAFFR, HVEM, ICAM-1, lymphocyte function-associated antigen-1 (LFA-1), CD2, CDS, CD7, CD287, LIGHT, NKG2C, NKG2D, SLAMF7, NKp80, NKp30, NKp44, NKp46, CD160, B7-H3, and a ligand that specifically binds with CD83, and the like.

The intracellular signaling domain can comprise the entire intracellular portion, or the entire native intracellular signaling domain, of the molecule from which it is derived, or a functional fragment or derivative thereof.

The term "4-1BB" refers to a member of the TNFR superfamily with an amino acid sequence provided as GenBank Acc. No. AAA62478.2, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like; and a "4-1BB costimulatory domain" is defined as amino acid residues 214-255 of GenBank Acc. No. AAA62478.2, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like. In one aspect, the "4-1BB costimulatory domain" is the sequence provided as SEQ ID NO:14 or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like.

"Immune effector cell," as that term is used herein, refers to a cell that is involved in an immune response, e.g., in the promotion of an immune effector response. Examples of immune effector cells include T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, mast cells, and myeloic-derived phagocytes.

"Immune effector function or immune effector response," as that term is used herein, refers to function or response, e.g., of an immune effector cell, that enhances or promotes an immune attack of a target cell. E.g., an immune effector function or response refers a property of a T or NK cell that promotes killing or the inhibition of growth or proliferation, of a target cell. In the case of a T cell, primary stimulation and co-stimulation are examples of immune effector function or response.

The term "encoding" refers to the inherent property of specific sequences of nucleotides in a polynucleotide, such as a gene, a cDNA, or an mRNA, to serve as templates for synthesis of other polymers and macromolecules in biological processes having either a defined sequence of nucleotides (e.g., rRNA, tRNA and mRNA) or a defined sequence of amino acids and the biological properties resulting therefrom. Thus, a gene, cDNA, or RNA, encodes a protein if transcription and translation of mRNA corresponding to that gene produces the protein in a cell or other biological system. Both the coding strand, the nucleotide sequence of which is identical to the mRNA sequence and is usually provided in sequence listings, and the non-coding strand, used as the template for transcription of a gene or cDNA, can be referred to as encoding the protein or other product of that gene or cDNA.

Unless otherwise specified, a "nucleotide sequence encoding an amino acid sequence" includes all nucleotide sequences that are degenerate versions of each other and that encode the same amino acid sequence. The phrase nucleotide sequence that encodes a protein or a RNA may also include introns to the extent that the nucleotide sequence encoding the protein may in some version contain an intron(s).

The term "effective amount" or "therapeutically effective amount" are used interchangeably herein, and refer to an amount of a compound, formulation, material, or composition, as described herein effective to achieve a particular biological result.

The term "endogenous" refers to any material from or produced inside an organism, cell, tissue or system.

The term "exogenous" refers to any material introduced from or produced outside an organism, cell, tissue or system.

The term "expression" refers to the transcription and/or translation of a particular nucleotide sequence driven by a promoter.

The term "transfer vector" refers to a composition of matter which comprises an isolated nucleic acid and which can be used to deliver the isolated nucleic acid to the interior of a cell. Numerous vectors are known in the art including, but not limited to, linear polynucleotides, polynucleotides associated with ionic or amphiphilic compounds, plasmids, and viruses. Thus, the term "transfer vector" includes an

autonomously replicating plasmid or a virus. The term should also be construed to further include non-plasmid and non-viral compounds which facilitate transfer of nucleic acid into cells, such as, for example, a polylysine compound, liposome, and the like. Examples of viral transfer vectors include, but are not limited to, adenoviral vectors, adeno-associated virus vectors, retroviral vectors, lentiviral vectors, and the like.

The term "expression vector" refers to a vector comprising a recombinant polynucleotide comprising expression control sequences operatively linked to a nucleotide sequence to be expressed. An expression vector comprises sufficient cis-acting elements for expression; other elements for expression can be supplied by the host cell or in an in vitro expression system. Expression vectors include all those known in the art, including cosmids, plasmids (e.g., naked or contained in liposomes) and viruses (e.g., lentiviruses, retroviruses, adenoviruses, and adeno-associated viruses) that incorporate the recombinant polynucleotide.

The term "homologous" or "identity" refers to the subunit sequence identity between two polymeric molecules, e.g., between two nucleic acid molecules, such as, two DNA molecules or two RNA molecules, or between two polypeptide molecules. When a subunit position in both of the two molecules is occupied by the same monomeric subunit; e.g., if a position in each of two DNA molecules is occupied by adenine, then they are homologous or identical at that position. The homology between two sequences is a direct function of the number of matching or homologous positions; e.g., if half (e.g., five positions in a polymer ten subunits in length) of the positions in two sequences are homologous, the two sequences are 50% homologous; if 90% of the positions (e.g., 9 of 10), are matched or homologous, the two sequences are 90% homologous.

"Humanized" forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')2 or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. For the most part, humanized antibodies and antibody fragments thereof are human immunoglobulins (recipient antibody or antibody fragment) in which residues from a complementary-determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity, and capacity. In some instances, Fv framework region (FR) residues of the human immunoglobulin are replaced by corresponding non-human residues. Furthermore, a humanized antibody/antibody fragment can comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. These modifications can further refine and optimize antibody or antibody fragment performance. In general, the humanized

antibody or antibody fragment thereof will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or a significant portion of the FR regions are those of a human immunoglobulin sequence. The humanized antibody or antibody fragment can also comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin. For further details, see Jones et al., Nature, 321: 522-525, 1986; Reichmann et al., Nature, 332: 323-329, 1988; Presta, Curr. Op. Struct. Biol., 2: 593-596, 1992.

"Fully human" refers to an immunoglobulin, such as an antibody or antibody fragment, where the whole molecule is of human origin or consists of an amino acid sequence identical to a human form of the antibody or immunoglobulin.

The term "isolated" means altered or removed from the natural state. For example, a nucleic acid or a peptide naturally present in a living animal is not "isolated," but the same nucleic acid or peptide partially or completely separated from the coexisting materials of its natural state is "isolated." An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell.

The term "operably linked" or "transcriptional control" refers to functional linkage between a regulatory sequence and a heterologous nucleic acid sequence resulting in expression of the latter. For example, a first nucleic acid sequence is operably linked with a second nucleic acid sequence when the first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Operably linked DNA sequences can be contiguous with each other and, e.g., where necessary to join two protein coding regions, are in the same reading frame.

The term "parenteral" administration of an immunogenic composition includes, e.g., subcutaneous (s.c.), intravenous (i.v.), intramuscular (i.m.), or intrasternal injection, intratumoral, or infusion techniques.

The term "nucleic acid" or "polynucleotide" refers to deoxyribonucleic acids (DNA) or ribonucleic acids (RNA) and polymers thereof in either single- or double-stranded form. Unless specifically limited, the term encompasses nucleic acids containing known analogues of natural nucleotides that have similar binding properties as the reference nucleic acid and are metabolized in a manner similar to naturally occurring nucleotides. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g., degenerate codon substitutions), alleles, orthologs, SNPs, and complementary sequences as well as the sequence explicitly indicated. Specifically,

degenerate codon substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzer et al., Nucleic Acid Res. 19:5081 (1991); Ohtsuka et al., J. Biol. Chem. 260:2605-2608 (1985); and Rossolini et al., Mol. Cell. Probes 8:91-98 (1994)).

The terms "peptide," "polypeptide," and "protein" are used interchangeably, and refer to a compound comprised of amino acid residues covalently linked by peptide bonds. A protein or peptide must contain at least two amino acids, and no limitation is placed on the maximum number of amino acids that can comprise a protein's or peptide's sequence. Polypeptides include any peptide or protein comprising two or more amino acids joined to each other by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, for example, and to longer chains, which generally are referred to in the art as proteins, of which there are many types. "Polypeptides" include, for example, biologically active fragments, substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. A polypeptide includes a natural peptide, a recombinant peptide, or a combination thereof.

The term "promoter" refers to a DNA sequence recognized by the synthetic machinery of the cell, or introduced synthetic machinery, required to initiate the specific transcription of a polynucleotide sequence.

The term "promoter/regulatory sequence" refers to a nucleic acid sequence which is required for expression of a gene product operably linked to the promoter/regulatory sequence. In some instances, this sequence may be the core promoter sequence and in other instances, this sequence may also include an enhancer sequence and other regulatory elements which are required for expression of the gene product. The promoter/regulatory sequence may, for example, be one which expresses the gene product in a tissue specific manner.

The term "constitutive" promoter refers to a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a cell under most or all physiological conditions of the cell.

The term "inducible" promoter refers to a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a cell substantially only when an inducer which corresponds to the promoter is present in the cell.

The term "tissue-specific" promoter refers to a nucleotide sequence which, when operably linked with a polynucleotide encodes or specified by a gene, causes the gene product to be produced in a cell substantially only if the cell is a cell of the tissue type corresponding to the promoter.

The terms "cancer associated antigen" or "tumor antigen" interchangeably refers to a molecule (typically a protein, carbohydrate or lipid) that is expressed on the surface of a cancer cell, either entirely or as a fragment (e.g., MHC/peptide), and which is useful for the preferential targeting of a pharmacological agent to the cancer cell. In some embodiments, a tumor antigen is a marker expressed by both normal cells and cancer cells, e.g., a lineage marker, e.g., CD19 on B cells. In some embodiments, a tumor antigen is a cell surface molecule that is overexpressed in a cancer cell in comparison to a normal cell, for instance, 1-fold over expression, 2-fold overexpression, 3-fold overexpression or more in comparison to a normal cell. In some enbodiments, a tumor antigen is a cell surface molecule that is inappropriately synthesized in the cancer cell, for instance, a molecule that contains deletions, additions or mutations in comparison to the molecule expressed on a normal cell. In some embodiments, a tumor antigen will be expressed exclusively on the cell surface of a cancer cell, entirely or as a fragment (e.g., MHC/peptide), and not synthesized or expressed on the surface of a normal cell. In some embodiments, the CARs of the present invention includes CARs comprising an antigen binding domain (e.g., antibody or antibody fragment) that binds to a MHC presented peptide. Normally, peptides derived from endogenous proteins fill the pockets of Major histocompatibility complex (MHC) class I molecules, and are recognized by T cell receptors (TCRs) on CD8 + T lymphocytes. The MHC class I complexes are constitutively expressed by all nucleated cells. In cancer, virus-specific and/or tumor-specific peptide/MHC complexes represent a unique class of cell surface targets for immunotherapy. TCR-like antibodies targeting peptides derived from viral or tumor antigens in the context of human leukocyte antigen (HLA)-A1 or HLA-A2 have been described (see, e.g., Sastry et al., J Virol. 2011 85(5):1935-1942; Sergeeva et al., Blood, 2011 117(16):4262-4272; Verma et al., J Immunol 2010 184(4):2156-2165; Willemsen et al., Gene Ther 2001 8(21) :1601-1608 ; Dao et al., Sci Transl Med 2013 5(176) :176ra33 ; Tassev et al., Cancer Gene Ther 2012 19(2):84-100). For example, TCR-like antibody can be identified from screening a library, such as a human scFv phage displayed library.

The term "tumor-supporting antigen" or "cancer-supporting antigen" interchangeably refer to a molecule (typically a protein, carbohydrate or lipid) that is expressed on the surface of a cell that is, itself, not cancerous, but supports the cancer cells, e.g., by promoting their growth or survival e.g., resistance to immune cells. Exemplary cells of this type include stromal cells and myeloid-derived suppressor cells (MDSCs). The tumor-supporting antigen itself need not play a role in supporting the tumor cells so long as the antigen is present on a cell that supports cancer cells.

The term "flexible polypeptide linker" or "linker" as used in the context of a scFv refers to a peptide linker that consists of amino acids such as glycine and/or serine residues used alone or in combination, to link variable heavy and variable light chain regions together. In one embodiment, the flexible polypeptide linker is a Gly/Ser linker and comprises the amino acid sequence (Gly-Gly-Gly-Ser)n, where n is a positive integer equal to or greater than 1. For example, n=1, n=2, n=3. n=4, n=5 and n=6, n=7, n=8, n=9 and n=10 (SEQ ID NO:6592). In one embodiment, the flexible polypeptide linkers include, but are not limited to, (Gly4 Ser)4 (SEQ ID NO:6593) or (Gly4 Ser)3 (SEQ ID NO:6594). In another embodiment, the linkers include multiple repeats of (Gly2Ser), (GlySer) or (Gly3Ser) (SEQ ID NO:6595). Also included within the scope of the invention are linkers described in WO2012/138475, incorporated herein by reference).

As used herein in connection with a messenger RNA (mRNA), a 5' cap (also termed an RNA cap, an RNA 7-methylguanosine cap or an RNA m7G cap) is a modified guanine nucleotide that has been added to the "front" or 5' end of a eukaryotic messenger RNA shortly after the start of transcription. The 5' cap consists of a terminal group which is linked to the first transcribed nucleotide. Its presence is critical for recognition by the ribosome and protection from RNases. Cap addition is coupled to transcription, and occurs co-transcriptionally, such that each influences the other. Shortly after the start of transcription, the 5' end of the mRNA being synthesized is bound by a cap-synthesizing complex associated with RNA polymerase. This enzymatic complex catalyzes the chemical reactions that are required for mRNA capping. Synthesis proceeds as a multi-step biochemical reaction. The capping moiety can be modified to modulate functionality of mRNA such as its stability or efficiency of translation.

As used herein, "in vitro transcribed RNA" refers to RNA, preferably mRNA, that has been synthesized in vitro. Generally, the in vitro transcribed RNA is generated from an in vitro transcription vector. The in vitro transcription vector comprises a template that is used to generate the in vitro transcribed RNA.

As used herein, a "poly(A)" is a series of adenosines attached by polyadenylation to the mRNA. In the preferred embodiment of a construct for transient expression, the polyA is between 50 and 5000 (SEQ ID NO: 6596), preferably greater than 64, more preferably greater than 100, most preferably greater than 300 or 400. poly(A) sequences can be modified chemically or enzymatically to modulate mRNA functionality such as localization, stability or efficiency of translation.

As used herein, "polyadenylation" refers to the covalent linkage of a polyadenylyl moiety, or its modified variant, to a messenger RNA molecule. In eukaryotic organisms, most messenger RNA (mRNA) molecules are polyadenylated at the 3' end. The 3' poly(A) tail is a long sequence of adenine nucleotides (often several hundred) added to the pre-mRNA through the action of an enzyme, polyadenylate

polymerase. In higher eukaryotes, the poly(A) tail is added onto transcripts that contain a specific sequence, the polyadenylation signal. The poly(A) tail and the protein bound to it aid in protecting mRNA from degradation by exonucleases. Polyadenylation is also important for transcription termination, export of the mRNA from the nucleus, and translation. Polyadenylation occurs in the nucleus immediately after transcription of DNA into RNA, but additionally can also occur later in the cytoplasm. After transcription has been terminated, the mRNA chain is cleaved through the action of an endonuclease complex associated with RNA polymerase. The cleavage site is usually characterized by the presence of the base sequence AAUAAA near the cleavage site. After the mRNA has been cleaved, adenosine residues are added to the free 3' end at the cleavage site.

As used herein, "transient" refers to expression of a non-integrated transgene for a period of hours, days or weeks, wherein the period of time of expression is less than the period of time for expression of the gene if integrated into the genome or contained within a stable plasmid replicon in the host cell.

As used herein, the terms "treat", "treatment" and "treating" refer to the reduction or amelioration of the progression, severity and/or duration of a proliferative disorder, or the amelioration of one or more symptoms (preferably, one or more discernible symptoms) of a proliferative disorder resulting from the administration of one or more therapies (e.g., one or more therapeutic agents such as a CAR of the invention). In specific embodiments, the terms "treat", "treatment" and "treating" refer to the amelioration of at least one measurable physical parameter of a proliferative disorder, such as growth of a tumor, not necessarily discernible by the patient. In other embodiments the terms "treat", "treatment" and "treating" - refer to the inhibition of the progression of a proliferative disorder, either physically by, e.g., stabilization of a discernible symptom, physiologically by, e.g., stabilization of a physical parameter, or both. In other embodiments the terms "treat", "treatment" and "treating" refer to the reduction or stabilization of tumor size or cancerous cell count.

The term "signal transduction pathway" refers to the biochemical relationship between a variety of signal transduction molecules that play a role in the transmission of a signal from one portion of a cell to another portion of a cell. The phrase "cell surface receptor" includes molecules and complexes of molecules capable of receiving a signal and transmitting signal across the membrane of a cell.

The term "subject" is intended to include living organisms in which an immune response can be elicited (e.g., mammals, human).

The term, a "substantially purified" cell refers to a cell that is essentially free of other cell types. A substantially purified cell also refers to a cell which has been separated from other cell types with which it

is normally associated in its naturally occurring state. In some instances, a population of substantially purified cells refers to a homogenous population of cells. In other instances, this term refers simply to cell that have been separated from the cells with which they are naturally associated in their natural state. In some aspects, the cells are cultured in vitro. In other aspects, the cells are not cultured in vitro.

The term “therapeutic” as used herein means a treatment. A therapeutic effect is obtained by reduction, suppression, remission, or eradication of a disease state.

The term “prophylaxis” as used herein means the prevention of or protective treatment for a disease or disease state.

In the context of the present invention, "tumor antigen" or "hyperproliferative disorder antigen" or "antigen associated with a hyperproliferative disorder" refers to antigens that are common to specific hyperproliferative disorders. In certain aspects, the hyperproliferative disorder antigens of the present invention are derived from, cancers including but not limited to primary or metastatic melanoma, thymoma, lymphoma, sarcoma, lung cancer, liver cancer, non-Hodgkin lymphoma, Hodgkin lymphoma, leukemias, uterine cancer, cervical cancer, bladder cancer, kidney cancer and adenocarcinomas such as breast cancer, prostate cancer, ovarian cancer, pancreatic cancer, and the like.

The term “transfected” or “transformed” or “transduced” refers to a process by which exogenous nucleic acid is transferred or introduced into the host cell. A “transfected” or “transformed” or “transduced” cell is one which has been transfected, transformed or transduced with exogenous nucleic acid. The cell includes the primary subject cell and its progeny.

The term “specifically binds,” refers to a molecule recognizing and binding with a binding partner (e.g., a protein or nucleic acid) present in a sample, but which molecule does not substantially recognize or bind other molecules in the sample.

“Membrane anchor” or “membrane tethering domain”, as that term is used herein, refers to a polypeptide or moiety, e.g., a myristoyl group, sufficient to anchor an extracellular or intracellular domain to the plasma membrane.

The term “bioequivalent” refers to an amount of an agent other than the reference compound (e.g., RAD001), required to produce an effect equivalent to the effect produced by the reference dose or reference amount of the reference compound (e.g., RAD001). In an embodiment the effect is the level of mTOR inhibition, e.g., as measured by P70 S6 kinase inhibition, e.g., as evaluated in an in vivo or in vitro assay, e.g., as measured by an assay described herein, e.g., the Boulay assay. In an embodiment, the

effect is alteration of the ratio of PD-1 positive/PD-1 negative T cells, as measured by cell sorting. In an embodiment a bioequivalent amount or dose of an mTOR inhibitor is the amount or dose that achieves the same level of P70 S6 kinase inhibition as does the reference dose or reference amount of a reference compound. In an embodiment, a bioequivalent amount or dose of an mTOR inhibitor is the amount or dose that achieves the same level of alteration in the ratio of PD-1 positive/PD-1 negative T cells as does the reference dose or reference amount of a reference compound.

The term "low, immune enhancing, dose" when used in conjunction with an mTOR inhibitor, e.g., an allosteric mTOR inhibitor, e.g., RAD001 or rapamycin, or a catalytic mTOR inhibitor, refers to a dose of mTOR inhibitor that partially, but not fully, inhibits mTOR activity, e.g., as measured by the inhibition of P70 S6 kinase activity. Methods for evaluating mTOR activity, e.g., by inhibition of P70 S6 kinase, are discussed herein. The dose is insufficient to result in complete immune suppression but is sufficient to enhance the immune response. In an embodiment, the low, immune enhancing, dose of mTOR inhibitor results in a decrease in the number of PD-1 positive T cells and/or an increase in the number of PD-1 negative T cells, or an increase in the ratio of PD-1 negative T cells/PD-1 positive T cells. In an embodiment, the low, immune enhancing, dose of mTOR inhibitor results in an increase in the number of naive T cells. In an embodiment, the low, immune enhancing, dose of mTOR inhibitor results in one or more of the following:

an increase in the expression of one or more of the following markers: CD62Lhigh, CD127high, CD27+, and BCL2, e.g., on memory T cells, e.g., memory T cell precursors;

a decrease in the expression of KLRG1, e.g., on memory T cells, e.g., memory T cell precursors; and

an increase in the number of memory T cell precursors, e.g., cells with any one or combination of the following characteristics: increased CD62Lhigh, increased CD127high, increased CD27+, decreased KLRG1, and increased BCL2;

wherein any of the changes described above occurs, e.g., at least transiently, e.g., as compared to a non-treated subject.

"Refractory" as used herein refers to a disease, e.g., cancer, that does not respond to a treatment. In embodiments, a refractory cancer can be resistant to a treatment before or at the beginning of the treatment. In other embodiments, the refractory cancer can become resistant during a treatment. A refractory cancer is also called a resistant cancer.

"Relapsed" as used herein refers to the return of a disease (e.g., cancer) or the signs and symptoms of a disease such as cancer after a period of improvement, e.g., after prior treatment of a therapy, e.g., cancer therapy.

Ranges: throughout this disclosure, various aspects of the invention can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the invention. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. As another example, a range such as 95-99% identity, includes something with 95%, 96%, 97%, 98% or 99% identity, and includes subranges such as 96-99%, 96-98%, 96-97%, 97-99%, 97-98% and 98-99% identity. This applies regardless of the breadth of the range.

DETAILED DESCRPTION

The gRNA molecules, compositions and methods described herein relate to genome editing in eukaryotic cells using a CRISPR/Cas system, e.g., a Cas9 system. In particular, the gRNA molecules, compositions and methods described herein relate to regulation of expression of (or expression of functional versions of) target molecules that have an effect on the function of a transplanted cell, for example a cell for cancer immunotherapy. In an aspect, the transplanted cell is an immune effector cell, e.g., an NK cell or T cell. In an aspect, the cell is an allogeneic cell. In an aspect, the cell has been, is or will be engineered to express a chimeric antigen receptor. Thus, provided herein are compositions and methods for altering, e.g., inhibiting or reducing, the expression and/or function (e.g., the level of expression of a functional version) of a gene product which may improve the efficacy (for example, by reducing or eliminating undesirable immunogenicity (such as a host versus graft response or a graft versus host response)), function, proliferation, stimulation or survival of a transplanted cell, for example a transplanted immune effector cell, for example a NK cell or T cell, for example a T cell engineered to express a chimeric antigen receptor (CAR), for example an allogeneic CAR-expressing T cell for immunotherapy.

In aspects, the gene products are allogeneic T cell targets such as a component of the T cell receptor, e.g., CD3zeta, CD3 epsilon, CD3 gamma, CD3 delta, T cell receptor (TCR) alpha or TCR beta; an HLA molecule or beta-2 micoglobulin (B2M), e.g., an HLA-A, an HLA-B, an HLA-C or B2M; a CIITA molecule; or a target for an immunosuppressant, e.g., glucocorticoid receptor, deoxycytidine kinase, an FKBP, CD52 or a cyclophilin family member; and combinations thereof. Without being bound by theory

it is believed that inhibition or elimination of the level of an allogeneic T cell target or level of expression of an allogeneic T cell target gene product (e.g., via alteration of the gene) may improve the function of a cell, e.g., a transplanted cell, e.g., a transplanted immune effector cell, e.g., a CART cell, e.g., an allogeneic CART cell, by reducing or eliminating a graft vs. host response, a host vs. graft response, or will render said transplanted cell resistant to immunosuppressant therapy.

In an aspect, compositions and methods described herein can be used to improve cell, e.g., T cell, e.g., CAR-engineered T cell, e.g., allogeneic CAR-engineered T cell function (for example, by reducing or eliminating undesirable immunogenicity (such as a host versus graft response or a graft versus host response)), survival, proliferation and/or efficacy by altering the gene of a component of the T cell receptor (TCR), e.g., CD3zeta, CD3 epsilon, CD3 gamma, CD3 delta, T cell receptor (TCR) alpha, e.g., constant region of TCR alpha, or TCR beta, e.g., constant region 1 or constant region 2 of TCR beta gene. While not wishing to be bound by theory, it is considered that reduced or absent expression of functional T-cell receptor components reduces or eliminates the presence of TCR on the surface of said cell, thereby reducing or preventing graft vs. host disease by eliminating T cell receptor recognition of and response to host tissues. This approach, therefore, could be used to generate "off the shelf" T cells (Torikai et al., 2012 Blood 119, 5697-5705).

In an aspect, compositions and methods described herein can be used to improve cell, e.g., T cell, e.g., CAR-engineered T cell, e.g., allogeneic CAR-engineered T cell function (for example, by reducing or eliminating undesirable immunogenicity (such as a host versus graft response or a graft versus host response)), survival, proliferation and/or efficacy by altering the gene of a component of the major histocompatibility complex, e.g., an HLA protein or B2M, e.g., HLA-A, HLA-B, HLA-C or B2M (encoded by the B2M gene), or protein which regulates expression of one or more components of the major histocompatibility complex, e.g., NLRC5. While not wishing to be bound by theory, it is considered that reduced or absent expression of a mismatch (e.g., one that does not match the type of the subject receiving the cell therapy) HLA protein (or component) reduces or eliminate host vs. graft disease by eliminating host T cell receptor recognition of and response to mismatched (e.g., allogeneic) graft tissue. This approach, therefore, could be used to generate "off the shelf" T cells.

In an aspect, compositions and methods described herein can be used to improve cell, e.g., T cell, e.g., CAR-engineered T cell, e.g., allogeneic CAR-engineered T cell function (for example, by reducing or eliminating undesirable immunogenicity (such as a host versus graft response or a graft versus host response)), survival, proliferation and/or efficacy by altering a gene of a component of the major histocompatibility complex class II or a regulator of MHC class II expression, e.g., CIITA (encoded by

the CIITA gene), RFXANK, RFX5, or RFXAP, and combinations thereof, e.g., CIITA. While not wishing to be bound by theory, it is believed that reducing or eliminating the expression of a regulator of MHC class II expression, e.g., CIITA, will reduce or eliminate the expression of MHC class II molecules on the allogeneic cell, thereby reducing or eliminating expression of a mismatch (e.g., one that does not match the type of the subject receiving the cell therapy) MHC class II protein (or component), thereby reducing or eliminating host vs. graft disease by, e.g., eliminating host T cell receptor recognition of and response to mismatched (e.g., allogeneic) graft tissue, e.g., allogeneic T cell, e.g., allogeneic CART cell, as described herein. This approach, therefore, could be used to generate "off the shelf" T cells.

In an aspect, it may be beneficial to reduce or eliminate expression of both one or more MHC class I molecules and one or more MHC II molecules, e.g., in a T cell, e.g., in an allogeneic T cell, e.g., in an allogeneic CART cell, e.g., as described herein, to further reduce or eliminate the host versus graft disease response upon administration of the cell. Thus, in embodimentsof the cells and methods of the invention, cells may be contacted with a composition of the invention (e.g., a composition comprising a gRNA and a Cas9 molecule) comprising a gRNA molecule, e.g., as described herein, to B2M (e.g., such that expression of one or more MHC class I molecules is reduced or eliminated in said cell) and a composition of the invention (e.g., a composition comprising a gRNA and a Cas9 molecule) comprising a gRNA molecule, e.g., as described herein, to CIITA (e.g., such that expression of one or more MHC class II molecules is reduced or eliminated). In embodiments of the cells and methods of the invention, the cell may also be contacted with a composition of the invention (e.g., a composition comprising a gRNA and a Cas9 molecule) comprising a gRNA molecule, e.g., as described herein, to a component of the TCR, e.g., to TRAC and/or TRBC (e.g., such that expression of the T cell receptor, e.g., one or more components of the TCR is reduced or eliminated). In an embodiment, a cell of the invention has reduced or eliminated expression of TCR (e.g., as detected by flow cytometry), reduced or eliminated expression of one or more MHC class I molecules (e.g., as detected by flow cytometry), and reduced or eliminated expression of one or more MHC class II molecules (e.g., as detected by flow cytometry). In an embodiment, a cell of the invention has reduced or eliminated expression of TRAC, reduced or eliminated expression of B2M, and reduced or eliminated expression of CIITA. In an embodiment, a cell of the invention has reduced or eliminated expression of TRAC, reduced or eliminated expression of NLRC5, and reduced or eliminated expression of CIITA. In embodiments, the reduced or eliminated expression is measured relative to a similar cell that has not been treated with a composition or CRISPR system of the invention. In embodiments, the cell is an immune effector cell, e.g., a T cell or NK cell, e.g., a T cell, e.g., as described herein. In embodiments the cell is a T cell which is engineered to express a chimeric antigen receptor (CAR), e.g., as described herein. In embodiments, the CAR is a BCMA CAR, e.g., as described herein.

In an embodiment, the invention provides a cell, e.g., an immune effector cell, e.g., a T cell or NK cell, e.g., a T cell, engineered to express a BCMA CAR which is TCR-/B2M-/CIITA- or TCR-/NLRC5-/CIITA-. In embodiments, the cell is a human cell. In embodiments, the cell is allogeneic relative to a subject to be administered said cell. In embodiments, the reduced or eliminated expression of TCR, B2M, NLRC5 and/or CIITA is accomplished by introducing into said cell a composition, CRISPR system, or gRNA of the invention, e.g., as described herein, or by a method as described herein.

In an aspect, compositions and methods described herein can be used to improve cell, e.g., T cell, e.g., CAR-engineered T cell, e.g., allogeneic CAR-engineered T cell function (for example, by reducing or eliminating undesirable immunogenicity (such as a host versus graft response or a graft versus host response)), survival, proliferation and/or efficacy by altering the gene of a target for an immunosuppressant, e.g., glucocorticoid receptor (GR) (encoded by NR3C1). Without being bound by theory, it is considered that absent or reduced expression of functional GR on a cell therapy product allows that cell therapy product to function in the presence of an immunosuppressive such as a corticosteroid such as dexamethasone, said immunosuppressive being administered to, for example, reduce or eliminate host vs. graft disease. This approach, therefore, could be used to generate "off the shelf" T cells.

In an aspect, compositions and methods described herein can be used to improve cell, e.g., T cell, e.g., CAR-engineered T cell, e.g., allogeneic CAR-engineered T cell function (for example, by reducing or eliminating undesirable immunogenicity (such as a host versus graft response or a graft versus host response)), survival, proliferation and/or efficacy by altering the gene of a target for an immunosuppressant, e.g., CD52 (encoded by CD52). Without being bound by theory, it is considered that absent or reduced expression of functional CD52 on a cell therapy product allows that cell therapy product to function in the presence of an immunosuppressive such as an anti-CD52 antibody or antigen-binding fragment thereof such as alemtuzumab (CAMPATH®), said immunosuppressive being administered to, for example, reduce or eliminate host vs. graft disease. This approach, therefore, could be used to generate "off the shelf" T cells.

In an aspect, compositions and methods described herein can be used to improve cell, e.g., T cell, e.g., CAR-engineered T cell, e.g., allogeneic CAR-engineered T cell function (for example, by reducing or eliminating undesirable immunogenicity (such as a host versus graft response or a graft versus host response)), survival, proliferation and/or efficacy by altering the gene of a target for an immunosuppressant, e.g., an FKBP family member, e.g., FKBP12 (encoded by FKBP1A). Without being bound by theory, it is considered that absent or reduced expression of functional FKBP12 on a cell

therapy product allows that cell therapy product to function in the presence of an immunosuppressive such as FK506 (or FKBP12-binding fragment or analog thereof), cyclosporine, rapamycin or rapalog, or mTor inhibitor such as RAD001, said immunosuppressive being administered to, for example, reduce or eliminate host vs. graft disease. This approach, therefore, could be used to generate "off the shelf" T cells.

In an aspect, compositions and methods described herein can be used to improve cell, e.g., T cell, e.g., CAR-engineered T cell, e.g., allogeneic CAR-engineered T cell function (for example, by reducing or eliminating undesirable immunogenicity (such as a host versus graft response or a graft versus host response)), survival, proliferation and/or efficacy by altering the gene of a target for an immunosuppressant, e.g., deoxycytdine kinase (encoded by DCK). Without being bound by theory, it is considered that absent or reduced expression of functional deoxycytdine kinase on a cell therapy product allows that cell therapy product to function in the presence of an immunosuppressive a nucleoside analog-based drug such as cytarabine (cytosine arabinoside) or gemcitabine], said immunosuppressive being administered to, for example, reduce or eliminate host vs. graft disease or treat a cancer. This approach, therefore, could be used to generate "off the shelf" T cells.

In aspects, the gene products are inhibitory molecules, e.g., immune checkpoint proteins, e.g., PD-1, PD-L1, PD-L2, CTLA4, TIM3, LAG3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta. Without being bound by theory, it is believed that inhibition or elimination of the level of an inhibitory molecule or level of expression of inhibitory molecule gene product (e.g., via alteration of the gene) may improve the function of a cell, e.g., a transplanted cell, e.g., a transplanted immune effector cell, e.g., a CART cell, e.g., an allogeneic CART cell, by reducing or eliminating the inhibitory effects mediated by said inhibitory molecule.

In one aspect, the compositions and methods described herein can be used to decrease the effect of immune suppressive factors on cells, e.g., CAR engineered T cells, by altering the gene of an inhibitory molecule, e.g., PD1. While not wishing to be bound by theory, it is considered that reduced or absent expression of Programed Cell Death 1 (PD-1) (encoded by PDCD1) abrogates the induction of a suppressed or non-responsive state ("anergy").

In one aspect, the compositions and methods described herein can be used to decrease the effect of immune suppressive factors on cells, e.g., CAR engineered T cells, by altering the gene of an inhibitory molecule, e.g., Tim3. While not wishing to be bound by theory, it is considered that reduced or absent

expression of Tim3 (encoded by HAVCR2) abrogates the induction of a suppressed or non-responsive state ("anergy").

In one aspect, the compositions and methods described herein can be used to decrease the effect of immune suppressive factors on cells, e.g., CAR engineered T cells, by altering the gene of an inhibitory molecule, e.g., CTLA4 gene. While not wishing to be bound by theory, it is considered that reduced or absent expression of cytotoxic T –lymphocyte associated antigen 4 (encoded by CTLA4) abrogates the induction of a suppressed or non-responsive state ("anergy").

In one aspect, the compositions and methods described herein can be used to decrease the effect of immune suppressive factors on cells, e.g., CAR engineered T cells, by altering the gene of an inhibitory molecule, e.g., Lag3 gene. While not wishing to be bound by theory, it is considered that reduced or absent expression of Lymphocyte-activation gene 3 (Lag3) (encoded by LAG3) abrogates the induction of a suppressed or non-responsive state ("anergy").

In one aspect, the compositions and methods described herein can be used to decrease the effect of immune suppressive factors on cells, e.g., CAR engineered T cells, by altering the gene of an inhibitory molecule, e.g., PD-L1 gene. While not wishing to be bound by theory, it is considered that reduced or absent expression of Programmed Death Ligand 1 (PD-L1, also known as CD274 and B7-H1) (encoded by CD274) abrogates the induction of a suppressed or non-responsive state ("anergy").

In one aspect, the compositions and methods described herein can be used to decrease the effect of immune suppressive factors on cells, e.g., CAR engineered T cells, by altering the gene of a downstream effector molecule of an inhibitory molecule, e.g., Tyrosine-protein phosphatase non-receptor type 1 gene. While not wishing to be bound by theory, it is considered that reduced or absent expression of functional tyrosine-protein phosphatase non-receptor type 1, also known as protein-tyrosine phosphatase 1B, (encoded by PTPN1) abrogates the induction of a suppressed or non-responsive state ("anergy") by affecting signaling through an inhibitory molecule.

In aspects, the compositions and methods described herein may be used in combination to generate cells, e.g., transplanted cells, e.g., allogeneic cells, e.g., immune effector cells, e.g., NK cells or T cells, e.g., CAR-engineered T cells with enhanced efficacy (for example, by reducing or eliminating undesirable immunogenicity (such as a host versus graft response or a graft versus host response)), survival, proliferation and/or stimulation relative to unmodified cells.

In one approach, the compositions and methods described herein may be used to generate cells in which levels or expression levels of a functional component of TCR have been reduced or eliminated and in

which levels or expression levels of a functional MHC have been reduced or eliminated. In one embodiment, cells have reduced or eliminated levels or expression levels of TCR alpha and HLA-A. In one embodiment, cells have reduced or eliminated levels or expression levels of TCR alpha and HLA-B. In one embodiment, cells have reduced or eliminated levels or expression levels of TCR alpha and HLA-C. In one embodiment, cells have reduced or eliminated levels or expression levels of TCR alpha and B2M. In one embodiment, cells have reduced or eliminated levels or expression levels of TCR alpha and NLRC5. In one embodiment, cells have reduced or eliminated levels or expression levels of TCR beta and HLA-A. In one embodiment, cells have reduced or eliminated levels or expression levels of TCR beta and HLA-B. In one embodiment, cells have reduced or eliminated levels or expression levels of TCR beta and HLA-C. In one embodiment, cells have reduced or eliminated levels or expression levels of TCR beta and B2M. In one embodiment, cells have reduced or eliminated levels or expression levels of TCR beta and NLRC5. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3zeta and HLA-A. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3zeta and HLA-B. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3zeta and HLA-C. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3zeta and B2M. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3zeta and NLRC5. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3epsilon and HLA-A. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3epsilon and HLA-B. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3epsilon and HLA-C. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3epsilon and B2M. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3epsilon and NLRC5. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3gamma and HLA-A. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3gamma and HLA-B. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3gamma and HLA-C. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3gamma and B2M. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3gamma and NLRC5. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3delta and HLA-A. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3delta and HLA-B. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3delta and HLA-C. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3delta and B2M. In one embodiment, cells have reduced or eliminated levels or expression levels of CD3delta and NLRC5. In any of the aforementioned embodiments, the cells may have reduced or eliminated levels or expression levels of CIITA. In an embodiment, the cells have reduced or eliminated levels or expression levels of

TRAC, B2M and CIITA. In an embodiment, the cells have reduced or eliminated levels or expression levels of TRBC, B2M and CIITA. In an embodiment, the cells have reduced or eliminated levels or expression levels of TRAC, TRBC, B2M and CIITA. In an embodiment, the cells have reduced or eliminated levels or expression levels of TRAC, NLRC5 and CIITA. In an embodiment, the cells have reduced or eliminated levels or expression levels of TRBC, NLRC5 and CIITA. In an embodiment, the cells have reduced or eliminated levels or expression levels of TRAC, TRBC, NLRC5 and CIITA. In any of the aforementioned embodiments, the cells may additionally have reduced or eliminated levels or expression levels of one or more inhibitory molecules or downstream effectors of an inhibitory molecule. In one aspect, the one or more inhibitory molecules comprises PD-1. In one aspect, the one or more inhibitory molecules comprises PD-L1. In one aspect, the one or more inhibitory molecules comprises Lag3. In one aspect, the one or more inhibitory molecules comprises Tim3. In one aspect, the one or more inhibitory molecules comprises CTLA4. In one aspect, the one or more inhibitory molecules comprises PTPN1. In one aspect, the one or more inhibitory molecules comprises PD-1 and PD-L1. In one aspect, the one or more inhibitory molecules comprises PD-1 and Lag3. In one aspect, the one or more inhibitory molecules comprises PD-1 and Tim3. In one aspect, the one or more inhibitory molecules comprises PD-1 and CTLA4. In one aspect, the one or more inhibitory molecules comprises PD-L1 and Lag3. In one aspect, the one or more inhibitory molecules comprises PD-L1 and Tim3. In one aspect, the one or more inhibitory molecules comprises PD-L1 and CTLA4. In one aspect, the one or more inhibitory molecules comprises Tim3 and Lag3. In one aspect, the one or more inhibitory molecules comprises Tim3 and CTLA4. In one aspect, the one or more inhibitory molecules comprises Lag3 and CTLA4. In one aspect, the one or more inhibitory molecules comprises , PD-1, PD-L1 and Lag3. In one aspect, the one or more inhibitory molecules comprises, PD-1, PD-L1 and Tim3. In one aspect, the one or more inhibitory molecules comprises, PD-1, PD-L1 and CTLA-4. In one aspect, the one or more inhibitory molecules comprises, PD-1, Tim3 and Lag3. In one aspect, the one or more inhibitory molecules comprises, PD-L1, Tim3 and Lag3. In one aspect, the one or more inhibitory molecules comprises, CTLA4, Tim3 and Lag3.

In one aspect, the compositions and methods described herein may be used to generate cells, e.g., T cells, e.g., CAR-engineered T cells, in which levels or expression levels of two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules have been reduced or eliminated. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises PD-1 and PD-L1. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises PD-1 and Lag3. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises PD-1 and Tim3. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises PD-1 and CTLA4. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4,

inhibitory molecules comprises PD-L1 and Lag3. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises PD-L1 and Tim3. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises PD-L1 and CTLA4. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises Tim3 and Lag3. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises Tim3 and CTLA4. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises Lag3 and CTLA4. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises , PD-1, PD-L1 and Lag3. . In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises, PD-1, PD-L1 and Tim3. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises, PD-1, PD-L1 and CTLA-4. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises, PD-1, Tim3 and Lag3. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises, PD-L1, Tim3 and Lag3. In one aspect, the two or more, e.g., 2, e.g., 3, e.g., 4, inhibitory molecules comprises, CTLA4, Tim3 and Lag3.

In embodiments in which the cells have reduced or eliminated levels or expression levels of TCR alpha, the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: SEQ ID NO: 5816 to SEQ ID NO: 5965 or SEQ ID NO: 5528 to SEQ ID NO: 5623, for example, SEQ ID NO: 5569, SEQ ID NO: 5587, SEQ ID NO: 5592 or SEQ ID NO: 5586, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: SEQ ID NO: 5816 to SEQ ID NO: 5965 or SEQ ID NO: 5528 to SEQ ID NO: 5623.

In embodiments in which the cells have reduced or eliminated levels or expression levels of TCR beta, the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 5966 to SEQ ID NO: 6097 or SEQ ID NO: 5624 to SEQ ID NO: 5643, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 5966 to SEQ ID NO: 6097 or SEQ ID NO: 5624 to SEQ ID NO: 5643. In embodiments in which the cells have reduced or eliminated levels or expression levels of TCR beta, the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 6098 to SEQ ID NO: 6226 or SEQ ID NO: 5644 to SEQ ID NO: 5719, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 6098 to SEQ ID NO: 6226 or SEQ ID NO: 5644 to SEQ ID NO: 5719.

In embodiments in which the cells have reduced or eliminated levels or expression levels of CD3zeta (encoded by CD247 gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 84 to SEQ ID NO: 392, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 84 to SEQ ID NO: 392.

In embodiments in which the cells have reduced or eliminated levels or expression levels of CD3epsilon (encoded by CD3E gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 533 to SEQ ID NO: 839, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 533 to SEQ ID NO: 839.

In embodiments in which the cells have reduced or eliminated levels or expression levels of CD3delta (encoded by CD3D gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 393 to SEQ ID NO: 532, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 393 to SEQ ID NO: 532.

In embodiments in which the cells have reduced or eliminated levels or expression levels of CD3gamma (encoded by CD3G gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 840 to SEQ ID NO: 968, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 840 to SEQ ID NO: 968.

In embodiments in which the cells have reduced or eliminated levels or expression levels of B2M (encoded by B2M gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 1 to SEQ ID NO: 83 or SEQ ID NO: 5492 to SEQ ID NO: 5527, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 1 to SEQ ID NO: 83 or SEQ ID NO: 5492 to SEQ ID NO: 5527.

In embodiments in which the cells have reduced or eliminated levels or expression levels of NLRC5 (encoded by NLRC5 gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 8622 to SEQ ID NO: 10089, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, or 20 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 8622 to SEQ ID NO: 10089.

In embodiments in which the cells have reduced or eliminated levels or expression levels of HLA-A (encoded by HLA-A gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 969 to SEQ ID NO: 1345, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 969 to SEQ ID NO: 1345.

In embodiments in which the cells have reduced or eliminated levels or expression levels of HLA-B (encoded by HLA-B gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 1346 to SEQ ID NO: 1698, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 1346 to SEQ ID NO: 1698.

In embodiments in which the cells have reduced or eliminated levels or expression levels of HLA-C (encoded by HLA-C gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 1699 to SEQ ID NO: 2068, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 1699 to SEQ ID NO: 2068.

In embodiments in which the cells have reduced or eliminated levels or expression levels of CIITA (encoded by CTIIA gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising any one of SEQ ID NO: 6750 to SEQ ID NO: 7716, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 6750 to SEQ ID NO: 7716. In embodiments, the gRNA molecule comprises a targeting domain comprises any one of SEQ ID NO: 7717 to SEQ ID NO: 7804.

In embodiments in which the cells have reduced or eliminated levels or expression levels of GR (encoded by NR3C1 gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 2069 to SEQ ID NO: 2941, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 2069 to SEQ ID NO: 2941.

In embodiments in which the cells have reduced or eliminated levels or expression levels of FKBP12 (encoded by FKBP1A gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 6325 to SEQ ID NO: 6583, or a gRNA molecule

comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 6325 to SEQ ID NO: 6583.

In embodiments in which the cells have reduced or eliminated levels or expression levels of CD52 (encoded by CD52 gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 6227 to SEQ ID NO: 6324, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 6227 to SEQ ID NO: 6324.

In embodiments in which the cells have reduced or eliminated levels or expression levels of DCK (encoded by DCK gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 5278 to SEQ ID NO: 5491, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 5278 to SEQ ID NO: 5491.

In embodiments in which the cells have reduced or eliminated levels or expression levels of PD-L1 (encoded by CD274 gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 2942 to SEQ ID NO: 3270, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 2942 to SEQ ID NO: 3270.

In embodiments in which the cells have reduced or eliminated levels or expression levels of Tim3 (encoded by HAVCR2 gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 3271 to SEQ ID NO: 3541, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 3271 to SEQ ID NO: 3541.

In embodiments in which the cells have reduced or eliminated levels or expression levels of Lag3 (encoded by LAG3 gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 3542 to SEQ ID NO: 4032, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 3542 to SEQ ID NO: 4032.

In embodiments in which the cells have reduced or eliminated levels or expression levels of PD-1 (encoded by PDCD1 gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 4033 to SEQ ID NO: 4589 or SEQ ID NO: 5720 to SEQ ID NO: 5815, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20,

21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 4033 to SEQ ID NO: 4589 or SEQ ID NO: 5720 to SEQ ID NO: 5815. In one embodiment, the gRNA molecule comprises a targeting domain comprising SEQ ID NO: 5775, or comprises a targeting domain comprising or consisting of 17, 18, or 19 consecutive nucleotides of SEQ ID NO: 5775.

In embodiments in which the cells have reduced or eliminated levels or expression levels of Tyrosine-protein phosphatase non-receptor type 1 (encoded by PTPN1 gene), the cells preferably comprise, or at one time comprised, a gRNA molecule comprising a targeting domain comprising SEQ ID NO: 4590 to SEQ ID NO: 5277, or a gRNA molecule comprising a targeting domain consisting of 17, 18, 19, 20, 21, 22, 23, 24 or 25 consecutive nucleotides, preferably 20 consecutive nucleotides, of SEQ ID NO: 4590 to SEQ ID NO: 5277.

In any of the aforementioned aspects and embodiments the cell is an autologous cell. In any of the aforementioned aspects and embodiments, the cell is an allogeneic cell. In any of the aforementioned embodiments and aspects, the cell is or will be engineered to express a chimeric antigen receptor (CAR), e.g., as described herein. In any of the aforementioned aspects and embodiments, the cell is a T cell.

Additional features of the gRNA molecule, the CRISPR systems, Cas9 molecules, cells, CAR molecules, and methods of the invention are described in detail below.

I. gRNA Molecules

A gRNA molecule may have a number of domains, as described more fully below, however, a gRNA molecule typically comprises at least a crRNA domain (comprising a targeting domain) and a tracr. The gRNA molecules of the invention, used as a component of a CRISPR system, are useful for modifying (e.g., modifying the sequence) DNA at or near a target site. Such modifications include deletions and or insertions that result in, for example, reduced or eliminated expression of a functional product of the gene comprising the target site. These uses, and additional uses, are described more fully below.

In an embodiment, a unimolecular, or sgRNA comprises, preferably from 5' to 3' : a crRNA (which contains a targeting domain complementary to a target sequence and a region that forms part of a flagpole (i.e., a crRNA flagpole region)); a loop; and a tracr (which contains a domain complementary to the crRNA flagpole region, and a domain which additionally binds a nuclease or other effector molecule, e.g., a Cas molecule, e.g., aCas9 molecule), and may take the following format (from 5' to 3'):

[targeting domain] – [crRNA flagpole region] – [optional first flagpole extension] – [loop] – [optional first tracr extension] – [tracr flagpole region] – [tracr nuclease binding domain].

In embodiments, the tracr nuclease binding domain binds to a Cas protein, e.g., a Cas9 protein.

In an embodiment, a bimolecular, or dgRNA comprises two polynucleotides; the first, preferably from 5' to 3': a crRNA (which contains a targeting domain complementary to a target sequence and a region tha tforms part of a flagpole; and the second, preferrably from 5' to 3': a tracr (which contains a domain complementary to the crRNA flagpole region, and a domain which additionally binds a nuclease or other effector molecule, e.g., a Cas molecule, e.g., Cas9 molecule), and may take the following format (from 5' to 3'):

Polynucleotide 1 (crRNA): [targeting domain] – [crRNA flagpole region] – [optional first flagpole extension] – [optional second flagpole extension]

Polynucleotide 2 (tracr): [optional first tracr extension] – [tracr flagpole region] - [tracr nuclease binding domain]

In embodiments, the tracr nuclease binding domain binds to a Cas protein, e.g., a Cas9 protein.

In some aspects, the targeting domain comprises or consists of a targeting domain sequence described herein, e.g., a targeting domain described in Table 1, 2, 3, 4, 5, 6, 6b, or 6c, or a targeting domain comprising or consisting of 17, 18, 19, 20, 21, 22, 23, 24, or 25 (preferably 20) consecutive nucleotides of a targeting domain sequence described in Table 1, 2, 3, 4, 5, 6, 6b, or 6c.

In some aspects, the flagpole, e.g., the crRNA flagpole region, comprises, from 5' to 3': GUUUUAGAGCUA (SEQ ID NO: 6584).

In some aspects, the flagpole, e.g., the crRNA flagpole region, comprises, from 5' to 3': GUUUAAGAGCUA (SEQ ID NO: 6585).

In some aspects the loop comprises, from 5' to 3': GAAA (SEQ ID NO: 6588).

In some aspects the tracr comprises, from 5' to 3': UAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUG C (SEQ ID NO: 6589) and is preferably used in a gRNA molecule comprising SEQ ID NO: 6584.

In some aspects the tracr comprises, from 5' to 3': UAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUG C (SEQ ID NO: 6590) and is preferably used in a gRNA molecule comprising SEQ ID NO: 6585.

In some aspects, the gRNA may also comprise, at the 3' end, additional U nucleic acids. For example the gRNA may comprise an additional 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 U nucleic acids at the 3' end (SEQ ID NO: 10806). In an embodiment, the gRNA comprises an additional 4 U nucleic acids at the 3' end. In

the case of dgRNA, one or more of the polynucleotides of the dgRNA (e.g., the polynucleotide comprising the targeting domain and the polynucleotide comprising the tracr) may comprise, at the 3' end, additional U nucleic acids. For example, the case of dgRNA, one or more of the polynucleotides of the dgRNA (e.g., the polynucleotide comprising the targeting domain and the polynucleotide comprising the tracr) may comprise an additional 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 U nucleic acids at the 3' end (SEQ ID NO: 10806). In an embodiment, in the case of dgRNA, one or more of the polynucleotides of the dgRNA (e.g., the polynucleotide comprising the targeting domain and the polynucleotide comprising the tracr) comprises an additional 4 U nucleic acids at the 3' end. In an embodiment of a dgRNA, only the polynucleotide comprising the tracr comprises the additional U nucleic acid(s), e.g., 4 U nucleic acids. In an emebodiment of a dgRNA, only the polynucleotide comprising the targeting domain comprises the additional U nucleic acid(s). In an embodiment of a dgRNA, both the polynucleotide comprising the targeting domain and the polynucleotide comprising the tracr comprise the additional U nucleic acids, e.g., 4 U nucleic acids.

In some aspects, the gRNA may also comprise, at the 3' end, additional A nucleic acids. For example the gRNA may comprise an additional 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 A nucleic acids at the 3' end (SEQ ID NO: 10809). In an embodiment, the gRNA comprises an additional 4 A nucleic acids at the 3' end. In the case of dgRNA, one or more of the polynucleotides of the dgRNA (e.g., the polynucleotide comprising the targeting domain and the polynucleotide comprising the tracr) may comprise, at the 3' end, additional A nucleic acids. For example, the case of dgRNA, one or more of the polynucleotides of the dgRNA (e.g., the polynucleotide comprising the targeting domain and the polynucleotide comprising the tracr) may comprise an additional 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 A nucleic acids at the 3' end (SEQ ID NO: 10809). In an embodiment, in the case of dgRNA, one or more of the polynucleotides of the dgRNA (e.g., the polynucleotide comprising the targeting domain and the polynucleotide comprising the tracr) comprises an additional 4 A nucleic acids at the 3' end. In an embodiment of a dgRNA, only the polynucleotide comprising the tracr comprises the additional A nucleic acid(s), e.g., 4 A nucleic acids. In an emebodiment of a dgRNA, only the polynucleotide comprising the targeting domain comprises the additional A nucleic acid(s). In an embodiment of a dgRNA, both the polynucleotide comprising the targeting domain and the polynucleotide comprising the tracr comprise the additional U nucleic acids, e.g., 4 A nucleic acids.

In embodiments, one or more of the polynucleotides of the gRNA molecule may comprise a cap at the 5' end.

In an embodiment, a unimolecular, or sgRNA comprises, preferably from 5' to 3' : a crRNA (which contains a targeting domain complementary to a target sequence; a crRNA flagpole region; first flagpole

extension; a loop; a first tracr extension (which contains a domain complementary to at least a portion of the first flagpole extension); and a tracr (which contains a domain complementary to the crRNA flagpole region, and a domain which additionally binds a Cas9 molecule). In some aspects, the targeting domain comprises a targeting domain sequence described herein, e.g., a targeting domain described in Table 1, 2, 3, 4, 5, 6, 6b, or 6c, or a targeting domain comprising or consisting of 17, 18, 19, 20, 21, 22, 23, 24, or 25 (preferably 20) consecutive nucleotides of a targeting domain sequence described in Table 1, 2, 3, 4, 5, 6, 6b, or 6c, for example the 3' 17, 18, 19, 20, 21, 22, 23, 24 or 25 (preferably 20) consecutive nucleotides of a targeting domain sequence described in Table 1, 2, 3, 4, 5, 6, 6b, or 6c.

In aspects comprising a first flagpole extension and/or a first tracr extension, the flagpole, loop and tracr sequences may be as described above. In general any first flagpole extension and first tracr extension may be employed, provided that they are complementary. In embodiments, the first flagpole extension and first tracr extension consist of 3, 4, 5, 6, 7, 8, 9, 10 or more complementary nucleotides.

In some aspects, the first flagpole extension comprises, from 5' to 3': UGCUG (SEQ ID NO: 6586). In some aspects, the first flagpole extension consists of SEQ ID NO: 6586.

In some aspects, the first tracr extension comprises, from 5' to 3': CAGCA (SEQ ID NO: 6591). In some aspects, the first tracr extension consists of SEQ ID NO: 6591.

In an embodiment, a dgRNA comprises two nucleic acid molecules. In some aspects, the dgRNA comprises a first nucleic acid which contains, preferably from 5' to 3' : a targeting domain complementary to a target sequence; a crRNA flagpole region; optionally a first flagpole extension; and, optionally, a second flagpole extension; and a second nucleic acid (which may be referred to herein as a tracr), and comprises at least a domain which binds a Cas molecule, e.g., a Cas9 molecule) comprising preferably from 5' to 3': optionally a first tracr extension; and a tracr (which contains a domain complementary to the crRNA flagpole region, and a domain which additionally binds a Cas, e.g., Cas9, molecule). The second nucleic acid may additionally comprise, at the 3' end (e.g., 3' to the tracr) additional U nucleic acids. For example the tracr may comprise an additional 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 U nucleic acids at the 3' end (e.g., 3' to the tracr) (SEQ ID NO: 10806). The second nucleic acid may additionally or alternately comprise, at the 3' end (e.g., 3' to the tracr) additional A nucleic acids. For example the tracr may comprise an additional 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 A nucleic acids at the 3' end (e.g., 3' to the tracr) (SEQ ID NO: 10809). In some aspects, the targeting domain comprises a targeting domain sequence described herein, e.g., a targeting domain described in Table 1, 2, 3, 4, 5, 6, 6b, or 6c, or a targeting domain comprising or consisting of 17, 18, 19, 20, 21, 22, 23, 24, or 25 (preferably 20) consecutive nucleotides of a targeting domain sequence described in Table 1, 2, 3, 4, 5, 6, 6b, or 6c.

In aspects involving a dgRNA, the crRNA flagpole region, optional first flagpole extension, optional first tracr extension and tracr sequences may be as described above.

In some aspects, the optional second flagpole extension comprises, from 5' to 3': UUUUG (SEQ ID NO: 6587).

In embodiments, the 3' 1, 2, 3, 4, or 5 nucleotides, the 5' 1, 2, 3, 4, or 5 nucleotides, or both the 3' and 5' 1, 2, 3, 4, or 5 nucleotides of the gRNA molecule (and in the case of a dgRNA molecule, the polynucleotide comprising the targeting domain and/or the polynucleotide comprising the tracr) are modified nucleic acids, as described more fully in section XIII, below.

The domains are discussed briefly below:

1) The Targeting Domain:

Guidance on the selection of targeting domains can be found, e.g., in Fu Y el al. NAT BIOTECHNOL 2014 (doi: 10.1038/nbt.2808) and Sternberg SH el al. NATURE 2014 (doi: 10.1038/naturel3011).

The targeting domain comprises a nucleotide sequence that is complementary, e.g., at least 80, 85, 90, 95, or 99% complementary, e.g., fully complementary, to the target sequence on the target nucleic acid. The targeting domain is part of an RNA molecule and will therefore comprise the base uracil (U), while any DNA encoding the gRNA molecule will comprise the base thymine (T). While not wishing to be bound by theory, it is believed that the complementarity of the targeting domain with the target sequence contributes to specificity of the interaction of the gRNA molecule/Cas9 molecule complex with a target nucleic acid. It is understood that in a targeting domain and target sequence pair, the uracil bases in the targeting domain will pair with the adenine bases in the target sequence.

In an embodiment, the targeting domain is 5 to 50, e.g., 10 to 40, e.g., 10 to 30, e.g., 15 to 30, e.g., 15 to 25 nucleotides in length. In an embodiment, the targeting domain is 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25 nucleotides in length. In an embodiment, the targeting domain is 16 nucleotides in length. In an embodiment, the targeting domain is 17 nucleotides in length. In an embodiment, the targeting domain is 18 nucleotides in length. In an embodiment, the targeting domain is 19 nucleotides in length. In an embodiment, the targeting domain is 20 nucleotides in length. In an embodiment, the targeting domain is 21 nucleotides in length. In an embodiment, the targeting domain is 22 nucleotides in length. In an embodiment, the targeting domain is 23 nucleotides in length. In an embodiment, the targeting domain is 24 nucleotides in length. In an embodiment, the targeting domain is 25 nucleotides in length. In embodiments, the aforementioned 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleotides comprise the 5'-16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleotides from a targeting domain described in Table 1, 2, 3, 4,

5, 6, 6b, or 6c. In embodiments, the aforementioned 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleotides comprise the 3'- 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleotides from a targeting domain described in Table 1, 2, 3, 4, 5, 6, 6b, or 6c.

Without being bound by theory, it is believed that the 8, 9 or 10 nucleic acids of the targeting domain disposed at the 3' end of the targeting domain is important for targeting the target sequence, and may thus be referred to as the "core" region of the targeting domain. In an embodiment, the core domain is fully complementary with the target sequence.

The strand of the target nucleic acid with which the targeting domain is complementary is referred to herein as the target sequence. In some aspects, the target sequence is disposed on a chromosome, e.g., is a target within a gene. In some aspects the target sequence is disposed within an exon of a gene. In some aspects the target sequence is disposed within an intron of a gene. In some aspects, the target sequence comprises, or is proximal (e.g., within 10, 20, 30, 40, 50, 100, 200, 300, 400, 500, or 1000 nucleic acids) to a binding site of a regulatory element, e.g., a promoter or transcription factor binding site, of a gene of interest. Some or all of the nucleotides of the domain can have a modification, e.g., modification found in Section XIII herein.

2) crRNA Flagpole Region:

The flagpole contains portions from both the crRNA and the tracr. The crRNA flagpole region is complementary with a portion of the tracr, and in an embodiment, has sufficient complementarity to a portion of the tracr to form a duplexed region under at least some physiological conditions, for example, normal physiological conditions. In an embodiment, the crRNA flagpole region is 5 to 30 nucleotides in length. In an embodiment, the crRNA flagpole region is 5 to 25 nucleotides in length. The crRNA flagpole region can share homology with, or be derived from, a naturally occurring portion of the repeat sequence from a bacterial CRISPR array. In an embodiment, it has at least 50% homology with a crRNA flagpole region disclosed herein, e.g., an S. pyogenes, or S. thermophilus, crRNA flagpole region.

In an embodiment, the flagpole, e.g., the crRNA flagpole region, comprises SEQ ID NO: 6584. In an embodiment, the flagpole, e.g., the crRNA flagpole region, comprises sequence having at least 50%, 60%, 70%, 80%, 85%, 90%, 95% or 99% homology with SEQ ID NO: 6584. In an embodiment, the flagpole, e.g., the crRNA flagpole region, comprises at least 5, 6, 7, 8, 9, 10, or 11 nucleotides of SEQ ID NO: 6584. In an embodiment, the flagpole, e.g., the crRNA flagpole region, comprises SEQ ID NO: 6585. In an embodiment, the flagpole comprises sequence having at least 50%, 60%, 70%, 80%, 85%, 90%, 95% or 99% homology with SEQ ID NO: 6585. In an embodiment, the flagpole, e.g., the crRNA flagpole region, comprises at least 5, 6, 7, 8, 9, 10, or 11 nucleotides of SEQ ID NO: 6585.

Some or all of the nucleotides of the domain can have a modification, e.g., modification described in Section XIII herein.

3) First Flagpole Extension

When a tracr comprising a first tracr extension is used, the crRNA may comprise a first flagpole extension. In general any first flagpole extension and first tracr extension may be employed, provided that they are complementary. In embodiments, the first flagpole extension and first tracr extension consist of 3, 4, 5, 6, 7, 8, 9, 10 or more complementary nucleotides.

The first flagpole extension may comprise nucleotides that are complementary, e.g., 80%, 85%, 90%, 95% or 99%, e.g., fully complementary, with nucleotides of the first tracr extension. In some aspects, the first flagpole extension nucleotides that hybridize with complementary nucleotides of the first tracr extension are contiguous. In some aspects, the first flagpole extension nucleotides that hybridize with complementary nucleotides of the first tracr extension are discontinuous, e.g., comprises two or more regions of hybridization separated by nucleotides that do not base pair with nucleotides of the first tracr extension. In some aspects, the first flagpole extension comprises at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more nucleotides. In some aspects, the first flagpole extension comprises, from 5' to 3': UGCUG (SEQ ID NO: 6586). In some aspects, the first flagpole extension consists of SEQ ID NO: 6586. In some aspects the first flagpole extension comprises nucleic acid that is at least 80%, 85%, 90%, 95% or 99% homology to SEQ ID NO: 6586.

Some or all of the nucleotides of the first tracr extension can have a modification, e.g., modification found in Section XIII herein.

3) The Loop

A loop serves to link the crRNA flagpole region (or optionally the first flagpole extension, when present) with the tracr (or optionally the first tracr extension, when present) of a sgRNA. The loop can link the crRNA flagpole region and tracr covalently or non-covalently. In an embodiment, the linkage is covalent. In an embodiment, the loop covalently couples the crRNA flagpole region and tracr. In an embodiment, the loop covalently couples the first flagpole extension and the first tracr extension. In an embodiment, the loop is, or comprises, a covalent bond interposed between the crRNA flagpole region and the domain of the tracr which hybridizes to the crRNA flagpole region. Typically, the loop comprises one or more, e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides.

In dgRNA molecules the two molecules can be associated by virtue of the hybridization between at least a portion of the crRNA (e.g., the crRNA flagpole region) and at least a portion of the tracr (e.g., the domain of the tracr which is complementary to the crRNA flagpole region).

A wide variety of loops are suitable for use in sgRNAs. Loops can consist of a covalent bond, or be as short as one or a few nucleotides, e.g., 1 , 2, 3, 4, or 5 nucleotides in length. In an embodiment, a loop is 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, or 25 or more nucleotides in length. In an embodiment, a loop is 2 to 50, 2 to 40, 2 to 30, 2 to 20, 2 to 10, or 2 to 5 nucleotides in length. In an embodiment, a loop shares homology with, or is derived from, a naturally occurring sequence. In an embodiment, the loop has at least 50% homology with a loop disclosed herein. In an embodiment, the loop comprises SEQ ID NO: 6588.

Some or all of the nucleotides of the domain can have a modification, e.g., modification described in Section XIII herein.

4) The Second Flagpole Extension

In an embodiment, a dgRNA can comprise additional sequence, 3' to the crRNA flagpole region or, when present, the first flagpole extension, referred to herein as the second flagpole extension. In an embodiment, the second flagpole extension is, 2-10, 2-9, 2-8, 2-7, 2-6, 2-5, or 2-4 nucleotides in length. In an embodiment, the second flagpole extension is 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more nucleotides in length. In an embodiment, the second flagpole extension comprises SEQ ID NO: 6587.

5) The Tracr:

The tracr is the nucleic acid sequence required for nuclease, e.g., Cas9, binding. Without being bound by theory, it is believed that each Cas9 species is associated with a particular tracr sequence. Tracr sequences are utilized in both sgRNA and in dgRNA systems. In an embodiment, the tracr comprises sequence from, or derived from, an *S. pyogenes* tracr. In some aspects, the tracr has a portion that hybridizes to the flagpole portion of the crRNA, e.g., has sufficient complementarity to the crRNA flagpole region to form a duplexed region under at least some physiological conditions (sometimes referred to herein as the tracr flagpole region or a tracr domain complementary to the crRNA flagpole region). In embodiments, the domain of the tracr that hybridizes with the crRNA flagpole region comprises at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides that hybridize with complementary nucleotides of the crRNA flagpole region. In some aspects, the tracr nucleotides that hybridize with complementary nucleotides of the crRNA flagpole region are contiguous. In some aspects, the tracr nucleotides that hybridize with complementary nucleotides of the crRNA flagpole region are discontinuous, e.g., comprises two or more regions of hybridization separated by nucleotides that do not base pair with nucleotides of the crRNA flagpole region. In some aspects, the portion of the tracr that

hybridizes to the crRNA flagpole region comprises, from 5' to 3': UAGCAAGUUAAAA (SEQ ID NO: 6597. In some aspects, the portion of the tracr that hybridizes to the crRNA flagpole regioncomprises, from 5' to 3': UAGCAAGUUUAAA (SEQ ID NO: 6598). In embodiments, the sequence that hybridizes with the crRNA flagpole region is disposed on the tracr 5'- to the sequence of the tracr that additionally binds a nuclease, e.g., a Cas molecule, e.g., a Cas9 molecule.

The tracr further comprises a domain that additionally binds to a nuclease, e.g., a Cas molecule, e.g., a Cas9 molecule. Without being bound by theory, it is believed that Cas9 from different species bind to different tracr sequences. In some aspects, the tracr comprises sequence that binds to a *S. pyogenes* Cas9 molecule. In some aspects, the tracr comprises sequence that binds to a Cas9 molecule disclosed herein. In some aspects, the domain that additionally binds a Cas9 molecule comprises, from 5' to 3': UAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGC (SEQ ID NO: 6599). In some aspects the domain that additionally binds a Cas9 molecule comprises, from 5' to 3': UAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 6600).

In some embodiments, the tracr comprises SEQ ID NO: 6589. In some embodiments, the tracr comprises SEQ ID NO: 6590.

Some or all of the nucleotides of the tracr can have a modification, e.g., modification found in Section XIII herein. In embodiments, the gRNA (e.g., the sgRNA or the tracr and/or crRNA of a dgRNA), e.g., any of the gRNA or gRNA components described above, comprises an inverted abasic residue at the 5' end, the 3' end or both the 5' and 3' end of the gRNA. In embodiments, the gRNA (e.g., the sgRNA or the tracr and/or crRNA of a dgRNA), e.g., any of the gRNA or gRNA components described above, comprises one or more phosphorothioate bonds between residues at the 5' end of the polynucleotide, for example, a phosphrothioate bond between the first two 5' residues, between each of the first three 5' residues, between each of the first four 5' residues, or between each of the first five 5' residues. In embodiments, the gRNA or gRNA component may alternatviely or additionally comprise one or more phosphorothioate bonds between residues at the 3' end of the polynucleotide, for example, a phosphrothioate bond between the first two 3' residues, between each of the first three 3' residues, between each of the first four 3' residues, or between each of the first five 3' residues. In an embodiment, the gRNA (e.g., the sgRNA or the tracr and/or crRNA of a dgRNA), e.g., any of the gRNA or gRNA components described above, comprises a phosphorothioate bond between each of the first four 5' residues (e.g., comprises, e.g., consists of, three phosphorothioate bonds at the 5' end(s)), and a phosphorothioate bond between each of the first four 3' residues (e.g., comprises, e.g., consists of, three phosphorothioate bonds at the 3' end(s)). In an embodiment, any of the phosphorothioate modificaitons

described above are combined with an inverted abasic residue at the 5' end, the 3' end, or both the 5' and 3' ends of the polynucleotide. In such embodiments, the inverted abasic nucleotide may be linked to the 5' and/or 3' nucelotide by a phosphate bond or a phosphorothioate bond. In embodiments, the gRNA (e.g., the sgRNA or the tracr and/or crRNA of a dgRNA), e.g., any of the gRNA or gRNA components described above, comprises one or more nucleotides that include a 2' O-methyl modification. In embodiments, each of the first 1, 2, 3, or more of the 5' residues comprise a 2' O-methyl modification. In embodiments, each of the first 1, 2, 3, or more of the 3' residues comprise a 2' O-methyl modification. In embodiments, the 4th-to-terminal, 3rd-to-terminal, and 2nd-to-terminal 3' residues comprise a 2' O-methyl modification. In embodiments, each of the first 1, 2, 3 or more of the 5' residues comprise a 2' O-methyl modification, and each of the first 1, 2, 3 or more of the 3' residues comprise a 2' O-methyl modification. In an embodiment, each of the first 3 of the 5' residues comprise a 2' O-methyl modification, and each of the first 3 of the 3' residues comprise a 2' O-methyl modification. In embodiments, each of the first 3 of the 5' residues comprise a 2' O-methyl modification, and the 4th-to-terminal, 3rd-to-terminal, and 2nd-to-terminal 3' residues comprise a 2' O-methyl modification. In embodiments, any of the 2' O-methyl modfications, e.g., as described above, may be combined with one or more phosphorothioate modifications, e.g., as described above, and/or one or more inverted abasic modifications, e.g., as described above.In an embodiment, the gRNA (e.g., the sgRNA or the tracr and/or crRNA of a dgRNA), e.g., any of the gRNA or gRNA components described above, comprises, e.g., consists of, a phosphorothioate bond between each of the first four 5' residues (e.g., comprises, e.g., consists of three phosphorothioate bonds at the 5' end of the polynucleotide(s)), a phosphorothioate bond between each of the first four 3' residues (e.g., comprises, e.g., consists of three phosphorothioate bonds at the 5' end of the polynucleotide(s)), a 2' O-methyl modification at each of the first three 5' residues, and a 2' O-methyl modification at each of the first three 3' residues. In an embodiment, the gRNA (e.g., the sgRNA or the tracr and/or crRNA of a dgRNA), e.g., any of the gRNA or gRNA components described above, comprises, e.g., consists of, a phosphorothioate bond between each of the first four 5' residues (e.g., comprises, e.g., consists of three phosphorothioate bonds at the 5' end of the polynucleotide(s)), a phosphorothioate bond between each of the first four 3' residues (e.g., comprises, e.g., consists of three phosphorothioate bonds at the 5' end of the polynucleotide(s)), a 2' O-methyl modification at each of the first three 5' residues, and a 2' O-methyl modification at each of the 4th-to-terminal, 3rd-to-terminal, and 2nd-to-terminal 3' residues.

In an embodiment, the gRNA (e.g., the sgRNA or the tracr and/or crRNA of a dgRNA), e.g., any of the gRNA or gRNA components described above, comprises, e.g., consists of, a phosphorothioate bond between each of the first four 5' residues (e.g., comprises, e.g., consists of three phosphorothioate bonds at the 5' end of the polynucleotide(s)), a phosphorothioate bond between each of the first four 3' residues

(e.g., comprises, e.g., consists of three phosphorothioate bonds at the 5' end of the polynucleotide(s)), a 2' O-methyl modification at each of the first three 5' residues, a 2' O-methyl modification at each of the first three 3' residues , and an additional inverted abasic residue at each of the 5' and 3' ends.

In an embodiment, the gRNA (e.g., the sgRNA or the tracr and/or crRNA of a dgRNA), e.g., any of the gRNA or gRNA components described above, comprises, e.g., consists of, a phosphorothioate bond between each of the first four 5' residues (e.g., comprises, e.g., consists of three phosphorothioate bonds at the 5' end of the polynucleotide(s)), a phosphorothioate bond between each of the first four 3' residues (e.g., comprises, e.g., consists of three phosphorothioate bonds at the 5' end of the polynucleotide(s)), a 2' O-methyl modification at each of the first three 5' residues, and a 2' O-methyl modification at each of the 4^{th}-to-terminal, 3^{rd}-to-terminal, and 2^{nd}-to-terminal 3' residues, and an additional inverted abasic residue at each of the 5' and 3' ends

In embodiments, the gRNA is a dgRNA and comprises, e.g., consists of:

crRNA:

mN*mN*mN*NNNNNNNNNNNNNNNNNNGUUUUAGAGCUAU*mG*mC*mU (SEQ ID NO: 10797), where m indicates a base with 2'O-Methyl modification, * indicates a phosphorothioate bond, and N's indicate the residues of the targeting domain, e.g., as described herein, (optionally with an inverted abasic residue at the 5' and/or 3' terminus); and

tracr:

AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUUUUU (SEQ ID NO: 6660) (optionally with an inverted abasic residue at the 5' and/or 3' terminus).

In embodiments, the gRNA is a dgRNA and comprises, e.g., consists of:

crRNA:

mN*mN*mN*NNNNNNNNNNNNNNNNNNGUUUUAGAGCUAU*mG*mC*mU (SEQ ID NO: 10797), where m indicates a base with 2'O-Methyl modification, * indicates a phosphorothioate bond, and N's indicate the residues of the targeting domain, e.g., as described herein, (optionally with an inverted abasic residue at the 5' and/or 3' terminus); and

tracr:

mA*mA*mC*AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU*mU*mU*mU (SEQ ID NO: 10798), where m indicates a base with 2'O-

Methyl modification, * indicates a phosphorothioate bond, and N's indicate the residues of the targeting domain (optionally with an inverted abasic residue at the 5' and/or 3' terminus).

In embodiments, the gRNA is a dgRNA and comprises, e.g., consists of:

crRNA:

mN*mN*mN*NNNNNNNNNNNNNNNNNGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO:), where m indicates a base with 2'O-Methyl modification, * indicates a phosphorothioate bond, and N's indicate the residues of the targeting domain, e.g., as described herein, (optionally with an inverted abasic residue at the 5' and/or 3' terminus); and

tracr:

AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUUUUU (SEQ ID NO: 6660) (optionally with an inverted abasic residue at the 5' and/or 3' terminus).

In embodiments, the gRNA is a dgRNA and comprises, e.g., consists of:

crRNA:

mN*mN*mN*NNNNNNNNNNNNNNNNNGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO:), where m indicates a base with 2'O-Methyl modification, * indicates a phosphorothioate bond, and N's indicate the residues of the targeting domain, e.g., as described herein, (optionally with an inverted abasic residue at the 5' and/or 3' terminus); and

tracr:

mA*mA*mC*AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU*mU*mU*mU (SEQ ID NO: 10798), where m indicates a base with 2'O-Methyl modification, and * indicates a phosphorothioate bond (optionally with an inverted abasic residue at the 5' and/or 3' terminus).

In embodiments, the gRNA is a sgRNA and comprises, e.g., consists of:

mN*mN*mN*NNNNNNNNNNNNNNNNNGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCU*mU*mU*mU (SEQ ID NO: 10799), where m indicates a base with 2'O-Methyl modification, * indicates a phosphorothioate bond, and N's indicate the residues of the targeting domain, e.g., as described herein, (optionally with an inverted abasic residue at the 5' and/or 3' terminus).

In embodiments, the gRNA is a sgRNA and comprises, e.g., consists of:

mN*mN*mN*NNNNNNNNNNNNNNNNNGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAG GCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U , where m indicates a base with 2'O-Methyl modification, * indicates a phosphorothioate bond, and N's indicate the residues of the targeting domain, e.g., as described herein, (optionally with an inverted abasic residue at the 5' and/or 3' terminus).

6) First Tracr Extension

Where the gRNA comprises a first flagpole extension, the tracr may comprise a first tracr extension. The first tracr extension may comprise nucleotides that are complementary, e.g., 80%, 85%, 90%, 95% or 99%, e.g., fully complementary, with nucleotides of the first flagpole extension. In some aspects, the first tracr extension nucleotides that hybridize with complementary nucleotides of the first flagpole extension are contiguous. In some aspects, the first tracr extension nucleotides that hybridize with complementary nucleotides of the first flagpole extension are discontinuous, e.g., comprises two or more regions of hybridization separated by nucleotides that do not base pair with nucleotides of the first flagpole extension. In some aspects, the first tracr extension comprises at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more nucleotides. In some aspects, the first tracr extension comprises SEQ ID NO: 6591. In some aspects the first tracr extension comprises nucleic acid that is at least 80%, 85%, 90%, 95% or 99% homology to SEQ ID NO: 6591.

Some or all of the nucleotides of the first tracr extension can have a modification, e.g., modification found in Section XIII herein.

In some embodiments, the sgRNA may comprise, from 5' to 3', disposed 3' to the targeting domain:

a)
GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAG UGGCACCGAGUCGGUGC (SEQ ID NO: 6601);

b)

GUUUAAGAGCUAGAAAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAG UGGCACCGAGUCGGUGC (SEQ ID NO: 6602);

c)

GUUUUAGAGCUAUGCUGGAAACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAA CUUGAAAAAGUGGCACCGAGUCGGUGC (SEQ ID NO: 6603);

d)

GUUUAAGAGCUAUGCUGGAAACAGCAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAA CUUGAAAAAGUGGCACCGAGUCGGUGC (SEQ ID NO: 6604);

e) any of a) to d), above, further comprising, at the 3' end, at least 1, 2, 3, 4, 5, 6 or 7 uracil (U) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 uracil (U) nucleotides;

f) any of a) to d), above, further comprising, at the 3' end, at least 1, 2, 3, 4, 5, 6 or 7 adenine (A) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 adenine (A) nucleotides; or

g) any of a) to f), above, further comprising, at the 5' end (e.g., at the 5' terminus, e.g., 5' to the targeting domain), at least 1, 2, 3, 4, 5, 6 or 7 adenine (A) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 adenine (A) nucleotides.

In an embodiment, a sgRNA of the invention comprises, e.g., consists of, from 5' to 3': [targeting domain]-GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAG UGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7811).

In an embodiment, a sgRNA of the invention comprises, e.g., consists of, from 5' to 3': [targeting domain]-GUUUAAGAGCUAUGCUGGAAACAGCAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAA CUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7807).

In embodiments, any of a) to g) above is disposed directly 3' to the targeting domain.

In some embodiments, the dgRNA may comprise:

A crRNA comprising, from 5' to 3', preferrably disposed directly 3' to the targeting domain:

a) GUUUUAGAGCUA (SEQ ID NO: 6584);

b) GUUUAAGAGCUA (SEQ ID NO: 6585);

c) GUUUUAGAGCUAUGCUG (SEQ ID NO: 6605);

d) GUUUAAGAGCUAUGCUG (SEQ ID NO: 6606);

e) GUUUUAGAGCUAUGCUGUUUUG (SEQ ID NO: 6607);

f) GUUUAAGAGCUAUGCUGUUUUG (SEQ ID NO: 6608); or

g) GUUUUAGAGCUAUGCU (SEQ ID NO: 7806):

and a tracr comprising, from 5' to 3':

a)
UAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUG
C (SEQ ID NO: 6589);

b)
UAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUG
C (SEQ ID NO: 6590);

c)
CAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGU
CGGUGC (SEQ ID NO: 6609);

d)
CAGCAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGU
CGGUGC (SEQ ID NO: 6610);

e)
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA
GUCGGUGCUUUUUUU (SEQ ID NO: 6660);

f)
AACAGCAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA
GUCGGUGCUUUUUUU (SEQ ID NO: 6661);

g)
GUUUAAGAGCUAUGCUGGAAACAGCAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAA
CUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7807);

h)
AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUC
GGUGCUUU (SEQ ID NO: 7808);

i)
GUUGGAACCAUUCAAAACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUG
AAAAAGUGGCACCGAGUCGGUGCUUU (SEQ ID NO: 7809);

j)
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA
GUCGGUGC (SEQ ID NO: 7820);

k) any of a) to j), above, further comprising, at the 3' end, at least 1, 2, 3, 4, 5, 6 or 7 uracil (U) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 uracil (U) nucleotides;

l) any of a) to j), above, further comprising, at the 3' end, at least 1, 2, 3, 4, 5, 6 or 7 adenine (A) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 adenine (A) nucleotides; or

m) any of a) to l), above, further comprising, at the 5' end (e.g., at the 5' terminus), at least 1, 2, 3, 4, 5, 6 or 7 adenine (A) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 adenine (A) nucleotides.

In an embodiment, the sequence of k), above comprises the 3' sequence UUUUUU, e.g., if a U6 promoter is used for transcription. In an embodiment, the sequence of k), above, comprises the 3' sequence UUUU, e.g., if an HI promoter is used for transcription. In an embodiment, sequence of k), above, comprises variable numbers of 3' U's depending, e.g., on the termination signal of the pol-III promoter used. In an embodiment, the sequence of k), above, comprises variable 3' sequence derived from the DNA template if a T7 promoter is used. In an embodiment, the sequence of k), above, comprises variable 3' sequence derived from the DNA template, e.g., if in vitro transcription is used to generate the RNA molecule. In an embodiment, the sequence of k), above, comprises variable 3' sequence derived from the DNA template, e.g, if a pol-II promoter is used to drive transcription.

In an embodiment, the crRNA comprises SEQ ID NO: 6607 and the tracr comprises, e.g., consists of AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA GUCGGUGCUUUUUUU (SEQ ID NO: 6660).

In an embodiment, the crRNA comprises SEQ ID NO: 6608 and the tracr comprises, e.g., consists of, AACAGCAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA GUCGGUGCUUUUUUU (SEQ ID NO: 6661).

In an embodiment, the crRNA comprises, e.g., consists of, a targeting domain and, disposed 3' to the targeting domain (e.g., disposed directly 3' to the targeting domain), a sequence comprising, e.g., consisting of, GUUUUAGAGCUAUGCU (SEQ ID NO: 7806), and the tracr comprises, e.g., consists of, GUUUAAGAGCUAUGCUGGAAACAGCAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAA CUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7807).

In an embodiment, the crRNA comprises, e.g., consists of, a targeting domain and, disposed 3' to the targeting domain (e.g., disposed directly 3' to the targeting domain), a sequence comprising, e.g.,

consisting of, GUUUUAGAGCUAUGCU (SEQ ID NO: 7806), and the tracr comprises, e.g., consists of, AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUU (SEQ ID NO: 7808).

In an embodiment, the crRNA comprises, e.g., consists of, a targeting domain and, disposed 3' to the targeting domain (e.g., disposed directly 3' to the targeting domain), a sequence comprising, e.g., consisting of, GUUUUAGAGCUAUGCUGUUUUG (SEQ ID NO: 6607), and the tracr comprises, e.g., consists of, GUUGGAACCAUUCAAAACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUU (SEQ ID NO: 7809).

7) Targeting Domains Useful for Altering Expression of Allogeneic T Cell Targets, Inhibitory Molecules and/or Downstream Effectors of An Inhibitory Molecule

Provided in the tables below are targeting domains for gRNA molecules for use in the compositions and methods of the present invention, for example, in altering expression of or altering a Allogeneic T Cell Target gene, Inhibitory Molecule gene and/or a Downstream Effectors of An Inhibitory Molecule gene.

Table 1: gRNA Targeting Domains for Exemplary Allogeneic T Cell Targets

Id.	Target	Target Region (e.g., Exon)	Strand	Genomic Location (hg38)	Guide RNA Targeting Domain Sequence	SEQ ID NO:
567_1_1	B2M	Exon 1	+	chr15:44711469-44711494	UGGCUGGGCACGCGUUUAAUAUAAG	1
567_1_2	B2M	Exon 1	+	chr15:44711472-44711497	CUGGGCACGCGUUUAAUAUAAGUGG	2
567_1_3	B2M	Exon 1	+	chr15:44711483-44711508	UUUAAUAUAAGUGGAGGCGUCGCGC	3
567_1_4	B2M	Exon 1	+	chr15:44711486-44711511	AAUAUAAGUGGAGGCGUCGCGCUGG	4
567_1_5	B2M	Exon 1	+	chr15:44711487-44711512	AUAUAAGUGGAGGCGUCGCGCUGGC	5
567_1_6	B2M	Exon 1	+	chr15:44711512-44711537	GGGCAUUCCUGAAGCUGACAGCAUU	6
567_1_7	B2M	Exon 1	+	chr15:44711513-44711538	GGCAUUCCUGAAGCUGACAGCAUUC	7
567_1_8	B2M	Exon 1	+	chr15:44711534-44711559	AUUCGGGCCGAGAUGUCUCGCUCCG	8
567_1_9	B2M	Exon 1	+	chr15:44711568-44711593	CUGUGCUCGCGCUACUCUCUCUUUC	9
567_1_10	B2M	Exon 1	+	chr15:44711573-44711598	CUCGCGCUACUCUCUCUUUCUGGCC	10
567_1_11	B2M	Exon 1	+	chr15:44711576-	GCGCUACUCUCUCU	11

				44711601	UUCUGGCCUGG	
567_1_12	B2M	Exon 1	-	chr15:44711466-44711491	AUAUUAAACGCGUGCCCAGCCAAUC	12
567_1_13	B2M	Exon 1	-	chr15:44711522-44711547	UCUCGGCCCGAAUGCUGUCAGCUUC	13
567_1_14	B2M	Exon 1	-	chr15:44711544-44711569	GCUAAGGCCACGGAGCGAGACAUCU	14
567_1_15	B2M	Exon 1	-	chr15:44711559-44711584	AGUAGCGCGAGCACAGCUAAGGCCA	15
567_1_16	B2M	Exon 1	-	chr15:44711565-44711590	AGAGAGAGUAGCGCGAGCACAGCUA	16
567_1_17	B2M	Exon 1	-	chr15:44711599-44711624	GAGAGACUCACGCUGGAUAGCCUCC	17
567_1_18	B2M	Exon 1	-	chr15:44711611-44711636	GCGGGAGGGUAGGAGAGACUCACGC	18
567_2_1	B2M	Exon 2	+	chr15:44715412-44715437	UAUUCCUCAGGUACUCCAAAGAUUC	19
567_2_2	B2M	Exon 2	+	chr15:44715440-44715465	UUUACUCACGUCAUCCAGCAGAGAA	20
567_2_3	B2M	Exon 2	+	chr15:44715473-44715498	CAAAUUUCCUGAAUUGCUAUGUGUC	21
567_2_4	B2M	Exon 2	+	chr15:44715474-44715499	AAAUUUCCUGAAUUGCUAUGUGUCU	22
567_2_5	B2M	Exon 2	+	chr15:44715515-44715540	ACAUUGAAGUUGACUUACUGAAGAA	23
567_2_6	B2M	Exon 2	+	chr15:44715535-44715560	AAGAAUGGAGAGAGAAUUGAAAAAG	24
567_2_7	B2M	Exon 2	+	chr15:44715562-44715587	GAGCAUUCAGACUUGUCUUUCAGCA	25
567_2_8	B2M	Exon 2	+	chr15:44715567-44715592	UUCAGACUUGUCUUUCAGCAAGGAC	26
567_2_9	B2M	Exon 2	+	chr15:44715672-44715697	UUUGUCACAGCCCAAGAUAGUUAAG	27
567_2_10	B2M	Exon 2	+	chr15:44715673-44715698	UUGUCACAGCCCAAGAUAGUUAAGU	28
567_2_11	B2M	Exon 2	+	chr15:44715674-44715699	UGUCACAGCCCAAGAUAGUUAAGUG	29
567_2_12	B2M	Exon 2	-	chr15:44715410-44715435	AUCUUUGGAGUACCUGAGGAAUAUC	30
567_2_13	B2M	Exon 2	-	chr15:44715411-44715436	AAUCUUUGGAGUACCUGAGGAAUAU	31
567_2_14	B2M	Exon 2	-	chr15:44715419-44715444	UAAACCUGAAUCUUUGGAGUACCUG	32
567_2_15	B2M	Exon 2	-	chr15:44715430-44715455	GAUGACGUGAGUAAACCUGAAUCUU	33
567_2_16	B2M	Exon 2	-	chr15:44715457-44715482	GGAAAUUUGACUUUCCAUUCUCUGC	34
567_2_17	B2M	Exon 2	-	chr15:44715483-44715508	AUGAAACCCAGACACAUAGCAAUUC	35

567_2_18	B2M	Exon 2	-	chr15:44715511-44715536	UCAGUAAGUCAACUUCAAUGUCGGA	36
567_2_19	B2M	Exon 2	-	chr15:44715515-44715540	UUCUUCAGUAAGUCAACUUCAAUGU	37
567_2_20	B2M	Exon 2	-	chr15:44715629-44715654	CAGGCAUACUCAUCUUUUUCAGUGG	38
567_2_21	B2M	Exon 2	-	chr15:44715630-44715655	GCAGGCAUACUCAUCUUUUUCAGUG	39
567_2_22	B2M	Exon 2	-	chr15:44715631-44715656	GGCAGGCAUACUCAUCUUUUUCAGU	40
567_2_23	B2M	Exon 2	-	chr15:44715632-44715657	CGGCAGGCAUACUCAUCUUUUUCAG	41
567_2_24	B2M	Exon 2	-	chr15:44715653-44715678	GACAAAGUCACAUGGUUCACACGGC	42
567_2_25	B2M	Exon 2	-	chr15:44715657-44715682	CUGUGACAAAGUCACAUGGUUCACA	43
567_2_26	B2M	Exon 2	-	chr15:44715666-44715691	UAUCUUGGGCUGUGACAAAGUCACA	44
567_2_27	B2M	Exon 2	-	chr15:44715685-44715710	AAGACUUACCCCACUUAACUAUCUU	45
567_2_28	B2M	Exon 2	-	chr15:44715686-44715711	UAAGACUUACCCCACUUAACUAUCU	46
567_3_1	B2M	Exon 3	+	chr15:44716326-44716351	AGAUCGAGACAUGUAAGCAGCAUCA	47
567_3_2	B2M	Exon 3	+	chr15:44716329-44716354	UCGAGACAUGUAAGCAGCAUCAUGG	48
567_3_3	B2M	Exon 3	-	chr15:44716313-44716338	AUGUCUCGAUCUAUGAAAAAGACAG	49
567_4_1	B2M	Exon 4	+	chr15:44717599-44717624	UUUUCAGGUUUGAAGAUGCCGCAUU	50
567_4_2	B2M	Exon 4	+	chr15:44717604-44717629	AGGUUUGAAGAUGCCGCAUUUGGAU	51
567_4_3	B2M	Exon 4	+	chr15:44717681-44717706	CACUUACACUUUAUGCACAAAAUGU	52
567_4_4	B2M	Exon 4	+	chr15:44717682-44717707	ACUUACACUUUAUGCACAAAAUGUA	53
567_4_5	B2M	Exon 4	+	chr15:44717702-44717727	AUGUAGGGUUAUAAUAAUGUUAACA	54
567_4_6	B2M	Exon 4	+	chr15:44717764-44717789	GUCUCCAUGUUUGAUGUAUCUGAGC	55
567_4_7	B2M	Exon 4	+	chr15:44717776-44717801	GAUGUAUCUGAGCAGGUUGCUCCAC	56
567_4_8	B2M	Exon 4	+	chr15:44717786-44717811	AGCAGGUUGCUCCACAGGUAGCUCU	57
567_4_9	B2M	Exon 4	+	chr15:44717789-44717814	AGGUUGCUCCACAGGUAGCUCUAGG	58
567_4_10	B2M	Exon 4	+	chr15:44717790-44717815	GGUUGCUCCACAGGUAGCUCUAGGA	59
567_4_11	B2M	Exon 4	+	chr15:44717794-44717819	GCUCCACAGGUAGCUCUAGGAGGGC	60

567_4_12	B2M	Exon 4	+	chr15:44717805-44717830	AGCUCUAGGAGGGCUGGCAACUUAG	61
567_4_13	B2M	Exon 4	+	chr15:44717808-44717833	UCUAGGAGGGCUGGCAACUUAGAGG	62
567_4_14	B2M	Exon 4	+	chr15:44717809-44717834	CUAGGAGGGCUGGCAACUUAGAGGU	63
567_4_15	B2M	Exon 4	+	chr15:44717810-44717835	UAGGAGGGCUGGCAACUUAGAGGUG	64
567_4_16	B2M	Exon 4	+	chr15:44717846-44717871	AUUCUCUUAUCCAACAUCAACAUCU	65
567_4_17	B2M	Exon 4	+	chr15:44717945-44717970	CAAUUUACAUACUCUGCUUAGAAUU	66
567_4_18	B2M	Exon 4	+	chr15:44717946-44717971	AAUUUACAUACUCUGCUUAGAAUUU	67
567_4_19	B2M	Exon 4	+	chr15:44717947-44717972	AUUUACAUACUCUGCUUAGAAUUUG	68
567_4_20	B2M	Exon 4	+	chr15:44717948-44717973	UUUACAUACUCUGCUUAGAAUUUGG	69
567_4_21	B2M	Exon 4	+	chr15:44717973-44717998	GGGAAAAUUUAGAAAUAUAAUUGAC	70
567_4_22	B2M	Exon 4	+	chr15:44717981-44718006	UUAGAAAUAUAAUUGACAGGAUUAU	71
567_4_23	B2M	Exon 4	+	chr15:44718056-44718081	UACUUCUUAUACAUUUGAUAAAGUA	72
567_4_24	B2M	Exon 4	+	chr15:44718061-44718086	CUUAUACAUUUGAUAAAGUAAGGCA	73
567_4_25	B2M	Exon 4	+	chr15:44718067-44718092	CAUUUGAUAAAGUAAGGCAUGGUUG	74
567_4_26	B2M	Exon 4	+	chr15:44718076-44718101	AAGUAAGGCAUGGUUGUGGGUUAAUC	75
567_4_27	B2M	Exon 4	-	chr15:44717589-44717614	CUUCAAACCUGAAAAGAAAAGAAAA	76
567_4_28	B2M	Exon 4	-	chr15:44717620-44717645	AUUUGGAAUUCAUCCAAUCCAAAUG	77
567_4_29	B2M	Exon 4	-	chr15:44717642-44717667	UAUUAAAAAGCAAGCAAGCAGAAUU	78
567_4_30	B2M	Exon 4	-	chr15:44717771-44717796	GCAACCUGCUCAGAUACAUCAAACA	79
567_4_31	B2M	Exon 4	-	chr15:44717800-44717825	UUGCCAGCCCUCCUAGAGCUACCUG	80
567_4_32	B2M	Exon 4	-	chr15:44717859-44717884	UCAAAUCUGACCAAGAUGUUGAUGU	81
567_4_33	B2M	Exon 4	-	chr15:44717947-44717972	CAAAUUCUAAGCAGAGUAUGUAAAU	82
567_4_34	B2M	Exon 4	-	chr15:44718119-44718144	CAAGUUUUAUGAUUUAUUUAACUUG	83
919_8_1	CD247	Exon 8	+	chr1:167430647-167430672	CACUGAAGCAUUUAUUAUGCAAAAU	84
919_8_2	CD247	Exon 8	+	chr1:167430651-167430676	GAAGCAUUUAUUAUGCAAAAUAGGA	85

919_8_3	CD247	Exon 8	+	chr1:167430719-167430744	CAGAGUAGAGAGCGUUUUCCAUCCA	86
919_8_4	CD247	Exon 8	+	chr1:167430763-167430788	ACGCAGCAGUAUCCUAGUACAUUGA	87
919_8_5	CD247	Exon 8	+	chr1:167430764-167430789	CGCAGCAGUAUCCUAGUACAUUGAC	88
919_8_6	CD247	Exon 8	+	chr1:167430792-167430817	UUUUUCCUGUCCUGCCACUGUCCGC	89
919_8_7	CD247	Exon 8	+	chr1:167430793-167430818	UUUUCCUGUCCUGCCACUGUCCGCU	90
919_8_8	CD247	Exon 8	+	chr1:167430803-167430828	CUGCCACUGUCCGCUGGGCAGUUAU	91
919_8_9	CD247	Exon 8	+	chr1:167430816-167430841	CUGGGCAGUUAUAGGUCCCAUGUGU	92
919_8_10	CD247	Exon 8	+	chr1:167430817-167430842	UGGGCAGUUAUAGGUCCCAUGUGUU	93
919_8_11	CD247	Exon 8	+	chr1:167430830-167430855	GUCCCAUGUGUUGGGUCUUCCUGCG	94
919_8_12	CD247	Exon 8	+	chr1:167430882-167430907	UCGCUGAAAGCGUGAAGUGAAUCAA	95
919_8_13	CD247	Exon 8	+	chr1:167430962-167430987	AUGCCACUUUGUGCACAGCUCAUCA	96
919_8_14	CD247	Exon 8	+	chr1:167430982-167431007	CAUCAAGGUCAGUCUGUUCAUCUUC	97
919_8_15	CD247	Exon 8	+	chr1:167430998-167431023	UUCAUCUUCUGGCCCCUGUAGCACA	98
919_8_16	CD247	Exon 8	+	chr1:167431011-167431036	CCCUGUAGCACAUGGUACAGUUCAA	99
919_8_17	CD247	Exon 8	+	chr1:167431016-167431041	UAGCACAUGGUACAGUUCAAUGGUG	100
919_8_18	CD247	Exon 8	+	chr1:167431024-167431049	GGUACAGUUCAAUGGUGCGGCACAG	101
919_8_19	CD247	Exon 8	+	chr1:167431031-167431056	UUCAAUGGUGCGGCACAGAGGCCUG	102
919_8_20	CD247	Exon 8	+	chr1:167431035-167431060	AUGGUGCGGCACAGAGGCCUGAGGC	103
919_8_21	CD247	Exon 8	+	chr1:167431036-167431061	UGGUGCGGCACAGAGGCCUGAGGCA	104
919_8_22	CD247	Exon 8	+	chr1:167431039-167431064	UGCGGCACAGAGGCCUGAGGCAGGG	105
919_8_23	CD247	Exon 8	+	chr1:167431058-167431083	GCAGGGAGGCUCCCGCUGCCCUCGC	106
919_8_24	CD247	Exon 8	+	chr1:167431064-167431089	AGGCUCCCGCUGCCCUCGCAGGCCC	107
919_8_25	CD247	Exon 8	+	chr1:167431113-167431138	ACCUUCCCAUGCCCCUGCAGCUCCC	108
919_8_26	CD247	Exon 8	+	chr1:167431123-167431148	GCCCCUGCAGCUCCCUGGUUGCACC	109
919_8_27	CD247	Exon 8	+	chr1:167431129-167431154	GCAGCUCCCUGGUUGCACCUGGCCU	110

919_8_28	CD247	Exon 8	+	chr1:167431156-167431181	GCUCCUUUCCAUCUGCCCCUCUGCC	111
919_8_29	CD247	Exon 8	+	chr1:167431169-167431194	UGCCCCUCUGCCCGGCCCUCUCACC	112
919_8_30	CD247	Exon 8	+	chr1:167431170-167431195	GCCCCUCUGCCCGGCCCUCUCACCA	113
919_8_31	CD247	Exon 8	+	chr1:167431173-167431198	CCUCUGCCCGGCCCUCUCACCAGGG	114
919_8_32	CD247	Exon 8	+	chr1:167431183-167431208	GCCCUCUCACCAGGGAGGCACAACA	115
919_8_33	CD247	Exon 8	+	chr1:167431206-167431231	CAUGGCCCAGUACAGUUACCUUGAA	116
919_8_34	CD247	Exon 8	+	chr1:167431209-167431234	GGCCCAGUACAGUUACCUUGAAAGG	117
919_8_35	CD247	Exon 8	+	chr1:167431215-167431240	GUACAGUUACCUUGAAAGGAGGUGA	118
919_8_36	CD247	Exon 8	+	chr1:167431243-167431268	UGACAACAGAAGCCAAAUUUACAGC	119
919_8_37	CD247	Exon 8	+	chr1:167431282-167431307	UCAGACACAGAGUGAUACAGACAUU	120
919_8_38	CD247	Exon 8	+	chr1:167431283-167431308	CAGACACAGAGUGAUACAGACAUUA	121
919_8_39	CD247	Exon 8	+	chr1:167431311-167431336	CAUGUGCUAGCAUCUGCGCUUUCUC	122
919_8_40	CD247	Exon 8	+	chr1:167431312-167431337	AUGUGCUAGCAUCUGCGCUUUCUCU	123
919_8_41	CD247	Exon 8	+	chr1:167431313-167431338	UGUGCUAGCAUCUGCGCUUUCUCUG	124
919_8_42	CD247	Exon 8	+	chr1:167431351-167431376	ACAGACUCAACAACUCAGCUGUGAG	125
919_8_43	CD247	Exon 8	+	chr1:167431371-167431396	GUGAGAGGCAGUGCGCCCGCCUCCC	126
919_8_44	CD247	Exon 8	+	chr1:167431372-167431397	UGAGAGGCAGUGCGCCCGCCUCCCA	127
919_8_45	CD247	Exon 8	+	chr1:167431381-167431406	GUGCGCCCGCCUCCCAGGGAGAACG	128
919_8_46	CD247	Exon 8	+	chr1:167431391-167431416	CUCCCAGGGAGAACGAGGAACCGCC	129
919_8_47	CD247	Exon 8	+	chr1:167431398-167431423	GGAGAACGAGGAACCGCCAGGAGAC	130
919_8_48	CD247	Exon 8	+	chr1:167431415-167431440	CAGGAGACAGGUCUACCUGCACCAC	131
919_8_49	CD247	Exon 8	+	chr1:167431426-167431451	UCUACCUGCACCACCGGCAAACCAG	132
919_8_50	CD247	Exon 8	+	chr1:167431427-167431452	CUACCUGCACCACCGGCAAACCAGA	133
919_8_51	CD247	Exon 8	+	chr1:167431434-167431459	CACCACCGGCAAACCAGAGGGCCCA	134
919_8_52	CD247	Exon 8	+	chr1:167431439-167431464	CCGGCAAACCAGAGGGCCCAAGGCC	135

919_8_53	CD247	Exon 8	+	chr1:167431440-167431465	CGGCAAACCAGAGGGCCCAAGGCCA	136
919_8_54	CD247	Exon 8	+	chr1:167431453-167431478	GGCCCAAGGCCAGGGCCGUAAGCCC	137
919_8_55	CD247	Exon 8	+	chr1:167431454-167431479	GCCCAAGGCCAGGGCCGUAAGCCCU	138
919_8_56	CD247	Exon 8	+	chr1:167431479-167431504	GGGAGUACACUCCCUUAAAGAGUGC	139
919_8_57	CD247	Exon 8	+	chr1:167431480-167431505	GGAGUACACUCCCUUAAAGAGUGCA	140
919_8_58	CD247	Exon 8	+	chr1:167431501-167431526	UGCAGGGACAACAGUCUGUGUGUGA	141
919_8_59	CD247	Exon 8	+	chr1:167431506-167431531	GGACAACAGUCUGUGUGUGAAGGUU	142
919_8_60	CD247	Exon 8	+	chr1:167431541-167431566	UAUAACCAAAGCAUCCUGUACAUAA	143
919_8_61	CD247	Exon 8	+	chr1:167431542-167431567	AUAACCAAAGCAUCCUGUACAUAAA	144
919_8_62	CD247	Exon 8	+	chr1:167431543-167431568	UAACCAAAGCAUCCUGUACAUAAAG	145
919_8_63	CD247	Exon 8	+	chr1:167431556-167431581	CUGUACAUAAAGGGGAAUACUUCAG	146
919_8_64	CD247	Exon 8	+	chr1:167431574-167431599	ACUUCAGUGGCUGAGAAGAGUGAAC	147
919_8_65	CD247	Exon 8	+	chr1:167431575-167431600	CUUCAGUGGCUGAGAAGAGUGAACC	148
919_8_66	CD247	Exon 8	+	chr1:167431609-167431634	AUGCUUCAUCCUGUGUCUCAUAAUC	149
919_8_67	CD247	Exon 8	+	chr1:167431610-167431635	UGCUUCAUCCUGUGUCUCAUAAUCU	150
919_8_68	CD247	Exon 8	+	chr1:167431620-167431645	UGUGUCUCAUAAUCUGGGCGUCUGC	151
919_8_69	CD247	Exon 8	+	chr1:167431625-167431650	CUCAUAAUCUGGGCGUCUGCAGGUC	152
919_8_70	CD247	Exon 8	+	chr1:167431636-167431661	GGCGUCUGCAGGUCUGGCCUUUGAG	153
919_8_71	CD247	Exon 8	+	chr1:167431649-167431674	CUGGCCUUUGAGUGGUGAAAUCCCC	154
919_8_72	CD247	Exon 8	+	chr1:167431661-167431686	UGGUGAAAUCCCCUGGCUGUUAGCG	155
919_8_73	CD247	Exon 8	+	chr1:167431662-167431687	GGUGAAAUCCCCUGGCUGUUAGCGA	156
919_8_74	CD247	Exon 8	+	chr1:167431663-167431688	GUGAAAUCCCCUGGCUGUUAGCGAG	157
919_8_75	CD247	Exon 8	+	chr1:167431664-167431689	UGAAAUCCCCUGGCUGUUAGCGAGG	158
919_8_76	CD247	Exon 8	+	chr1:167431668-167431693	AUCCCCUGGCUGUUAGCGAGGGGGC	159
919_8_77	CD247	Exon 8	+	chr1:167431669-167431694	UCCCCUGGCUGUUAGCGAGGGGGCA	160

919_8_78	CD247	Exon 8	+	chr1:167431683-167431708	GCGAGGGGGCAGGGCCUGCAUGUGA	161
919_8_79	CD247	Exon 8	+	chr1:167431684-167431709	CGAGGGGGCAGGGCCUGCAUGUGAA	162
919_8_80	CD247	Exon 8	+	chr1:167431693-167431718	AGGGCCUGCAUGUGAAGGGCGUCGU	163
919_8_81	CD247	Exon 8	+	chr1:167431702-167431727	AUGUGAAGGGCGUCGUAGGUGUCCU	164
919_8_82	CD247	Exon 8	+	chr1:167431705-167431730	UGAAGGGCGUCGUAGGUGUCCUUGG	165
919_8_83	CD247	Exon 8	+	chr1:167431722-167431747	GUCCUUGGUGGCUGUACUGAGACCC	166
919_8_84	CD247	Exon 8	-	chr1:167430692-167430717	UUUUUUCUACUGUUUUAAUUUAUAC	167
919_8_85	CD247	Exon 8	-	chr1:167430740-167430765	GUCAUUACAGGGCACAGGCCAUGGA	168
919_8_86	CD247	Exon 8	-	chr1:167430744-167430769	CUGCGUCAUUACAGGGCACAGGCCA	169
919_8_87	CD247	Exon 8	-	chr1:167430750-167430775	AUACUGCUGCGUCAUUACAGGGCAC	170
919_8_88	CD247	Exon 8	-	chr1:167430756-167430781	ACUAGGAUACUGCUGCGUCAUUACA	171
919_8_89	CD247	Exon 8	-	chr1:167430757-167430782	UACUAGGAUACUGCUGCGUCAUUAC	172
919_8_90	CD247	Exon 8	-	chr1:167430778-167430803	GACAGGAAAAACCCGUCAAUGUACU	173
919_8_91	CD247	Exon 8	-	chr1:167430800-167430825	ACUGCCCAGCGGACAGUGGCAGGAC	174
919_8_92	CD247	Exon 8	-	chr1:167430805-167430830	CUAUAACUGCCCAGCGGACAGUGGC	175
919_8_93	CD247	Exon 8	-	chr1:167430809-167430834	GGACCUAUAACUGCCCAGCGGACAG	176
919_8_94	CD247	Exon 8	-	chr1:167430816-167430841	ACACAUGGGACCUAUAACUGCCCAG	177
919_8_95	CD247	Exon 8	-	chr1:167430835-167430860	GGCCUCGCAGGAAGACCCAACACAU	178
919_8_96	CD247	Exon 8	-	chr1:167430836-167430861	AGGCCUCGCAGGAAGACCCAACACA	179
919_8_97	CD247	Exon 8	-	chr1:167430852-167430877	AAAAUCAUCUUUGUGAAGGCCUCGC	180
919_8_98	CD247	Exon 8	-	chr1:167430861-167430886	GCGAAUGACAAAAUCAUCUUUGUGA	181
919_8_99	CD247	Exon 8	-	chr1:167430913-167430938	GAAUAAAGUGCUGCGGAGCAAGAGG	182
919_8_100	CD247	Exon 8	-	chr1:167430916-167430941	UGUGAAUAAAGUGCUGCGGAGCAAG	183
919_8_101	CD247	Exon 8	-	chr1:167430925-167430950	GUUACACAGUGUGAAUAAAGUGCUG	184
919_8_102	CD247	Exon 8	-	chr1:167430952-167430977	UGCACAAAGUGGCAUAAAAAACAUG	185

919_8_103	CD247	Exon 8	-	chr1:167430968-167430993	UGACCUUGAUGAGCUGUGCACAAAG	186
919_8_104	CD247	Exon 8	-	chr1:167431013-167431038	CAUUGAACUGUACCAUGUGCUACAG	187
919_8_105	CD247	Exon 8	-	chr1:167431014-167431039	CCAUUGAACUGUACCAUGUGCUACA	188
919_8_106	CD247	Exon 8	-	chr1:167431015-167431040	ACCAUUGAACUGUACCAUGUGCUAC	189
919_8_107	CD247	Exon 8	-	chr1:167431055-167431080	AGGGCAGCGGGAGCCUCCCUGCCUC	190
919_8_108	CD247	Exon 8	-	chr1:167431072-167431097	GUCAGCCAGGGCCUGCGAGGGCAGC	191
919_8_109	CD247	Exon 8	-	chr1:167431073-167431098	GGUCAGCCAGGGCCUGCGAGGGCAG	192
919_8_110	CD247	Exon 8	-	chr1:167431079-167431104	GGGGAGGGUCAGCCAGGGCCUGCGA	193
919_8_111	CD247	Exon 8	-	chr1:167431080-167431105	AGGGGAGGGUCAGCCAGGGCCUGCG	194
919_8_112	CD247	Exon 8	-	chr1:167431089-167431114	UGGGCGGGCAGGGGAGGGUCAGCCA	195
919_8_113	CD247	Exon 8	-	chr1:167431090-167431115	GUGGGCGGGCAGGGGAGGGUCAGCC	196
919_8_114	CD247	Exon 8	-	chr1:167431099-167431124	CAUGGGAAGGUGGGCGGGCAGGGGA	197
919_8_115	CD247	Exon 8	-	chr1:167431100-167431125	GCAUGGGAAGGUGGGCGGGCAGGGG	198
919_8_116	CD247	Exon 8	-	chr1:167431103-167431128	GGGGCAUGGGAAGGUGGGCGGGCAG	199
919_8_117	CD247	Exon 8	-	chr1:167431104-167431129	AGGGGCAUGGGAAGGUGGGCGGGCA	200
919_8_118	CD247	Exon 8	-	chr1:167431105-167431130	CAGGGGCAUGGGAAGGUGGGCGGGC	201
919_8_119	CD247	Exon 8	-	chr1:167431109-167431134	GCUGCAGGGGCAUGGGAAGGUGGGC	202
919_8_120	CD247	Exon 8	-	chr1:167431110-167431135	AGCUGCAGGGGCAUGGGAAGGUGGG	203
919_8_121	CD247	Exon 8	-	chr1:167431113-167431138	GGGAGCUGCAGGGGCAUGGGAAGGU	204
919_8_122	CD247	Exon 8	-	chr1:167431114-167431139	AGGGAGCUGCAGGGGCAUGGGAAGG	205
919_8_123	CD247	Exon 8	-	chr1:167431117-167431142	ACCAGGGAGCUGCAGGGGCAUGGGA	206
919_8_124	CD247	Exon 8	-	chr1:167431121-167431146	UGCAACCAGGGAGCUGCAGGGGCAU	207
919_8_125	CD247	Exon 8	-	chr1:167431122-167431147	GUGCAACCAGGGAGCUGCAGGGGCA	208
919_8_126	CD247	Exon 8	-	chr1:167431127-167431152	GCCAGGUGCAACCAGGGAGCUGCAG	209
919_8_127	CD247	Exon 8	-	chr1:167431128-167431153	GGCCAGGUGCAACCAGGGAGCUGCA	210

919_8_128	CD247	Exon 8	-	chr1:167431129-167431154	AGGCCAGGUGCAACCAGGGAGCUGC	211
919_8_129	CD247	Exon 8	-	chr1:167431138-167431163	AAGGAGCCUAGGCCAGGUGCAACCA	212
919_8_130	CD247	Exon 8	-	chr1:167431139-167431164	AAAGGAGCCUAGGCCAGGUGCAACC	213
919_8_131	CD247	Exon 8	-	chr1:167431149-167431174	GGGCAGAUGGAAAGGAGCCUAGGCC	214
919_8_132	CD247	Exon 8	-	chr1:167431154-167431179	CAGAGGGGCAGAUGGAAAGGAGCCU	215
919_8_133	CD247	Exon 8	-	chr1:167431162-167431187	GGGCCGGGCAGAGGGGCAGAUGGAA	216
919_8_134	CD247	Exon 8	-	chr1:167431167-167431192	UGAGAGGGCCGGGCAGAGGGGCAGA	217
919_8_135	CD247	Exon 8	-	chr1:167431174-167431199	UCCCUGGUGAGAGGGCCGGGCAGAG	218
919_8_136	CD247	Exon 8	-	chr1:167431175-167431200	CUCCCUGGUGAGAGGGCCGGGCAGA	219
919_8_137	CD247	Exon 8	-	chr1:167431176-167431201	CCUCCCUGGUGAGAGGGCCGGGCAG	220
919_8_138	CD247	Exon 8	-	chr1:167431182-167431207	GUUGUGCCUCCCUGGUGAGAGGGCC	221
919_8_139	CD247	Exon 8	-	chr1:167431183-167431208	UGUUGUGCCUCCCUGGUGAGAGGGC	222
919_8_140	CD247	Exon 8	-	chr1:167431187-167431212	GCCAUGUUGUGCCUCCCUGGUGAGA	223
919_8_141	CD247	Exon 8	-	chr1:167431188-167431213	GGCCAUGUUGUGCCUCCCUGGUGAG	224
919_8_142	CD247	Exon 8	-	chr1:167431195-167431220	UGUACUGGGCCAUGUUGUGCCUCCC	225
919_8_143	CD247	Exon 8	-	chr1:167431214-167431239	CACCUCCUUUCAAGGUAACUGUACU	226
919_8_144	CD247	Exon 8	-	chr1:167431215-167431240	UCACCUCCUUUCAAGGUAACUGUAC	227
919_8_145	CD247	Exon 8	-	chr1:167431227-167431252	CUGUUGUCACCUUCACCUCCUUUCA	228
919_8_146	CD247	Exon 8	-	chr1:167431258-167431283	AGUGGCUUCACUCCUGCUGUAAAUU	229
919_8_147	CD247	Exon 8	-	chr1:167431281-167431306	AUGUCUGUAUCACUCUGUGUCUGAG	230
919_8_148	CD247	Exon 8	-	chr1:167431389-167431414	CGGUUCCUCGUUCUCCCUGGGAGGC	231
919_8_149	CD247	Exon 8	-	chr1:167431390-167431415	GCGGUUCCUCGUUCUCCCUGGGAGG	232
919_8_150	CD247	Exon 8	-	chr1:167431393-167431418	CUGGCGGUUCCUCGUUCUCCCUGGG	233
919_8_151	CD247	Exon 8	-	chr1:167431396-167431421	CUCCUGGCGGUUCCUCGUUCUCCCU	234
919_8_152	CD247	Exon 8	-	chr1:167431397-167431422	UCUCCUGGCGGUUCCUCGUUCUCCC	235

919_8_153	CD247	Exon 8	-	chr1:167431414-167431439	UGGUGCAGGUAGACCUGUCUCCUGG	236
919_8_154	CD247	Exon 8	-	chr1:167431417-167431442	CGGUGGUGCAGGUAGACCUGUCUCC	237
919_8_155	CD247	Exon 8	-	chr1:167431433-167431458	GGGCCCUCUGGUUUGCCGGUGGUGC	238
919_8_156	CD247	Exon 8	-	chr1:167431439-167431464	GGCCUUGGGCCCUCUGGUUUGCCGG	239
919_8_157	CD247	Exon 8	-	chr1:167431442-167431467	CCUGGCCUUGGGCCCUCUGGUUUGC	240
919_8_158	CD247	Exon 8	-	chr1:167431450-167431475	CUUACGGCCCUGGCCUUGGGCCCUC	241
919_8_159	CD247	Exon 8	-	chr1:167431458-167431483	UCCCAGGGCUUACGGCCCUGGCCUU	242
919_8_160	CD247	Exon 8	-	chr1:167431459-167431484	CUCCCAGGGCUUACGGCCCUGGCCU	243
919_8_161	CD247	Exon 8	-	chr1:167431465-167431490	AGUGUACUCCCAGGGCUUACGGCCC	244
919_8_162	CD247	Exon 8	-	chr1:167431471-167431496	UAAGGGAGUGUACUCCCAGGGCUUA	245
919_8_163	CD247	Exon 8	-	chr1:167431478-167431503	CACUCUUUAAGGGAGUGUACUCCCA	246
919_8_164	CD247	Exon 8	-	chr1:167431479-167431504	GCACUCUUUAAGGGAGUGUACUCCC	247
919_8_165	CD247	Exon 8	-	chr1:167431493-167431518	AGACUGUUGUCCCUGCACUCUUUAA	248
919_8_166	CD247	Exon 8	-	chr1:167431494-167431519	CAGACUGUUGUCCCUGCACUCUUUA	249
919_8_167	CD247	Exon 8	-	chr1:167431549-167431574	AUUCCCCUUUAUGUACAGGAUGCUU	250
919_8_168	CD247	Exon 8	-	chr1:167431558-167431583	CACUGAAGUAUUCCCCUUUAUGUAC	251
919_8_169	CD247	Exon 8	-	chr1:167431601-167431626	GACACAGGAUGAAGCAUUUACAACC	252
919_8_170	CD247	Exon 8	-	chr1:167431621-167431646	UGCAGACGCCCAGAUUAUGAGACAC	253
919_8_171	CD247	Exon 8	-	chr1:167431656-167431681	ACAGCCAGGGGAUUUCACCACUCAA	254
919_8_172	CD247	Exon 8	-	chr1:167431673-167431698	GCCCUGCCCCCUCGCUAACAGCCAG	255
919_8_173	CD247	Exon 8	-	chr1:167431674-167431699	GGCCCUGCCCCCUCGCUAACAGCCA	256
919_8_174	CD247	Exon 8	-	chr1:167431675-167431700	AGGCCCUGCCCCCUCGCUAACAGCC	257
919_8_175	CD247	Exon 8	-	chr1:167431700-167431725	GACACCUACGACGCCCUUCACAUGC	258
919_8_176	CD247	Exon 8	-	chr1:167431727-167431752	CGCCAGGGUCUCAGUACAGCCACCA	259
919_7_1	CD247	Exon 7	+	chr1:167432999-167433024	UGAAGGGACGCCGGCAGCUCCUACC	260

919_7_2	CD247	Exon 7	+	chr1:167433005-167433030	GACGCCGGCAGCUCCUACCUGGUAA	261
919_7_3	CD247	Exon 7	+	chr1:167433029-167433054	AAGGCCAUCGUGCCCCUUGCCCCUC	262
919_7_4	CD247	Exon 7	+	chr1:167433035-167433060	AUCGUGCCCCUUGCCCCUCCGGCGC	263
919_7_5	CD247	Exon 7	+	chr1:167433043-167433068	CCUUGCCCCUCCGGCGCUGGUUGUU	264
919_7_6	CD247	Exon 7	+	chr1:167433044-167433069	CUUGCCCCUCCGGCGCUGGUUGUUU	265
919_7_7	CD247	Exon 7	-	chr1:167433012-167433037	AUGGCCUUUACCAGGUAGGAGCUGC	266
919_7_8	CD247	Exon 7	-	chr1:167433021-167433046	AGGGGCACGAUGGCCUUUACCAGGU	267
919_7_9	CD247	Exon 7	-	chr1:167433025-167433050	GGCAAGGGGCACGAUGGCCUUUACC	268
919_7_10	CD247	Exon 7	-	chr1:167433036-167433061	AGCGCCGGAGGGGCAAGGGGCACGA	269
919_7_11	CD247	Exon 7	-	chr1:167433044-167433069	AAACAACCAGCGCCGGAGGGGCAAG	270
919_7_12	CD247	Exon 7	-	chr1:167433045-167433070	CAAACAACCAGCGCCGGAGGGGCAA	271
919_7_13	CD247	Exon 7	-	chr1:167433046-167433071	CCAAACAACCAGCGCCGGAGGGGCA	272
919_7_14	CD247	Exon 7	-	chr1:167433051-167433076	CACUCCCAAACAACCAGCGCCGGAG	273
919_7_15	CD247	Exon 7	-	chr1:167433052-167433077	UCACUCCCAAACAACCAGCGCCGGA	274
919_7_16	CD247	Exon 7	-	chr1:167433053-167433078	UUCACUCCCAAACAACCAGCGCCGG	275
919_7_17	CD247	Exon 7	-	chr1:167433056-167433081	CAUUUCACUCCCAAACAACCAGCGC	276
919_6_1	CD247	Exon 6	+	chr1:167434020-167434045	UCGCCUUUCAUCCCAAUCUCACUGU	277
919_6_2	CD247	Exon 6	+	chr1:167434060-167434085	UAUCUUUCUGCAGUUCCUGCAGAAG	278
919_6_3	CD247	Exon 6	+	chr1:167434061-167434086	AUCUUUCUGCAGUUCCUGCAGAAGA	279
919_6_4	CD247	Exon 6	+	chr1:167434066-167434091	UCUGCAGUUCCUGCAGAAGAGGGCG	280
919_6_5	CD247	Exon 6	-	chr1:167434021-167434046	UACAGUGAGAUUGGGAUGAAAGGCG	281
919_6_6	CD247	Exon 6	-	chr1:167434026-167434051	AGGCCUACAGUGAGAUUGGGAUGAA	282
919_6_7	CD247	Exon 6	-	chr1:167434034-167434059	GAUGGCGGAGGCCUACAGUGAGAUU	283
919_6_8	CD247	Exon 6	-	chr1:167434035-167434060	AGAUGGCGGAGGCCUACAGUGAGAU	284
919_6_9	CD247	Exon 6	-	chr1:167434051-167434076	GAACUGCAGAAAGAUAAGAUGGCGG	285

919_6_10	CD247	Exon 6	-	chr1:167434054-167434079	CAGGAACUGCAGAAAGAUAAGAUGG	286
919_6_11	CD247	Exon 6	-	chr1:167434057-167434082	CUGCAGGAACUGCAGAAAGAUAAGA	287
919_5_1	CD247	Exon 5	+	chr1:167435380-167435405	GAGGUCUCCUCUACUCACAUUGUAC	288
919_5_2	CD247	Exon 5	+	chr1:167435391-167435416	UACUCACAUUGUACAGGCCUUCCUG	289
919_5_3	CD247	Exon 5	+	chr1:167435392-167435417	ACUCACAUUGUACAGGCCUUCCUGA	290
919_5_4	CD247	Exon 5	+	chr1:167435411-167435436	UCCUGAGGGUUCUUCCUUCUCUGCU	291
919_5_5	CD247	Exon 5	+	chr1:167435422-167435447	CUUCCUUCUCUGCUAGGAAAGACAA	292
919_5_6	CD247	Exon 5	+	chr1:167435423-167435448	UUCCUUCUCUGCUAGGAAAGACAAC	293
919_5_7	CD247	Exon 5	-	chr1:167435390-167435415	AGGAAGGCCUGUACAAUGUGAGUAG	294
919_5_8	CD247	Exon 5	-	chr1:167435411-167435436	AGCAGAGAAGGAAGAACCCUCAGGA	295
919_5_9	CD247	Exon 5	-	chr1:167435415-167435440	UCCUAGCAGAGAAGGAAGAACCCUC	296
919_5_10	CD247	Exon 5	-	chr1:167435428-167435453	UUCCCGUUGUCUUUCCUAGCAGAGA	297
919_4_1	CD247	Exon 4	+	chr1:167438544-167438569	CACAGGAAGGUAGAGGAACCCCUAC	298
919_4_2	CD247	Exon 4	+	chr1:167438562-167438587	CCCCUACCGGCUUUCCCCCCAUCUC	299
919_4_3	CD247	Exon 4	+	chr1:167438563-167438588	CCCUACCGGCUUUCCCCCAUCUCA	300
919_4_4	CD247	Exon 4	+	chr1:167438569-167438594	CGGCUUUCCCCCCAUCUCAGGGUCC	301
919_4_5	CD247	Exon 4	-	chr1:167438565-167438590	CCUGAGAUGGGGGGAAAGCCGGUAG	302
919_4_6	CD247	Exon 4	-	chr1:167438566-167438591	CCCUGAGAUGGGGGGAAAGCCGGUA	303
919_4_7	CD247	Exon 4	-	chr1:167438567-167438592	ACCCUGAGAUGGGGGGAAAGCCGGU	304
919_4_8	CD247	Exon 4	-	chr1:167438571-167438596	CGGGACCCUGAGAUGGGGGGAAAGC	305
919_4_9	CD247	Exon 4	-	chr1:167438579-167438604	GACGUGGCCGGGACCCUGAGAUGGG	306
919_4_10	CD247	Exon 4	-	chr1:167438580-167438605	AGACGUGGCCGGGACCCUGAGAUGG	307
919_4_11	CD247	Exon 4	-	chr1:167438581-167438606	GAGACGUGGCCGGGACCCUGAGAUG	308
919_4_12	CD247	Exon 4	-	chr1:167438582-167438607	AGAGACGUGGCCGGGACCCUGAGAU	309
919_4_13	CD247	Exon 4	-	chr1:167438583-167438608	AAGAGACGUGGCCGGGACCCUGAGA	310

919_4_14	CD247	Exon 4	-	chr1:167438595-167438620	GAUGUUUUGGACAAGAGACGUGGCC	311
919_4_15	CD247	Exon 4	-	chr1:167438596-167438621	CGAUGUUUUGGACAAGAGACGUGGC	312
919_4_16	CD247	Exon 4	-	chr1:167438600-167438625	AGUACGAUGUUUUGGACAAGAGACG	313
919_4_17	CD247	Exon 4	-	chr1:167438613-167438638	GGACGAAGAGAGGAGUACGAUGUUU	314
919_4_18	CD247	Exon 4	-	chr1:167438628-167438653	UAGGAGCUCAAUCUAGGACGAAGAG	315
919_4_19	CD247	Exon 4	-	chr1:167438639-167438664	CUUAUCUGUUAUAGGAGCUCAAUCU	316
919_3_1	CD247	Exon 3	+	chr1:167439328-167439353	GCGAGGCUGACUUACGUUAUAGAGC	317
919_3_2	CD247	Exon 3	+	chr1:167439334-167439359	CUGACUUACGUUAUAGAGCUGGUUC	318
919_3_3	CD247	Exon 3	+	chr1:167439343-167439368	GUUAUAGAGCUGGUUCUGGCCCUGC	319
919_3_4	CD247	Exon 3	+	chr1:167439350-167439375	AGCUGGUUCUGGCCCUGCUGGUACG	320
919_3_5	CD247	Exon 3	+	chr1:167439351-167439376	GCUGGUUCUGGCCCUGCUGGUACGC	321
919_3_6	CD247	Exon 3	+	chr1:167439352-167439377	CUGGUUCUGGCCCUGCUGGUACGCG	322
919_3_7	CD247	Exon 3	+	chr1:167439353-167439378	UGGUUCUGGCCCUGCUGGUACGCGG	323
919_3_8	CD247	Exon 3	-	chr1:167439365-167439390	GCGCAGACGCCCCCGCGUACCAGCA	324
919_3_9	CD247	Exon 3	-	chr1:167439366-167439391	AGCGCAGACGCCCCCGCGUACCAGC	325
919_3_10	CD247	Exon 3	-	chr1:167439394-167439419	UUUGCUUUCUGUGUUGCAGUUCAGC	326
919_2_1	CD247	Exon 2	+	chr1:167440648-167440673	CCCAGUGGUACCCACCUUCACUCUC	327
919_2_2	CD247	Exon 2	+	chr1:167440655-167440680	GUACCCACCUUCACUCUCAGGAACA	328
919_2_3	CD247	Exon 2	+	chr1:167440684-167440709	AGUGAGAAUGACACCAUAGAUGAAG	329
919_2_4	CD247	Exon 2	+	chr1:167440699-167440724	AUAGAUGAAGAGGAUUCCAUCCAGC	330
919_2_5	CD247	Exon 2	+	chr1:167440712-167440737	AUUCCAUCCAGCAGGUAGCAGAGUU	331
919_2_6	CD247	Exon 2	+	chr1:167440713-167440738	UUCCAUCCAGCAGGUAGCAGAGUUU	332
919_2_7	CD247	Exon 2	+	chr1:167440723-167440748	CAGGUAGCAGAGUUUGGGAUCCAGC	333
919_2_8	CD247	Exon 2	+	chr1:167440761-167440786	GUGCCUCUGUGCCAAGAGAUAAAGC	334
919_2_9	CD247	Exon 2	-	chr1:167440641-167440666	AAGGUGGGUACCACUGGGCUUUGGG	335

919_2_10	CD247	Exon 2	-	chr1:167440644-167440669	GUGAAGGUGGGUACCACUGGGCUUU	336
919_2_11	CD247	Exon 2	-	chr1:167440645-167440670	AGUGAAGGUGGGUACCACUGGGCUU	337
919_2_12	CD247	Exon 2	-	chr1:167440651-167440676	CCUGAGAGUGAAGGUGGGUACCACU	338
919_2_13	CD247	Exon 2	-	chr1:167440652-167440677	UCCUGAGAGUGAAGGUGGGUACCAC	339
919_2_14	CD247	Exon 2	-	chr1:167440661-167440686	CUGCCUUGUUCCUGAGAGUGAAGGU	340
919_2_15	CD247	Exon 2	-	chr1:167440662-167440687	ACUGCCUUGUUCCUGAGAGUGAAGG	341
919_2_16	CD247	Exon 2	-	chr1:167440665-167440690	CUCACUGCCUUGUUCCUGAGAGUGA	342
919_2_17	CD247	Exon 2	-	chr1:167440700-167440725	UGCUGGAUGGAAUCCUCUUCAUCUA	343
919_2_18	CD247	Exon 2	-	chr1:167440718-167440743	AUCCCAAACUCUGCUACCUGCUGGA	344
919_2_19	CD247	Exon 2	-	chr1:167440722-167440747	CUGGAUCCCAAACUCUGCUACCUGC	345
919_2_20	CD247	Exon 2	-	chr1:167440746-167440771	ACAGAGGCACAGAGCUUUGGCCUGC	346
919_2_21	CD247	Exon 2	-	chr1:167440754-167440779	CUCUUGGCACAGAGGCACAGAGCUU	347
919_2_22	CD247	Exon 2	-	chr1:167440767-167440792	UGACCAGCUUUAUCUCUUGGCACAG	348
919_1_1	CD247	Exon 1	+	chr1:167518389-167518414	UCGACACGUCGGCCCUACCUGUAAU	349
919_1_2	CD247	Exon 1	+	chr1:167518405-167518430	ACCUGUAAUCGGCAACUGUGCCUGC	350
919_1_3	CD247	Exon 1	+	chr1:167518409-167518434	GUAAUCGGCAACUGUGCCUGCAGGA	351
919_1_4	CD247	Exon 1	+	chr1:167518415-167518440	GGCAACUGUGCCUGCAGGAUGGCCG	352
919_1_5	CD247	Exon 1	+	chr1:167518461-167518486	UCAUCUUGUCCUUUCCCUCAGAAAG	353
919_1_6	CD247	Exon 1	+	chr1:167518465-167518490	CUUGUCCUUUCCCUCAGAAAGAGGC	354
919_1_7	CD247	Exon 1	+	chr1:167518466-167518491	UUGUCCUUUCCCUCAGAAAGAGGCU	355
919_1_8	CD247	Exon 1	+	chr1:167518469-167518494	UCCUUUCCCUCAGAAAGAGGCUGGG	356
919_1_9	CD247	Exon 1	+	chr1:167518475-167518500	CCCUCAGAAAGAGGCUGGGAGGCAG	357
919_1_10	CD247	Exon 1	+	chr1:167518481-167518506	GAAAGAGGCUGGGAGGCAGAGGCUG	358
919_1_11	CD247	Exon 1	+	chr1:167518487-167518512	GGCUGGGAGGCAGAGGCUGAGGCAG	359
919_1_12	CD247	Exon 1	+	chr1:167518490-167518515	UGGGAGGCAGAGGCUGAGGCAGCGG	360

919_1_13	CD247	Exon 1	+	chr1:167518494-167518519	AGGCAGAGGCUGAGGCAGCGGUGGC	361
919_1_14	CD247	Exon 1	+	chr1:167518495-167518520	GGCAGAGGCUGAGGCAGCGGUGGCC	362
919_1_15	CD247	Exon 1	+	chr1:167518499-167518524	GAGGCUGAGGCAGCGGUGGCCGGGA	363
919_1_16	CD247	Exon 1	+	chr1:167518504-167518529	UGAGGCAGCGGUGGCCGGGACGGUU	364
919_1_17	CD247	Exon 1	+	chr1:167518512-167518537	CGGUGGCCGGGACGGUUAGGAGAAA	365
919_1_18	CD247	Exon 1	+	chr1:167518524-167518549	CGGUUAGGAGAAAAGGAGUCUCUGC	366
919_1_19	CD247	Exon 1	+	chr1:167518550-167518575	GGUUUUAUUCUGCAGCUACCUCCCC	367
919_1_20	CD247	Exon 1	+	chr1:167518556-167518581	AUUCUGCAGCUACCUCCCCAGGAAG	368
919_1_21	CD247	Exon 1	+	chr1:167518559-167518584	CUGCAGCUACCUCCCCAGGAAGUGG	369
919_1_22	CD247	Exon 1	+	chr1:167518566-167518591	UACCUCCCCAGGAAGUGGAGGACUG	370
919_1_23	CD247	Exon 1	+	chr1:167518567-167518592	ACCUCCCCAGGAAGUGGAGGACUGU	371
919_1_24	CD247	Exon 1	+	chr1:167518568-167518593	CCUCCCCAGGAAGUGGAGGACUGUG	372
919_1_25	CD247	Exon 1	+	chr1:167518594-167518619	GGCCUUUGAGAAAGCACCUGCCGAC	373
919_1_26	CD247	Exon 1	+	chr1:167518595-167518620	GCCUUUGAGAAAGCACCUGCCGACA	374
919_1_27	CD247	Exon 1	-	chr1:167518385-167518410	CAGGUAGGGCCGACGUGUCGACGGC	375
919_1_28	CD247	Exon 1	-	chr1:167518389-167518414	AUUACAGGUAGGGCCGACGUGUCGA	376
919_1_29	CD247	Exon 1	-	chr1:167518404-167518429	CAGGCACAGUUGCCGAUUACAGGUA	377
919_1_30	CD247	Exon 1	-	chr1:167518405-167518430	GCAGGCACAGUUGCCGAUUACAGGU	378
919_1_31	CD247	Exon 1	-	chr1:167518409-167518434	UCCUGCAGGCACAGUUGCCGAUUAC	379
919_1_32	CD247	Exon 1	-	chr1:167518428-167518453	GCGCUUUUCACCGCGGCCAUCCUGC	380
919_1_33	CD247	Exon 1	-	chr1:167518440-167518465	AUGAAGUGGAAGGCGCUUUUCACCG	381
919_1_34	CD247	Exon 1	-	chr1:167518455-167518480	GAGGGAAAGGACAAGAUGAAGUGGA	382
919_1_35	CD247	Exon 1	-	chr1:167518459-167518484	UUCUGAGGGAAAGGACAAGAUGAAG	383
919_1_36	CD247	Exon 1	-	chr1:167518473-167518498	GCCUCCCAGCCUCUUUCUGAGGGAA	384
919_1_37	CD247	Exon 1	-	chr1:167518478-167518503	CCUCUGCCUCCCAGCCUCUUUCUGA	385

919_1_38	CD247	Exon 1	-	chr1:167518479-167518504	GCCUCUGCCUCCCAGCCUCUUUCUG	386
919_1_39	CD247	Exon 1	-	chr1:167518521-167518546	GAGACUCCUUUUCUCCUAACCGUCC	387
919_1_40	CD247	Exon 1	-	chr1:167518571-167518596	CCCCACAGUCCUCCACUUCCUGGGG	388
919_1_41	CD247	Exon 1	-	chr1:167518574-167518599	AGGCCCCACAGUCCUCCACUUCCUG	389
919_1_42	CD247	Exon 1	-	chr1:167518575-167518600	AAGGCCCCACAGUCCUCCACUUCCU	390
919_1_43	CD247	Exon 1	-	chr1:167518576-167518601	AAAGGCCCCACAGUCCUCCACUUCC	391
919_1_44	CD247	Exon 1	-	chr1:167518599-167518624	GCCCUGUCGGCAGGUGCUUUCUCAA	392
915_5_1	CD3D	Exon 5	+	chr11:118339059-118339084	AGCCCAGGCACCUGCUGAGUGAAAG	393
915_5_2	CD3D	Exon 5	+	chr11:118339072-118339097	GCUGAGUGAAAGAGGAUAUAUUUAU	394
915_5_3	CD3D	Exon 5	+	chr11:118339085-118339110	GGAUAUAUUUAUUGGCUGAGCAAGA	395
915_5_4	CD3D	Exon 5	+	chr11:118339086-118339111	GAUAUAUUUAUUGGCUGAGCAAGAA	396
915_5_5	CD3D	Exon 5	+	chr11:118339090-118339115	UAUUUAUUGGCUGAGCAAGAAGGGA	397
915_5_6	CD3D	Exon 5	+	chr11:118339099-118339124	GCUGAGCAAGAAGGGAAGGUACAGU	398
915_5_7	CD3D	Exon 5	+	chr11:118339105-118339130	CAAGAAGGGAAGGUACAGUUGGUAA	399
915_5_8	CD3D	Exon 5	+	chr11:118339132-118339157	GCUGCUUCUAGAAGCCACCAGUCUC	400
915_5_9	CD3D	Exon 5	+	chr11:118339164-118339189	CUUGUUCCGAGCCCAGUUUCCUCCA	401
915_5_10	CD3D	Exon 5	+	chr11:118339167-118339192	GUUCCGAGCCCAGUUUCCUCCAAGG	402
915_5_11	CD3D	Exon 5	+	chr11:118339194-118339219	GCUGUACUGAGCAUCAUCUCGAUCU	403
915_5_12	CD3D	Exon 5	+	chr11:118339197-118339222	GUACUGAGCAUCAUCUCGAUCUCGG	404
915_5_13	CD3D	Exon 5	+	chr11:118339198-118339223	UACUGAGCAUCAUCUCGAUCUCGGA	405
915_5_14	CD3D	Exon 5	+	chr11:118339199-118339224	ACUGAGCAUCAUCUCGAUCUCGGAG	406
915_5_15	CD3D	Exon 5	+	chr11:118339209-118339234	AUCUCGAUCUCGGAGGGGCUAAGAG	407
915_5_16	CD3D	Exon 5	+	chr11:118339223-118339248	GGGGCUAAGAGAGGAGAAGAGAAAA	408
915_5_17	CD3D	Exon 5	-	chr11:118339054-118339079	ACUCAGCAGGUGCCUGGGCUUCUUA	409
915_5_18	CD3D	Exon 5	-	chr11:118339064-118339089	AUCCUCUUUCACUCAGCAGGUGCCU	410

915_5_19	CD3D	Exon 5	-	chr11:118339065-118339090	UAUCCUCUUUCACUCAGCAGGUGCC	411
915_5_20	CD3D	Exon 5	-	chr11:118339072-118339097	AUAAAUAUAUCCUCUUUCACUCAGC	412
915_5_21	CD3D	Exon 5	-	chr11:118339149-118339174	UCGGAACAAGUGAACCUGAGACUGG	413
915_5_22	CD3D	Exon 5	-	chr11:118339152-118339177	GGCUCGGAACAAGUGAACCUGAGAC	414
915_5_23	CD3D	Exon 5	-	chr11:118339173-118339198	CAGCCACCUUGGAGGAAACUGGGCU	415
915_5_24	CD3D	Exon 5	-	chr11:118339178-118339203	CAGUACAGCCACCUUGGAGGAAACU	416
915_5_25	CD3D	Exon 5	-	chr11:118339179-118339204	UCAGUACAGCCACCUUGGAGGAAAC	417
915_5_26	CD3D	Exon 5	-	chr11:118339186-118339211	AUGAUGCUCAGUACAGCCACCUUGG	418
915_5_27	CD3D	Exon 5	-	chr11:118339189-118339214	GAGAUGAUGCUCAGUACAGCCACCU	419
915_4_1	CD3D	Exon 4	+	chr11:118339435-118339460	CCCCUCAACGCUCACCUGAUAGACC	420
915_4_2	CD3D	Exon 4	+	chr11:118339463-118339488	UCAUUCCUCAACAGAGCUUGUGUGU	421
915_4_3	CD3D	Exon 4	-	chr11:118339431-118339456	UAUCAGGUGAGCGUUGAGGGGAAGG	422
915_4_4	CD3D	Exon 4	-	chr11:118339434-118339459	GUCUAUCAGGUGAGCGUUGAGGGGA	423
915_4_5	CD3D	Exon 4	-	chr11:118339438-118339463	CCAGGUCUAUCAGGUGAGCGUUGAG	424
915_4_6	CD3D	Exon 4	-	chr11:118339439-118339464	ACCAGGUCUAUCAGGUGAGCGUUGA	425
915_4_7	CD3D	Exon 4	-	chr11:118339440-118339465	GACCAGGUCUAUCAGGUGAGCGUUG	426
915_4_8	CD3D	Exon 4	-	chr11:118339452-118339477	CUGUUGAGGAAUGACCAGGUCUAUC	427
915_4_9	CD3D	Exon 4	-	chr11:118339461-118339486	ACACAAGCUCUGUUGAGGAAUGACC	428
915_4_10	CD3D	Exon 4	-	chr11:118339471-118339496	AGCUGCCGACACACAAGCUCUGUUG	429
915_3_1	CD3D	Exon 3	+	chr11:118339802-118339827	AGCAAAGCAGAAGACUCCCAAAGCA	430
915_3_2	CD3D	Exon 3	+	chr11:118339812-118339837	AAGACUCCCAAAGCAAGGAGCAGAG	431
915_3_3	CD3D	Exon 3	+	chr11:118339845-118339870	ACAUCAGUGACAAUGAUGCCAGCCA	432
915_3_4	CD3D	Exon 3	+	chr11:118339848-118339873	UCAGUGACAAUGAUGCCAGCCACGG	433
915_3_5	CD3D	Exon 3	+	chr11:118339852-118339877	UGACAAUGAUGCCAGCCACGGUGGC	434
915_3_6	CD3D	Exon 3	+	chr11:118339874-118339899	GGCUGGAUCCAGCUCCACACAGCUC	435

915_3_7	CD3D	Exon 3	+	chr11:118339884-118339909	AGCUCCACACAGCUCUGGCACACUG	436
915_3_8	CD3D	Exon 3	+	chr11:118339885-118339910	GCUCCACACAGCUCUGGCACACUGU	437
915_3_9	CD3D	Exon 3	+	chr11:118339886-118339911	CUCCACACAGCUCUGGCACACUGUG	438
915_3_10	CD3D	Exon 3	+	chr11:118339887-118339912	UCCACACAGCUCUGGCACACUGUGG	439
915_3_11	CD3D	Exon 3	+	chr11:118339891-118339916	CACAGCUCUGGCACACUGUGGGGGA	440
915_3_12	CD3D	Exon 3	+	chr11:118339892-118339917	ACAGCUCUGGCACACUGUGGGGGAA	441
915_3_13	CD3D	Exon 3	+	chr11:118339895-118339920	GCUCUGGCACACUGUGGGGGAAGGG	442
915_3_14	CD3D	Exon 3	+	chr11:118339902-118339927	CACACUGUGGGGGAAGGGAGGAGAG	443
915_3_15	CD3D	Exon 3	-	chr11:118339769-118339794	GACUGGAAGGCUGUCUGGGGGUUAG	444
915_3_16	CD3D	Exon 3	-	chr11:118339776-118339801	GACAUGAGACUGGAAGGCUGUCUGG	445
915_3_17	CD3D	Exon 3	-	chr11:118339777-118339802	GGACAUGAGACUGGAAGGCUGUCUG	446
915_3_18	CD3D	Exon 3	-	chr11:118339778-118339803	UGGACAUGAGACUGGAAGGCUGUCU	447
915_3_19	CD3D	Exon 3	-	chr11:118339779-118339804	CUGGACAUGAGACUGGAAGGCUGUC	448
915_3_20	CD3D	Exon 3	-	chr11:118339787-118339812	CUGCUUUGCUGGACAUGAGACUGGA	449
915_3_21	CD3D	Exon 3	-	chr11:118339791-118339816	UCUUCUGCUUUGCUGGACAUGAGAC	450
915_3_22	CD3D	Exon 3	-	chr11:118339803-118339828	UUGCUUUGGGAGUCUUCUGCUUUGC	451
915_3_23	CD3D	Exon 3	-	chr11:118339821-118339846	UCAUUGCCACUCUGCUCCUUGCUUU	452
915_3_24	CD3D	Exon 3	-	chr11:118339822-118339847	GUCAUUGCCACUCUGCUCCUUGCUU	453
915_3_25	CD3D	Exon 3	-	chr11:118339866-118339891	UGGAGCUGGAUCCAGCCACCGUGGC	454
915_3_26	CD3D	Exon 3	-	chr11:118339870-118339895	UGUGUGGAGCUGGAUCCAGCCACCG	455
915_3_27	CD3D	Exon 3	-	chr11:118339885-118339910	ACAGUGUGCCAGAGCUGUGUGGAGC	456
915_3_28	CD3D	Exon 3	-	chr11:118339891-118339916	UCCCCCACAGUGUGCCAGAGCUGUG	457
915_2_1	CD3D	Exon 2	+	chr11:118340367-118340392	CACGUACUUCGAUAAUGAACUUGCA	458
915_2_2	CD3D	Exon 2	+	chr11:118340422-118340447	UCCCAUUACACCUAUAUAUUCCUCG	459
915_2_3	CD3D	Exon 2	+	chr11:118340423-118340448	CCCAUUACACCUAUAUAUUCCUCGU	460

915_2_4	CD3D	Exon 2	+	chr11:118340429-118340454	ACACCUAUAUAUUCCUCGUGGGUCC	461
915_2_5	CD3D	Exon 2	+	chr11:118340444-118340469	UCGUGGGUCCAGGAUGCGUUUUCCC	462
915_2_6	CD3D	Exon 2	+	chr11:118340505-118340530	ACCGUUCCCUCUACCCAUGUGAUGC	463
915_2_7	CD3D	Exon 2	+	chr11:118340548-118340573	ACACUCUGUCCUCAAGUUCCUCUAU	464
915_2_8	CD3D	Exon 2	+	chr11:118340559-118340584	UCAAGUUCCUCUAUAGGUAUCUUGA	465
915_2_9	CD3D	Exon 2	+	chr11:118340560-118340585	CAAGUUCCUCUAUAGGUAUCUUGAA	466
915_2_10	CD3D	Exon 2	+	chr11:118340561-118340586	AAGUUCCUCUAUAGGUAUCUUGAAG	467
915_2_11	CD3D	Exon 2	+	chr11:118340572-118340597	UAGGUAUCUUGAAGGGGCUCACUAA	468
915_2_12	CD3D	Exon 2	+	chr11:118340573-118340598	AGGUAUCUUGAAGGGGCUCACUAAA	469
915_2_13	CD3D	Exon 2	+	chr11:118340574-118340599	GGUAUCUUGAAGGGGCUCACUAAAG	470
915_2_14	CD3D	Exon 2	-	chr11:118340352-118340377	GAAGUACGUGCUUCCUGAACCCUUU	471
915_2_15	CD3D	Exon 2	-	chr11:118340353-118340378	CGAAGUACGUGCUUCCUGAACCCUU	472
915_2_16	CD3D	Exon 2	-	chr11:118340410-118340435	AGGUGUAAUGGGACAGAUAUAUACA	473
915_2_17	CD3D	Exon 2	-	chr11:118340426-118340451	CCCACGAGGAAUAUAUAGGUGUAAU	474
915_2_18	CD3D	Exon 2	-	chr11:118340427-118340452	ACCCACGAGGAAUAUAUAGGUGUAA	475
915_2_19	CD3D	Exon 2	-	chr11:118340435-118340460	CAUCCUGGACCCACGAGGAAUAUAU	476
915_2_20	CD3D	Exon 2	-	chr11:118340445-118340470	UGGGAAAACGCAUCCUGGACCCACG	477
915_2_21	CD3D	Exon 2	-	chr11:118340455-118340480	AGACUGGACCUGGGAAAACGCAUCC	478
915_2_22	CD3D	Exon 2	-	chr11:118340469-118340494	UCUCAGACAUUACAAGACUGGACCU	479
915_2_23	CD3D	Exon 2	-	chr11:118340470-118340495	CUCUCAGACAUUACAAGACUGGACC	480
915_2_24	CD3D	Exon 2	-	chr11:118340476-118340501	ACACUGCUCUCAGACAUUACAAGAC	481
915_2_25	CD3D	Exon 2	-	chr11:118340505-118340530	GCAUCACAUGGGUAGAGGGAACGGU	482
915_2_26	CD3D	Exon 2	-	chr11:118340506-118340531	AGCAUCACAUGGGUAGAGGGAACGG	483
915_2_27	CD3D	Exon 2	-	chr11:118340509-118340534	ACCAGCAUCACAUGGGUAGAGGGAA	484
915_2_28	CD3D	Exon 2	-	chr11:118340514-118340539	GCAAUACCAGCAUCACAUGGGUAGA	485

915_2_29	CD3D	Exon 2	-	chr11:118340515-118340540	UGCAAUACCAGCAUCACAUGGGUAG	486
915_2_30	CD3D	Exon 2	-	chr11:118340521-118340546	GUGAAUUGCAAUACCAGCAUCACAU	487
915_2_31	CD3D	Exon 2	-	chr11:118340522-118340547	UGUGAAUUGCAAUACCAGCAUCACA	488
915_2_32	CD3D	Exon 2	-	chr11:118340560-118340585	UUCAAGAUACCUAUAGAGGAACUUG	489
915_2_33	CD3D	Exon 2	-	chr11:118340569-118340594	GUGAGCCCCUUCAAGAUACCUAUAG	490
915_1_1	CD3D	Exon 1	+	chr11:118342538-118342563	UGGAGUAGCCUUACCUUGCGAGAGA	491
915_1_2	CD3D	Exon 1	+	chr11:118342539-118342564	GGAGUAGCCUUACCUUGCGAGAGAA	492
915_1_3	CD3D	Exon 1	+	chr11:118342553-118342578	UUGCGAGAGAAGGGUAGCCAGUACC	493
915_1_4	CD3D	Exon 1	+	chr11:118342589-118342614	AAACGUGCUAUGUUCCAUCUCCCAG	494
915_1_5	CD3D	Exon 1	+	chr11:118342614-118342639	CGGAACUCAUCCAGUAGAUAAAGCC	495
915_1_6	CD3D	Exon 1	+	chr11:118342634-118342659	AAGCCAGGUCACCGAACUAUCAGCC	496
915_1_7	CD3D	Exon 1	+	chr11:118342635-118342660	AGCCAGGUCACCGAACUAUCAGCCU	497
915_1_8	CD3D	Exon 1	+	chr11:118342667-118342692	AGCUGCCCUCCCCUAGCUGACUCAC	498
915_1_9	CD3D	Exon 1	+	chr11:118342673-118342698	CCUCCCCUAGCUGACUCACAGGUAC	499
915_1_10	CD3D	Exon 1	+	chr11:118342680-118342705	UAGCUGACUCACAGGUACCGGAAAG	500
915_1_11	CD3D	Exon 1	+	chr11:118342687-118342712	CUCACAGGUACCGGAAAGAGGAGAG	501
915_1_12	CD3D	Exon 1	+	chr11:118342688-118342713	UCACAGGUACCGGAAAGAGGAGAGU	502
915_1_13	CD3D	Exon 1	+	chr11:118342689-118342714	CACAGGUACCGGAAAGAGGAGAGUG	503
915_1_14	CD3D	Exon 1	+	chr11:118342690-118342715	ACAGGUACCGGAAAGAGGAGAGUGG	504
915_1_15	CD3D	Exon 1	+	chr11:118342693-118342718	GGUACCGGAAAGAGGAGAGUGGGGG	505
915_1_16	CD3D	Exon 1	+	chr11:118342734-118342759	CUGCUUCUCUGCUUUCUGCCGUUGA	506
915_1_17	CD3D	Exon 1	+	chr11:118342737-118342762	CUUCUCUGCUUUCUGCCGUUGAUGG	507
915_1_18	CD3D	Exon 1	+	chr11:118342738-118342763	UUCUCUGCUUUCUGCCGUUGAUGGU	508
915_1_19	CD3D	Exon 1	-	chr11:118342530-118342555	AAGGUAAGGCUACUCCAGGUGGGUG	509
915_1_20	CD3D	Exon 1	-	chr11:118342531-118342556	CAAGGUAAGGCUACUCCAGGUGGGU	510

915_1_21	CD3D	Exon 1	-	chr11:118342532-118342557	GCAAGGUAAGGCUACUCCAGGUGGG	511
915_1_22	CD3D	Exon 1	-	chr11:118342535-118342560	CUCGCAAGGUAAGGCUACUCCAGGU	512
915_1_23	CD3D	Exon 1	-	chr11:118342536-118342561	UCUCGCAAGGUAAGGCUACUCCAGG	513
915_1_24	CD3D	Exon 1	-	chr11:118342539-118342564	UUCUCUCGCAAGGUAAGGCUACUCC	514
915_1_25	CD3D	Exon 1	-	chr11:118342549-118342574	CUGGCUACCCUUCUCUCGCAAGGUA	515
915_1_26	CD3D	Exon 1	-	chr11:118342554-118342579	UGGUACUGGCUACCCUUCUCUCGCA	516
915_1_27	CD3D	Exon 1	-	chr11:118342573-118342598	AGCACGUUUCUCUCUGGCCUGGUAC	517
915_1_28	CD3D	Exon 1	-	chr11:118342579-118342604	GAACAUAGCACGUUUCUCUCUGGCC	518
915_1_29	CD3D	Exon 1	-	chr11:118342584-118342609	AGAUGGAACAUAGCACGUUUCUCUC	519
915_1_30	CD3D	Exon 1	-	chr11:118342606-118342631	CUACUGGAUGAGUUCCGCUGGGAGA	520
915_1_31	CD3D	Exon 1	-	chr11:118342612-118342637	CUUUAUCUACUGGAUGAGUUCCGCU	521
915_1_32	CD3D	Exon 1	-	chr11:118342613-118342638	GCUUUAUCUACUGGAUGAGUUCCGC	522
915_1_33	CD3D	Exon 1	-	chr11:118342627-118342652	AGUUCGGUGACCUGGCUUUAUCUAC	523
915_1_34	CD3D	Exon 1	-	chr11:118342640-118342665	CACCCAGGCUGAUAGUUCGGUGACC	524
915_1_35	CD3D	Exon 1	-	chr11:118342648-118342673	GCAGCUCUCACCCAGGCUGAUAGUU	525
915_1_36	CD3D	Exon 1	-	chr11:118342660-118342685	AGCUAGGGGAGGGCAGCUCUCACCC	526
915_1_37	CD3D	Exon 1	-	chr11:118342675-118342700	CGGUACCUGUGAGUCAGCUAGGGGA	527
915_1_38	CD3D	Exon 1	-	chr11:118342676-118342701	CCGGUACCUGUGAGUCAGCUAGGGG	528
915_1_39	CD3D	Exon 1	-	chr11:118342679-118342704	UUUCCGGUACCUGUGAGUCAGCUAG	529
915_1_40	CD3D	Exon 1	-	chr11:118342680-118342705	CUUUCCGGUACCUGUGAGUCAGCUA	530
915_1_41	CD3D	Exon 1	-	chr11:118342681-118342706	UCUUUCCGGUACCUGUGAGUCAGCU	531
915_1_42	CD3D	Exon 1	-	chr11:118342700-118342725	AGUUCCUCCCCCACUCUCCUCUUUC	532
916_1_1	CD3E	Exon 1	+	chr11:118304575-118304600	CAGGUAUUGUCAGAGUCCUCUUGUU	533
916_1_2	CD3E	Exon 1	+	chr11:118304584-118304609	UCAGAGUCCUCUUGUUUGGCCUUCU	534
916_1_3	CD3E	Exon 1	+	chr11:118304588-118304613	AGUCCUCUUGUUUGGCCUUCUAGGA	535

916_1_4	CD3E	Exon 1	+	chr11:118304594-118304619	CUUGUUUGGCCUUCUAGGAAGGCUG	536
916_1_5	CD3E	Exon 1	+	chr11:118304595-118304620	UUGUUUGGCCUUCUAGGAAGGCUGU	537
916_1_6	CD3E	Exon 1	+	chr11:118304621-118304646	GGACCCAGCUUUCUUCAACCAGUCC	538
916_1_7	CD3E	Exon 1	+	chr11:118304624-118304649	CCCAGCUUUCUUCAACCAGUCCAGG	539
916_1_8	CD3E	Exon 1	+	chr11:118304627-118304652	AGCUUUCUUCAACCAGUCCAGGUGG	540
916_1_9	CD3E	Exon 1	+	chr11:118304655-118304680	CCUCUGCCUUGAACGUUUCCAAGUG	541
916_1_10	CD3E	Exon 1	+	chr11:118304668-118304693	CGUUUCCAAGUGAGGUAAAACCCGC	542
916_1_11	CD3E	Exon 1	+	chr11:118304676-118304701	AGUGAGGUAAAACCCGCAGGCCCAG	543
916_1_12	CD3E	Exon 1	+	chr11:118304696-118304721	CCCAGAGGCCUCUCUACUUCCUGUG	544
916_1_13	CD3E	Exon 1	+	chr11:118304697-118304722	CCAGAGGCCUCUCUACUUCCUGUGU	545
916_1_14	CD3E	Exon 1	+	chr11:118304698-118304723	CAGAGGCCUCUCUACUUCCUGUGUG	546
916_1_15	CD3E	Exon 1	+	chr11:118304730-118304755	GAAACCCUCCUCCCCUCCCAGCCUC	547
916_1_16	CD3E	Exon 1	+	chr11:118304749-118304774	AGCCUCAGGUGCCUGCUUCAGAAAA	548
916_1_17	CD3E	Exon 1	-	chr11:118304572-118304597	AAGAGGACUCUGACAAUACCUGGAG	549
916_1_18	CD3E	Exon 1	-	chr11:118304573-118304598	CAAGAGGACUCUGACAAUACCUGGA	550
916_1_19	CD3E	Exon 1	-	chr11:118304574-118304599	ACAAGAGGACUCUGACAAUACCUGG	551
916_1_20	CD3E	Exon 1	-	chr11:118304577-118304602	CAAACAAGAGGACUCUGACAAUACC	552
916_1_21	CD3E	Exon 1	-	chr11:118304594-118304619	CAGCCUUCCUAGAAGGCCAAACAAG	553
916_1_22	CD3E	Exon 1	-	chr11:118304606-118304631	AGCUGGGUCCCACAGCCUUCCUAGA	554
916_1_23	CD3E	Exon 1	-	chr11:118304627-118304652	CCACCUGGACUGGUUGAAGAAAGCU	555
916_1_24	CD3E	Exon 1	-	chr11:118304628-118304653	UCCACCUGGACUGGUUGAAGAAAGC	556
916_1_25	CD3E	Exon 1	-	chr11:118304642-118304667	UCAAGGCAGAGGCCUCCACCUGGAC	557
916_1_26	CD3E	Exon 1	-	chr11:118304647-118304672	AACGUUCAAGGCAGAGGCCUCCACC	558
916_1_27	CD3E	Exon 1	-	chr11:118304658-118304683	CCUCACUUGGAAACGUUCAAGGCAG	559
916_1_28	CD3E	Exon 1	-	chr11:118304664-118304689	GUUUUACCUCACUUGGAAACGUUCA	560

916_1_29	CD3E	Exon 1	-	chr11:118304676-118304701	CUGGGCCUGCGGGUUUUACCUCACU	561
916_1_30	CD3E	Exon 1	-	chr11:118304691-118304716	GAAGUAGAGAGGCCUCUGGGCCUGC	562
916_1_31	CD3E	Exon 1	-	chr11:118304692-118304717	GGAAGUAGAGAGGCCUCUGGGCCUG	563
916_1_32	CD3E	Exon 1	-	chr11:118304699-118304724	CCACACAGGAAGUAGAGAGGCCUCU	564
916_1_33	CD3E	Exon 1	-	chr11:118304700-118304725	CCCACACAGGAAGUAGAGAGGCCUC	565
916_1_34	CD3E	Exon 1	-	chr11:118304707-118304732	UCUGAACCCCACACAGGAAGUAGAG	566
916_1_35	CD3E	Exon 1	-	chr11:118304718-118304743	GGAGGAGGGUUUCUGAACCCCACAC	567
916_1_36	CD3E	Exon 1	-	chr11:118304737-118304762	GGCACCUGAGGCUGGGAGGGGAGGA	568
916_1_37	CD3E	Exon 1	-	chr11:118304738-118304763	AGGCACCUGAGGCUGGGAGGGGAGG	569
916_1_38	CD3E	Exon 1	-	chr11:118304741-118304766	AGCAGGCACCUGAGGCUGGGGAGGGG	570
916_1_39	CD3E	Exon 1	-	chr11:118304744-118304769	UGAAGCAGGCACCUGAGGCUGGGAG	571
916_1_40	CD3E	Exon 1	-	chr11:118304745-118304770	CUGAAGCAGGCACCUGAGGCUGGGA	572
916_1_41	CD3E	Exon 1	-	chr11:118304746-118304771	UCUGAAGCAGGCACCUGAGGCUGGG	573
916_1_42	CD3E	Exon 1	-	chr11:118304749-118304774	UUUUCUGAAGCAGGCACCUGAGGCU	574
916_1_43	CD3E	Exon 1	-	chr11:118304750-118304775	AUUUUCUGAAGCAGGCACCUGAGGC	575
916_1_44	CD3E	Exon 1	-	chr11:118304754-118304779	CACCAUUUUCUGAAGCAGGCACCUG	576
916_1_45	CD3E	Exon 1	-	chr11:118304763-118304788	AGAGAGACUCACCAUUUUCUGAAGC	577
916_2_1	CD3E	Exon 2	+	chr11:118304883-118304908	UUUUUUCCAGAAGUAGUAAGUCUGC	578
916_2_2	CD3E	Exon 2	+	chr11:118304934-118304959	CAGUCCCAUGAAACAAAGAUGCAGU	579
916_2_3	CD3E	Exon 2	+	chr11:118304935-118304960	AGUCCCAUGAAACAAAGAUGCAGUC	580
916_2_4	CD3E	Exon 2	+	chr11:118304945-118304970	AACAAAGAUGCAGUCGGGCACUCAC	581
916_2_5	CD3E	Exon 2	+	chr11:118304955-118304980	CAGUCGGGCACUCACUGGAGAGUUC	582
916_2_6	CD3E	Exon 2	+	chr11:118304956-118304981	AGUCGGGCACUCACUGGAGAGUUCU	583
916_2_7	CD3E	Exon 2	+	chr11:118304974-118304999	GAGUUCUGGGCCUCUGCCUCUUAUC	584
916_2_8	CD3E	Exon 2	+	chr11:118304982-118305007	GGCCUCUGCCUCUUAUCAGGUGAGU	585

916_2_9	CD3E	Exon 2	+	chr11:118304986-118305011	UCUGCCUCUUAUCAGGUGAGUAGGA	586
916_2_10	CD3E	Exon 2	+	chr11:118304991-118305016	CUCUUAUCAGGUGAGUAGGAUGGAG	587
916_2_11	CD3E	Exon 2	+	chr11:118304996-118305021	AUCAGGUGAGUAGGAUGGAGUGGAA	588
916_2_12	CD3E	Exon 2	+	chr11:118304997-118305022	UCAGGUGAGUAGGAUGGAGUGGAAA	589
916_2_13	CD3E	Exon 2	-	chr11:118304892-118304917	CGGAGGCCAGCAGACUUACUACUUC	590
916_2_14	CD3E	Exon 2	-	chr11:118304914-118304939	GACUGUUACUUUACUAAGAUGGCGG	591
916_2_15	CD3E	Exon 2	-	chr11:118304917-118304942	UGGGACUGUUACUUUACUAAGAUGG	592
916_2_16	CD3E	Exon 2	-	chr11:118304920-118304945	UCAUGGGACUGUUACUUUACUAAGA	593
916_2_17	CD3E	Exon 2	-	chr11:118304941-118304966	GUGCCCGACUGCAUCUUUGUUUCAU	594
916_2_18	CD3E	Exon 2	-	chr11:118304942-118304967	AGUGCCCGACUGCAUCUUUGUUUCA	595
916_2_19	CD3E	Exon 2	-	chr11:118304987-118305012	AUCCUACUCACCUGAUAAGAGGCAG	596
916_2_20	CD3E	Exon 2	-	chr11:118304993-118305018	CACUCCAUCCUACUCACCUGAUAAG	597
916_3_1	CD3E	Exon 3	+	chr11:118307263-118307288	UUUUUUUUCUUAUUUAUUUUCUAGU	598
916_3_2	CD3E	Exon 3	+	chr11:118307270-118307295	UCUUAUUUAUUUUCUAGUUGGCGUU	599
916_3_3	CD3E	Exon 3	+	chr11:118307271-118307296	CUUAUUUAUUUUCUAGUUGGCGUUU	600
916_3_4	CD3E	Exon 3	+	chr11:118307272-118307297	UUAUUUAUUUUCUAGUUGGCGUUUG	601
916_3_5	CD3E	Exon 3	+	chr11:118307273-118307298	UAUUUAUUUUCUAGUUGGCGUUUGG	602
916_3_6	CD3E	Exon 3	+	chr11:118307281-118307306	UUCUAGUUGGCGUUUGGGGGCAAGA	603
916_4_1	CD3E	Exon 4	+	chr11:118308413-118308438	GUUUCCUUUUCAGGUAAUGAAGAAA	604
916_4_2	CD3E	Exon 4	+	chr11:118308414-118308439	UUUCCUUUUCAGGUAAUGAAGAAAU	605
916_4_3	CD3E	Exon 4	-	chr11:118308420-118308445	UUACCCAUUUCUUCAUUACCUGAAA	606
916_5_1	CD3E	Exon 5	+	chr11:118312128-118312153	GCUGUUUCCUUUUUUCAUUUUCAGG	607
916_5_2	CD3E	Exon 5	+	chr11:118312155-118312180	GUAUUACACAGACACGUGAGUUUAU	608
916_5_3	CD3E	Exon 5	-	chr11:118312138-118312163	UGUAAUACCACCUGAAAAUGAAAAA	609
916_6_1	CD3E	Exon 6	+	chr11:118312611-118312636	CCCCAGCAUAUAAAGUCUCCAUCUC	610

916_6_2	CD3E	Exon 6	+	chr11:118312647-118312672	UAAUAUUGACAUGCCCUCAGUAUCC	611
916_6_3	CD3E	Exon 6	+	chr11:118312663-118312688	UCAGUAUCCUGGAUCUGAAAUACUA	612
916_6_4	CD3E	Exon 6	+	chr11:118312686-118312711	UAUGGCAACACAAUGAUAAAAACAU	613
916_6_5	CD3E	Exon 6	+	chr11:118312689-118312714	GGCAACACAAUGAUAAAAACAUAGG	614
916_6_6	CD3E	Exon 6	+	chr11:118312697-118312722	AAUGAUAAAAACAUAGGCGGUGAUG	615
916_6_7	CD3E	Exon 6	+	chr11:118312713-118312738	GCGGUGAUGAGGAUGAUAAAAACAU	616
916_6_8	CD3E	Exon 6	+	chr11:118312724-118312749	GAUGAUAAAAACAUAGGCAGUGAUG	617
916_6_9	CD3E	Exon 6	+	chr11:118312742-118312767	AGUGAUGAGGAUCACCUGUCACUGA	618
916_6_10	CD3E	Exon 6	+	chr11:118312757-118312782	CUGUCACUGAAGGAAUUUUCAGAAU	619
916_6_11	CD3E	Exon 6	+	chr11:118312767-118312792	AGGAAUUUUCAGAAUUGGAGCAAAG	620
916_6_12	CD3E	Exon 6	+	chr11:118312791-118312816	GUGGUUAUUAUGUCUGCUACCCCAG	621
916_6_13	CD3E	Exon 6	+	chr11:118312831-118312856	AGAUGCGAACUUUUAUCUCUACCUG	622
916_6_14	CD3E	Exon 6	+	chr11:118312832-118312857	GAUGCGAACUUUUAUCUCUACCUGA	623
916_6_15	CD3E	Exon 6	+	chr11:118312839-118312864	ACUUUUAUCUCUACCUGAGGGCAAG	624
916_6_16	CD3E	Exon 6	+	chr11:118312848-118312873	UCUACCUGAGGGCAAGAGGUAAUCC	625
916_6_17	CD3E	Exon 6	+	chr11:118312861-118312886	AAGAGGUAAUCCAGGUCUCCAGAAC	626
916_6_18	CD3E	Exon 6	-	chr11:118312596-118312621	UAUGCUGGGGAGAAAGAAGGGAAAU	627
916_6_19	CD3E	Exon 6	-	chr11:118312603-118312628	GACUUUAUAUGCUGGGGAGAAAGAA	628
916_6_20	CD3E	Exon 6	-	chr11:118312604-118312629	AGACUUUAUAUGCUGGGGAGAAAGA	629
916_6_21	CD3E	Exon 6	-	chr11:118312614-118312639	CCAGAGAUGGAGACUUUAUAUGCUG	630
916_6_22	CD3E	Exon 6	-	chr11:118312615-118312640	UCCAGAGAUGGAGACUUUAUAUGCU	631
916_6_23	CD3E	Exon 6	-	chr11:118312616-118312641	UUCCAGAGAUGGAGACUUUAUAUGC	632
916_6_24	CD3E	Exon 6	-	chr11:118312632-118312657	GUCAAUAUUACUGUGGUUCCAGAGA	633
916_6_25	CD3E	Exon 6	-	chr11:118312644-118312669	UACUGAGGGCAUGUCAAUAUUACUG	634
916_6_26	CD3E	Exon 6	-	chr11:118312663-118312688	UAGUAUUUCAGAUCCAGGAUACUGA	635

916_6_27	CD3E	Exon 6	-	chr11:118312664-118312689	AUAGUAUUUCAGAUCCAGGAUACUG	636
916_6_28	CD3E	Exon 6	-	chr11:118312673-118312698	UGUGUUGCCAUAGUAUUUCAGAUCC	637
916_6_29	CD3E	Exon 6	-	chr11:118312759-118312784	CAAUUCUGAAAAUUCCUUCAGUGAC	638
916_6_30	CD3E	Exon 6	-	chr11:118312813-118312838	CGCAUCUUCUGGUUUGCUUCCUCUG	639
916_6_31	CD3E	Exon 6	-	chr11:118312814-118312839	UCGCAUCUUCUGGUUUGCUUCCUCU	640
916_6_32	CD3E	Exon 6	-	chr11:118312815-118312840	UUCGCAUCUUCUGGUUUGCUUCCUC	641
916_6_33	CD3E	Exon 6	-	chr11:118312829-118312854	GGUAGAGAUAAAAGUUCGCAUCUUC	642
916_6_34	CD3E	Exon 6	-	chr11:118312855-118312880	GAGACCUGGAUUACCUCUUGCCCUC	643
916_7_1	CD3E	Exon 7	+	chr11:118313696-118313721	CCCCCCACAGUGUGUGAGAACUGCA	644
916_7_2	CD3E	Exon 7	+	chr11:118313702-118313727	ACAGUGUGUGAGAACUGCAUGGAGA	645
916_7_3	CD3E	Exon 7	+	chr11:118313714-118313739	AACUGCAUGGAGAUGGAUGUGAUGU	646
916_7_4	CD3E	Exon 7	+	chr11:118313717-118313742	UGCAUGGAGAUGGAUGUGAUGUCGG	647
916_7_5	CD3E	Exon 7	+	chr11:118313735-118313760	AUGUCGGUGGCCACAAUUGUCAUAG	648
916_7_6	CD3E	Exon 7	+	chr11:118313751-118313776	UUGUCAUAGUGGACAUCUGCAUCAC	649
916_7_7	CD3E	Exon 7	+	chr11:118313752-118313777	UGUCAUAGUGGACAUCUGCAUCACU	650
916_7_8	CD3E	Exon 7	+	chr11:118313753-118313778	GUCAUAGUGGACAUCUGCAUCACUG	651
916_7_9	CD3E	Exon 7	+	chr11:118313754-118313779	UCAUAGUGGACAUCUGCAUCACUGG	652
916_7_10	CD3E	Exon 7	+	chr11:118313768-118313793	UGCAUCACUGGGGGCUUGCUGCUGC	653
916_7_11	CD3E	Exon 7	+	chr11:118313779-118313804	GGGCUUGCUGCUGCUGGUUUACUAC	654
916_7_12	CD3E	Exon 7	+	chr11:118313795-118313820	GUUUACUACUGGAGCAAGAAUAGAA	655
916_7_13	CD3E	Exon 7	+	chr11:118313801-118313826	UACUGGAGCAAGAAUAGAAAGGCCA	656
916_7_14	CD3E	Exon 7	+	chr11:118313820-118313845	AGGCCAAGGCCAAGCCUGUGACACG	657
916_7_15	CD3E	Exon 7	+	chr11:118313825-118313850	AAGGCCAAGCCUGUGACACGAGGAG	658
916_7_16	CD3E	Exon 7	+	chr11:118313826-118313851	AGGCCAAGCCUGUGACACGAGGAGC	659
916_7_17	CD3E	Exon 7	+	chr11:118313832-118313857	AGCCUGUGACACGAGGAGCGGGUGC	660

916_7_18	CD3E	Exon 7	+	chr11:118313835-118313860	CUGUGACACGAGGAGCGGGUGCUGG	661
916_7_19	CD3E	Exon 7	+	chr11:118313839-118313864	GACACGAGGAGCGGGUGCUGGCGGC	662
916_7_20	CD3E	Exon 7	+	chr11:118313845-118313870	AGGAGCGGGUGCUGGCGGCAGGCAA	663
916_7_21	CD3E	Exon 7	+	chr11:118313846-118313871	GGAGCGGGUGCUGGCGGCAGGCAAA	664
916_7_22	CD3E	Exon 7	+	chr11:118313847-118313872	GAGCGGGUGCUGGCGGCAGGCAAAG	665
916_7_23	CD3E	Exon 7	+	chr11:118313852-118313877	GGUGCUGGCGGCAGGCAAAGGGGUA	666
916_7_24	CD3E	Exon 7	+	chr11:118313858-118313883	GGCGGCAGGCAAAGGGGUAAGGCUG	667
916_7_25	CD3E	Exon 7	-	chr11:118313684-118313709	ACACUGUGGGGGGUGGGGUGGGGAG	668
916_7_26	CD3E	Exon 7	-	chr11:118313689-118313714	CUCACACACUGUGGGGGGUGGGGUG	669
916_7_27	CD3E	Exon 7	-	chr11:118313690-118313715	UCUCACACACUGUGGGGGGUGGGGU	670
916_7_28	CD3E	Exon 7	-	chr11:118313691-118313716	UUCUCACACACUGUGGGGGGUGGGG	671
916_7_29	CD3E	Exon 7	-	chr11:118313694-118313719	CAGUUCUCACACACUGUGGGGGGUG	672
916_7_30	CD3E	Exon 7	-	chr11:118313695-118313720	GCAGUUCUCACACACUGUGGGGGGU	673
916_7_31	CD3E	Exon 7	-	chr11:118313696-118313721	UGCAGUUCUCACACACUGUGGGGGG	674
916_7_32	CD3E	Exon 7	-	chr11:118313699-118313724	CCAUGCAGUUCUCACACACUGUGGG	675
916_7_33	CD3E	Exon 7	-	chr11:118313700-118313725	UCCAUGCAGUUCUCACACACUGUGG	676
916_7_34	CD3E	Exon 7	-	chr11:118313701-118313726	CUCCAUGCAGUUCUCACACACUGUG	677
916_7_35	CD3E	Exon 7	-	chr11:118313702-118313727	UCUCCAUGCAGUUCUCACACACUGU	678
916_7_36	CD3E	Exon 7	-	chr11:118313703-118313728	AUCUCCAUGCAGUUCUCACACACUG	679
916_7_37	CD3E	Exon 7	-	chr11:118313748-118313773	AUGCAGAUGUCCACUAUGACAAUUG	680
916_7_38	CD3E	Exon 7	-	chr11:118313826-118313851	GCUCCUCGUGUCACAGGCUUGGCCU	681
916_7_39	CD3E	Exon 7	-	chr11:118313832-118313857	GCACCCGCUCCUCGUGUCACAGGCU	682
916_7_40	CD3E	Exon 7	-	chr11:118313837-118313862	CGCCAGCACCCGCUCCUCGUGUCAC	683
916_8_1	CD3E	Exon 8	+	chr11:118314431-118314456	CCUCCUUCCUCCGCAGGACAAAACA	684
916_8_2	CD3E	Exon 8	+	chr11:118314436-118314461	UUCCUCCGCAGGACAAAACAAGGAG	685

916_8_3	CD3E	Exon 8	+	chr11:118314467-118314492	CCACCUGUUCCCAACCCAGACUAUG	686
916_8_4	CD3E	Exon 8	+	chr11:118314475-118314500	UCCCAACCCAGACUAUGAGGUAACG	687
916_8_5	CD3E	Exon 8	+	chr11:118314476-118314501	CCCAACCCAGACUAUGAGGUAACGU	688
916_8_6	CD3E	Exon 8	+	chr11:118314486-118314511	ACUAUGAGGUAACGUGGGAUAGAAA	689
916_8_7	CD3E	Exon 8	+	chr11:118314487-118314512	CUAUGAGGUAACGUGGGAUAGAAAU	690
916_8_8	CD3E	Exon 8	-	chr11:118314432-118314457	UUGUUUUGUCCUGCGGAGGAAGGAG	691
916_8_9	CD3E	Exon 8	-	chr11:118314433-118314458	CUUGUUUUGUCCUGCGGAGGAAGGA	692
916_8_10	CD3E	Exon 8	-	chr11:118314434-118314459	CCUUGUUUUGUCCUGCGGAGGAAGG	693
916_8_11	CD3E	Exon 8	-	chr11:118314437-118314462	UCUCCUUGUUUUGUCCUGCGGAGGA	694
916_8_12	CD3E	Exon 8	-	chr11:118314441-118314466	GGCCUCUCCUUGUUUUGUCCUGCGG	695
916_8_13	CD3E	Exon 8	-	chr11:118314444-118314469	GGUGGCCUCUCCUUGUUUUGUCCUG	696
916_8_14	CD3E	Exon 8	-	chr11:118314467-118314492	CAUAGUCUGGGUUGGGAACAGGUGG	697
916_8_15	CD3E	Exon 8	-	chr11:118314470-118314495	CCUCAUAGUCUGGGUUGGGAACAGG	698
916_8_16	CD3E	Exon 8	-	chr11:118314473-118314498	UUACCUCAUAGUCUGGGUUGGGAAC	699
916_8_17	CD3E	Exon 8	-	chr11:118314479-118314504	CCCACGUUACCUCAUAGUCUGGGUU	700
916_8_18	CD3E	Exon 8	-	chr11:118314480-118314505	UCCCACGUUACCUCAUAGUCUGGGU	701
916_8_19	CD3E	Exon 8	-	chr11:118314484-118314509	UCUAUCCCACGUUACCUCAUAGUCU	702
916_8_20	CD3E	Exon 8	-	chr11:118314485-118314510	UUCUAUCCCACGUUACCUCAUAGUC	703
916_9_1	CD3E	Exon 9	+	chr11:118315466-118315491	CUCUCUAUUUCACCCCCAGCCCAUC	704
916_9_2	CD3E	Exon 9	+	chr11:118315471-118315496	UAUUUCACCCCCAGCCCAUCCGGAA	705
916_9_3	CD3E	Exon 9	+	chr11:118315478-118315503	CCCCCAGCCCAUCCGGAAAGGCCAG	706
916_9_4	CD3E	Exon 9	+	chr11:118315479-118315504	CCCCAGCCCAUCCGGAAAGGCCAGC	707
916_9_5	CD3E	Exon 9	+	chr11:118315492-118315517	GGAAAGGCCAGCGGGACCUGUAUUC	708
916_9_6	CD3E	Exon 9	+	chr11:118315522-118315547	UGAAUCAGAGACGCAUCUGACCCUC	709
916_9_7	CD3E	Exon 9	+	chr11:118315542-118315567	CCCUCUGGAGAACACUGCCUCCCGC	710

916_9_8	CD3E	Exon 9	+	chr11:118315548-118315573	GGAGAACACUGCCUCCCGCUGGCCC	711
916_9_9	CD3E	Exon 9	+	chr11:118315586-118315611	AGUCCCCCUGCGACUCCCUGUUUCC	712
916_9_10	CD3E	Exon 9	+	chr11:118315587-118315612	GUCCCCCUGCGACUCCCUGUUUCCU	713
916_9_11	CD3E	Exon 9	+	chr11:118315597-118315622	GACUCCCUGUUUCCUGGGCUAGUCU	714
916_9_12	CD3E	Exon 9	+	chr11:118315632-118315657	GAGAGAGAAUCGUUCCUCAGCCUCA	715
916_9_13	CD3E	Exon 9	+	chr11:118315689-118315714	GCUCCCUCCUCCCUGCCUUCUCUGC	716
916_9_14	CD3E	Exon 9	+	chr11:118315760-118315785	UCAUCAGUAGUCACACCCUCACAGC	717
916_9_15	CD3E	Exon 9	+	chr11:118315777-118315802	CUCACAGCUGGCCUGCCCUCUUGCC	718
916_9_16	CD3E	Exon 9	+	chr11:118315812-118315837	UUUGUGCUAUUCACUCCCUUCCCUU	719
916_9_17	CD3E	Exon 9	+	chr11:118315921-118315946	CGCCGUCCCCUUUUGCAGCCCUCUC	720
916_9_18	CD3E	Exon 9	+	chr11:118315922-118315947	GCCGUCCCCUUUUGCAGCCCUCUCU	721
916_9_19	CD3E	Exon 9	+	chr11:118315923-118315948	CCGUCCCCUUUUGCAGCCCUCUCUG	722
916_9_20	CD3E	Exon 9	+	chr11:118315927-118315952	CCCCUUUUGCAGCCCUCUCUGGGGA	723
916_9_21	CD3E	Exon 9	+	chr11:118315932-118315957	UUUGCAGCCCUCUCUGGGGAUGGAC	724
916_9_22	CD3E	Exon 9	+	chr11:118315933-118315958	UUGCAGCCCUCUCUGGGGAUGGACU	725
916_9_23	CD3E	Exon 9	+	chr11:118315949-118315974	GGAUGGACUGGGUAAAUGUUGACAG	726
916_9_24	CD3E	Exon 9	+	chr11:118315973-118315998	GAGGCCCUGCCCCGUUCACAGAUCC	727
916_9_25	CD3E	Exon 9	+	chr11:118316062-118316087	ACUCCCUCCACCCCCCUCCACUGU	728
916_9_26	CD3E	Exon 9	+	chr11:118316069-118316094	CCACCCCCCCUCCACUGUAGGCCAC	729
916_9_27	CD3E	Exon 9	+	chr11:118316073-118316098	CCCCCCUCCACUGUAGGCCACUGGA	730
916_9_28	CD3E	Exon 9	+	chr11:118316139-118316164	GAGAGAGAAAAAAAUAAACUGUAUU	731
916_9_29	CD3E	Exon 9	-	chr11:118315465-118315490	AUGGGCUGGGGGUGAAAUAGAGAGG	732
916_9_30	CD3E	Exon 9	-	chr11:118315466-118315491	GAUGGGCUGGGGGUGAAAUAGAGAG	733
916_9_31	CD3E	Exon 9	-	chr11:118315467-118315492	GGAUGGGCUGGGGGUGAAAUAGAGA	734
916_9_32	CD3E	Exon 9	-	chr11:118315468-118315493	CGGAUGGGCUGGGGGUGAAAUAGAG	735

916_9_33	CD3E	Exon 9	-	chr11:118315481-118315506	CCGCUGGCCUUUCCGGAUGGGCUGG	736
916_9_34	CD3E	Exon 9	-	chr11:118315482-118315507	CCCGCUGGCCUUUCCGGAUGGGCUG	737
916_9_35	CD3E	Exon 9	-	chr11:118315483-118315508	UCCCGCUGGCCUUUCCGGAUGGGCU	738
916_9_36	CD3E	Exon 9	-	chr11:118315484-118315509	GUCCCGCUGGCCUUUCCGGAUGGGC	739
916_9_37	CD3E	Exon 9	-	chr11:118315488-118315513	ACAGGUCCCGCUGGCCUUUCCGGAU	740
916_9_38	CD3E	Exon 9	-	chr11:118315489-118315514	UACAGGUCCCGCUGGCCUUUCCGGA	741
916_9_39	CD3E	Exon 9	-	chr11:118315493-118315518	AGAAUACAGGUCCCGCUGGCCUUUC	742
916_9_40	CD3E	Exon 9	-	chr11:118315502-118315527	AUUCAGGCCAGAAUACAGGUCCCGC	743
916_9_41	CD3E	Exon 9	-	chr11:118315511-118315536	GCGUCUCUGAUUCAGGCCAGAAUAC	744
916_9_42	CD3E	Exon 9	-	chr11:118315523-118315548	AGAGGGUCAGAUGCGUCUCUGAUUC	745
916_9_43	CD3E	Exon 9	-	chr11:118315545-118315570	CCAGCGGGAGGCAGUGUUCUCCAGA	746
916_9_44	CD3E	Exon 9	-	chr11:118315546-118315571	GCCAGCGGGAGGCAGUGUUCUCCAG	747
916_9_45	CD3E	Exon 9	-	chr11:118315562-118315587	UGGAGAGGAGACCUGGGCCAGCGGG	748
916_9_46	CD3E	Exon 9	-	chr11:118315565-118315590	GACUGGAGAGGAGACCUGGGCCAGC	749
916_9_47	CD3E	Exon 9	-	chr11:118315566-118315591	GGACUGGAGAGGAGACCUGGGCCAG	750
916_9_48	CD3E	Exon 9	-	chr11:118315573-118315598	CGCAGGGGGACUGGAGAGGAGACCU	751
916_9_49	CD3E	Exon 9	-	chr11:118315574-118315599	UCGCAGGGGGACUGGAGAGGAGACC	752
916_9_50	CD3E	Exon 9	-	chr11:118315582-118315607	ACAGGGAGUCGCAGGGGGACUGGAG	753
916_9_51	CD3E	Exon 9	-	chr11:118315587-118315612	AGGAAACAGGGAGUCGCAGGGGGAC	754
916_9_52	CD3E	Exon 9	-	chr11:118315592-118315617	AGCCCAGGAAACAGGGAGUCGCAGG	755
916_9_53	CD3E	Exon 9	-	chr11:118315593-118315618	UAGCCCAGGAAACAGGGAGUCGCAG	756
916_9_54	CD3E	Exon 9	-	chr11:118315594-118315619	CUAGCCCAGGAAACAGGGAGUCGCA	757
916_9_55	CD3E	Exon 9	-	chr11:118315595-118315620	ACUAGCCCAGGAAACAGGGAGUCGC	758
916_9_56	CD3E	Exon 9	-	chr11:118315604-118315629	GGGUCCAAGACUAGCCCAGGAAACA	759
916_9_57	CD3E	Exon 9	-	chr11:118315605-118315630	GGGGUCCAAGACUAGCCCAGGAAAC	760

916_9_58	CD3E	Exon 9	-	chr11:118315612-118315637	CUCUCGUGGGGUCCAAGACUAGCCC	761
916_9_59	CD3E	Exon 9	-	chr11:118315629-118315654	GGCUGAGGAACGAUUCUCUCUCGUG	762
916_9_60	CD3E	Exon 9	-	chr11:118315630-118315655	AGGCUGAGGAACGAUUCUCUCUCGU	763
916_9_61	CD3E	Exon 9	-	chr11:118315631-118315656	GAGGCUGAGGAACGAUUCUCUCUCG	764
916_9_62	CD3E	Exon 9	-	chr11:118315649-118315674	UCCCGCGGAGUUCACCAUGAGGCUG	765
916_9_63	CD3E	Exon 9	-	chr11:118315655-118315680	CCGACCUCCCGCGGAGUUCACCAUG	766
916_9_64	CD3E	Exon 9	-	chr11:118315722-118315747	GAGGAAGCAGCAAUAUUUUAGGACU	767
916_9_65	CD3E	Exon 9	-	chr11:118315723-118315748	AGAGGAAGCAGCAAUAUUUUAGGAC	768
916_9_66	CD3E	Exon 9	-	chr11:118315728-118315753	AAGGAAGAGGAAGCAGCAAUAUUUU	769
916_9_67	CD3E	Exon 9	-	chr11:118315746-118315771	ACUACUGAUGAUGCUUCAAAGGAAG	770
916_9_68	CD3E	Exon 9	-	chr11:118315752-118315777	GGUGUGACUACUGAUGAUGCUUCAA	771
916_9_69	CD3E	Exon 9	-	chr11:118315778-118315803	UGGCAAGAGGGCAGGCCAGCUGUGA	772
916_9_70	CD3E	Exon 9	-	chr11:118315779-118315804	CUGGCAAGAGGGCAGGCCAGCUGUG	773
916_9_71	CD3E	Exon 9	-	chr11:118315791-118315816	CAAAUAAAUAUCCUGGCAAGAGGGC	774
916_9_72	CD3E	Exon 9	-	chr11:118315795-118315820	AGCACAAAUAAAUAUCCUGGCAAGA	775
916_9_73	CD3E	Exon 9	-	chr11:118315796-118315821	UAGCACAAAUAAAUAUCCUGGCAAG	776
916_9_74	CD3E	Exon 9	-	chr11:118315803-118315828	GAGUGAAUAGCACAAAUAAAUAUCC	777
916_9_75	CD3E	Exon 9	-	chr11:118315830-118315855	ACGGAGAAGUUACAUCCAAAGGGAA	778
916_9_76	CD3E	Exon 9	-	chr11:118315831-118315856	AACGGAGAAGUUACAUCCAAAGGGA	779
916_9_77	CD3E	Exon 9	-	chr11:118315835-118315860	ACUGAACGGAGAAGUUACAUCCAAA	780
916_9_78	CD3E	Exon 9	-	chr11:118315836-118315861	AACUGAACGGAGAAGUUACAUCCAA	781
916_9_79	CD3E	Exon 9	-	chr11:118315854-118315879	CAUGCAAGAAAAGGAGGGAACUGAA	782
916_9_80	CD3E	Exon 9	-	chr11:118315864-118315889	GGACAACUUACAUGCAAGAAAAGGA	783
916_9_81	CD3E	Exon 9	-	chr11:118315865-118315890	GGGACAACUUACAUGCAAGAAAAGG	784
916_9_82	CD3E	Exon 9	-	chr11:118315868-118315893	UGGGGGACAACUUACAUGCAAGAAA	785

916_9_83	CD3E	Exon 9	-	chr11:118315890-118315915	AAGUAGAUGGAAUACUUUGGGAUGG	786
916_9_84	CD3E	Exon 9	-	chr11:118315891-118315916	AAAGUAGAUGGAAUACUUUGGGAUG	787
916_9_85	CD3E	Exon 9	-	chr11:118315892-118315917	AAAAGUAGAUGGAAUACUUUGGGAU	788
916_9_86	CD3E	Exon 9	-	chr11:118315893-118315918	GAAAAGUAGAUGGAAUACUUUGGGA	789
916_9_87	CD3E	Exon 9	-	chr11:118315897-118315922	GAUAGAAAAGUAGAUGGAAUACUUU	790
916_9_88	CD3E	Exon 9	-	chr11:118315898-118315923	CGAUAGAAAAGUAGAUGGAAUACUU	791
916_9_89	CD3E	Exon 9	-	chr11:118315908-118315933	AAGGGGACGGCGAUAGAAAAGUAGA	792
916_9_90	CD3E	Exon 9	-	chr11:118315926-118315951	CCCCAGAGAGGGCUGCAAAAGGGGA	793
916_9_91	CD3E	Exon 9	-	chr11:118315930-118315955	CCAUCCCCAGAGAGGCUGCAAAAG	794
916_9_92	CD3E	Exon 9	-	chr11:118315931-118315956	UCCAUCCCCAGAGAGGGCUGCAAAA	795
916_9_93	CD3E	Exon 9	-	chr11:118315932-118315957	GUCCAUCCCCAGAGAGGGCUGCAAA	796
916_9_94	CD3E	Exon 9	-	chr11:118315942-118315967	CAUUUACCCAGUCCAUCCCCAGAGA	797
916_9_95	CD3E	Exon 9	-	chr11:118315943-118315968	ACAUUUACCCAGUCCAUCCCCAGAG	798
916_9_96	CD3E	Exon 9	-	chr11:118315980-118316005	AGGGCCAGGAUCUGUGAACGGGGCA	799
916_9_97	CD3E	Exon 9	-	chr11:118315981-118316006	CAGGGCCAGGAUCUGUGAACGGGGC	800
916_9_98	CD3E	Exon 9	-	chr11:118315985-118316010	GGCUCAGGGCCAGGAUCUGUGAACG	801
916_9_99	CD3E	Exon 9	-	chr11:118315986-118316011	UGGCUCAGGGCCAGGAUCUGUGAAC	802
916_9_100	CD3E	Exon 9	-	chr11:118315987-118316012	CUGGCUCAGGGCCAGGAUCUGUGAA	803
916_9_101	CD3E	Exon 9	-	chr11:118315999-118316024	AGGAGCACAGGGCUGGCUCAGGGCC	804
916_9_102	CD3E	Exon 9	-	chr11:118316004-118316029	GAGGGAGGAGCACAGGGCUGGCUCA	805
916_9_103	CD3E	Exon 9	-	chr11:118316005-118316030	GGAGGGAGGAGCACAGGGCUGGCUC	806
916_9_104	CD3E	Exon 9	-	chr11:118316011-118316036	GUUGGGGGAGGGAGGAGCACAGGGC	807
916_9_105	CD3E	Exon 9	-	chr11:118316015-118316040	GAGUGUUGGGGGAGGGAGGAGCACA	808
916_9_106	CD3E	Exon 9	-	chr11:118316016-118316041	GGAGUGUUGGGGGAGGGAGGAGCAC	809
916_9_107	CD3E	Exon 9	-	chr11:118316024-118316049	GUUGGUAGGGAGUGUUGGGGGAGGG	810

916_9_108	CD3E	Exon 9	-	chr11:118316027-118316052	GGGGUUGGUAGGGAGUGUUGGGGGA	811
916_9_109	CD3E	Exon 9	-	chr11:118316028-118316053	GGGGGUUGGUAGGGAGUGUUGGGGG	812
916_9_110	CD3E	Exon 9	-	chr11:118316031-118316056	UUAGGGGGUUGGUAGGGAGUGUUGG	813
916_9_111	CD3E	Exon 9	-	chr11:118316032-118316057	AUUAGGGGGUUGGUAGGGAGUGUUG	814
916_9_112	CD3E	Exon 9	-	chr11:118316033-118316058	GAUUAGGGGGUUGGUAGGGAGUGUU	815
916_9_113	CD3E	Exon 9	-	chr11:118316034-118316059	GGAUUAGGGGGUUGGUAGGGAGUGU	816
916_9_114	CD3E	Exon 9	-	chr11:118316042-118316067	GGAGUAGGGGAUUAGGGGGUUGGUA	817
916_9_115	CD3E	Exon 9	-	chr11:118316043-118316068	GGGAGUAGGGGAUUAGGGGGUUGGU	818
916_9_116	CD3E	Exon 9	-	chr11:118316047-118316072	UGGAGGGAGUAGGGGAUUAGGGGGU	819
916_9_117	CD3E	Exon 9	-	chr11:118316051-118316076	GGGGUGGAGGGAGUAGGGGAUUAGG	820
916_9_118	CD3E	Exon 9	-	chr11:118316052-118316077	GGGGGUGGAGGGAGUAGGGGAUUAG	821
916_9_119	CD3E	Exon 9	-	chr11:118316053-118316078	GGGGGGUGGAGGGAGUAGGGGAUUA	822
916_9_120	CD3E	Exon 9	-	chr11:118316054-118316079	GGGGGGGUGGAGGGAGUAGGGGAUU	823
916_9_121	CD3E	Exon 9	-	chr11:118316060-118316085	AGUGGAGGGGGGGUGGAGGGAGUAG	824
916_9_122	CD3E	Exon 9	-	chr11:118316061-118316086	CAGUGGAGGGGGGGUGGAGGGAGUA	825
916_9_123	CD3E	Exon 9	-	chr11:118316062-118316087	ACAGUGGAGGGGGGGUGGAGGGAGU	826
916_9_124	CD3E	Exon 9	-	chr11:118316068-118316093	UGGCCUACAGUGGAGGGGGGGUGGA	827
916_9_125	CD3E	Exon 9	-	chr11:118316069-118316094	GUGGCCUACAGUGGAGGGGGGGUGG	828
916_9_126	CD3E	Exon 9	-	chr11:118316072-118316097	CCAGUGGCCUACAGUGGAGGGGGGG	829
916_9_127	CD3E	Exon 9	-	chr11:118316075-118316100	CAUCCAGUGGCCUACAGUGGAGGGG	830
916_9_128	CD3E	Exon 9	-	chr11:118316076-118316101	CCAUCCAGUGGCCUACAGUGGAGGG	831
916_9_129	CD3E	Exon 9	-	chr11:118316077-118316102	ACCAUCCAGUGGCCUACAGUGGAGG	832
916_9_130	CD3E	Exon 9	-	chr11:118316078-118316103	GACCAUCCAGUGGCCUACAGUGGAG	833
916_9_131	CD3E	Exon 9	-	chr11:118316079-118316104	UGACCAUCCAGUGGCCUACAGUGGA	834
916_9_132	CD3E	Exon 9	-	chr11:118316080-118316105	AUGACCAUCCAGUGGCCUACAGUGG	835

916_9_133	CD3E	Exon 9	-	chr11:118316083-118316108	CAAAUGACCAUCCAGUGGCCUACAG	836
916_9_134	CD3E	Exon 9	-	chr11:118316093-118316118	UACGGAGAUGCAAAUGACCAUCCAG	837
916_9_135	CD3E	Exon 9	-	chr11:118316116-118316141	UCAGCUGAGGAGCAGAGCACAUUUA	838
916_9_136	CD3E	Exon 9	-	chr11:118316134-118316159	AGUUUAUUUUUUUCUCUCUCAGCUG	839
917_1_1	CD3G	Exon 1	+	chr11:118344359-118344384	AGGCUGGCUGGCUGGCUGGCUGCUA	840
917_1_2	CD3G	Exon 1	+	chr11:118344360-118344385	GGCUGGCUGGCUGGCUGGCUGCUAA	841
917_1_3	CD3G	Exon 1	+	chr11:118344380-118344405	GCUAAGGGCUGCUCCACGCUUUUGC	842
917_1_4	CD3G	Exon 1	+	chr11:118344383-118344408	AAGGGCUGCUCCACGCUUUUGCCGG	843
917_1_5	CD3G	Exon 1	+	chr11:118344399-118344424	UUUUGCCGGAGGACAGAGACUGACA	844
917_1_6	CD3G	Exon 1	+	chr11:118344405-118344430	CGGAGGACAGAGACUGACAUGGAAC	845
917_1_7	CD3G	Exon 1	+	chr11:118344406-118344431	GGAGGACAGAGACUGACAUGGAACA	846
917_1_8	CD3G	Exon 1	+	chr11:118344407-118344432	GAGGACAGAGACUGACAUGGAACAG	847
917_1_9	CD3G	Exon 1	+	chr11:118344411-118344436	ACAGAGACUGACAUGGAACAGGGGA	848
917_1_10	CD3G	Exon 1	+	chr11:118344412-118344437	CAGAGACUGACAUGGAACAGGGGAA	849
917_1_11	CD3G	Exon 1	+	chr11:118344417-118344442	ACUGACAUGGAACAGGGGAAGGGCC	850
917_1_12	CD3G	Exon 1	+	chr11:118344432-118344457	GGGAAGGGCCUGGCUGUCCUCAUCC	851
917_1_13	CD3G	Exon 1	+	chr11:118344451-118344476	UCAUCCUGGCUAUCAUUCUUCUUCA	852
917_1_14	CD3G	Exon 1	+	chr11:118344456-118344481	CUGGCUAUCAUUCUUCUUCAAGGUA	853
917_1_15	CD3G	Exon 1	+	chr11:118344457-118344482	UGGCUAUCAUUCUUCUUCAAGGUAA	854
917_1_16	CD3G	Exon 1	+	chr11:118344466-118344491	UUCUUCUUCAAGGUAAGGGCCUACU	855
917_1_17	CD3G	Exon 1	+	chr11:118344467-118344492	UCUUCUUCAAGGUAAGGGCCUACUA	856
917_1_18	CD3G	Exon 1	+	chr11:118344468-118344493	CUUCUUCAAGGUAAGGGCCUACUAG	857
917_1_19	CD3G	Exon 1	+	chr11:118344473-118344498	UCAAGGUAAGGGCCUACUAGGGGUC	858
917_1_20	CD3G	Exon 1	-	chr11:118344323-118344348	UCACUGGCUCCACCCAUCACUGUUG	859
917_1_21	CD3G	Exon 1	-	chr11:118344324-118344349	AUCACUGGCUCCACCCAUCACUGUU	860

917_1_22	CD3G	Exon 1	-	chr11:118344325-118344350	GAUCACUGGCUCCACCCAUCACUGU	861
917_1_23	CD3G	Exon 1	-	chr11:118344344-118344369	GUCGGUCGGACACGUCGUCGAUCAC	862
917_1_24	CD3G	Exon 1	-	chr11:118344396-118344421	CAGUCUCUGUCCUCCGGCAAAAGCG	863
917_1_25	CD3G	Exon 1	-	chr11:118344407-118344432	CUGUUCCAUGUCAGUCUCUGUCCUC	864
917_1_26	CD3G	Exon 1	-	chr11:118344443-118344468	AAUGAUAGCCAGGAUGAGGACAGCC	865
917_1_27	CD3G	Exon 1	-	chr11:118344452-118344477	UUGAAGAAGAAUGAUAGCCAGGAUG	866
917_1_28	CD3G	Exon 1	-	chr11:118344458-118344483	CUUACCUUGAAGAAGAAUGAUAGCC	867
917_2_1	CD3G	Exon 2	+	chr11:118349007-118349032	CUCUCUUCUGUCUUUACAGGUACUU	868
917_2_2	CD3G	Exon 2	+	chr11:118349023-118349048	CAGGUACUUUGGCCCAGUCAAUCAA	869
917_2_3	CD3G	Exon 2	+	chr11:118349027-118349052	UACUUUGGCCCAGUCAAUCAAAGGU	870
917_2_4	CD3G	Exon 2	+	chr11:118349035-118349060	CCCAGUCAAUCAAAGGUAGGAGAAA	871
917_2_5	CD3G	Exon 2	-	chr11:118349038-118349063	CCAUUUCUCCUACCUUUGAUUGACU	872
917_2_6	CD3G	Exon 2	-	chr11:118349039-118349064	GCCAUUUCUCCUACCUUUGAUUGAC	873
917_3_1	CD3G	Exon 3	+	chr11:118349726-118349751	GCUUUUCUCAUUUCAGGAAACCACU	874
917_3_2	CD3G	Exon 3	+	chr11:118349732-118349757	CUCAUUUCAGGAAACCACUUGGUUA	875
917_3_3	CD3G	Exon 3	+	chr11:118349754-118349779	UUAAGGUGUAUGACUAUCAAGAAGA	876
917_3_4	CD3G	Exon 3	+	chr11:118349759-118349784	GUGUAUGACUAUCAAGAAGAUGGUU	877
917_3_5	CD3G	Exon 3	+	chr11:118349800-118349825	UGAUGCAGAAGCCAAAAAUAUCACA	878
917_3_6	CD3G	Exon 3	+	chr11:118349811-118349836	CCAAAAAUAUCACAUGGUUUAAAGA	879
917_3_7	CD3G	Exon 3	+	chr11:118349812-118349837	CAAAAAUAUCACAUGGUUUAAAGAU	880
917_3_8	CD3G	Exon 3	+	chr11:118349823-118349848	CAUGGUUUAAAGAUGGGAAGAUGAU	881
917_3_9	CD3G	Exon 3	+	chr11:118349851-118349876	CUUCCUAACUGAAGAUAAAAAAAAA	882
917_3_10	CD3G	Exon 3	+	chr11:118349858-118349883	ACUGAAGAUAAAAAAAAAUGGAAUC	883
917_3_11	CD3G	Exon 3	+	chr11:118349859-118349884	CUGAAGAUAAAAAAAAAUGGAAUCU	884
917_3_12	CD3G	Exon 3	+	chr11:118349873-118349898	AAAUGGAAUCUGGGAAGUAAUGCCA	885

917_3_13	CD3G	Exon 3	+	chr11:118349883-118349908	UGGGAAGUAAUGCCAAGGACCCUCG	886
917_3_14	CD3G	Exon 3	+	chr11:118349884-118349909	GGGAAGUAAUGCCAAGGACCCUCGA	887
917_3_15	CD3G	Exon 3	+	chr11:118349901-118349926	ACCCUCGAGGGAUGUAUCAGUGUAA	888
917_3_16	CD3G	Exon 3	+	chr11:118349960-118349985	UAUUACAGAAGUAUGUAAUCCCCUU	889
917_3_17	CD3G	Exon 3	-	chr11:118349724-118349749	UGGUUUCCUGAAAUGAGAAAAGCCG	890
917_3_18	CD3G	Exon 3	-	chr11:118349749-118349774	UUGAUAGUCAUACACCUUAACCAAG	891
917_3_19	CD3G	Exon 3	-	chr11:118349814-118349839	CCAUCUUUAAACCAUGUGAUAUUUU	892
917_3_20	CD3G	Exon 3	-	chr11:118349857-118349882	AUUCCAUUUUUUUUAUCUUCAGUU	893
917_3_21	CD3G	Exon 3	-	chr11:118349898-118349923	CACUGAUACAUCCCUCGAGGGUCCU	894
917_3_22	CD3G	Exon 3	-	chr11:118349905-118349930	UCCUUUACACUGAUACAUCCCUCGA	895
917_3_23	CD3G	Exon 3	-	chr11:118349906-118349931	AUCCUUUACACUGAUACAUCCCUCG	896
917_3_24	CD3G	Exon 3	-	chr11:118349951-118349976	ACAUACUUCUGUAAUACACUUGGAG	897
917_3_25	CD3G	Exon 3	-	chr11:118349956-118349981	GGAUUACAUACUUCUGUAAUACACU	898
917_4_1	CD3G	Exon 4	+	chr11:118350566-118350591	UUGAACUAAAUGCAGCCACCAUAUC	899
917_4_2	CD3G	Exon 4	+	chr11:118350611-118350636	UCGUCAGCAUUUUCGUCCUUGCUGU	900
917_4_3	CD3G	Exon 4	+	chr11:118350612-118350637	CGUCAGCAUUUUCGUCCUUGCUGUU	901
917_4_4	CD3G	Exon 4	+	chr11:118350613-118350638	GUCAGCAUUUUCGUCCUUGCUGUUG	902
917_4_5	CD3G	Exon 4	+	chr11:118350629-118350654	UUGCUGUUGGGGUCUACUUCAUUGC	903
917_4_6	CD3G	Exon 4	+	chr11:118350634-118350659	GUUGGGGUCUACUUCAUUGCUGGAC	904
917_4_7	CD3G	Exon 4	+	chr11:118350638-118350663	GGGUCUACUUCAUUGCUGGACAGGA	905
917_4_8	CD3G	Exon 4	+	chr11:118350656-118350681	GACAGGAUGGAGUUCGCCAGUCGAG	906
917_4_9	CD3G	Exon 4	-	chr11:118350540-118350565	GCAGUUCUGACACACUGUAGGGAAA	907
917_4_10	CD3G	Exon 4	-	chr11:118350546-118350571	UUCAAUGCAGUUCUGACACACUGUA	908
917_4_11	CD3G	Exon 4	-	chr11:118350547-118350572	GUUCAAUGCAGUUCUGACACACUGU	909
917_4_12	CD3G	Exon 4	-	chr11:118350584-118350609	UCAGCAAAGAGAAAGCCAGAUAUGG	910

917_4_13	CD3G	Exon 4	-	chr11:118350587-118350612	AUUUCAGCAAAGAGAAAGCCAGAUA	911
917_4_14	CD3G	Exon 4	-	chr11:118350630-118350655	AGCAAUGAAGUAGACCCCAACAGCA	912
917_4_15	CD3G	Exon 4	-	chr11:118350675-118350700	UAAGAGCAUUCUUUUACCUCUCGAC	913
917_5_1	CD3G	Exon 5	+	chr11:118351644-118351669	CUGUUGCCCAAUGACCAGCUCUACC	914
917_5_2	CD3G	Exon 5	+	chr11:118351649-118351674	GCCCAAUGACCAGCUCUACCAGGUA	915
917_5_3	CD3G	Exon 5	+	chr11:118351650-118351675	CCCAAUGACCAGCUCUACCAGGUAA	916
917_5_4	CD3G	Exon 5	+	chr11:118351651-118351676	CCAAUGACCAGCUCUACCAGGUAAG	917
917_5_5	CD3G	Exon 5	-	chr11:118351653-118351678	CCCUUACCUGGUAGAGCUGGUCAUU	918
917_5_6	CD3G	Exon 5	-	chr11:118351654-118351679	CCCCUUACCUGGUAGAGCUGGUCAU	919
917_5_7	CD3G	Exon 5	-	chr11:118351661-118351686	UCUUCAUCCCCUUACCUGGUAGAGC	920
917_5_8	CD3G	Exon 5	-	chr11:118351670-118351695	CUCUUUUAUUCUUCAUCCCCUUACC	921
917_6_1	CD3G	Exon 6	+	chr11:118352385-118352410	CUGUGCUGUCCUUUCCAGCCCCUCA	922
917_6_2	CD3G	Exon 6	+	chr11:118352419-118352444	AAGAUGACCAGUACAGCCACCUUCA	923
917_6_3	CD3G	Exon 6	+	chr11:118352432-118352457	CAGCCACCUUCAAGGAAACCAGUUG	924
917_6_4	CD3G	Exon 6	+	chr11:118352435-118352460	CCACCUUCAAGGAAACCAGUUGAGG	925
917_6_5	CD3G	Exon 6	+	chr11:118352448-118352473	AACCAGUUGAGGAGGAAUUGAACUC	926
917_6_6	CD3G	Exon 6	+	chr11:118352460-118352485	AGGAAUUGAACUCAGGACUCAGAGU	927
917_6_7	CD3G	Exon 6	+	chr11:118352463-118352488	AAUUGAACUCAGGACUCAGAGUAGG	928
917_6_8	CD3G	Exon 6	+	chr11:118352464-118352489	AUUGAACUCAGGACUCAGAGUAGGU	929
917_6_9	CD3G	Exon 6	-	chr11:118352397-118352422	CUUCUCGAUCCUUGAGGGGCUGGAA	930
917_6_10	CD3G	Exon 6	-	chr11:118352402-118352427	GUCAUCUUCUCGAUCCUUGAGGGGC	931
917_6_11	CD3G	Exon 6	-	chr11:118352406-118352431	ACUGGUCAUCUUCUCGAUCCUUGAG	932
917_6_12	CD3G	Exon 6	-	chr11:118352407-118352432	UACUGGUCAUCUUCUCGAUCCUUGA	933
917_6_13	CD3G	Exon 6	-	chr11:118352408-118352433	GUACUGGUCAUCUUCUCGAUCCUUG	934
917_6_14	CD3G	Exon 6	-	chr11:118352429-118352454	CUGGUUUCCUUGAAGGUGGCUGUAC	935

917_6_15	CD3G	Exon 6	-	chr11:118352438-118352463	CCUCCUCAACUGGUUUCCUUGAAGG	936
917_6_16	CD3G	Exon 6	-	chr11:118352441-118352466	AUUCCUCCUCAACUGGUUUCCUUGA	937
917_6_17	CD3G	Exon 6	-	chr11:118352453-118352478	GUCCUGAGUUCAAUUCCUCCUCAAC	938
917_7_1	CD3G	Exon 7	+	chr11:118353096-118353121	AUUGCAAUUUUUCUUUUUUCAGUCC	939
917_7_2	CD3G	Exon 7	+	chr11:118353142-118353167	UUCCCAGAAUCAAAGCAAUGCAUUU	940
917_7_3	CD3G	Exon 7	+	chr11:118353188-118353213	ACUUUCAGCCCUAAAUCUAGACUCA	941
917_7_4	CD3G	Exon 7	+	chr11:118353208-118353233	ACUCAAGGUUCCCAGAGAUGACAAA	942
917_7_5	CD3G	Exon 7	+	chr11:118353218-118353243	CCCAGAGAUGACAAAUGGAGAAGAA	943
917_7_6	CD3G	Exon 7	+	chr11:118353236-118353261	AGAAGAAAGGCCAUCAGAGCAAAUU	944
917_7_7	CD3G	Exon 7	+	chr11:118353237-118353262	GAAGAAAGGCCAUCAGAGCAAAUUU	945
917_7_8	CD3G	Exon 7	+	chr11:118353238-118353263	AAGAAAGGCCAUCAGAGCAAAUUUG	946
917_7_9	CD3G	Exon 7	+	chr11:118353239-118353264	AGAAAGGCCAUCAGAGCAAAUUUGG	947
917_7_10	CD3G	Exon 7	+	chr11:118353298-118353323	ACUGUGUUUCAGAAGCGCCACCUAU	948
917_7_11	CD3G	Exon 7	+	chr11:118353299-118353324	CUGUGUUUCAGAAGCGCCACCUAUU	949
917_7_12	CD3G	Exon 7	+	chr11:118353300-118353325	UGUGUUUCAGAAGCGCCACCUAUUG	950
917_7_13	CD3G	Exon 7	+	chr11:118353342-118353367	AAAAUGAAAAGAUCAAAUAACCCCC	951
917_7_14	CD3G	Exon 7	-	chr11:118353122-118353147	GGGAACUGAAUAGGAGGAGAACACC	952
917_7_15	CD3G	Exon 7	-	chr11:118353133-118353158	GCUUUGAUUCUGGGAACUGAAUAGG	953
917_7_16	CD3G	Exon 7	-	chr11:118353136-118353161	AUUGCUUUGAUUCUGGGAACUGAAU	954
917_7_17	CD3G	Exon 7	-	chr11:118353147-118353172	UUCCAAAAUGCAUUGCUUUGAUUCU	955
917_7_18	CD3G	Exon 7	-	chr11:118353148-118353173	UUUCCAAAAUGCAUUGCUUUGAUUC	956
917_7_19	CD3G	Exon 7	-	chr11:118353179-118353204	AUUUAGGGCUGAAAGUCUCUCUGCU	957
917_7_20	CD3G	Exon 7	-	chr11:118353199-118353224	UCUGGGAACCUUGAGUCUAGAUUUA	958
917_7_21	CD3G	Exon 7	-	chr11:118353200-118353225	CUCUGGGAACCUUGAGUCUAGAUUU	959
917_7_22	CD3G	Exon 7	-	chr11:118353221-118353246	CCUUUCUUCUCCAUUUGUCAUCUCU	960

917_7_23	CD3G	Exon 7	-	chr11:118353222-118353247	GCCUUUCUUCUCCAUUUGUCAUCUC	961
917_7_24	CD3G	Exon 7	-	chr11:118353249-118353274	UGAGAAACCCCCAAAUUUGCUCUGA	962
917_7_25	CD3G	Exon 7	-	chr11:118353318-118353343	UUCUUUUACAAUUUUCCCCAAUAGG	963
917_7_26	CD3G	Exon 7	-	chr11:118353321-118353346	UUUUUCUUUUACAAUUUUCCCCAAU	964
917_7_27	CD3G	Exon 7	-	chr11:118353365-118353390	ACAAAAAAUUAUAUUCAAAUCCAGG	965
917_7_28	CD3G	Exon 7	-	chr11:118353366-118353391	CACAAAAAAUUAUAUUCAAAUCCAG	966
917_7_29	CD3G	Exon 7	-	chr11:118353367-118353392	ACACAAAAAAUUAUAUUCAAAUCCA	967
917_7_30	CD3G	Exon 7	-	chr11:118353368-118353393	AACACAAAAAAUUAUAUUCAAAUCC	968
3105_1_1	HLA-A	Exon 1	+	chr6:29942466-29942491	CCAGAGAAGCCAAUCAGUGUCGUCG	969
3105_1_2	HLA-A	Exon 1	+	chr6:29942498-29942523	UGUUCUAAAGCCCGCACGCACCCAC	970
3105_1_3	HLA-A	Exon 1	+	chr6:29942499-29942524	GUUCUAAAGCCCGCACGCACCCACC	971
3105_1_4	HLA-A	Exon 1	+	chr6:29942525-29942550	GGACUCAGAUUCUCCCCAGACGCCG	972
3105_1_5	HLA-A	Exon 1	+	chr6:29942529-29942554	UCAGAUUCUCCCCAGACGCCGAGGA	973
3105_1_6	HLA-A	Exon 1	+	chr6:29942538-29942563	CCCCAGACGCCGAGGAUGGCCGUCA	974
3105_1_7	HLA-A	Exon 1	+	chr6:29942568-29942593	CCCCGAACCCUCCUCCUGCUACUCU	975
3105_1_8	HLA-A	Exon 1	+	chr6:29942569-29942594	CCCGAACCCUCCUCCUGCUACUCUC	976
3105_1_9	HLA-A	Exon 1	+	chr6:29942570-29942595	CCGAACCCUCCUCCUGCUACUCUCG	977
3105_1_10	HLA-A	Exon 1	+	chr6:29942571-29942596	CGAACCCUCCUCCUGCUACUCUCGG	978
3105_1_11	HLA-A	Exon 1	+	chr6:29942577-29942602	CUCCUCCUGCUACUCUCGGGGGCCC	979
3105_1_12	HLA-A	Exon 1	+	chr6:29942594-29942619	GGGGGCCCUGGCCCUGACCCAGACC	980
3105_1_13	HLA-A	Exon 1	+	chr6:29942595-29942620	GGGGCCCUGGCCCUGACCCAGACCU	981
3105_1_14	HLA-A	Exon 1	+	chr6:29942598-29942623	GCCCUGGCCCUGACCCAGACCUGGG	982
3105_1_15	HLA-A	Exon 1	+	chr6:29942599-29942624	CCCUGGCCCUGACCCAGACCUGGGC	983
3105_1_16	HLA-A	Exon 1	+	chr6:29942608-29942633	UGACCCAGACCUGGGCGGGUGAGUG	984
3105_1_17	HLA-A	Exon 1	+	chr6:29942609-29942634	GACCCAGACCUGGGCGGGUGAGUGC	985

3105_1_18	HLA-A	Exon 1	+	chr6:29942610-29942635	ACCCAGACCUGGGCGGGUGAGUGCG	986
3105_1_19	HLA-A	Exon 1	+	chr6:29942614-29942639	AGACCUGGGCGGGUGAGUGCGGGGU	987
3105_1_20	HLA-A	Exon 1	+	chr6:29942615-29942640	GACCUGGGCGGGUGAGUGCGGGGUC	988
3105_1_21	HLA-A	Exon 1	+	chr6:29942618-29942643	CUGGGCGGGUGAGUGCGGGGUCGGG	989
3105_1_22	HLA-A	Exon 1	+	chr6:29942619-29942644	UGGGCGGGUGAGUGCGGGGUCGGGA	990
3105_1_23	HLA-A	Exon 1	-	chr6:29942450-29942475	CUUCUCUGGAAACCCGACACCCAAU	991
3105_1_24	HLA-A	Exon 1	-	chr6:29942451-29942476	GCUUCUCUGGAAACCCGACACCCAA	992
3105_1_25	HLA-A	Exon 1	-	chr6:29942469-29942494	CCGCGACGACACUGAUUGGCUUCUC	993
3105_1_26	HLA-A	Exon 1	-	chr6:29942478-29942503	GAACAGCGACCGCGACGACACUGAU	994
3105_1_27	HLA-A	Exon 1	-	chr6:29942511-29942536	AAUCUGAGUCCCGGUGGGUGCGUGC	995
3105_1_28	HLA-A	Exon 1	-	chr6:29942512-29942537	GAAUCUGAGUCCCGGUGGGUGCGUG	996
3105_1_29	HLA-A	Exon 1	-	chr6:29942521-29942546	GUCUGGGGAGAAUCUGAGUCCCGGU	997
3105_1_30	HLA-A	Exon 1	-	chr6:29942522-29942547	CGUCUGGGGAGAAUCUGAGUCCCGG	998
3105_1_31	HLA-A	Exon 1	-	chr6:29942525-29942550	CGGCGUCUGGGGAGAAUCUGAGUCC	999
3105_1_32	HLA-A	Exon 1	-	chr6:29942541-29942566	CCAUGACGGCCAUCCUCGGCGUCUG	1000
3105_1_33	HLA-A	Exon 1	-	chr6:29942542-29942567	GCCAUGACGGCCAUCCUCGGCGUCU	1001
3105_1_34	HLA-A	Exon 1	-	chr6:29942543-29942568	CGCCAUGACGGCCAUCCUCGGCGUC	1002
3105_1_35	HLA-A	Exon 1	-	chr6:29942550-29942575	UUCGGGGCGCCAUGACGGCCAUCCU	1003
3105_1_36	HLA-A	Exon 1	-	chr6:29942560-29942585	AGGAGGAGGGUUCGGGGCGCCAUGA	1004
3105_1_37	HLA-A	Exon 1	-	chr6:29942571-29942596	CCGAGAGUAGCAGGAGGAGGGUUCG	1005
3105_1_38	HLA-A	Exon 1	-	chr6:29942572-29942597	CCCGAGAGUAGCAGGAGGAGGGUUC	1006
3105_1_39	HLA-A	Exon 1	-	chr6:29942573-29942598	CCCCGAGAGUAGCAGGAGGAGGGUU	1007
3105_1_40	HLA-A	Exon 1	-	chr6:29942578-29942603	AGGGCCCCCGAGAGUAGCAGGAGGA	1008
3105_1_41	HLA-A	Exon 1	-	chr6:29942579-29942604	CAGGGCCCCCGAGAGUAGCAGGAGG	1009
3105_1_42	HLA-A	Exon 1	-	chr6:29942582-29942607	GGCCAGGGCCCCCGAGAGUAGCAGG	1010

3105_1_43	HLA-A	Exon 1	-	chr6:29942585-29942610	CAGGGCCAGGGCCCCCGAGAGUAGC	1011
3105_1_44	HLA-A	Exon 1	-	chr6:29942602-29942627	CCCGCCCAGGUCUGGGUCAGGGCCA	1012
3105_1_45	HLA-A	Exon 1	-	chr6:29942603-29942628	ACCCGCCCAGGUCUGGGUCAGGGCC	1013
3105_1_46	HLA-A	Exon 1	-	chr6:29942608-29942633	CACUCACCCGCCCAGGUCUGGGUCA	1014
3105_1_47	HLA-A	Exon 1	-	chr6:29942609-29942634	GCACUCACCCGCCCAGGUCUGGGUC	1015
3105_1_48	HLA-A	Exon 1	-	chr6:29942614-29942639	ACCCCGCACUCACCCGCCCAGGUCU	1016
3105_1_49	HLA-A	Exon 1	-	chr6:29942615-29942640	GACCCCGCACUCACCCGCCCAGGUC	1017
3105_1_50	HLA-A	Exon 1	-	chr6:29942620-29942645	CUCCCGACCCCGCACUCACCCGCCC	1018
3105_2_1	HLA-A	Exon 2	+	chr6:29942745-29942770	CUCGCCCCCAGGCUCCCACUCCAUG	1019
3105_2_2	HLA-A	Exon 2	+	chr6:29942769-29942794	GAGGUAUUUCUUCACAUCCGUGUCC	1020
3105_2_3	HLA-A	Exon 2	+	chr6:29942774-29942799	AUUUCUUCACAUCCGUGUCCCGGCC	1021
3105_2_4	HLA-A	Exon 2	+	chr6:29942780-29942805	UCACAUCCGUGUCCCGGCCCGGCCG	1022
3105_2_5	HLA-A	Exon 2	+	chr6:29942781-29942806	CACAUCCGUGUCCCGGCCCGGCCGC	1023
3105_2_6	HLA-A	Exon 2	+	chr6:29942782-29942807	ACAUCCGUGUCCCGGCCCGGCCGCG	1024
3105_2_7	HLA-A	Exon 2	+	chr6:29942803-29942828	CGCGGGGAGCCCCGCUUCAUCGCCG	1025
3105_2_8	HLA-A	Exon 2	+	chr6:29942804-29942829	GCGGGGAGCCCCGCUUCAUCGCCGU	1026
3105_2_9	HLA-A	Exon 2	+	chr6:29942812-29942837	CCCCGCUUCAUCGCCGUGGGCUACG	1027
3105_2_10	HLA-A	Exon 2	+	chr6:29942832-29942857	CUACGUGGACGACACGCAGUUCGUG	1028
3105_2_11	HLA-A	Exon 2	+	chr6:29942859-29942884	GUUCGACAGCGACGCCGCGAGCCAG	1029
3105_2_12	HLA-A	Exon 2	+	chr6:29942863-29942888	GACAGCGACGCCGCGAGCCAGAGGA	1030
3105_2_13	HLA-A	Exon 2	+	chr6:29942871-29942896	CGCCGCGAGCCAGAGGAUGGAGCCG	1031
3105_2_14	HLA-A	Exon 2	+	chr6:29942872-29942897	GCCGCGAGCCAGAGGAUGGAGCCGC	1032
3105_2_15	HLA-A	Exon 2	+	chr6:29942880-29942905	CCAGAGGAUGGAGCCGCGGGCGCCG	1033
3105_2_16	HLA-A	Exon 2	+	chr6:29942890-29942915	GAGCCGCGGGCGCCGUGGAUAGAGC	1034
3105_2_17	HLA-A	Exon 2	+	chr6:29942893-29942918	CCGCGGGCGCCGUGGAUAGAGCAGG	1035

3105_2_18	HLA-A	Exon 2	+	chr6:29942894-29942919	CGCGGGCGCCGUGGAUAGAGCAGGA	1036
3105_2_19	HLA-A	Exon 2	+	chr6:29942895-29942920	GCGGGCGCCGUGGAUAGAGCAGGAG	1037
3105_2_20	HLA-A	Exon 2	+	chr6:29942899-29942924	GCGCCGUGGAUAGAGCAGGAGGGGC	1038
3105_2_21	HLA-A	Exon 2	+	chr6:29942907-29942932	GAUAGAGCAGGAGGGGCCGGAGUAU	1039
3105_2_22	HLA-A	Exon 2	+	chr6:29942908-29942933	AUAGAGCAGGAGGGGCCGGAGUAUU	1040
3105_2_23	HLA-A	Exon 2	+	chr6:29942914-29942939	CAGGAGGGGCCGGAGUAUUGGGACC	1041
3105_2_24	HLA-A	Exon 2	+	chr6:29942922-29942947	GCCGGAGUAUUGGGACCAGGAGACA	1042
3105_2_25	HLA-A	Exon 2	+	chr6:29942932-29942957	UGGGACCAGGAGACACGGAAUGUGA	1043
3105_2_26	HLA-A	Exon 2	+	chr6:29942956-29942981	AAGGCCCAGUCACAGACUGACCGAG	1044
3105_2_27	HLA-A	Exon 2	+	chr6:29942962-29942987	CAGUCACAGACUGACCGAGUGGACC	1045
3105_2_28	HLA-A	Exon 2	+	chr6:29942963-29942988	AGUCACAGACUGACCGAGUGGACCU	1046
3105_2_29	HLA-A	Exon 2	+	chr6:29942964-29942989	GUCACAGACUGACCGAGUGGACCUG	1047
3105_2_30	HLA-A	Exon 2	+	chr6:29942975-29943000	ACCGAGUGGACCUGGGGACCCUGCG	1048
3105_2_31	HLA-A	Exon 2	+	chr6:29942995-29943020	CUGCGCGGCUACUACAACCAGAGCG	1049
3105_2_32	HLA-A	Exon 2	+	chr6:29942999-29943024	GCGGCUACUACAACCAGAGCGAGGC	1050
3105_2_33	HLA-A	Exon 2	+	chr6:29943012-29943037	CCAGAGCGAGGCCGGUGAGUGACCC	1051
3105_2_34	HLA-A	Exon 2	+	chr6:29943016-29943041	AGCGAGGCCGGUGAGUGACCCCGGC	1052
3105_2_35	HLA-A	Exon 2	+	chr6:29943017-29943042	GCGAGGCCGGUGAGUGACCCCGGCC	1053
3105_2_36	HLA-A	Exon 2	+	chr6:29943018-29943043	CGAGGCCGGUGAGUGACCCCGGCCG	1054
3105_2_37	HLA-A	Exon 2	+	chr6:29943019-29943044	GAGGCCGGUGAGUGACCCCGGCCGG	1055
3105_2_38	HLA-A	Exon 2	-	chr6:29942742-29942767	GGAGUGGGAGCCUGGGGGCGAGCAG	1056
3105_2_39	HLA-A	Exon 2	-	chr6:29942752-29942777	AAUACCUCAUGGAGUGGGAGCCUGG	1057
3105_2_40	HLA-A	Exon 2	-	chr6:29942753-29942778	AAAUACCUCAUGGAGUGGGAGCCUG	1058
3105_2_41	HLA-A	Exon 2	-	chr6:29942754-29942779	GAAAUACCUCAUGGAGUGGGAGCCU	1059
3105_2_42	HLA-A	Exon 2	-	chr6:29942755-29942780	AGAAAUACCUCAUGGAGUGGGAGCC	1060

3105_2_43	HLA-A	Exon 2	-	chr6:29942762-29942787	GAUGUGAAGAAAUACCUCAUGGAGU	1061
3105_2_44	HLA-A	Exon 2	-	chr6:29942763-29942788	GGAUGUGAAGAAAUACCUCAUGGAG	1062
3105_2_45	HLA-A	Exon 2	-	chr6:29942768-29942793	GACACGGAUGUGAAGAAAUACCUCA	1063
3105_2_46	HLA-A	Exon 2	-	chr6:29942789-29942814	GGCUCCCCGCGGCCGGGCCGGGACA	1064
3105_2_47	HLA-A	Exon 2	-	chr6:29942795-29942820	AAGCGGGGCUCCCCGCGGCCGGGCC	1065
3105_2_48	HLA-A	Exon 2	-	chr6:29942796-29942821	GAAGCGGGGCUCCCCGCGGCCGGGC	1066
3105_2_49	HLA-A	Exon 2	-	chr6:29942800-29942825	CGAUGAAGCGGGGCUCCCCGCGGCC	1067
3105_2_50	HLA-A	Exon 2	-	chr6:29942801-29942826	GCGAUGAAGCGGGGCUCCCCGCGGC	1068
3105_2_51	HLA-A	Exon 2	-	chr6:29942805-29942830	CACGGCGAUGAAGCGGGGCUCCCCG	1069
3105_2_52	HLA-A	Exon 2	-	chr6:29942815-29942840	CCACGUAGCCCACGGCGAUGAAGCG	1070
3105_2_53	HLA-A	Exon 2	-	chr6:29942816-29942841	UCCACGUAGCCCACGGCGAUGAAGC	1071
3105_2_54	HLA-A	Exon 2	-	chr6:29942817-29942842	GUCCACGUAGCCCACGGCGAUGAAG	1072
3105_2_55	HLA-A	Exon 2	-	chr6:29942828-29942853	AACUGCGUGUCGUCCACGUAGCCCA	1073
3105_2_56	HLA-A	Exon 2	-	chr6:29942876-29942901	GCCCGCGGCUCCAUCCUCUGGCUCG	1074
3105_2_57	HLA-A	Exon 2	-	chr6:29942883-29942908	CCACGGCGCCCGCGGCUCCAUCCUC	1075
3105_2_58	HLA-A	Exon 2	-	chr6:29942896-29942921	CCUCCUGCUCUAUCCACGGCGCCCG	1076
3105_2_59	HLA-A	Exon 2	-	chr6:29942905-29942930	ACUCCGGCCCCUCCUGCUCUAUCCA	1077
3105_2_60	HLA-A	Exon 2	-	chr6:29942926-29942951	UCCGUGUCUCCUGGUCCCAAUACUC	1078
3105_2_61	HLA-A	Exon 2	-	chr6:29942940-29942965	CUGGGCCUUCACAUUCCGUGUCUCC	1079
3105_2_62	HLA-A	Exon 2	-	chr6:29942963-29942988	AGGUCCACUCGGUCAGUCUGUGACU	1080
3105_2_63	HLA-A	Exon 2	-	chr6:29942964-29942989	CAGGUCCACUCGGUCAGUCUGUGAC	1081
3105_2_64	HLA-A	Exon 2	-	chr6:29942979-29943004	GCCGCGCAGGGUCCCCAGGUCCACU	1082
3105_2_65	HLA-A	Exon 2	-	chr6:29942988-29943013	GUUGUAGUAGCCGCGCAGGGUCCCC	1083
3105_2_66	HLA-A	Exon 2	-	chr6:29942996-29943021	UCGCUCUGGUUGUAGUAGCCGCGCA	1084
3105_2_67	HLA-A	Exon 2	-	chr6:29942997-29943022	CUCGCUCUGGUUGUAGUAGCCGCGC	1085

3105_2_68	HLA-A	Exon 2	-	chr6:29943015-29943040	CCGGGGUCACUCACCGGCCUCGCUC	1086
3105_2_69	HLA-A	Exon 2	-	chr6:29943026-29943051	UGCGCCCCCGGCCGGGGUCACUCAC	1087
3105_3_1	HLA-A	Exon 3	+	chr6:29943267-29943292	GUUCUCACACCAUCCAGAUAAUGUA	1088
3105_3_2	HLA-A	Exon 3	+	chr6:29943278-29943303	AUCCAGAUAAUGUAUGGCUGCGACG	1089
3105_3_3	HLA-A	Exon 3	+	chr6:29943279-29943304	UCCAGAUAAUGUAUGGCUGCGACGU	1090
3105_3_4	HLA-A	Exon 3	+	chr6:29943280-29943305	CCAGAUAAUGUAUGGCUGCGACGUG	1091
3105_3_5	HLA-A	Exon 3	+	chr6:29943284-29943309	AUAAUGUAUGGCUGCGACGUGGGGU	1092
3105_3_6	HLA-A	Exon 3	+	chr6:29943288-29943313	UGUAUGGCUGCGACGUGGGGUCGGA	1093
3105_3_7	HLA-A	Exon 3	+	chr6:29943289-29943314	GUAUGGCUGCGACGUGGGGUCGGAC	1094
3105_3_8	HLA-A	Exon 3	+	chr6:29943303-29943328	UGGGGUCGGACGGGCGCUUCCUCCG	1095
3105_3_9	HLA-A	Exon 3	+	chr6:29943304-29943329	GGGGUCGGACGGGCGCUUCCUCCGC	1096
3105_3_10	HLA-A	Exon 3	+	chr6:29943310-29943335	GGACGGGCGCUUCCUCCGCGGGUAC	1097
3105_3_11	HLA-A	Exon 3	+	chr6:29943314-29943339	GGGCGCUUCCUCCGCGGGUACCGGC	1098
3105_3_12	HLA-A	Exon 3	+	chr6:29943327-29943352	GCGGGUACCGGCAGGACGCCUACGA	1099
3105_3_13	HLA-A	Exon 3	+	chr6:29943332-29943357	UACCGGCAGGACGCCUACGACGGCA	1100
3105_3_14	HLA-A	Exon 3	+	chr6:29943353-29943378	GGCAAGGAUUACAUCGCCCUGAACG	1101
3105_3_15	HLA-A	Exon 3	+	chr6:29943367-29943392	CGCCCUGAACGAGGACCUGCGCUCU	1102
3105_3_16	HLA-A	Exon 3	+	chr6:29943374-29943399	AACGAGGACCUGCGCUCUUGGACCG	1103
3105_3_17	HLA-A	Exon 3	+	chr6:29943377-29943402	GAGGACCUGCGCUCUUGGACCGCGG	1104
3105_3_18	HLA-A	Exon 3	+	chr6:29943383-29943408	CUGCGCUCUUGGACCGCGGCGGACA	1105
3105_3_19	HLA-A	Exon 3	+	chr6:29943386-29943411	CGCUCUUGGACCGCGGCGGACAUGG	1106
3105_3_20	HLA-A	Exon 3	+	chr6:29943409-29943434	GGCGGCUCAGAUCACCAAGCGCAAG	1107
3105_3_21	HLA-A	Exon 3	+	chr6:29943410-29943435	GCGGCUCAGAUCACCAAGCGCAAGU	1108
3105_3_22	HLA-A	Exon 3	+	chr6:29943413-29943438	GCUCAGAUCACCAAGCGCAAGUGGG	1109
3105_3_23	HLA-A	Exon 3	+	chr6:29943416-29943441	CAGAUCACCAAGCGCAAGUGGGAGG	1110

3105_3_24	HLA-A	Exon 3	+	chr6:29943425-29943450	AAGCGCAAGUGGGAGGCGGCCCAUG	1111
3105_3_25	HLA-A	Exon 3	+	chr6:29943428-29943453	CGCAAGUGGGAGGCGGCCCAUGAGG	1112
3105_3_26	HLA-A	Exon 3	+	chr6:29943449-29943474	GAGGCGGAGCAGUUGAGAGCCUACC	1113
3105_3_27	HLA-A	Exon 3	+	chr6:29943453-29943478	CGGAGCAGUUGAGAGCCUACCUGGA	1114
3105_3_28	HLA-A	Exon 3	+	chr6:29943464-29943489	AGAGCCUACCUGGAUGGCACGUGCG	1115
3105_3_29	HLA-A	Exon 3	+	chr6:29943469-29943494	CUACCUGGAUGGCACGUGCGUGGAG	1116
3105_3_30	HLA-A	Exon 3	+	chr6:29943485-29943510	UGCGUGGAGUGGCUCCGCAGAUACC	1117
3105_3_31	HLA-A	Exon 3	+	chr6:29943492-29943517	AGUGGCUCCGCAGAUACCUGGAGAA	1118
3105_3_32	HLA-A	Exon 3	+	chr6:29943493-29943518	GUGGCUCCGCAGAUACCUGGAGAAC	1119
3105_3_33	HLA-A	Exon 3	+	chr6:29943497-29943522	CUCCGCAGAUACCUGGAGAACGGGA	1120
3105_3_34	HLA-A	Exon 3	+	chr6:29943515-29943540	AACGGGAAGGAGACGCUGCAGCGCA	1121
3105_3_35	HLA-A	Exon 3	+	chr6:29943516-29943541	ACGGGAAGGAGACGCUGCAGCGCAC	1122
3105_3_36	HLA-A	Exon 3	+	chr6:29943523-29943548	GGAGACGCUGCAGCGCACGGGUACC	1123
3105_3_37	HLA-A	Exon 3	+	chr6:29943524-29943549	GAGACGCUGCAGCGCACGGGUACCA	1124
3105_3_38	HLA-A	Exon 3	+	chr6:29943525-29943550	AGACGCUGCAGCGCACGGGUACCAG	1125
3105_3_39	HLA-A	Exon 3	+	chr6:29943531-29943556	UGCAGCGCACGGGUACCAGGGGCCA	1126
3105_3_40	HLA-A	Exon 3	+	chr6:29943532-29943557	GCAGCGCACGGGUACCAGGGGCCAC	1127
3105_3_41	HLA-A	Exon 3	+	chr6:29943533-29943558	CAGCGCACGGGUACCAGGGGCCACG	1128
3105_3_42	HLA-A	Exon 3	-	chr6:29943252-29943277	GUGUGAGAACCUGGCCCCGACCCCG	1129
3105_3_43	HLA-A	Exon 3	-	chr6:29943266-29943291	ACAUUAUCUGGAUGGUGUGAGAACC	1130
3105_3_44	HLA-A	Exon 3	-	chr6:29943279-29943304	ACGUCGCAGCCAUACAUUAUCUGGA	1131
3105_3_45	HLA-A	Exon 3	-	chr6:29943283-29943308	CCCCACGUCGCAGCCAUACAUUAUC	1132
3105_3_46	HLA-A	Exon 3	-	chr6:29943325-29943350	GUAGGCGUCCUGCCGGUACCCGCGG	1133
3105_3_47	HLA-A	Exon 3	-	chr6:29943328-29943353	GUCGUAGGCGUCCUGCCGGUACCCG	1134
3105_3_48	HLA-A	Exon 3	-	chr6:29943337-29943362	AUCCUUGCCGUCGUAGGCGUCCUGC	1135

3105_3_49	HLA-A	Exon 3	-	chr6:29943348-29943373	AGGGCGAUGUAAUCCUUGCCGUCGU	1136
3105_3_50	HLA-A	Exon 3	-	chr6:29943372-29943397	GUCCAAGAGCGCAGGUCCUCGUUCA	1137
3105_3_51	HLA-A	Exon 3	-	chr6:29943373-29943398	GGUCCAAGAGCGCAGGUCCUCGUUC	1138
3105_3_52	HLA-A	Exon 3	-	chr6:29943385-29943410	CAUGUCCGCCGCGGUCCAAGAGCGC	1139
3105_3_53	HLA-A	Exon 3	-	chr6:29943399-29943424	GUGAUCUGAGCCGCCAUGUCCGCCG	1140
3105_3_54	HLA-A	Exon 3	-	chr6:29943426-29943451	UCAUGGGCCGCCUCCCACUUGCGCU	1141
3105_3_55	HLA-A	Exon 3	-	chr6:29943447-29943472	UAGGCUCUCAACUGCUCCGCCUCAU	1142
3105_3_56	HLA-A	Exon 3	-	chr6:29943448-29943473	GUAGGCUCUCAACUGCUCCGCCUCA	1143
3105_3_57	HLA-A	Exon 3	-	chr6:29943471-29943496	CACUCCACGCACGUGCCAUCCAGGU	1144
3105_3_58	HLA-A	Exon 3	-	chr6:29943475-29943500	GAGCCACUCCACGCACGUGCCAUCC	1145
3105_3_59	HLA-A	Exon 3	-	chr6:29943502-29943527	CUCCUUCCCGUUCUCCAGGUAUCUG	1146
3105_3_60	HLA-A	Exon 3	-	chr6:29943511-29943536	CUGCAGCGUCUCCUUCCCGUUCUCC	1147
3105_4_1	HLA-A	Exon 4	+	chr6:29944141-29944166	ACCCACCACCCCAUCUCUGACCAUG	1148
3105_4_2	HLA-A	Exon 4	+	chr6:29944152-29944177	CAUCUCUGACCAUGAGGCCACCCUG	1149
3105_4_3	HLA-A	Exon 4	+	chr6:29944158-29944183	UGACCAUGAGGCCACCCUGAGGUGC	1150
3105_4_4	HLA-A	Exon 4	+	chr6:29944159-29944184	GACCAUGAGGCCACCCUGAGGUGCU	1151
3105_4_5	HLA-A	Exon 4	+	chr6:29944165-29944190	GAGGCCACCCUGAGGUGCUGGGCCC	1152
3105_4_6	HLA-A	Exon 4	+	chr6:29944166-29944191	AGGCCACCCUGAGGUGCUGGGCCCU	1153
3105_4_7	HLA-A	Exon 4	+	chr6:29944180-29944205	UGCUGGGCCCUGGGCUUCUACCCUG	1154
3105_4_8	HLA-A	Exon 4	+	chr6:29944197-29944222	CUACCCUGCGGAGAUCACACUGACC	1155
3105_4_9	HLA-A	Exon 4	+	chr6:29944203-29944228	UGCGGAGAUCACACUGACCUGGCAG	1156
3105_4_10	HLA-A	Exon 4	+	chr6:29944204-29944229	GCGGAGAUCACACUGACCUGGCAGC	1157
3105_4_11	HLA-A	Exon 4	+	chr6:29944208-29944233	AGAUCACACUGACCUGGCAGCGGGA	1158
3105_4_12	HLA-A	Exon 4	+	chr6:29944209-29944234	GAUCACACUGACCUGGCAGCGGGAU	1159
3105_4_13	HLA-A	Exon 4	+	chr6:29944210-29944235	AUCACACUGACCUGGCAGCGGGAUG	1160

3105_4_14	HLA-A	Exon 4	+	chr6:29944213-29944238	ACACUGACCUGGCAGCGGGAUGGGG	1161
3105_4_15	HLA-A	Exon 4	+	chr6:29944225-29944250	CAGCGGGAUGGGGAGGACCAGACCC	1162
3105_4_16	HLA-A	Exon 4	+	chr6:29944231-29944256	GAUGGGGAGGACCAGACCCAGGACA	1163
3105_4_17	HLA-A	Exon 4	+	chr6:29944240-29944265	GACCAGACCCAGGACACGGAGCUCG	1164
3105_4_18	HLA-A	Exon 4	+	chr6:29944248-29944273	CCAGGACACGGAGCUCGUGGAGACC	1165
3105_4_19	HLA-A	Exon 4	+	chr6:29944256-29944281	CGGAGCUCGUGGAGACCAGGCCUGC	1166
3105_4_20	HLA-A	Exon 4	+	chr6:29944257-29944282	GGAGCUCGUGGAGACCAGGCCUGCA	1167
3105_4_21	HLA-A	Exon 4	+	chr6:29944258-29944283	GAGCUCGUGGAGACCAGGCCUGCAG	1168
3105_4_22	HLA-A	Exon 4	+	chr6:29944262-29944287	UCGUGGAGACCAGGCCUGCAGGGGA	1169
3105_4_23	HLA-A	Exon 4	+	chr6:29944278-29944303	UGCAGGGGAUGGAACCUUCCAGAAG	1170
3105_4_24	HLA-A	Exon 4	+	chr6:29944279-29944304	GCAGGGGAUGGAACCUUCCAGAAGU	1171
3105_4_25	HLA-A	Exon 4	+	chr6:29944282-29944307	GGGGAUGGAACCUUCCAGAAGUGGG	1172
3105_4_26	HLA-A	Exon 4	+	chr6:29944288-29944313	GGAACCUUCCAGAAGUGGGCGGCUG	1173
3105_4_27	HLA-A	Exon 4	+	chr6:29944291-29944316	ACCUUCCAGAAGUGGGCGGCUGUGG	1174
3105_4_28	HLA-A	Exon 4	+	chr6:29944301-29944326	AGUGGGCGGCUGUGGUGGUGCCUUC	1175
3105_4_29	HLA-A	Exon 4	+	chr6:29944306-29944331	GCGGCUGUGGUGGUGCCUUCUGGAG	1176
3105_4_30	HLA-A	Exon 4	+	chr6:29944339-29944364	AGAUACACCUGCCAUGUGCAGCAUG	1177
3105_4_31	HLA-A	Exon 4	+	chr6:29944340-29944365	GAUACACCUGCCAUGUGCAGCAUGA	1178
3105_4_32	HLA-A	Exon 4	+	chr6:29944368-29944393	UCUGCCCAAGCCCCUCACCCUGAGA	1179
3105_4_33	HLA-A	Exon 4	+	chr6:29944369-29944394	CUGCCCAAGCCCCUCACCCUGAGAU	1180
3105_4_34	HLA-A	Exon 4	+	chr6:29944370-29944395	UGCCCAAGCCCCUCACCCUGAGAUG	1181
3105_4_35	HLA-A	Exon 4	+	chr6:29944375-29944400	AAGCCCCUCACCCUGAGAUGGGGUA	1182
3105_4_36	HLA-A	Exon 4	+	chr6:29944378-29944403	CCCCUCACCCUGAGAUGGGGUAAGG	1183
3105_4_37	HLA-A	Exon 4	+	chr6:29944379-29944404	CCCUCACCCUGAGAUGGGGUAAGGA	1184
3105_4_38	HLA-A	Exon 4	+	chr6:29944385-29944410	CCCUGAGAUGGGGUAAGGAGGGAGA	1185

3105_4_39	HLA-A	Exon 4	+	chr6:29944386-29944411	CCUGAGAUGGGGUAAGGAGGGAGAU	1186
3105_4_40	HLA-A	Exon 4	+	chr6:29944387-29944412	CUGAGAUGGGGUAAGGAGGGAGAUG	1187
3105_4_41	HLA-A	Exon 4	+	chr6:29944388-29944413	UGAGAUGGGGUAAGGAGGGAGAUGG	1188
3105_4_42	HLA-A	Exon 4	-	chr6:29944116-29944141	CAUAUGUGUCUUGGGGGGGUCUGAC	1189
3105_4_43	HLA-A	Exon 4	-	chr6:29944117-29944142	UCAUAUGUGUCUUGGGGGGGUCUGA	1190
3105_4_44	HLA-A	Exon 4	-	chr6:29944125-29944150	GUGGUGGGUCAUAUGUGUCUUGGGG	1191
3105_4_45	HLA-A	Exon 4	-	chr6:29944126-29944151	GGUGGUGGGUCAUAUGUGUCUUGGG	1192
3105_4_46	HLA-A	Exon 4	-	chr6:29944127-29944152	GGGUGGUGGGUCAUAUGUGUCUUGG	1193
3105_4_47	HLA-A	Exon 4	-	chr6:29944128-29944153	GGGGUGGUGGGUCAUAUGUGUCUUG	1194
3105_4_48	HLA-A	Exon 4	-	chr6:29944129-29944154	UGGGGUGGUGGGUCAUAUGUGUCUU	1195
3105_4_49	HLA-A	Exon 4	-	chr6:29944130-29944155	AUGGGGUGGUGGGUCAUAUGUGUCU	1196
3105_4_50	HLA-A	Exon 4	-	chr6:29944145-29944170	GCCUCAUGGUCAGAGAUGGGGUGGU	1197
3105_4_51	HLA-A	Exon 4	-	chr6:29944146-29944171	GGCCUCAUGGUCAGAGAUGGGGUGG	1198
3105_4_52	HLA-A	Exon 4	-	chr6:29944149-29944174	GGUGGCCUCAUGGUCAGAGAUGGGG	1199
3105_4_53	HLA-A	Exon 4	-	chr6:29944152-29944177	CAGGGUGGCCUCAUGGUCAGAGAUG	1200
3105_4_54	HLA-A	Exon 4	-	chr6:29944153-29944178	UCAGGGUGGCCUCAUGGUCAGAGAU	1201
3105_4_55	HLA-A	Exon 4	-	chr6:29944154-29944179	CUCAGGGUGGCCUCAUGGUCAGAGA	1202
3105_4_56	HLA-A	Exon 4	-	chr6:29944164-29944189	GGCCCAGCACCUCAGGGUGGCCUCA	1203
3105_4_57	HLA-A	Exon 4	-	chr6:29944172-29944197	AAGCCCAGGGCCCAGCACCUCAGGG	1204
3105_4_58	HLA-A	Exon 4	-	chr6:29944175-29944200	UAGAAGCCCAGGGCCCAGCACCUCA	1205
3105_4_59	HLA-A	Exon 4	-	chr6:29944176-29944201	GUAGAAGCCCAGGGCCCAGCACCUC	1206
3105_4_60	HLA-A	Exon 4	-	chr6:29944190-29944215	GUGAUCUCCGCAGGGUAGAAGCCCA	1207
3105_4_61	HLA-A	Exon 4	-	chr6:29944191-29944216	UGUGAUCUCCGCAGGGUAGAAGCCC	1208
3105_4_62	HLA-A	Exon 4	-	chr6:29944203-29944228	CUGCCAGGUCAGUGUGAUCUCCGCA	1209
3105_4_63	HLA-A	Exon 4	-	chr6:29944204-29944229	GCUGCCAGGUCAGUGUGAUCUCCGC	1210

3105_4_64	HLA-A	Exon 4	-	chr6:29944223-29944248	GUCUGGUCCUCCCCAUCCCGCUGCC	1211
3105_4_65	HLA-A	Exon 4	-	chr6:29944245-29944270	CUCCACGAGCUCCGUGUCCUGGGUC	1212
3105_4_66	HLA-A	Exon 4	-	chr6:29944250-29944275	CUGGUCUCCACGAGCUCCGUGUCCU	1213
3105_4_67	HLA-A	Exon 4	-	chr6:29944251-29944276	CCUGGUCUCCACGAGCUCCGUGUCC	1214
3105_4_68	HLA-A	Exon 4	-	chr6:29944274-29944299	UGGAAGGUUCCAUCCCUGCAGGCC	1215
3105_4_69	HLA-A	Exon 4	-	chr6:29944279-29944304	ACUUCUGGAAGGUUCCAUCCCCUGC	1216
3105_4_70	HLA-A	Exon 4	-	chr6:29944295-29944320	ACCACCACAGCCGCCCACUUCUGGA	1217
3105_4_71	HLA-A	Exon 4	-	chr6:29944299-29944324	AGGCACCACCACAGCCGCCCACUUC	1218
3105_4_72	HLA-A	Exon 4	-	chr6:29944324-29944349	AGGUGUAUCUCUGCUCCUCUCCAGA	1219
3105_4_73	HLA-A	Exon 4	-	chr6:29944349-29944374	GGCAGACCCUCAUGCUGCACAUGGC	1220
3105_4_74	HLA-A	Exon 4	-	chr6:29944353-29944378	CUUGGGCAGACCCUCAUGCUGCACA	1221
3105_4_75	HLA-A	Exon 4	-	chr6:29944375-29944400	UACCCCAUCUCAGGGUGAGGGGCUU	1222
3105_4_76	HLA-A	Exon 4	-	chr6:29944376-29944401	UUACCCCAUCUCAGGGUGAGGGGCU	1223
3105_4_77	HLA-A	Exon 4	-	chr6:29944381-29944406	CCUCCUUACCCCAUCUCAGGGUGAG	1224
3105_4_78	HLA-A	Exon 4	-	chr6:29944382-29944407	CCCUCCUUACCCCAUCUCAGGGUGA	1225
3105_4_79	HLA-A	Exon 4	-	chr6:29944383-29944408	UCCCUCCUUACCCCAUCUCAGGGUG	1226
3105_4_80	HLA-A	Exon 4	-	chr6:29944388-29944413	CCAUCUCCCUCCUUACCCCAUCUCA	1227
3105_4_81	HLA-A	Exon 4	-	chr6:29944389-29944414	CCCAUCUCCCUCCUUACCCCAUCUC	1228
3105_5_1	HLA-A	Exon 5	+	chr6:29944504-29944529	UCUUCCCAGCCCACCAUCCCCAUCG	1229
3105_5_2	HLA-A	Exon 5	+	chr6:29944505-29944530	CUUCCCAGCCCACCAUCCCCAUCGU	1230
3105_5_3	HLA-A	Exon 5	+	chr6:29944517-29944542	CCAUCCCCAUCGUGGGCAUCAUUGC	1231
3105_5_4	HLA-A	Exon 5	+	chr6:29944522-29944547	CCCAUCGUGGGCAUCAUUGCUGGCC	1232
3105_5_5	HLA-A	Exon 5	+	chr6:29944532-29944557	GCAUCAUUGCUGGCCUGGUUCUCCU	1233
3105_5_6	HLA-A	Exon 5	+	chr6:29944547-29944572	UGGUUCUCCUUGGAGCUGUGAUCAC	1234
3105_5_7	HLA-A	Exon 5	+	chr6:29944555-29944580	CUUGGAGCUGUGAUCACUGGAGCUG	1235

3105_5_8	HLA-A	Exon 5	+	chr6:29944572-29944597	UGGAGCUGUGGUCGCUGCCGUGAUG	1236
3105_5_9	HLA-A	Exon 5	+	chr6:29944575-29944600	AGCUGUGGUCGCUGCCGUGAUGUGG	1237
3105_5_10	HLA-A	Exon 5	+	chr6:29944578-29944603	UGUGGUCGCUGCCGUGAUGUGGAGG	1238
3105_5_11	HLA-A	Exon 5	+	chr6:29944589-29944614	CCGUGAUGUGGAGGAGGAAGAGCUC	1239
3105_5_12	HLA-A	Exon 5	+	chr6:29944592-29944617	UGAUGUGGAGGAGGAAGAGCUCAGG	1240
3105_5_13	HLA-A	Exon 5	+	chr6:29944598-29944623	GGAGGAGGAAGAGCUCAGGUGGAGA	1241
3105_5_14	HLA-A	Exon 5	+	chr6:29944599-29944624	GAGGAGGAAGAGCUCAGGUGGAGAA	1242
3105_5_15	HLA-A	Exon 5	+	chr6:29944600-29944625	AGGAGGAAGAGCUCAGGUGGAGAAG	1243
3105_5_16	HLA-A	Exon 5	+	chr6:29944606-29944631	AAGAGCUCAGGUGGAGAAGGGGUGA	1244
3105_5_17	HLA-A	Exon 5	+	chr6:29944607-29944632	AGAGCUCAGGUGGAGAAGGGGUGAA	1245
3105_5_18	HLA-A	Exon 5	+	chr6:29944610-29944635	GCUCAGGUGGAGAAGGGGUGAAGGG	1246
3105_5_19	HLA-A	Exon 5	+	chr6:29944611-29944636	CUCAGGUGGAGAAGGGGUGAAGGGU	1247
3105_5_20	HLA-A	Exon 5	+	chr6:29944612-29944637	UCAGGUGGAGAAGGGGUGAAGGGUG	1248
3105_5_21	HLA-A	Exon 5	-	chr6:29944477-29944502	GCUCUGGGAAAAGAGGGGAAGGUGA	1249
3105_5_22	HLA-A	Exon 5	-	chr6:29944478-29944503	AGCUCUGGGAAAAGAGGGGAAGGUG	1250
3105_5_23	HLA-A	Exon 5	-	chr6:29944483-29944508	AAGACAGCUCUGGGAAAAGAGGGGA	1251
3105_5_24	HLA-A	Exon 5	-	chr6:29944487-29944512	UGGGAAGACAGCUCUGGGAAAAGAG	1252
3105_5_25	HLA-A	Exon 5	-	chr6:29944488-29944513	CUGGGAAGACAGCUCUGGGAAAAGA	1253
3105_5_26	HLA-A	Exon 5	-	chr6:29944489-29944514	GCUGGGAAGACAGCUCUGGGAAAAG	1254
3105_5_27	HLA-A	Exon 5	-	chr6:29944497-29944522	GAUGGUGGGCUGGGAAGACAGCUCU	1255
3105_5_28	HLA-A	Exon 5	-	chr6:29944498-29944523	GGAUGGUGGGCUGGGAAGACAGCUC	1256
3105_5_29	HLA-A	Exon 5	-	chr6:29944511-29944536	AUGCCCACGAUGGGGAUGGUGGGCU	1257
3105_5_30	HLA-A	Exon 5	-	chr6:29944512-29944537	GAUGCCCACGAUGGGGAUGGUGGGC	1258
3105_5_31	HLA-A	Exon 5	-	chr6:29944516-29944541	CAAUGAUGCCCACGAUGGGGAUGGU	1259
3105_5_32	HLA-A	Exon 5	-	chr6:29944517-29944542	GCAAUGAUGCCCACGAUGGGGAUGG	1260

3105_5_33	HLA-A	Exon 5	-	chr6:29944520-29944545	CCAGCAAUGAUGCCCACGAUGGGGA	1261
3105_5_34	HLA-A	Exon 5	-	chr6:29944524-29944549	CAGGCCAGCAAUGAUGCCCACGAUG	1262
3105_5_35	HLA-A	Exon 5	-	chr6:29944525-29944550	CCAGGCCAGCAAUGAUGCCCACGAU	1263
3105_5_36	HLA-A	Exon 5	-	chr6:29944526-29944551	ACCAGGCCAGCAAUGAUGCCCACGA	1264
3105_5_37	HLA-A	Exon 5	-	chr6:29944548-29944573	AGUGAUCACAGCUCCAAGGAGAACC	1265
3105_5_38	HLA-A	Exon 5	-	chr6:29944557-29944582	CACAGCUCCAGUGAUCACAGCUCCA	1266
3105_5_39	HLA-A	Exon 5	-	chr6:29944592-29944617	CCUGAGCUCUUCCUCCUCCACAUCA	1267
3105_6_1	HLA-A	Exon 6	+	chr6:29945040-29945065	GACAUUUUCUUCUCACAGAUAGAAA	1268
3105_6_2	HLA-A	Exon 6	+	chr6:29945043-29945068	AUUUUCUUCUCACAGAUAGAAAAGG	1269
3105_6_3	HLA-A	Exon 6	+	chr6:29945044-29945069	UUUUCUUCUCACAGAUAGAAAAGGA	1270
3105_6_4	HLA-A	Exon 6	+	chr6:29945057-29945082	GAUAGAAAAGGAGGGAGUUACACUC	1271
3105_6_5	HLA-A	Exon 6	+	chr6:29945076-29945101	ACACUCAGGCUGCAAGUAAGUAUGA	1272
3105_6_6	HLA-A	Exon 6	+	chr6:29945079-29945104	CUCAGGCUGCAAGUAAGUAUGAAGG	1273
3105_7_1	HLA-A	Exon 7	+	chr6:29945223-29945248	UCUACCCCAGGCAGUGACAGUGCCC	1274
3105_7_2	HLA-A	Exon 7	+	chr6:29945224-29945249	CUACCCCAGGCAGUGACAGUGCCCA	1275
3105_7_3	HLA-A	Exon 7	+	chr6:29945254-29945279	CUGAUGUGUCCCUCACAGCUUGUAA	1276
3105_7_4	HLA-A	Exon 7	+	chr6:29945265-29945290	CUCACAGCUUGUAAAGGUGAGAGCU	1277
3105_7_5	HLA-A	Exon 7	+	chr6:29945268-29945293	ACAGCUUGUAAAGGUGAGAGCUUGG	1278
3105_7_6	HLA-A	Exon 7	-	chr6:29945230-29945255	GAGCCCUGGGCACUGUCACUGCCUG	1279
3105_7_7	HLA-A	Exon 7	-	chr6:29945231-29945256	AGAGCCCUGGGCACUGUCACUGCCU	1280
3105_7_8	HLA-A	Exon 7	-	chr6:29945232-29945257	CAGAGCCCUGGGCACUGUCACUGCC	1281
3105_7_9	HLA-A	Exon 7	-	chr6:29945248-29945273	GCUGUGAGGGACACAUCAGAGCCCU	1282
3105_7_10	HLA-A	Exon 7	-	chr6:29945249-29945274	AGCUGUGAGGGACACAUCAGAGCCC	1283
3105_7_11	HLA-A	Exon 7	-	chr6:29945266-29945291	AAGCUCUCACCUUUACAAGCUGUGA	1284
3105_7_12	HLA-A	Exon 7	-	chr6:29945267-29945292	CAAGCUCUCACCUUUACAAGCUGUG	1285

3105_8_1	HLA-A	Exon 8	+	chr6:29945445-29945470	UAUAGUGUGAGACAGCUGCCUUGUG	1286
3105_8_2	HLA-A	Exon 8	+	chr6:29945446-29945471	AUAGUGUGAGACAGCUGCCUUGUGU	1287
3105_8_3	HLA-A	Exon 8	+	chr6:29945455-29945480	GACAGCUGCCUUGUGUGGGACUGAG	1288
3105_8_4	HLA-A	Exon 8	+	chr6:29945517-29945542	AAGAACCCUGACUUUGUUUCUGCAA	1289
3105_8_5	HLA-A	Exon 8	+	chr6:29945545-29945570	CACCUGCAUGUGUCUGUGUUCGUGU	1290
3105_8_6	HLA-A	Exon 8	+	chr6:29945557-29945582	UCUGUGUUCGUGUAGGCAUAAUGUG	1291
3105_8_7	HLA-A	Exon 8	+	chr6:29945560-29945585	GUGUUCGUGUAGGCAUAAUGUGAGG	1292
3105_8_8	HLA-A	Exon 8	+	chr6:29945563-29945588	UUCGUGUAGGCAUAAUGUGAGGAGG	1293
3105_8_9	HLA-A	Exon 8	+	chr6:29945564-29945589	UCGUGUAGGCAUAAUGUGAGGAGGU	1294
3105_8_10	HLA-A	Exon 8	+	chr6:29945565-29945590	CGUGUAGGCAUAAUGUGAGGAGGUG	1295
3105_8_11	HLA-A	Exon 8	+	chr6:29945652-29945677	CCCAAUCAUCUUUCCUGUUCCAGAG	1296
3105_8_12	HLA-A	Exon 8	+	chr6:29945655-29945680	AAUCAUCUUUCCUGUUCCAGAGAGG	1297
3105_8_13	HLA-A	Exon 8	+	chr6:29945656-29945681	AUCAUCUUUCCUGUUCCAGAGAGGU	1298
3105_8_14	HLA-A	Exon 8	+	chr6:29945657-29945682	UCAUCUUUCCUGUUCCAGAGAGGUG	1299
3105_8_15	HLA-A	Exon 8	+	chr6:29945663-29945688	UUCCUGUUCCAGAGAGGUGGGGCUG	1300
3105_8_16	HLA-A	Exon 8	+	chr6:29945691-29945716	UGUCUCCAUCUCUGUCUCAACUUCA	1301
3105_8_17	HLA-A	Exon 8	+	chr6:29945775-29945800	UACUUUCUCAAAUUCUUGCCAUGAG	1302
3105_8_18	HLA-A	Exon 8	+	chr6:29945794-29945819	CAUGAGAGGUUGAUGAGUUAAUUAA	1303
3105_8_19	HLA-A	Exon 8	+	chr6:29945830-29945855	CCUAAAAUUUGAGAGACAAAAUAAA	1304
3105_8_20	HLA-A	Exon 8	-	chr6:29945466-29945491	AACUCUUGCCUCUCAGUCCCACACA	1305
3105_8_21	HLA-A	Exon 8	-	chr6:29945497-29945522	UUCUUCAAGUCACAAAGGGAAGGGC	1306
3105_8_22	HLA-A	Exon 8	-	chr6:29945501-29945526	AGGGUUCUUCAAGUCACAAAGGGAA	1307
3105_8_23	HLA-A	Exon 8	-	chr6:29945502-29945527	CAGGGUUCUUCAAGUCACAAAGGGA	1308
3105_8_24	HLA-A	Exon 8	-	chr6:29945506-29945531	AAGUCAGGGUUCUUCAAGUCACAAA	1309
3105_8_25	HLA-A	Exon 8	-	chr6:29945507-29945532	AAAGUCAGGGUUCUUCAAGUCACAA	1310

3105_8_26	HLA-A	Exon 8	-	chr6:29945525-29945550	AGGUGCCUUUGCAGAAACAAAGUCA	1311
3105_8_27	HLA-A	Exon 8	-	chr6:29945526-29945551	CAGGUGCCUUUGCAGAAACAAAGUC	1312
3105_8_28	HLA-A	Exon 8	-	chr6:29945550-29945575	UGCCUACACGAACACAGACACAUGC	1313
3105_8_29	HLA-A	Exon 8	-	chr6:29945599-29945624	GGUCAUGGUGGACAUGGGGGUGGGG	1314
3105_8_30	HLA-A	Exon 8	-	chr6:29945602-29945627	GAGGGUCAUGGUGGACAUGGGGGUG	1315
3105_8_31	HLA-A	Exon 8	-	chr6:29945603-29945628	AGAGGGUCAUGGUGGACAUGGGGGU	1316
3105_8_32	HLA-A	Exon 8	-	chr6:29945604-29945629	AAGAGGGUCAUGGUGGACAUGGGGG	1317
3105_8_33	HLA-A	Exon 8	-	chr6:29945607-29945632	GGGAAGAGGGUCAUGGUGGACAUGG	1318
3105_8_34	HLA-A	Exon 8	-	chr6:29945608-29945633	UGGGAAGAGGGUCAUGGUGGACAUG	1319
3105_8_35	HLA-A	Exon 8	-	chr6:29945609-29945634	GUGGGAAGAGGGUCAUGGUGGACAU	1320
3105_8_36	HLA-A	Exon 8	-	chr6:29945610-29945635	CGUGGGAAGAGGGUCAUGGUGGACA	1321
3105_8_37	HLA-A	Exon 8	-	chr6:29945616-29945641	GGUCAGCGUGGGAAGAGGGUCAUGG	1322
3105_8_38	HLA-A	Exon 8	-	chr6:29945619-29945644	ACAGGUCAGCGUGGGAAGAGGGUCA	1323
3105_8_39	HLA-A	Exon 8	-	chr6:29945625-29945650	GGGAGCACAGGUCAGCGUGGGAAGA	1324
3105_8_40	HLA-A	Exon 8	-	chr6:29945626-29945651	AGGGAGCACAGGUCAGCGUGGGAAG	1325
3105_8_41	HLA-A	Exon 8	-	chr6:29945632-29945657	UUGGGGAGGGAGCACAGGUCAGCGU	1326
3105_8_42	HLA-A	Exon 8	-	chr6:29945633-29945658	AUUGGGGAGGGAGCACAGGUCAGCG	1327
3105_8_43	HLA-A	Exon 8	-	chr6:29945642-29945667	GGAAAGAUGAUUGGGGAGGGAGCAC	1328
3105_8_44	HLA-A	Exon 8	-	chr6:29945650-29945675	CUGGAACAGGAAAGAUGAUUGGGGA	1329
3105_8_45	HLA-A	Exon 8	-	chr6:29945651-29945676	UCUGGAACAGGAAAGAUGAUUGGGG	1330
3105_8_46	HLA-A	Exon 8	-	chr6:29945654-29945679	CUCUCUGGAACAGGAAAGAUGAUUG	1331
3105_8_47	HLA-A	Exon 8	-	chr6:29945655-29945680	CCUCUCUGGAACAGGAAAGAUGAUU	1332
3105_8_48	HLA-A	Exon 8	-	chr6:29945656-29945681	ACCUCUCUGGAACAGGAAAGAUGAU	1333
3105_8_49	HLA-A	Exon 8	-	chr6:29945668-29945693	CACCUCAGCCCCACCUCUCUGGAAC	1334
3105_8_50	HLA-A	Exon 8	-	chr6:29945674-29945699	UGGAGACACCUCAGCCCCACCUCUC	1335

3105_8_51	HLA-A	Exon 8	-	chr6:29945699-29945724	GUGCACCAUGAAGUUGAGACAGAGA	1336
3105_8_52	HLA-A	Exon 8	-	chr6:29945743-29945768	ACUAAGGUUCUAAUUUUAAUAGGGA	1337
3105_8_53	HLA-A	Exon 8	-	chr6:29945747-29945772	UUAUACUAAGGUUCUAAUUUUAAUA	1338
3105_8_54	HLA-A	Exon 8	-	chr6:29945748-29945773	UUUAUACUAAGGUUCUAAUUUUAAU	1339
3105_8_55	HLA-A	Exon 8	-	chr6:29945764-29945789	AAUUUGAGAAAGUAAAUUUAUACUA	1340
3105_8_56	HLA-A	Exon 8	-	chr6:29945796-29945821	CUUUAAUUAACUCAUCAACCUCUCA	1341
3105_8_57	HLA-A	Exon 8	-	chr6:29945833-29945858	CCAUUUAUUUUGUCUCUCAAAUUUU	1342
3105_8_58	HLA-A	Exon 8	-	chr6:29945873-29945898	GCACAAGAAACACGUGGACUCUGGA	1343
3105_8_59	HLA-A	Exon 8	-	chr6:29945877-29945902	AUCAGCACAAGAAACACGUGGACUC	1344
3105_8_60	HLA-A	Exon 8	-	chr6:29945884-29945909	GCAACAAAUCAGCACAAGAAACACG	1345
3106_8_1	HLA-B	Exon 8	+	chr6:31353849-31353874	CUCAGCACAGCGAACAUGCAGAUUC	1346
3106_8_2	HLA-B	Exon 8	+	chr6:31353853-31353878	GCACAGCGAACAUGCAGAUUCUGGA	1347
3106_8_3	HLA-B	Exon 8	+	chr6:31353861-31353886	AACAUGCAGAUUCUGGAAGGUUCUC	1348
3106_8_4	HLA-B	Exon 8	+	chr6:31353888-31353913	GUCUUUAUUUGCUCUCUCAAAUUCC	1349
3106_8_5	HLA-B	Exon 8	+	chr6:31353974-31353999	UUAUAUUCAGAUUCUUAUUUUCAGU	1350
3106_8_6	HLA-B	Exon 8	+	chr6:31353975-31354000	UAUAUUCAGAUUCUUAUUUUCAGUA	1351
3106_8_7	HLA-B	Exon 8	+	chr6:31354022-31354047	AGUGCACGUAAAGUUGAGACAGAGA	1352
3106_8_8	HLA-B	Exon 8	+	chr6:31354046-31354071	AUGGAGACAUCCAGCCCCACCUCUC	1353
3106_8_9	HLA-B	Exon 8	+	chr6:31354064-31354089	ACCUCUCUGGAACAAGAAAGAUGAC	1354
3106_8_10	HLA-B	Exon 8	+	chr6:31354065-31354090	CCUCUCUGGAACAAGAAAGAUGACU	1355
3106_8_11	HLA-B	Exon 8	+	chr6:31354066-31354091	CUCUCUGGAACAAGAAAGAUGACUG	1356
3106_8_12	HLA-B	Exon 8	+	chr6:31354069-31354094	UCUGGAACAAGAAAGAUGACUGGGG	1357
3106_8_13	HLA-B	Exon 8	+	chr6:31354078-31354103	AGAAAGAUGACUGGGGAGGAAACAC	1358
3106_8_14	HLA-B	Exon 8	+	chr6:31354087-31354112	ACUGGGGAGGAAACACAGGUCAGCA	1359
3106_8_15	HLA-B	Exon 8	+	chr6:31354088-31354113	CUGGGGAGGAAACACAGGUCAGCAU	1360

3106_8_16	HLA-B	Exon 8	+	chr6:31354094-31354119	AGGAAACACAGGUCAGCAUGGGAAC	1361
3106_8_17	HLA-B	Exon 8	+	chr6:31354095-31354120	GGAAACACAGGUCAGCAUGGGAACA	1362
3106_8_18	HLA-B	Exon 8	+	chr6:31354096-31354121	GAAACACAGGUCAGCAUGGGAACAG	1363
3106_8_19	HLA-B	Exon 8	+	chr6:31354105-31354130	GUCAGCAUGGGAACAGGGGUCACAG	1364
3106_8_20	HLA-B	Exon 8	+	chr6:31354113-31354138	GGGAACAGGGGUCACAGUGGACACA	1365
3106_8_21	HLA-B	Exon 8	+	chr6:31354114-31354139	GGAACAGGGGUCACAGUGGACACAA	1366
3106_8_22	HLA-B	Exon 8	+	chr6:31354117-31354142	ACAGGGGUCACAGUGGACACAAGGG	1367
3106_8_23	HLA-B	Exon 8	+	chr6:31354118-31354143	CAGGGGUCACAGUGGACACAAGGGU	1368
3106_8_24	HLA-B	Exon 8	+	chr6:31354152-31354177	CUCCACCUCCUCACAUUAUGCUAAC	1369
3106_8_25	HLA-B	Exon 8	+	chr6:31354153-31354178	UCCACCUCCUCACAUUAUGCUAACA	1370
3106_8_26	HLA-B	Exon 8	+	chr6:31354170-31354195	UGCUAACAGGGACGCAGACACAUUC	1371
3106_8_27	HLA-B	Exon 8	+	chr6:31354197-31354222	GUGCCUUUGCAGAAAGAGAUGCCAG	1372
3106_8_28	HLA-B	Exon 8	+	chr6:31354215-31354240	AUGCCAGAGGCUCUUGAAGUCACAA	1373
3106_8_29	HLA-B	Exon 8	+	chr6:31354216-31354241	UGCCAGAGGCUCUUGAAGUCACAAA	1374
3106_8_30	HLA-B	Exon 8	+	chr6:31354217-31354242	GCCAGAGGCUCUUGAAGUCACAAAG	1375
3106_8_31	HLA-B	Exon 8	+	chr6:31354220-31354245	AGAGGCUCUUGAAGUCACAAAGGGG	1376
3106_8_32	HLA-B	Exon 8	+	chr6:31354268-31354293	CAGUCCCUCACAAGACAGCUGUCUC	1377
3106_8_33	HLA-B	Exon 8	-	chr6:31353914-31353939	UGGAUUAAUUAAAUAAGUCAAUUCC	1378
3106_8_34	HLA-B	Exon 8	-	chr6:31353939-31353964	UCAAAUAUUUGCUAUGAGAGGUUGA	1379
3106_8_35	HLA-B	Exon 8	-	chr6:31353946-31353971	UGUUUUCUCAAAUAUUUGCUAUGAG	1380
3106_8_36	HLA-B	Exon 8	-	chr6:31354059-31354084	CUUUCUUGUUCCAGAGAGGUGGGGC	1381
3106_8_37	HLA-B	Exon 8	-	chr6:31354063-31354088	UCAUCUUUCUUGUUCCAGAGAGGUG	1382
3106_8_38	HLA-B	Exon 8	-	chr6:31354064-31354089	GUCAUCUUUCUUGUUCCAGAGAGGU	1383
3106_8_39	HLA-B	Exon 8	-	chr6:31354065-31354090	AGUCAUCUUUCUUGUUCCAGAGAGG	1384
3106_8_40	HLA-B	Exon 8	-	chr6:31354068-31354093	CCCAGUCAUCUUUCUUGUUCCAGAG	1385

3106_8_41	HLA-B	Exon 8	-	chr6:31354157-31354182	UCCCUGUUAGCAUAAUGUGAGGAGG	1386
3106_8_42	HLA-B	Exon 8	-	chr6:31354160-31354185	GCGUCCCUGUUAGCAUAAUGUGAGG	1387
3106_8_43	HLA-B	Exon 8	-	chr6:31354163-31354188	UCUGCGUCCCUGUUAGCAUAAUGUG	1388
3106_8_44	HLA-B	Exon 8	-	chr6:31354203-31354228	GAGCCUCUGGCAUCUCUUUCUGCAA	1389
3106_8_45	HLA-B	Exon 8	-	chr6:31354221-31354246	UCCCCUUUGUGACUUCAAGAGCCUC	1390
3106_8_46	HLA-B	Exon 8	-	chr6:31354262-31354287	GCUGUCUUGUGAGGGACUGAGAUGC	1391
3106_8_47	HLA-B	Exon 8	-	chr6:31354275-31354300	GUAGCCUGAGACAGCUGUCUUGUGA	1392
3106_8_48	HLA-B	Exon 8	-	chr6:31354276-31354301	UGUAGCCUGAGACAGCUGUCUUGUG	1393
3106_7_1	HLA-B	Exon 7	+	chr6:31354485-31354510	AGCUGUGAGAGACACAUCAGAGCCC	1394
3106_7_2	HLA-B	Exon 7	+	chr6:31354486-31354511	GCUGUGAGAGACACAUCAGAGCCCU	1395
3106_7_3	HLA-B	Exon 7	+	chr6:31354502-31354527	CAGAGCCCUGGGCACUGUCGCUGCC	1396
3106_7_4	HLA-B	Exon 7	+	chr6:31354519-31354544	UCGCUGCCUGGAGUAGAACAAAAAC	1397
3106_7_5	HLA-B	Exon 7	-	chr6:31354466-31354491	ACAGCUUGAAAAGGUGAGAUUCUUG	1398
3106_7_6	HLA-B	Exon 7	-	chr6:31354467-31354492	CACAGCUUGAAAAGGUGAGAUUCUU	1399
3106_7_7	HLA-B	Exon 7	-	chr6:31354468-31354493	UCACAGCUUGAAAAGGUGAGAUUCU	1400
3106_7_8	HLA-B	Exon 7	-	chr6:31354480-31354505	CUGAUGUGUCUCUCACAGCUUGAAA	1401
3106_7_9	HLA-B	Exon 7	-	chr6:31354510-31354535	CUACUCCAGGCAGCGACAGUGCCCA	1402
3106_7_10	HLA-B	Exon 7	-	chr6:31354511-31354536	UCUACUCCAGGCAGCGACAGUGCCC	1403
3106_6_1	HLA-B	Exon 6	+	chr6:31354643-31354668	GAGUAGCUCCCUCCUUUUCCACCUG	1404
3106_6_2	HLA-B	Exon 6	+	chr6:31354644-31354669	AGUAGCUCCCUCCUUUUCCACCUGU	1405
3106_6_3	HLA-B	Exon 6	-	chr6:31354610-31354635	CGUGUAAGUGGUGGGGGUGGGAGUG	1406
3106_6_4	HLA-B	Exon 6	-	chr6:31354617-31354642	CAGGCUGCGUGUAAGUGGUGGGGGU	1407
3106_6_5	HLA-B	Exon 6	-	chr6:31354618-31354643	UCAGGCUGCGUGUAAGUGGUGGGGG	1408
3106_6_6	HLA-B	Exon 6	-	chr6:31354621-31354646	CUCUCAGGCUGCGUGUAAGUGGUGG	1409
3106_6_7	HLA-B	Exon 6	-	chr6:31354622-31354647	ACUCUCAGGCUGCGUGUAAGUGGUG	1410

3106_6_8	HLA-B	Exon 6	-	chr6:31354623-31354648	UACUCUCAGGCUGCGUGUAAGUGGU	1411
3106_6_9	HLA-B	Exon 6	-	chr6:31354624-31354649	CUACUCUCAGGCUGCGUGUAAGUGG	1412
3106_6_10	HLA-B	Exon 6	-	chr6:31354627-31354652	GAGCUACUCUCAGGCUGCGUGUAAG	1413
3106_6_11	HLA-B	Exon 6	-	chr6:31354641-31354666	GGUGGAAAAGGAGGGAGCUACUCUC	1414
3106_6_12	HLA-B	Exon 6	-	chr6:31354654-31354679	UUUUCUUCCCACAGGUGGAAAAGGA	1415
3106_6_13	HLA-B	Exon 6	-	chr6:31354655-31354680	AUUUUCUUCCCACAGGUGGAAAAGG	1416
3106_6_14	HLA-B	Exon 6	-	chr6:31354658-31354683	GACAUUUUCUUCCCACAGGUGGAAA	1417
3106_6_15	HLA-B	Exon 6	-	chr6:31354664-31354689	UCACAGGACAUUUUCUUCCCACAGG	1418
3106_5_1	HLA-B	Exon 5	+	chr6:31355140-31355165	CACAGCUCCGAUGACCACAACUGCU	1419
3106_5_2	HLA-B	Exon 5	+	chr6:31355149-31355174	GAUGACCACAACUGCUAGGACAGCC	1420
3106_5_3	HLA-B	Exon 5	+	chr6:31355171-31355196	GCCAGGCCAGCAACAAUGCCCACGA	1421
3106_5_4	HLA-B	Exon 5	+	chr6:31355172-31355197	CCAGGCCAGCAACAAUGCCCACGAU	1422
3106_5_5	HLA-B	Exon 5	+	chr6:31355173-31355198	CAGGCCAGCAACAAUGCCCACGAUG	1423
3106_5_6	HLA-B	Exon 5	+	chr6:31355177-31355202	CCAGCAACAAUGCCCACGAUGGGGA	1424
3106_5_7	HLA-B	Exon 5	+	chr6:31355180-31355205	GCAACAAUGCCCACGAUGGGGACGG	1425
3106_5_8	HLA-B	Exon 5	+	chr6:31355185-31355210	AAUGCCCACGAUGGGGACGGUGGAC	1426
3106_5_9	HLA-B	Exon 5	+	chr6:31355186-31355211	AUGCCCACGAUGGGGACGGUGGACU	1427
3106_5_10	HLA-B	Exon 5	+	chr6:31355193-31355218	CGAUGGGGACGGUGGACUGGGAAGA	1428
3106_5_11	HLA-B	Exon 5	+	chr6:31355199-31355224	GGACGGUGGACUGGGAAGACGGCUC	1429
3106_5_12	HLA-B	Exon 5	+	chr6:31355200-31355225	GACGGUGGACUGGGAAGACGGCUCU	1430
3106_5_13	HLA-B	Exon 5	+	chr6:31355205-31355230	UGGACUGGGAAGACGGCUCUGGGAA	1431
3106_5_14	HLA-B	Exon 5	+	chr6:31355208-31355233	ACUGGGAAGACGGCUCUGGGAAAGG	1432
3106_5_15	HLA-B	Exon 5	+	chr6:31355209-31355234	CUGGGAAGACGGCUCUGGGAAAGGA	1433
3106_5_16	HLA-B	Exon 5	+	chr6:31355210-31355235	UGGGAAGACGGCUCUGGGAAAGGAG	1434
3106_5_17	HLA-B	Exon 5	+	chr6:31355219-31355244	GGCUCUGGGAAAGGAGGGGAAGAUG	1435

3106_5_18	HLA-B	Exon 5	+	chr6:31355220-31355245	GCUCUGGGAAAGGAGGGGAAGAUGA	1436
3106_5_19	HLA-B	Exon 5	-	chr6:31355085-31355110	UCAGGUAGGGAAGGGGUGAGGGGUG	1437
3106_5_20	HLA-B	Exon 5	-	chr6:31355086-31355111	UUCAGGUAGGGAAGGGGUGAGGGGU	1438
3106_5_21	HLA-B	Exon 5	-	chr6:31355087-31355112	GUUCAGGUAGGGAAGGGGUGAGGGG	1439
3106_5_22	HLA-B	Exon 5	-	chr6:31355090-31355115	AGAGUUCAGGUAGGGAAGGGGUGAG	1440
3106_5_23	HLA-B	Exon 5	-	chr6:31355091-31355116	AAGAGUUCAGGUAGGGAAGGGGUGA	1441
3106_5_24	HLA-B	Exon 5	-	chr6:31355092-31355117	GAAGAGUUCAGGUAGGGAAGGGGUG	1442
3106_5_25	HLA-B	Exon 5	-	chr6:31355097-31355122	AGGAGGAAGAGUUCAGGUAGGGAAG	1443
3106_5_26	HLA-B	Exon 5	-	chr6:31355098-31355123	UAGGAGGAAGAGUUCAGGUAGGGAA	1444
3106_5_27	HLA-B	Exon 5	-	chr6:31355099-31355124	GUAGGAGGAAGAGUUCAGGUAGGGA	1445
3106_5_28	HLA-B	Exon 5	-	chr6:31355103-31355128	AUGUGUAGGAGGAAGAGUUCAGGUA	1446
3106_5_29	HLA-B	Exon 5	-	chr6:31355104-31355129	GAUGUGUAGGAGGAAGAGUUCAGGU	1447
3106_5_30	HLA-B	Exon 5	-	chr6:31355108-31355133	CUGUGAUGUGUAGGAGGAAGAGUUC	1448
3106_5_31	HLA-B	Exon 5	-	chr6:31355119-31355144	UGUGGUCGCUGCUGUGAUGUGUAGG	1449
3106_5_32	HLA-B	Exon 5	-	chr6:31355122-31355147	AGCUGUGGUCGCUGCUGUGAUGUGU	1450
3106_5_33	HLA-B	Exon 5	-	chr6:31355142-31355167	CUAGCAGUUGUGGUCAUCGGAGCUG	1451
3106_5_34	HLA-B	Exon 5	-	chr6:31355150-31355175	UGGCUGUCCUAGCAGUUGUGGUCAU	1452
3106_5_35	HLA-B	Exon 5	-	chr6:31355157-31355182	GCUGGCCUGGCUGUCCUAGCAGUUG	1453
3106_5_36	HLA-B	Exon 5	-	chr6:31355175-31355200	CCCAUCGUGGGCAUUGUUGCUGGCC	1454
3106_5_37	HLA-B	Exon 5	-	chr6:31355180-31355205	CCGUCCCCAUCGUGGGCAUUGUUGC	1455
3106_5_38	HLA-B	Exon 5	-	chr6:31355192-31355217	CUUCCCAGUCCACCGUCCCCAUCGU	1456
3106_5_39	HLA-B	Exon 5	-	chr6:31355193-31355218	UCUUCCCAGUCCACCGUCCCCAUCG	1457
3106_4_1	HLA-B	Exon 4	+	chr6:31355299-31355324	CUCAUCCCCCUCCUUACCCCAUCUC	1458
3106_4_2	HLA-B	Exon 4	+	chr6:31355300-31355325	UCAUCCCCCUCCUUACCCCAUCUCA	1459
3106_4_3	HLA-B	Exon 4	+	chr6:31355305-31355330	CCCCUCCUUACCCCAUCUCAGGGUG	1460

3106_4_4	HLA-B	Exon 4	+	chr6:31355306-31355331	CCCUCCUUACCCCAUCUCAGGGUGA	1461
3106_4_5	HLA-B	Exon 4	+	chr6:31355307-31355332	CCUCCUUACCCCAUCUCAGGGUGAG	1462
3106_4_6	HLA-B	Exon 4	+	chr6:31355313-31355338	UACCCCAUCUCAGGGUGAGGGGCUU	1463
3106_4_7	HLA-B	Exon 4	+	chr6:31355335-31355360	CUUCGGCAGCCCCUCAUGCUGUACA	1464
3106_4_8	HLA-B	Exon 4	+	chr6:31355364-31355389	AUGUGUAUCUCUGCUCUUCUCCAGA	1465
3106_4_9	HLA-B	Exon 4	+	chr6:31355389-31355414	AGGCACCACCACAGCUGCCCACUUC	1466
3106_4_10	HLA-B	Exon 4	+	chr6:31355393-31355418	ACCACCACAGCUGCCCACUUCUGGA	1467
3106_4_11	HLA-B	Exon 4	+	chr6:31355409-31355434	ACUUCUGGAAGGUUCUAUCUCCUGC	1468
3106_4_12	HLA-B	Exon 4	+	chr6:31355414-31355439	UGGAAGGUUCUAUCUCCUGCUGGUC	1469
3106_4_13	HLA-B	Exon 4	+	chr6:31355443-31355468	CUCCACAAGCUCAGUGUCCUGAGUU	1470
3106_4_14	HLA-B	Exon 4	+	chr6:31355465-31355490	GUUUGGUCCUCGCCAUCCCGCUGCC	1471
3106_4_15	HLA-B	Exon 4	+	chr6:31355484-31355509	GCUGCCAGGUCAGUGUGAUCUCCGC	1472
3106_4_16	HLA-B	Exon 4	+	chr6:31355485-31355510	CUGCCAGGUCAGUGUGAUCUCCGCA	1473
3106_4_17	HLA-B	Exon 4	+	chr6:31355497-31355522	UGUGAUCUCCGCAGGGUAGAAACCC	1474
3106_4_18	HLA-B	Exon 4	+	chr6:31355498-31355523	GUGAUCUCCGCAGGGUAGAAACCCA	1475
3106_4_19	HLA-B	Exon 4	+	chr6:31355512-31355537	GUAGAAACCCAGGGCCCAGCACCUC	1476
3106_4_20	HLA-B	Exon 4	+	chr6:31355513-31355538	UAGAAACCCAGGGCCCAGCACCUCA	1477
3106_4_21	HLA-B	Exon 4	+	chr6:31355516-31355541	AAACCCAGGGCCCAGCACCUCAGGG	1478
3106_4_22	HLA-B	Exon 4	+	chr6:31355524-31355549	GGCCCAGCACCUCAGGGUGGCCUCA	1479
3106_4_23	HLA-B	Exon 4	+	chr6:31355534-31355559	CUCAGGGUGGCCUCAUGGUCAGAGA	1480
3106_4_24	HLA-B	Exon 4	+	chr6:31355535-31355560	UCAGGGUGGCCUCAUGGUCAGAGAU	1481
3106_4_25	HLA-B	Exon 4	+	chr6:31355536-31355561	CAGGGUGGCCUCAUGGUCAGAGAUG	1482
3106_4_26	HLA-B	Exon 4	+	chr6:31355539-31355564	GGUGGCCUCAUGGUCAGAGAUGGGG	1483
3106_4_27	HLA-B	Exon 4	+	chr6:31355542-31355567	GGCCUCAUGGUCAGAGAUGGGGUGG	1484
3106_4_28	HLA-B	Exon 4	+	chr6:31355543-31355568	GCCUCAUGGUCAGAGAUGGGGUGGU	1485

3106_4_29	HLA-B	Exon 4	+	chr6:31355559-31355584	UGGGGUGGUGGGUCACGUGUGUCUU	1486
3106_4_30	HLA-B	Exon 4	+	chr6:31355560-31355585	GGGGUGGUGGGUCACGUGUGUCUUU	1487
3106_4_31	HLA-B	Exon 4	+	chr6:31355561-31355586	GGGUGGUGGGUCACGUGUGUCUUUG	1488
3106_4_32	HLA-B	Exon 4	+	chr6:31355562-31355587	GGUGGUGGGUCACGUGUGUCUUUGG	1489
3106_4_33	HLA-B	Exon 4	+	chr6:31355563-31355588	GUGGUGGGUCACGUGUGUCUUUGGG	1490
3106_4_34	HLA-B	Exon 4	+	chr6:31355571-31355596	UCACGUGUGUCUUUGGGGGGUCUGA	1491
3106_4_35	HLA-B	Exon 4	+	chr6:31355572-31355597	CACGUGUGUCUUUGGGGGUCUGAU	1492
3106_4_36	HLA-B	Exon 4	-	chr6:31355299-31355324	GAGAUGGGGUAAGGAGGGGGAUGAG	1493
3106_4_37	HLA-B	Exon 4	-	chr6:31355300-31355325	UGAGAUGGGGUAAGGAGGGGGAUGA	1494
3106_4_38	HLA-B	Exon 4	-	chr6:31355301-31355326	CUGAGAUGGGGUAAGGAGGGGGAUG	1495
3106_4_39	HLA-B	Exon 4	-	chr6:31355307-31355332	CUCACCCUGAGAUGGGGUAAGGAGG	1496
3106_4_40	HLA-B	Exon 4	-	chr6:31355308-31355333	CCUCACCCUGAGAUGGGGUAAGGAG	1497
3106_4_41	HLA-B	Exon 4	-	chr6:31355309-31355334	CCCUCACCCUGAGAUGGGGUAAGGA	1498
3106_4_42	HLA-B	Exon 4	-	chr6:31355310-31355335	CCCCUCACCCUGAGAUGGGGUAAGG	1499
3106_4_43	HLA-B	Exon 4	-	chr6:31355313-31355338	AAGCCCCUCACCCUGAGAUGGGGUA	1500
3106_4_44	HLA-B	Exon 4	-	chr6:31355318-31355343	UGCCGAAGCCCCUCACCCUGAGAUG	1501
3106_4_45	HLA-B	Exon 4	-	chr6:31355319-31355344	CUGCCGAAGCCCCUCACCCUGAGAU	1502
3106_4_46	HLA-B	Exon 4	-	chr6:31355320-31355345	GCUGCCGAAGCCCCUCACCCUGAGA	1503
3106_4_47	HLA-B	Exon 4	-	chr6:31355347-31355372	AUACACAUGCCAUGUACAGCAUGAG	1504
3106_4_48	HLA-B	Exon 4	-	chr6:31355348-31355373	GAUACACAUGCCAUGUACAGCAUGA	1505
3106_4_49	HLA-B	Exon 4	-	chr6:31355349-31355374	AGAUACACAUGCCAUGUACAGCAUG	1506
3106_4_50	HLA-B	Exon 4	-	chr6:31355387-31355412	AGUGGGCAGCUGUGGUGGUGCCUUC	1507
3106_4_51	HLA-B	Exon 4	-	chr6:31355397-31355422	ACCUUCCAGAAGUGGCAGCUGUGG	1508
3106_4_52	HLA-B	Exon 4	-	chr6:31355400-31355425	AGAACCUUCCAGAAGUGGGCAGCUG	1509
3106_4_53	HLA-B	Exon 4	-	chr6:31355409-31355434	GCAGGAGAUAGAACCUUCCAGAAGU	1510

3106_4_54	HLA-B	Exon 4	-	chr6:31355410-31355435	AGCAGGAGAUAGAACCUUCCAGAAG	1511
3106_4_55	HLA-B	Exon 4	-	chr6:31355432-31355457	CUGAGCUUGUGGAGACCAGACCAGC	1512
3106_4_56	HLA-B	Exon 4	-	chr6:31355448-31355473	GACCAAACUCAGGACACUGAGCUUG	1513
3106_4_57	HLA-B	Exon 4	-	chr6:31355463-31355488	CAGCGGGAUGGCGAGGACCAAACUC	1514
3106_4_58	HLA-B	Exon 4	-	chr6:31355475-31355500	ACACUGACCUGGCAGCGGGAUGGCG	1515
3106_4_59	HLA-B	Exon 4	-	chr6:31355480-31355505	AGAUCACACUGACCUGGCAGCGGGA	1516
3106_4_60	HLA-B	Exon 4	-	chr6:31355484-31355509	GCGGAGAUCACACUGACCUGGCAGC	1517
3106_4_61	HLA-B	Exon 4	-	chr6:31355485-31355510	UGCGGAGAUCACACUGACCUGGCAG	1518
3106_4_62	HLA-B	Exon 4	-	chr6:31355491-31355516	CUACCCUGCGGAGAUCACACUGACC	1519
3106_4_63	HLA-B	Exon 4	-	chr6:31355508-31355533	UGCUGGGCCCUGGGUUUCUACCCUG	1520
3106_4_64	HLA-B	Exon 4	-	chr6:31355522-31355547	AGGCCACCCUGAGGUGCUGGGCCCU	1521
3106_4_65	HLA-B	Exon 4	-	chr6:31355523-31355548	GAGGCCACCCUGAGGUGCUGGGCCC	1522
3106_4_66	HLA-B	Exon 4	-	chr6:31355529-31355554	GACCAUGAGGCCACCCUGAGGUGCU	1523
3106_4_67	HLA-B	Exon 4	-	chr6:31355530-31355555	UGACCAUGAGGCCACCCUGAGGUGC	1524
3106_4_68	HLA-B	Exon 4	-	chr6:31355536-31355561	CAUCUCUGACCAUGAGGCCACCCUG	1525
3106_4_69	HLA-B	Exon 4	-	chr6:31355547-31355572	ACCCACCACCCCAUCUCUGACCAUG	1526
3106_3_1	HLA-B	Exon 3	+	chr6:31356173-31356198	CUCCAGCUUGUCCUUCCCGUUCUCC	1527
3106_3_2	HLA-B	Exon 3	+	chr6:31356182-31356207	GUCCUUCCCGUUCUCCAGGUAUCUG	1528
3106_3_3	HLA-B	Exon 3	+	chr6:31356209-31356234	GAGCCACUCCACGCACUCGCCCUCC	1529
3106_3_4	HLA-B	Exon 3	+	chr6:31356213-31356238	CACUCCACGCACUCGCCCUCCAGGU	1530
3106_3_5	HLA-B	Exon 3	+	chr6:31356236-31356261	GUAGGCUCUCCGCUGCUCCGCCUCA	1531
3106_3_6	HLA-B	Exon 3	+	chr6:31356237-31356262	UAGGCUCUCCGCUGCUCCGCCUCAC	1532
3106_3_7	HLA-B	Exon 3	+	chr6:31356257-31356282	CUCACGGGCCGCCUCCCACUUGCGC	1533
3106_3_8	HLA-B	Exon 3	+	chr6:31356258-31356283	UCACGGGCCGCCUCCCACUUGCGCU	1534
3106_3_9	HLA-B	Exon 3	+	chr6:31356282-31356307	UGGGUGAUCUGAGCCGCCGUGUCCG	1535

3106_3_10	HLA-B	Exon 3	+	chr6:31356285-31356310	GUGAUCUGAGCCGCCGUGUCCGCGG	1536
3106_3_11	HLA-B	Exon 3	+	chr6:31356291-31356316	UGAGCCGCCGUGUCCGCGGCGGUCC	1537
3106_3_12	HLA-B	Exon 3	+	chr6:31356299-31356324	CGUGUCCGCGGCGGUCCAGGAGCGC	1538
3106_3_13	HLA-B	Exon 3	+	chr6:31356311-31356336	GGUCCAGGAGCGCAGGUCCUCGUUC	1539
3106_3_14	HLA-B	Exon 3	+	chr6:31356312-31356337	GUCCAGGAGCGCAGGUCCUCGUUCA	1540
3106_3_15	HLA-B	Exon 3	+	chr6:31356336-31356361	AGGGCGAUGUAAUCCUUGCCGUCGU	1541
3106_3_16	HLA-B	Exon 3	+	chr6:31356344-31356369	GUAAUCCUUGCCGUCGUAGGCGUAC	1542
3106_3_17	HLA-B	Exon 3	+	chr6:31356356-31356381	GUCGUAGGCGUACUGGUCAUGCCCG	1543
3106_3_18	HLA-B	Exon 3	+	chr6:31356359-31356384	GUAGGCGUACUGGUCAUGCCCGCGG	1544
3106_3_19	HLA-B	Exon 3	+	chr6:31356362-31356387	GGCGUACUGGUCAUGCCCGCGGAGG	1545
3106_3_20	HLA-B	Exon 3	+	chr6:31356373-31356398	CAUGCCCGCGGAGGAGGCGCCCGUC	1546
3106_3_21	HLA-B	Exon 3	+	chr6:31356401-31356426	CCCCACGUCGCAGCCGUACAUGCUC	1547
3106_3_22	HLA-B	Exon 3	+	chr6:31356404-31356429	CACGUCGCAGCCGUACAUGCUCUGG	1548
3106_3_23	HLA-B	Exon 3	+	chr6:31356405-31356430	ACGUCGCAGCCGUACAUGCUCUGGA	1549
3106_3_24	HLA-B	Exon 3	-	chr6:31356151-31356176	GAGCGCGCUGGUACCAGGGGCAGUG	1550
3106_3_25	HLA-B	Exon 3	-	chr6:31356152-31356177	GGAGCGCGCUGGUACCAGGGGCAGU	1551
3106_3_26	HLA-B	Exon 3	-	chr6:31356153-31356178	UGGAGCGCGCUGGUACCAGGGGCAG	1552
3106_3_27	HLA-B	Exon 3	-	chr6:31356159-31356184	ACAAGCUGGAGCGCGCUGGUACCAG	1553
3106_3_28	HLA-B	Exon 3	-	chr6:31356160-31356185	GACAAGCUGGAGCGCGCUGGUACCA	1554
3106_3_29	HLA-B	Exon 3	-	chr6:31356161-31356186	GGACAAGCUGGAGCGCGCUGGUACC	1555
3106_3_30	HLA-B	Exon 3	-	chr6:31356168-31356193	ACGGGAAGGACAAGCUGGAGCGCGC	1556
3106_3_31	HLA-B	Exon 3	-	chr6:31356178-31356203	UACCUGGAGAACGGGAAGGACAAGC	1557
3106_3_32	HLA-B	Exon 3	-	chr6:31356187-31356212	CUCCGCAGAUACCUGGAGAACGGGA	1558
3106_3_33	HLA-B	Exon 3	-	chr6:31356191-31356216	GUGGCUCCGCAGAUACCUGGAGAAC	1559
3106_3_34	HLA-B	Exon 3	-	chr6:31356192-31356217	AGUGGCUCCGCAGAUACCUGGAGAA	1560

3106_3_35	HLA-B	Exon 3	-	chr6:31356199-31356224	UGCGUGGAGUGGCUCCGCAGAUACC	1561
3106_3_36	HLA-B	Exon 3	-	chr6:31356215-31356240	CUACCUGGAGGGCGAGUGCGUGGAG	1562
3106_3_37	HLA-B	Exon 3	-	chr6:31356220-31356245	AGAGCCUACCUGGAGGGCGAGUGCG	1563
3106_3_38	HLA-B	Exon 3	-	chr6:31356231-31356256	CGGAGCAGCGGAGAGCCUACCUGGA	1564
3106_3_39	HLA-B	Exon 3	-	chr6:31356232-31356257	GCGGAGCAGCGGAGAGCCUACCUGG	1565
3106_3_40	HLA-B	Exon 3	-	chr6:31356235-31356260	GAGGCGGAGCAGCGGAGAGCCUACC	1566
3106_3_41	HLA-B	Exon 3	-	chr6:31356248-31356273	GGAGGCGGCCCGUGAGGCGGAGCAG	1567
3106_3_42	HLA-B	Exon 3	-	chr6:31356256-31356281	CGCAAGUGGGAGGCGGCCCGUGAGG	1568
3106_3_43	HLA-B	Exon 3	-	chr6:31356259-31356284	CAGCGCAAGUGGGAGGCGGCCCGUG	1569
3106_3_44	HLA-B	Exon 3	-	chr6:31356268-31356293	CAGAUCACCCAGCGCAAGUGGGAGG	1570
3106_3_45	HLA-B	Exon 3	-	chr6:31356271-31356296	GCUCAGAUCACCCAGCGCAAGUGGG	1571
3106_3_46	HLA-B	Exon 3	-	chr6:31356274-31356299	GCGGCUCAGAUCACCCAGCGCAAGU	1572
3106_3_47	HLA-B	Exon 3	-	chr6:31356275-31356300	GGCGGCUCAGAUCACCCAGCGCAAG	1573
3106_3_48	HLA-B	Exon 3	-	chr6:31356298-31356323	CGCUCCUGGACCGCCGCGGACACGG	1574
3106_3_49	HLA-B	Exon 3	-	chr6:31356301-31356326	CUGCGCUCCUGGACCGCCGCGGACA	1575
3106_3_50	HLA-B	Exon 3	-	chr6:31356307-31356332	GAGGACCUGCGCUCCUGGACCGCCG	1576
3106_3_51	HLA-B	Exon 3	-	chr6:31356317-31356342	CGCCCUGAACGAGGACCUGCGCUCC	1577
3106_3_52	HLA-B	Exon 3	-	chr6:31356331-31356356	GGCAAGGAUUACAUCGCCCUGAACG	1578
3106_3_53	HLA-B	Exon 3	-	chr6:31356352-31356377	CAUGACCAGUACGCCUACGACGGCA	1579
3106_3_54	HLA-B	Exon 3	-	chr6:31356357-31356382	GCGGGCAUGACCAGUACGCCUACGA	1580
3106_3_55	HLA-B	Exon 3	-	chr6:31356380-31356405	GGGGCCGGACGGGCGCCUCCUCCGC	1581
3106_3_56	HLA-B	Exon 3	-	chr6:31356381-31356406	UGGGGCCGGACGGGCGCCUCCUCCG	1582
3106_3_57	HLA-B	Exon 3	-	chr6:31356395-31356420	GUACGGCUGCGACGUGGGGCCGGAC	1583
3106_3_58	HLA-B	Exon 3	-	chr6:31356396-31356421	UGUACGGCUGCGACGUGGGGCCGGA	1584
3106_3_59	HLA-B	Exon 3	-	chr6:31356400-31356425	AGCAUGUACGGCUGCGACGUGGGGC	1585

3106_3_60	HLA-B	Exon 3	-	chr6:31356404-31356429	CCAGAGCAUGUACGGCUGCGACGUG	1586
3106_3_61	HLA-B	Exon 3	-	chr6:31356405-31356430	UCCAGAGCAUGUACGGCUGCGACGU	1587
3106_3_62	HLA-B	Exon 3	-	chr6:31356406-31356431	CUCCAGAGCAUGUACGGCUGCGACG	1588
3106_3_63	HLA-B	Exon 3	-	chr6:31356417-31356442	CCUCUCACACCCUCCAGAGCAUGUA	1589
3106_2_1	HLA-B	Exon 2	+	chr6:31356662-31356687	UGCGCCCCGGGCCGGGGUCACUCAC	1590
3106_2_2	HLA-B	Exon 2	+	chr6:31356673-31356698	CCGGGGUCACUCACCGGCCUCGCUC	1591
3106_2_3	HLA-B	Exon 2	+	chr6:31356691-31356716	CUCGCUCUGGUUGUAGUAGCCGCGC	1592
3106_2_4	HLA-B	Exon 2	+	chr6:31356700-31356725	GUUGUAGUAGCCGCGCAGGUUCCGC	1593
3106_2_5	HLA-B	Exon 2	+	chr6:31356709-31356734	GCCGCGCAGGUUCCGCAGGCUCUCU	1594
3106_2_6	HLA-B	Exon 2	+	chr6:31356724-31356749	CAGGCUCUCUCGGUCAGUCUGUGCC	1595
3106_2_7	HLA-B	Exon 2	+	chr6:31356725-31356750	AGGCUCUCUCGGUCAGUCUGUGCCU	1596
3106_2_8	HLA-B	Exon 2	+	chr6:31356748-31356773	CUGGGCCUUGUAGAUCUGUGUGUUC	1597
3106_2_9	HLA-B	Exon 2	+	chr6:31356762-31356787	UCUGUGUGUUCCGGUCCCAAUACUC	1598
3106_2_10	HLA-B	Exon 2	+	chr6:31356783-31356808	ACUCCGGCCCCUCCUGCUCUAUCCA	1599
3106_2_11	HLA-B	Exon 2	+	chr6:31356792-31356817	CCUCCUGCUCUAUCCACGGCGCCCG	1600
3106_2_12	HLA-B	Exon 2	+	chr6:31356804-31356829	UCCACGGCGCCCGCGGCUCCUCUCU	1601
3106_2_13	HLA-B	Exon 2	+	chr6:31356812-31356837	GCCCGCGGCUCCUCUCUCGGACUCG	1602
3106_2_14	HLA-B	Exon 2	+	chr6:31356838-31356863	GGCGUCGCUGUCGAACCUCACGAAC	1603
3106_2_15	HLA-B	Exon 2	+	chr6:31356839-31356864	GCGUCGCUGUCGAACCUCACGAACU	1604
3106_2_16	HLA-B	Exon 2	+	chr6:31356871-31356896	GUCCACGUAGCCCACUGAGAUGAAG	1605
3106_2_17	HLA-B	Exon 2	+	chr6:31356872-31356897	UCCACGUAGCCCACUGAGAUGAAGC	1606
3106_2_18	HLA-B	Exon 2	+	chr6:31356873-31356898	CCACGUAGCCCACUGAGAUGAAGCG	1607
3106_2_19	HLA-B	Exon 2	+	chr6:31356883-31356908	CACUGAGAUGAAGCGGGGCUCCCCG	1608
3106_2_20	HLA-B	Exon 2	+	chr6:31356887-31356912	GAGAUGAAGCGGGGCUCCCCGCGGC	1609
3106_2_21	HLA-B	Exon 2	+	chr6:31356888-31356913	AGAUGAAGCGGGGCUCCCCGCGGCC	1610

3106_2_22	HLA-B	Exon 2	+	chr6:31356892-31356917	GAAGCGGGGCUCCCCGCGGCCGGGC	1611
3106_2_23	HLA-B	Exon 2	+	chr6:31356893-31356918	AAGCGGGGCUCCCCGCGGCCGGGCC	1612
3106_2_24	HLA-B	Exon 2	+	chr6:31356899-31356924	GGCUCCCCGCGGCCGGGCCGGGACA	1613
3106_2_25	HLA-B	Exon 2	+	chr6:31356902-31356927	UCCCCGCGGCCGGGCCGGGACACGG	1614
3106_2_26	HLA-B	Exon 2	+	chr6:31356920-31356945	GACACGGAGGUGUAGAAAUACCUCA	1615
3106_2_27	HLA-B	Exon 2	+	chr6:31356925-31356950	GGAGGUGUAGAAAUACCUCAUGGAG	1616
3106_2_28	HLA-B	Exon 2	+	chr6:31356926-31356951	GAGGUGUAGAAAUACCUCAUGGAGU	1617
3106_2_29	HLA-B	Exon 2	+	chr6:31356933-31356958	AGAAAUACCUCAUGGAGUGGGAGCC	1618
3106_2_30	HLA-B	Exon 2	+	chr6:31356934-31356959	GAAAUACCUCAUGGAGUGGGAGCCU	1619
3106_2_31	HLA-B	Exon 2	+	chr6:31356935-31356960	AAAUACCUCAUGGAGUGGGAGCCUG	1620
3106_2_32	HLA-B	Exon 2	+	chr6:31356936-31356961	AAUACCUCAUGGAGUGGGAGCCUGG	1621
3106_2_33	HLA-B	Exon 2	+	chr6:31356941-31356966	CUCAUGGAGUGGGAGCCUGGGGGUG	1622
3106_2_34	HLA-B	Exon 2	+	chr6:31356944-31356969	AUGGAGUGGGAGCCUGGGGGUGAGG	1623
3106_2_35	HLA-B	Exon 2	+	chr6:31356945-31356970	UGGAGUGGGAGCCUGGGGGUGAGGA	1624
3106_2_36	HLA-B	Exon 2	+	chr6:31356946-31356971	GGAGUGGGAGCCUGGGGGUGAGGAG	1625
3106_2_37	HLA-B	Exon 2	-	chr6:31356669-31356694	GAGGCCGGUGAGUGACCCCGGCCCG	1626
3106_2_38	HLA-B	Exon 2	-	chr6:31356670-31356695	CGAGGCCGGUGAGUGACCCCGGCCC	1627
3106_2_39	HLA-B	Exon 2	-	chr6:31356671-31356696	GCGAGGCCGGUGAGUGACCCCGGCC	1628
3106_2_40	HLA-B	Exon 2	-	chr6:31356676-31356701	CCAGAGCGAGGCCGGUGAGUGACCC	1629
3106_2_41	HLA-B	Exon 2	-	chr6:31356689-31356714	GCGGCUACUACAACCAGAGCGAGGC	1630
3106_2_42	HLA-B	Exon 2	-	chr6:31356693-31356718	CUGCGCGGCUACUACAACCAGAGCG	1631
3106_2_43	HLA-B	Exon 2	-	chr6:31356713-31356738	ACCGAGAGAGCCUGCGGAACCUGCG	1632
3106_2_44	HLA-B	Exon 2	-	chr6:31356724-31356749	GGCACAGACUGACCGAGAGAGCCUG	1633
3106_2_45	HLA-B	Exon 2	-	chr6:31356750-31356775	CGGAACACACAGAUCUACAAGGCCC	1634
3106_2_46	HLA-B	Exon 2	-	chr6:31356756-31356781	UGGGACCGGAACACACAGAUCUACA	1635

3106_2_47	HLA-B	Exon 2	-	chr6:31356775-31356800	GCAGGAGGGGCCGGAGUAUUGGGAC	1636
3106_2_48	HLA-B	Exon 2	-	chr6:31356780-31356805	AUAGAGCAGGAGGGGCCGGAGUAUU	1637
3106_2_49	HLA-B	Exon 2	-	chr6:31356781-31356806	GAUAGAGCAGGAGGGGCCGGAGUAU	1638
3106_2_50	HLA-B	Exon 2	-	chr6:31356789-31356814	GCGCCGUGGAUAGAGCAGGAGGGGC	1639
3106_2_51	HLA-B	Exon 2	-	chr6:31356793-31356818	GCGGGCGCCGUGGAUAGAGCAGGAG	1640
3106_2_52	HLA-B	Exon 2	-	chr6:31356794-31356819	CGCGGGCGCCGUGGAUAGAGCAGGA	1641
3106_2_53	HLA-B	Exon 2	-	chr6:31356795-31356820	CCGCGGGCGCCGUGGAUAGAGCAGG	1642
3106_2_54	HLA-B	Exon 2	-	chr6:31356798-31356823	GAGCCGCGGGCGCCGUGGAUAGAGC	1643
3106_2_55	HLA-B	Exon 2	-	chr6:31356808-31356833	UCCGAGAGAGGAGCCGCGGGCGCCG	1644
3106_2_56	HLA-B	Exon 2	-	chr6:31356816-31356841	GCCGCGAGUCCGAGAGAGGAGCCGC	1645
3106_2_57	HLA-B	Exon 2	-	chr6:31356817-31356842	CGCCGCGAGUCCGAGAGAGGAGCCG	1646
3106_2_58	HLA-B	Exon 2	-	chr6:31356825-31356850	GACAGCGACGCCGCGAGUCCGAGAG	1647
3106_2_59	HLA-B	Exon 2	-	chr6:31356856-31356881	CUACGUGGACGACACCCAGUUCGUG	1648
3106_2_60	HLA-B	Exon 2	-	chr6:31356876-31356901	CCCCGCUUCAUCUCAGUGGGCUACG	1649
3106_2_61	HLA-B	Exon 2	-	chr6:31356884-31356909	GCGGGGAGCCCCGCUUCAUCUCAGU	1650
3106_2_62	HLA-B	Exon 2	-	chr6:31356885-31356910	CGCGGGGAGCCCCGCUUCAUCUCAG	1651
3106_2_63	HLA-B	Exon 2	-	chr6:31356906-31356931	ACCUCCGUGUCCCGGCCCGGCCGCG	1652
3106_2_64	HLA-B	Exon 2	-	chr6:31356907-31356932	CACCUCCGUGUCCCGGCCCGGCCGC	1653
3106_2_65	HLA-B	Exon 2	-	chr6:31356908-31356933	ACACCUCCGUGUCCCGGCCCGGCCG	1654
3106_2_66	HLA-B	Exon 2	-	chr6:31356914-31356939	AUUUCUACACCUCCGUGUCCCGGCC	1655
3106_2_67	HLA-B	Exon 2	-	chr6:31356919-31356944	GAGGUAUUUCUACACCUCCGUGUCC	1656
3106_2_68	HLA-B	Exon 2	-	chr6:31356943-31356968	CUCACCCCCAGGCUCCCACUCCAUG	1657
3106_1_1	HLA-B	Exon 1	+	chr6:31357060-31357085	CAUUUCCCUCCCGACCCGCACUCAC	1658
3106_1_2	HLA-B	Exon 1	+	chr6:31357066-31357091	CCUCCCGACCCGCACUCACCGGCCC	1659
3106_1_3	HLA-B	Exon 1	+	chr6:31357072-31357097	GACCCGCACUCACCGGCCCAGGUCU	1660

3106_1_4	HLA-B	Exon 1	+	chr6:31357077-31357102	GCACUCACCGGCCCAGGUCUCGGUC	1661
3106_1_5	HLA-B	Exon 1	+	chr6:31357078-31357103	CACUCACCGGCCCAGGUCUCGGUCA	1662
3106_1_6	HLA-B	Exon 1	+	chr6:31357083-31357108	ACCGGCCCAGGUCUCGGUCAGGGCC	1663
3106_1_7	HLA-B	Exon 1	+	chr6:31357084-31357109	CCGGCCCAGGUCUCGGUCAGGGCCA	1664
3106_1_8	HLA-B	Exon 1	+	chr6:31357101-31357126	CAGGGCCAGGGCCGCCGAGAGCAGC	1665
3106_1_9	HLA-B	Exon 1	+	chr6:31357104-31357129	GGCCAGGGCCGCCGAGAGCAGCAGG	1666
3106_1_10	HLA-B	Exon 1	+	chr6:31357108-31357133	AGGGCCGCCGAGAGCAGCAGGAGGA	1667
3106_1_11	HLA-B	Exon 1	+	chr6:31357113-31357138	CGCCGAGAGCAGCAGGAGGACGGUU	1668
3106_1_12	HLA-B	Exon 1	+	chr6:31357114-31357139	GCCGAGAGCAGCAGGAGGACGGUUC	1669
3106_1_13	HLA-B	Exon 1	+	chr6:31357115-31357140	CCGAGAGCAGCAGGAGGACGGUUCG	1670
3106_1_14	HLA-B	Exon 1	+	chr6:31357135-31357160	GUUCGGGGCGCCAUGACCAGCAUCU	1671
3106_1_15	HLA-B	Exon 1	+	chr6:31357144-31357169	GCCAUGACCAGCAUCUCGGCGUCUG	1672
3106_1_16	HLA-B	Exon 1	+	chr6:31357159-31357184	UCGGCGUCUGAGGAGACUCUGAGUC	1673
3106_1_17	HLA-B	Exon 1	+	chr6:31357160-31357185	CGGCGUCUGAGGAGACUCUGAGUCC	1674
3106_1_18	HLA-B	Exon 1	+	chr6:31357163-31357188	CGUCUGAGGAGACUCUGAGUCCGGG	1675
3106_1_19	HLA-B	Exon 1	+	chr6:31357164-31357189	GUCUGAGGAGACUCUGAGUCCGGGU	1676
3106_1_20	HLA-B	Exon 1	+	chr6:31357171-31357196	GAGACUCUGAGUCCGGGUGGGUGCG	1677
3106_1_21	HLA-B	Exon 1	+	chr6:31357172-31357197	AGACUCUGAGUCCGGGUGGGUGCGU	1678
3106_1_22	HLA-B	Exon 1	+	chr6:31357173-31357198	GACUCUGAGUCCGGGUGGGUGCGUG	1679
3106_1_23	HLA-B	Exon 1	+	chr6:31357186-31357211	GGUGGGUGCGUGGGGACUUUAGAAC	1680
3106_1_24	HLA-B	Exon 1	+	chr6:31357187-31357212	GUGGGUGCGUGGGGACUUUAGAACU	1681
3106_1_25	HLA-B	Exon 1	+	chr6:31357194-31357219	CGUGGGGACUUUAGAACUGGGACCG	1682
3106_1_26	HLA-B	Exon 1	+	chr6:31357207-31357232	GAACUGGGACCGCGGCGACGCUGAU	1683
3106_1_27	HLA-B	Exon 1	-	chr6:31357068-31357093	CUGGGCCGGUGAGUGCGGGUCGGGA	1684
3106_1_28	HLA-B	Exon 1	-	chr6:31357069-31357094	CCUGGGCCGGUGAGUGCGGGUCGGG	1685

3106_1_29	HLA-B	Exon 1	-	chr6:31357072-31357097	AGACCUGGGCCGGUGAGUGCGGGUC	1686
3106_1_30	HLA-B	Exon 1	-	chr6:31357073-31357098	GAGACCUGGGCCGGUGAGUGCGGGU	1687
3106_1_31	HLA-B	Exon 1	-	chr6:31357077-31357102	GACCGAGACCUGGGCCGGUGAGUGC	1688
3106_1_32	HLA-B	Exon 1	-	chr6:31357078-31357103	UGACCGAGACCUGGGCCGGUGAGUG	1689
3106_1_33	HLA-B	Exon 1	-	chr6:31357087-31357112	CCCUGGCCCUGACCGAGACCUGGGC	1690
3106_1_34	HLA-B	Exon 1	-	chr6:31357091-31357116	GCGGCCCUGGCCCUGACCGAGACCU	1691
3106_1_35	HLA-B	Exon 1	-	chr6:31357092-31357117	GGCGGCCCUGGCCCUGACCGAGACC	1692
3106_1_36	HLA-B	Exon 1	-	chr6:31357109-31357134	GUCCUCCUGCUGCUCUCGGCGGCCC	1693
3106_1_37	HLA-B	Exon 1	-	chr6:31357115-31357140	CGAACCGUCCUCCUGCUGCUCUCGG	1694
3106_1_38	HLA-B	Exon 1	-	chr6:31357118-31357143	CCCCGAACCGUCCUCCUGCUGCUCU	1695
3106_1_39	HLA-B	Exon 1	-	chr6:31357148-31357173	UCCUCAGACGCCGAGAUGCUGGUCA	1696
3106_1_40	HLA-B	Exon 1	-	chr6:31357154-31357179	AGAGUCUCCUCAGACGCCGAGAUGC	1697
3106_1_41	HLA-B	Exon 1	-	chr6:31357186-31357211	GUUCUAAAGUCCCCACGCACCCACC	1698
3107_8_1	HLA-C	Exon 8	+	chr6:31268726-31268751	CUCAGCACAGCGAACAUGCAAAUUC	1699
3107_8_2	HLA-C	Exon 8	+	chr6:31268730-31268755	GCACAGCGAACAUGCAAAUUCUGGA	1700
3107_8_3	HLA-C	Exon 8	+	chr6:31268738-31268763	AACAUGCAAAUUCUGGAAGGUUCUC	1701
3107_8_4	HLA-C	Exon 8	+	chr6:31268765-31268790	GUCUUUAUUUGCUCUCUCAACUUCU	1702
3107_8_5	HLA-C	Exon 8	+	chr6:31268834-31268859	UAUUUGAGAACACAAAUUUAUAUUC	1703
3107_8_6	HLA-C	Exon 8	+	chr6:31268851-31268876	UUAUAUUCAGGUUCUUAACUUCAUU	1704
3107_8_7	HLA-C	Exon 8	+	chr6:31268852-31268877	UAUAUUCAGGUUCUUAACUUCAUUA	1705
3107_8_8	HLA-C	Exon 8	+	chr6:31268900-31268925	GUGCACCAUGAAUUUGAGACAGAGA	1706
3107_8_9	HLA-C	Exon 8	+	chr6:31268924-31268949	AUGGAGACAUCCAGCCCCACCUCUC	1707
3107_8_10	HLA-C	Exon 8	+	chr6:31268930-31268955	ACAUCCAGCCCCACCUCUCUGGAAC	1708
3107_8_11	HLA-C	Exon 8	+	chr6:31268942-31268967	ACCUCUCUGGAACAGGAAAGAUGAU	1709
3107_8_12	HLA-C	Exon 8	+	chr6:31268943-31268968	CCUCUCUGGAACAGGAAAGAUGAUC	1710

3107_8_13	HLA-C	Exon 8	+	chr6:31268944-31268969	CUCUCUGGAACAGGAAAGAUGAUCG	1711
3107_8_14	HLA-C	Exon 8	+	chr6:31268947-31268972	UCUGGAACAGGAAAGAUGAUCGGGG	1712
3107_8_15	HLA-C	Exon 8	+	chr6:31268948-31268973	CUGGAACAGGAAAGAUGAUCGGGGA	1713
3107_8_16	HLA-C	Exon 8	+	chr6:31268956-31268981	GGAAAGAUGAUCGGGGAGGGAACAC	1714
3107_8_17	HLA-C	Exon 8	+	chr6:31268965-31268990	AUCGGGGAGGGAACACAGGUCAGUG	1715
3107_8_18	HLA-C	Exon 8	+	chr6:31268966-31268991	UCGGGGAGGGAACACAGGUCAGUGU	1716
3107_8_19	HLA-C	Exon 8	+	chr6:31268967-31268992	CGGGGAGGGAACACAGGUCAGUGUG	1717
3107_8_20	HLA-C	Exon 8	+	chr6:31268972-31268997	AGGGAACACAGGUCAGUGUGGGGAC	1718
3107_8_21	HLA-C	Exon 8	+	chr6:31268973-31268998	GGGAACACAGGUCAGUGUGGGGACA	1719
3107_8_22	HLA-C	Exon 8	+	chr6:31268974-31268999	GGAACACAGGUCAGUGUGGGGACAG	1720
3107_8_23	HLA-C	Exon 8	+	chr6:31268980-31269005	CAGGUCAGUGUGGGGACAGGGGUCA	1721
3107_8_24	HLA-C	Exon 8	+	chr6:31268983-31269008	GUCAGUGUGGGGACAGGGGUCACGG	1722
3107_8_25	HLA-C	Exon 8	+	chr6:31268989-31269014	GUGGGGACAGGGGUCACGGUGGACA	1723
3107_8_26	HLA-C	Exon 8	+	chr6:31268990-31269015	UGGGGACAGGGGUCACGGUGGACAC	1724
3107_8_27	HLA-C	Exon 8	+	chr6:31268991-31269016	GGGGACAGGGGUCACGGUGGACACG	1725
3107_8_28	HLA-C	Exon 8	+	chr6:31268992-31269017	GGGACAGGGGUCACGGUGGACACGG	1726
3107_8_29	HLA-C	Exon 8	+	chr6:31268995-31269020	ACAGGGGUCACGGUGGACACGGGGG	1727
3107_8_30	HLA-C	Exon 8	+	chr6:31268996-31269021	CAGGGGUCACGGUGGACACGGGGGU	1728
3107_8_31	HLA-C	Exon 8	+	chr6:31269030-31269055	CUCCACCUCCUCACAUUAUGCUAAC	1729
3107_8_32	HLA-C	Exon 8	+	chr6:31269048-31269073	UGCUAACAGGAACGCAGACACAUUC	1730
3107_8_33	HLA-C	Exon 8	+	chr6:31269075-31269100	GUGCCUUUGCAGAAAGAGAUGCCAG	1731
3107_8_34	HLA-C	Exon 8	+	chr6:31269093-31269118	AUGCCAGAGGCUCUUGAAGUCACAA	1732
3107_8_35	HLA-C	Exon 8	+	chr6:31269098-31269123	AGAGGCUCUUGAAGUCACAAAGGAG	1733
3107_8_36	HLA-C	Exon 8	+	chr6:31269132-31269157	GAAAUCCUGCAUCUCAGUCCCACAC	1734
3107_8_37	HLA-C	Exon 8	+	chr6:31269145-31269170	UCAGUCCCACACAGGCAGCUGUCUC	1735

3107_8_38	HLA-C	Exon 8	-	chr6:31268816-31268841	UCAAAUAUUUGCUAUGAAGCGUUGA	1736
3107_8_39	HLA-C	Exon 8	-	chr6:31268908-31268933	UGUCUCCAUCUCUGUCUCAAAUUCA	1737
3107_8_40	HLA-C	Exon 8	-	chr6:31268937-31268962	CUUUCCUGUUCCAGAGAGGUGGGGC	1738
3107_8_41	HLA-C	Exon 8	-	chr6:31268941-31268966	UCAUCUUUCCUGUUCCAGAGAGGUG	1739
3107_8_42	HLA-C	Exon 8	-	chr6:31268942-31268967	AUCAUCUUUCCUGUUCCAGAGAGGU	1740
3107_8_43	HLA-C	Exon 8	-	chr6:31268943-31268968	GAUCAUCUUUCCUGUUCCAGAGAGG	1741
3107_8_44	HLA-C	Exon 8	-	chr6:31268946-31268971	CCCGAUCAUCUUUCCUGUUCCAGAG	1742
3107_8_45	HLA-C	Exon 8	-	chr6:31269035-31269060	UUCCUGUUAGCAUAAUGUGAGGAGG	1743
3107_8_46	HLA-C	Exon 8	-	chr6:31269038-31269063	GCGUUCCUGUUAGCAUAAUGUGAGG	1744
3107_8_47	HLA-C	Exon 8	-	chr6:31269041-31269066	UCUGCGUUCCUGUUAGCAUAAUGUG	1745
3107_8_48	HLA-C	Exon 8	-	chr6:31269081-31269106	GAGCCUCUGGCAUCUCUUUCUGCAA	1746
3107_8_49	HLA-C	Exon 8	-	chr6:31269099-31269124	UCUCCUUUGUGACUUCAAGAGCCUC	1747
3107_8_50	HLA-C	Exon 8	-	chr6:31269140-31269165	AGCUGCCUGUGUGGGACUGAGAUGC	1748
3107_8_51	HLA-C	Exon 8	-	chr6:31269153-31269178	UGUAGCCUGAGACAGCUGCCUGUGU	1749
3107_8_52	HLA-C	Exon 8	-	chr6:31269154-31269179	CUGUAGCCUGAGACAGCUGCCUGUG	1750
3107_7_1	HLA-C	Exon 7	+	chr6:31269344-31269369	AGUGAUGAGAGACUCAUCAGAGCCC	1751
3107_7_2	HLA-C	Exon 7	+	chr6:31269345-31269370	GUGAUGAGAGACUCAUCAGAGCCCU	1752
3107_7_3	HLA-C	Exon 7	+	chr6:31269361-31269386	CAGAGCCCUGGGCACUGUUGCUGCC	1753
3107_7_4	HLA-C	Exon 7	+	chr6:31269362-31269387	AGAGCCCUGGGCACUGUUGCUGCCU	1754
3107_7_5	HLA-C	Exon 7	+	chr6:31269363-31269388	GAGCCCUGGGCACUGUUGCUGCCUG	1755
3107_7_6	HLA-C	Exon 7	-	chr6:31269315-31269340	AAGGUGAGAUUCUGGGGAGCUGAAG	1756
3107_7_7	HLA-C	Exon 7	-	chr6:31269326-31269351	CAUCACUUGUAAAGGUGAGAUUCUG	1757
3107_7_8	HLA-C	Exon 7	-	chr6:31269327-31269352	UCAUCACUUGUAAAGGUGAGAUUCU	1758
3107_7_9	HLA-C	Exon 7	-	chr6:31269328-31269353	CUCAUCACUUGUAAAGGUGAGAUUC	1759
3107_7_10	HLA-C	Exon 7	-	chr6:31269339-31269364	CUGAUGAGUCUCUCAUCACUUGUAA	1760

3107_7_11	HLA-C	Exon 7	-	chr6:31269369-31269394	CUACCCCAGGCAGCAACAGUGCCCA	1761
3107_7_12	HLA-C	Exon 7	-	chr6:31269370-31269395	UCUACCCCAGGCAGCAACAGUGCCC	1762
3107_6_1	HLA-C	Exon 6	+	chr6:31269503-31269528	GAGCAGCUCCCUCCUUUUCCACCUG	1763
3107_6_2	HLA-C	Exon 6	+	chr6:31269504-31269529	AGCAGCUCCCUCCUUUUCCACCUGU	1764
3107_6_3	HLA-C	Exon 6	-	chr6:31269470-31269495	CGUGUAAGUGAUGGCGGCGGGCGUG	1765
3107_6_4	HLA-C	Exon 6	-	chr6:31269477-31269502	CAGGCUGCGUGUAAGUGAUGGCGGC	1766
3107_6_5	HLA-C	Exon 6	-	chr6:31269478-31269503	UCAGGCUGCGUGUAAGUGAUGGCGG	1767
3107_6_6	HLA-C	Exon 6	-	chr6:31269481-31269506	CUCUCAGGCUGCGUGUAAGUGAUGG	1768
3107_6_7	HLA-C	Exon 6	-	chr6:31269484-31269509	CUGCUCUCAGGCUGCGUGUAAGUGA	1769
3107_6_8	HLA-C	Exon 6	-	chr6:31269501-31269526	GGUGGAAAAGGAGGGAGCUGCUCUC	1770
3107_6_9	HLA-C	Exon 6	-	chr6:31269514-31269539	UUUUCUUCCCACAGGUGGAAAAGGA	1771
3107_6_10	HLA-C	Exon 6	-	chr6:31269515-31269540	AUUUUCUUCCCACAGGUGGAAAAGG	1772
3107_6_11	HLA-C	Exon 6	-	chr6:31269518-31269543	GGCAUUUUCUUCCCACAGGUGGAAA	1773
3107_6_12	HLA-C	Exon 6	-	chr6:31269524-31269549	UCAUAGGGCAUUUUCUUCCCACAGG	1774
3107_5_1	HLA-C	Exon 5	+	chr6:31269967-31269992	GAGCUCUUCCUCCUACACAUCAUAG	1775
3107_5_2	HLA-C	Exon 5	+	chr6:31269984-31270009	CAUCAUAGCGGUGACCACAGCUCCA	1776
3107_5_3	HLA-C	Exon 5	+	chr6:31269993-31270018	GGUGACCACAGCUCCAAGGACAGCU	1777
3107_5_4	HLA-C	Exon 5	+	chr6:31270002-31270027	AGCUCCAAGGACAGCUAGGACAACC	1778
3107_5_5	HLA-C	Exon 5	+	chr6:31270011-31270036	GACAGCUAGGACAACCAGGACAGCC	1779
3107_5_6	HLA-C	Exon 5	+	chr6:31270033-31270058	GCCAGGCCAGCAACGAUGCCCAUGA	1780
3107_5_7	HLA-C	Exon 5	+	chr6:31270034-31270059	CCAGGCCAGCAACGAUGCCCAUGAU	1781
3107_5_8	HLA-C	Exon 5	+	chr6:31270035-31270060	CAGGCCAGCAACGAUGCCCAUGAUG	1782
3107_5_9	HLA-C	Exon 5	+	chr6:31270039-31270064	CCAGCAACGAUGCCCAUGAUGGGGA	1783
3107_5_10	HLA-C	Exon 5	+	chr6:31270042-31270067	GCAACGAUGCCCAUGAUGGGGAUGG	1784
3107_5_11	HLA-C	Exon 5	+	chr6:31270043-31270068	CAACGAUGCCCAUGAUGGGGAUGGU	1785

3107_5_12	HLA-C	Exon 5	+	chr6:31270047-31270072	GAUGCCCAUGAUGGGGAUGGUGGGC	1786
3107_5_13	HLA-C	Exon 5	+	chr6:31270048-31270073	AUGCCCAUGAUGGGGAUGGUGGGCU	1787
3107_5_14	HLA-C	Exon 5	+	chr6:31270055-31270080	UGAUGGGGAUGGUGGGCUGGGAAGA	1788
3107_5_15	HLA-C	Exon 5	+	chr6:31270061-31270086	GGAUGGUGGGCUGGGAAGAUGGCUC	1789
3107_5_16	HLA-C	Exon 5	+	chr6:31270062-31270087	GAUGGUGGGCUGGGAAGAUGGCUCU	1790
3107_5_17	HLA-C	Exon 5	+	chr6:31270067-31270092	UGGGCUGGGAAGAUGGCUCUGGGAA	1791
3107_5_18	HLA-C	Exon 5	+	chr6:31270070-31270095	GCUGGGAAGAUGGCUCUGGGAAAGG	1792
3107_5_19	HLA-C	Exon 5	+	chr6:31270076-31270101	AAGAUGGCUCUGGGAAAGGAGGAGA	1793
3107_5_20	HLA-C	Exon 5	+	chr6:31270081-31270106	GGCUCUGGGAAAGGAGGAGAAGGUG	1794
3107_5_21	HLA-C	Exon 5	+	chr6:31270082-31270107	GCUCUGGGAAAGGAGGAGAAGGUGA	1795
3107_5_22	HLA-C	Exon 5	-	chr6:31269944-31269969	UCAGGUAGGGAAGGGGUGAAGAGCG	1796
3107_5_23	HLA-C	Exon 5	-	chr6:31269945-31269970	CUCAGGUAGGGAAGGGGUGAAGAGC	1797
3107_5_24	HLA-C	Exon 5	-	chr6:31269946-31269971	GCUCAGGUAGGGAAGGGGUGAAGAG	1798
3107_5_25	HLA-C	Exon 5	-	chr6:31269956-31269981	AGGAGGAAGAGCUCAGGUAGGGAAG	1799
3107_5_26	HLA-C	Exon 5	-	chr6:31269957-31269982	UAGGAGGAAGAGCUCAGGUAGGGAA	1800
3107_5_27	HLA-C	Exon 5	-	chr6:31269958-31269983	GUAGGAGGAAGAGCUCAGGUAGGGA	1801
3107_5_28	HLA-C	Exon 5	-	chr6:31269962-31269987	AUGUGUAGGAGGAAGAGCUCAGGUA	1802
3107_5_29	HLA-C	Exon 5	-	chr6:31269963-31269988	GAUGUGUAGGAGGAAGAGCUCAGGU	1803
3107_5_30	HLA-C	Exon 5	-	chr6:31269967-31269992	CUAUGAUGUGUAGGAGGAAGAGCUC	1804
3107_5_31	HLA-C	Exon 5	-	chr6:31269978-31270003	UGUGGUCACCGCUAUGAUGUGUAGG	1805
3107_5_32	HLA-C	Exon 5	-	chr6:31269981-31270006	AGCUGUGGUCACCGCUAUGAUGUGU	1806
3107_5_33	HLA-C	Exon 5	-	chr6:31270001-31270026	GUUGUCCUAGCUGUCCUUGGAGCUG	1807
3107_5_34	HLA-C	Exon 5	-	chr6:31270009-31270034	CUGUCCUGGUUGUCCUAGCUGUCCU	1808
3107_5_35	HLA-C	Exon 5	-	chr6:31270028-31270053	GGCAUCGUUGCUGGCCUGGCUGUCC	1809
3107_5_36	HLA-C	Exon 5	-	chr6:31270037-31270062	CCCAUCAUGGGCAUCGUUGCUGGCC	1810

3107_5_37	HLA-C	Exon 5	-	chr6:31270042-31270067	CCAUCCCCAUCAUGGGCAUCGUUGC	1811
3107_5_38	HLA-C	Exon 5	-	chr6:31270054-31270079	CUUCCCAGCCCACCAUCCCCAUCAU	1812
3107_5_39	HLA-C	Exon 5	-	chr6:31270055-31270080	UCUUCCCAGCCCACCAUCCCCAUCA	1813
3107_4_1	HLA-C	Exon 4	+	chr6:31270192-31270217	CCCAUUCCCCUCCUUACCCCAGCUC	1814
3107_4_2	HLA-C	Exon 4	+	chr6:31270193-31270218	CCAUUCCCCUCCUUACCCCAGCUCA	1815
3107_4_3	HLA-C	Exon 4	+	chr6:31270198-31270223	CCCCUCCUUACCCCAGCUCAGGGUG	1816
3107_4_4	HLA-C	Exon 4	+	chr6:31270199-31270224	CCCUCCUUACCCCAGCUCAGGGUGA	1817
3107_4_5	HLA-C	Exon 4	+	chr6:31270200-31270225	CCUCCUUACCCCAGCUCAGGGUGAG	1818
3107_4_6	HLA-C	Exon 4	+	chr6:31270228-31270253	CUCUUGCAGCCCCUCGUGCUGCAUA	1819
3107_4_7	HLA-C	Exon 4	+	chr6:31270257-31270282	ACGUGUAUCUCUGCUCUUGUCCAGA	1820
3107_4_8	HLA-C	Exon 4	+	chr6:31270282-31270307	AGGCACCACCACAGCUGCCCACUUC	1821
3107_4_9	HLA-C	Exon 4	+	chr6:31270286-31270311	ACCACCACAGCUGCCCACUUCUGGA	1822
3107_4_10	HLA-C	Exon 4	+	chr6:31270302-31270327	ACUUCUGGAAGGUUCCAUCUCCUGC	1823
3107_4_11	HLA-C	Exon 4	+	chr6:31270307-31270332	UGGAAGGUUCCAUCUCCUGCUGGCC	1824
3107_4_12	HLA-C	Exon 4	+	chr6:31270322-31270347	CCUGCUGGCCUGGUCUCCACAAGCU	1825
3107_4_13	HLA-C	Exon 4	+	chr6:31270330-31270355	CCUGGUCUCCACAAGCUCGGUGUCC	1826
3107_4_14	HLA-C	Exon 4	+	chr6:31270331-31270356	CUGGUCUCCACAAGCUCGGUGUCCU	1827
3107_4_15	HLA-C	Exon 4	+	chr6:31270336-31270361	CUCCACAAGCUCGGUGUCCUGGGUC	1828
3107_4_16	HLA-C	Exon 4	+	chr6:31270358-31270383	GUCUGGUCCUCCCCAUCCCGCUGCC	1829
3107_4_17	HLA-C	Exon 4	+	chr6:31270377-31270402	GCUGCCAGGUCAGUGUGAUCUCCGC	1830
3107_4_18	HLA-C	Exon 4	+	chr6:31270378-31270403	CUGCCAGGUCAGUGUGAUCUCCGCA	1831
3107_4_19	HLA-C	Exon 4	+	chr6:31270390-31270415	UGUGAUCUCCGCAGGGUAGAAGCCC	1832
3107_4_20	HLA-C	Exon 4	+	chr6:31270391-31270416	GUGAUCUCCGCAGGGUAGAAGCCCA	1833
3107_4_21	HLA-C	Exon 4	+	chr6:31270405-31270430	GUAGAAGCCCAGGGCCCAGCACCUC	1834
3107_4_22	HLA-C	Exon 4	+	chr6:31270406-31270431	UAGAAGCCCAGGGCCCAGCACCUCA	1835

3107_4_23	HLA-C	Exon 4	+	chr6:31270409-31270434	AAGCCCAGGGCCCAGCACCUCAGGG	1836
3107_4_24	HLA-C	Exon 4	+	chr6:31270417-31270442	GGCCCAGCACCUCAGGGUGGCCUCA	1837
3107_4_25	HLA-C	Exon 4	+	chr6:31270426-31270451	CCUCAGGGUGGCCUCAUGGUCAGAG	1838
3107_4_26	HLA-C	Exon 4	+	chr6:31270427-31270452	CUCAGGGUGGCCUCAUGGUCAGAGA	1839
3107_4_27	HLA-C	Exon 4	+	chr6:31270428-31270453	UCAGGGUGGCCUCAUGGUCAGAGAG	1840
3107_4_28	HLA-C	Exon 4	+	chr6:31270429-31270454	CAGGGUGGCCUCAUGGUCAGAGAGG	1841
3107_4_29	HLA-C	Exon 4	+	chr6:31270432-31270457	GGUGGCCUCAUGGUCAGAGAGGGGG	1842
3107_4_30	HLA-C	Exon 4	+	chr6:31270435-31270460	GGCCUCAUGGUCAGAGAGGGGGUGG	1843
3107_4_31	HLA-C	Exon 4	+	chr6:31270436-31270461	GCCUCAUGGUCAGAGAGGGGGUGGU	1844
3107_4_32	HLA-C	Exon 4	+	chr6:31270452-31270477	GGGGGUGGUGGGUCACGUGUGUCUU	1845
3107_4_33	HLA-C	Exon 4	+	chr6:31270453-31270478	GGGGUGGUGGGUCACGUGUGUCUUU	1846
3107_4_34	HLA-C	Exon 4	+	chr6:31270454-31270479	GGGUGGUGGGUCACGUGUGUCUUUG	1847
3107_4_35	HLA-C	Exon 4	+	chr6:31270455-31270480	GGUGGUGGGUCACGUGUGUCUUUGG	1848
3107_4_36	HLA-C	Exon 4	+	chr6:31270464-31270489	UCACGUGUGUCUUUGGGGGUUCUGA	1849
3107_4_37	HLA-C	Exon 4	+	chr6:31270465-31270490	CACGUGUGUCUUUGGGGGUUCUGAC	1850
3107_4_38	HLA-C	Exon 4	-	chr6:31270192-31270217	GAGCUGGGGUAAGGAGGGGAAUGGG	1851
3107_4_39	HLA-C	Exon 4	-	chr6:31270193-31270218	UGAGCUGGGGUAAGGAGGGGAAUGG	1852
3107_4_40	HLA-C	Exon 4	-	chr6:31270194-31270219	CUGAGCUGGGGUAAGGAGGGGAAUG	1853
3107_4_41	HLA-C	Exon 4	-	chr6:31270195-31270220	CCUGAGCUGGGGUAAGGAGGGGAAU	1854
3107_4_42	HLA-C	Exon 4	-	chr6:31270196-31270221	CCCUGAGCUGGGGUAAGGAGGGGAA	1855
3107_4_43	HLA-C	Exon 4	-	chr6:31270201-31270226	CCUCACCCUGAGCUGGGGUAAGGAG	1856
3107_4_44	HLA-C	Exon 4	-	chr6:31270202-31270227	CCCUCACCCUGAGCUGGGGUAAGGA	1857
3107_4_45	HLA-C	Exon 4	-	chr6:31270203-31270228	CCCCUCACCCUGAGCUGGGGUAAGG	1858
3107_4_46	HLA-C	Exon 4	-	chr6:31270206-31270231	GAGCCCCUCACCCUGAGCUGGGGUA	1859
3107_4_47	HLA-C	Exon 4	-	chr6:31270211-31270236	UGCAAGAGCCCCUCACCCUGAGCUG	1860

3107_4_48	HLA-C	Exon 4	-	chr6:31270212-31270237	CUGCAAGAGCCCCUCACCCUGAGCU	1861
3107_4_49	HLA-C	Exon 4	-	chr6:31270213-31270238	GCUGCAAGAGCCCCUCACCCUGAGC	1862
3107_4_50	HLA-C	Exon 4	-	chr6:31270240-31270265	AUACACGUGCCAUAUGCAGCACGAG	1863
3107_4_51	HLA-C	Exon 4	-	chr6:31270241-31270266	GAUACACGUGCCAUAUGCAGCACGA	1864
3107_4_52	HLA-C	Exon 4	-	chr6:31270242-31270267	AGAUACACGUGCCAUAUGCAGCACG	1865
3107_4_53	HLA-C	Exon 4	-	chr6:31270280-31270305	AGUGGGCAGCUGUGGUGGUGCCUUC	1866
3107_4_54	HLA-C	Exon 4	-	chr6:31270290-31270315	ACCUUCCAGAAGUGGGCAGCUGUGG	1867
3107_4_55	HLA-C	Exon 4	-	chr6:31270293-31270318	GGAACCUUCCAGAAGUGGGCAGCUG	1868
3107_4_56	HLA-C	Exon 4	-	chr6:31270302-31270327	GCAGGAGAUGGAACCUUCCAGAAGU	1869
3107_4_57	HLA-C	Exon 4	-	chr6:31270303-31270328	AGCAGGAGAUGGAACCUUCCAGAAG	1870
3107_4_58	HLA-C	Exon 4	-	chr6:31270319-31270344	UUGUGGAGACCAGGCCAGCAGGAGA	1871
3107_4_59	HLA-C	Exon 4	-	chr6:31270325-31270350	CCGAGCUUGUGGAGACCAGGCCAGC	1872
3107_4_60	HLA-C	Exon 4	-	chr6:31270333-31270358	CCAGGACACCGAGCUUGUGGAGACC	1873
3107_4_61	HLA-C	Exon 4	-	chr6:31270341-31270366	GACCAGACCCAGGACACCGAGCUUG	1874
3107_4_62	HLA-C	Exon 4	-	chr6:31270356-31270381	CAGCGGGAUGGGGAGGACCAGACCC	1875
3107_4_63	HLA-C	Exon 4	-	chr6:31270368-31270393	ACACUGACCUGGCAGCGGGAUGGGG	1876
3107_4_64	HLA-C	Exon 4	-	chr6:31270371-31270396	AUCACACUGACCUGGCAGCGGGAUG	1877
3107_4_65	HLA-C	Exon 4	-	chr6:31270372-31270397	GAUCACACUGACCUGGCAGCGGGAU	1878
3107_4_66	HLA-C	Exon 4	-	chr6:31270373-31270398	AGAUCACACUGACCUGGCAGCGGGA	1879
3107_4_67	HLA-C	Exon 4	-	chr6:31270377-31270402	GCGGAGAUCACACUGACCUGGCAGC	1880
3107_4_68	HLA-C	Exon 4	-	chr6:31270378-31270403	UGCGGAGAUCACACUGACCUGGCAG	1881
3107_4_69	HLA-C	Exon 4	-	chr6:31270384-31270409	CUACCCUGCGGAGAUCACACUGACC	1882
3107_4_70	HLA-C	Exon 4	-	chr6:31270401-31270426	UGCUGGGCCCUGGGCUUCUACCCUG	1883
3107_4_71	HLA-C	Exon 4	-	chr6:31270415-31270440	AGGCCACCCUGAGGUGCUGGGCCCU	1884
3107_4_72	HLA-C	Exon 4	-	chr6:31270416-31270441	GAGGCCACCCUGAGGUGCUGGGCCC	1885

3107_4_73	HLA-C	Exon 4	-	chr6:31270422-31270447	GACCAUGAGGCCACCCUGAGGUGCU	1886
3107_4_74	HLA-C	Exon 4	-	chr6:31270423-31270448	UGACCAUGAGGCCACCCUGAGGUGC	1887
3107_4_75	HLA-C	Exon 4	-	chr6:31270429-31270454	CCUCUCUGACCAUGAGGCCACCCUG	1888
3107_4_76	HLA-C	Exon 4	-	chr6:31270440-31270465	ACCCACCACCCCCUCUCUGACCAUG	1889
3107_3_1	HLA-C	Exon 3	+	chr6:31271079-31271104	CUGCAGCGUCUCCUUCCCGUUCUCC	1890
3107_3_2	HLA-C	Exon 3	+	chr6:31271088-31271113	CUCCUUCCCGUUCUCCAGGUAUCUG	1891
3107_3_3	HLA-C	Exon 3	+	chr6:31271115-31271140	GAGCCACUCCACGCACGUGCCCUCC	1892
3107_3_4	HLA-C	Exon 3	+	chr6:31271119-31271144	CACUCCACGCACGUGCCCUCCAGGU	1893
3107_3_5	HLA-C	Exon 3	+	chr6:31271142-31271167	GUAGGCUCUCAGCUGCUCCGCCGCA	1894
3107_3_6	HLA-C	Exon 3	+	chr6:31271143-31271168	UAGGCUCUCAGCUGCUCCGCCGCAC	1895
3107_3_7	HLA-C	Exon 3	+	chr6:31271163-31271188	CGCACGGGCCGCCUCCAACUUGCGC	1896
3107_3_8	HLA-C	Exon 3	+	chr6:31271164-31271189	GCACGGGCCGCCUCCAACUUGCGCU	1897
3107_3_9	HLA-C	Exon 3	+	chr6:31271179-31271204	AACUUGCGCUGGGUGAUCUGAGCCG	1898
3107_3_10	HLA-C	Exon 3	+	chr6:31271188-31271213	UGGGUGAUCUGAGCCGCGGUGUCCG	1899
3107_3_11	HLA-C	Exon 3	+	chr6:31271191-31271216	GUGAUCUGAGCCGCGGUGUCCGCGG	1900
3107_3_12	HLA-C	Exon 3	+	chr6:31271197-31271222	UGAGCCGCGGUGUCCGCGGCGGUCC	1901
3107_3_13	HLA-C	Exon 3	+	chr6:31271205-31271230	GGUGUCCGCGGCGGUCCAGGAGCGC	1902
3107_3_14	HLA-C	Exon 3	+	chr6:31271217-31271242	GGUCCAGGAGCGCAGGUCCUCGUUC	1903
3107_3_15	HLA-C	Exon 3	+	chr6:31271218-31271243	GUCCAGGAGCGCAGGUCCUCGUUCA	1904
3107_3_16	HLA-C	Exon 3	+	chr6:31271242-31271267	AGGGCGAUGUAAUCCUUGCCGUCGU	1905
3107_3_17	HLA-C	Exon 3	+	chr6:31271245-31271270	GCGAUGUAAUCCUUGCCGUCGUAGG	1906
3107_3_18	HLA-C	Exon 3	+	chr6:31271250-31271275	GUAAUCCUUGCCGUCGUAGGCGGAC	1907
3107_3_19	HLA-C	Exon 3	+	chr6:31271262-31271287	GUCGUAGGCGGACUGGUCAUACCCG	1908
3107_3_20	HLA-C	Exon 3	+	chr6:31271265-31271290	GUAGGCGGACUGGUCAUACCCGCGG	1909
3107_3_21	HLA-C	Exon 3	+	chr6:31271268-31271293	GGCGGACUGGUCAUACCCGCGGAGG	1910

3107_3_22	HLA-C	Exon 3	+	chr6:31271278-31271303	UCAUACCCGCGGAGGAGGCGCCCGU	1911
3107_3_23	HLA-C	Exon 3	+	chr6:31271279-31271304	CAUACCCGCGGAGGAGGCGCCCGUC	1912
3107_3_24	HLA-C	Exon 3	+	chr6:31271286-31271311	GCGGAGGAGGCGCCCGUCGGGCCCC	1913
3107_3_25	HLA-C	Exon 3	+	chr6:31271307-31271332	CCCCAGGUCGCAGCCAGACAUCCUC	1914
3107_3_26	HLA-C	Exon 3	+	chr6:31271310-31271335	CAGGUCGCAGCCAGACAUCCUCUGG	1915
3107_3_27	HLA-C	Exon 3	+	chr6:31271311-31271336	AGGUCGCAGCCAGACAUCCUCUGGA	1916
3107_3_28	HLA-C	Exon 3	+	chr6:31271324-31271349	ACAUCCUCUGGAGGGUGUGAGACCC	1917
3107_3_29	HLA-C	Exon 3	+	chr6:31271338-31271363	GUGUGAGACCCUGGCCCCGCCCCCG	1918
3107_3_30	HLA-C	Exon 3	-	chr6:31271057-31271082	CAGCGCGCAGGUACCAGGGGCAGUG	1919
3107_3_31	HLA-C	Exon 3	-	chr6:31271058-31271083	GCAGCGCGCAGGUACCAGGGGCAGU	1920
3107_3_32	HLA-C	Exon 3	-	chr6:31271059-31271084	UGCAGCGCGCAGGUACCAGGGGCAG	1921
3107_3_33	HLA-C	Exon 3	-	chr6:31271065-31271090	AGACGCUGCAGCGCGCAGGUACCAG	1922
3107_3_34	HLA-C	Exon 3	-	chr6:31271066-31271091	GAGACGCUGCAGCGCGCAGGUACCA	1923
3107_3_35	HLA-C	Exon 3	-	chr6:31271067-31271092	GGAGACGCUGCAGCGCGCAGGUACC	1924
3107_3_36	HLA-C	Exon 3	-	chr6:31271074-31271099	ACGGGAAGGAGACGCUGCAGCGCGC	1925
3107_3_37	HLA-C	Exon 3	-	chr6:31271093-31271118	CUCCGCAGAUACCUGGAGAACGGGA	1926
3107_3_38	HLA-C	Exon 3	-	chr6:31271097-31271122	GUGGCUCCGCAGAUACCUGGAGAAC	1927
3107_3_39	HLA-C	Exon 3	-	chr6:31271098-31271123	AGUGGCUCCGCAGAUACCUGGAGAA	1928
3107_3_40	HLA-C	Exon 3	-	chr6:31271105-31271130	UGCGUGGAGUGGCUCCGCAGAUACC	1929
3107_3_41	HLA-C	Exon 3	-	chr6:31271121-31271146	CUACCUGGAGGGCACGUGCGUGGAG	1930
3107_3_42	HLA-C	Exon 3	-	chr6:31271126-31271151	AGAGCCUACCUGGAGGGCACGUGCG	1931
3107_3_43	HLA-C	Exon 3	-	chr6:31271137-31271162	CGGAGCAGCUGAGAGCCUACCUGGA	1932
3107_3_44	HLA-C	Exon 3	-	chr6:31271138-31271163	GCGGAGCAGCUGAGAGCCUACCUGG	1933
3107_3_45	HLA-C	Exon 3	-	chr6:31271141-31271166	GCGGCGGAGCAGCUGAGAGCCUACC	1934
3107_3_46	HLA-C	Exon 3	-	chr6:31271162-31271187	CGCAAGUUGGAGGCGGCCCGUGCGG	1935

3107_3_47	HLA-C	Exon 3	-	chr6:31271165-31271190	CAGCGCAAGUUGGAGGCGGCCCGUG	1936
3107_3_48	HLA-C	Exon 3	-	chr6:31271174-31271199	CAGAUCACCCAGCGCAAGUUGGAGG	1937
3107_3_49	HLA-C	Exon 3	-	chr6:31271177-31271202	GCUCAGAUCACCCAGCGCAAGUUGG	1938
3107_3_50	HLA-C	Exon 3	-	chr6:31271180-31271205	GCGGCUCAGAUCACCCAGCGCAAGU	1939
3107_3_51	HLA-C	Exon 3	-	chr6:31271204-31271229	CGCUCCUGGACCGCCGCGGACACCG	1940
3107_3_52	HLA-C	Exon 3	-	chr6:31271213-31271238	GAGGACCUGCGCUCCUGGACCGCCG	1941
3107_3_53	HLA-C	Exon 3	-	chr6:31271223-31271248	CGCCCUGAACGAGGACCUGCGCUCC	1942
3107_3_54	HLA-C	Exon 3	-	chr6:31271237-31271262	GGCAAGGAUUACAUCGCCCUGAACG	1943
3107_3_55	HLA-C	Exon 3	-	chr6:31271258-31271283	UAUGACCAGUCCGCCUACGACGGCA	1944
3107_3_56	HLA-C	Exon 3	-	chr6:31271263-31271288	GCGGGUAUGACCAGUCCGCCUACGA	1945
3107_3_57	HLA-C	Exon 3	-	chr6:31271286-31271311	GGGGCCCGACGGGCGCCUCCUCCGC	1946
3107_3_58	HLA-C	Exon 3	-	chr6:31271287-31271312	UGGGGCCCGACGGGCGCCUCCUCCG	1947
3107_3_59	HLA-C	Exon 3	-	chr6:31271301-31271326	GUCUGGCUGCGACCUGGGGCCCGAC	1948
3107_3_60	HLA-C	Exon 3	-	chr6:31271302-31271327	UGUCUGGCUGCGACCUGGGGCCCGA	1949
3107_3_61	HLA-C	Exon 3	-	chr6:31271310-31271335	CCAGAGGAUGUCUGGCUGCGACCUG	1950
3107_3_62	HLA-C	Exon 3	-	chr6:31271311-31271336	UCCAGAGGAUGUCUGGCUGCGACCU	1951
3107_3_63	HLA-C	Exon 3	-	chr6:31271312-31271337	CUCCAGAGGAUGUCUGGCUGCGACC	1952
3107_3_64	HLA-C	Exon 3	-	chr6:31271323-31271348	GGUCUCACACCCUCCAGAGGAUGUC	1953
3107_3_65	HLA-C	Exon 3	-	chr6:31271331-31271356	GGGGCCAGGGUCUCACACCCUCCAG	1954
3107_2_1	HLA-C	Exon 2	+	chr6:31271584-31271609	CCGGGGUCACUCACCGUCCUCGCUC	1955
3107_2_2	HLA-C	Exon 2	+	chr6:31271602-31271627	CUCGCUCUGGUUGUAGUAGCCGCGC	1956
3107_2_3	HLA-C	Exon 2	+	chr6:31271611-31271636	GUUGUAGUAGCCGCGCAGGUUCCGC	1957
3107_2_4	HLA-C	Exon 2	+	chr6:31271620-31271645	GCCGCGCAGGUUCCGCAGGCUCACU	1958
3107_2_5	HLA-C	Exon 2	+	chr6:31271635-31271660	CAGGCUCACUCGGUCAGCCUGUGCC	1959
3107_2_6	HLA-C	Exon 2	+	chr6:31271659-31271684	CUGGCGCUUGUACUUCUGUGUCUCC	1960

3107_2_7	HLA-C	Exon 2	+	chr6:31271673-31271698	UCUGUGUCUCCCGGUCCCAAUACUC	1961
3107_2_8	HLA-C	Exon 2	+	chr6:31271694-31271719	ACUCCGGCCCCUCCUGCUCCACCCA	1962
3107_2_9	HLA-C	Exon 2	+	chr6:31271703-31271728	CCUCCUGCUCCACCCACGGCGCCCG	1963
3107_2_10	HLA-C	Exon 2	+	chr6:31271715-31271740	CCCACGGCGCCCGCGGCUCCCCUCU	1964
3107_2_11	HLA-C	Exon 2	+	chr6:31271723-31271748	GCCCGCGGCUCCCCUCUCGGACUCG	1965
3107_2_12	HLA-C	Exon 2	+	chr6:31271782-31271807	GUCCACGUAGCCCACUGAGAUGAAG	1966
3107_2_13	HLA-C	Exon 2	+	chr6:31271783-31271808	UCCACGUAGCCCACUGAGAUGAAGC	1967
3107_2_14	HLA-C	Exon 2	+	chr6:31271784-31271809	CCACGUAGCCCACUGAGAUGAAGCG	1968
3107_2_15	HLA-C	Exon 2	+	chr6:31271794-31271819	CACUGAGAUGAAGCGGGGCUCUCCG	1969
3107_2_16	HLA-C	Exon 2	+	chr6:31271798-31271823	GAGAUGAAGCGGGGCUCUCCGCGGC	1970
3107_2_17	HLA-C	Exon 2	+	chr6:31271799-31271824	AGAUGAAGCGGGGCUCUCCGCGGCC	1971
3107_2_18	HLA-C	Exon 2	+	chr6:31271803-31271828	GAAGCGGGGCUCUCCGCGGCCGGGC	1972
3107_2_19	HLA-C	Exon 2	+	chr6:31271804-31271829	AAGCGGGGCUCUCCGCGGCCGGGCC	1973
3107_2_20	HLA-C	Exon 2	+	chr6:31271810-31271835	GGCUCUCCGCGGCCGGGCCGGGACA	1974
3107_2_21	HLA-C	Exon 2	+	chr6:31271813-31271838	UCUCCGCGGCCGGGCCGGGACACGG	1975
3107_2_22	HLA-C	Exon 2	+	chr6:31271831-31271856	GACACGGCGGUGUCGAAAUACCUCA	1976
3107_2_23	HLA-C	Exon 2	+	chr6:31271836-31271861	GGCGGUGUCGAAAUACCUCAUGGAG	1977
3107_2_24	HLA-C	Exon 2	+	chr6:31271837-31271862	GCGGUGUCGAAAUACCUCAUGGAGU	1978
3107_2_25	HLA-C	Exon 2	+	chr6:31271844-31271869	CGAAAUACCUCAUGGAGUGGGAGCC	1979
3107_2_26	HLA-C	Exon 2	+	chr6:31271845-31271870	GAAAUACCUCAUGGAGUGGGAGCCU	1980
3107_2_27	HLA-C	Exon 2	+	chr6:31271846-31271871	AAAUACCUCAUGGAGUGGGAGCCUG	1981
3107_2_28	HLA-C	Exon 2	+	chr6:31271847-31271872	AAUACCUCAUGGAGUGGGAGCCUGG	1982
3107_2_29	HLA-C	Exon 2	+	chr6:31271852-31271877	CUCAUGGAGUGGGAGCCUGGGGGCG	1983
3107_2_30	HLA-C	Exon 2	+	chr6:31271855-31271880	AUGGAGUGGGAGCCUGGGGGCGAGG	1984
3107_2_31	HLA-C	Exon 2	+	chr6:31271856-31271881	UGGAGUGGGAGCCUGGGGGCGAGGA	1985

3107_2_32	HLA-C	Exon 2	+	chr6:31271857-31271882	GGAGUGGGAGCCUGGGGGCGAGGAG	1986
3107_2_33	HLA-C	Exon 2	-	chr6:31271580-31271605	GAGGACGGUGAGUGACCCCGGCCCG	1987
3107_2_34	HLA-C	Exon 2	-	chr6:31271581-31271606	CGAGGACGGUGAGUGACCCCGGCCC	1988
3107_2_35	HLA-C	Exon 2	-	chr6:31271582-31271607	GCGAGGACGGUGAGUGACCCCGGCC	1989
3107_2_36	HLA-C	Exon 2	-	chr6:31271587-31271612	CCAGAGCGAGGACGGUGAGUGACCC	1990
3107_2_37	HLA-C	Exon 2	-	chr6:31271600-31271625	GCGGCUACUACAACCAGAGCGAGGA	1991
3107_2_38	HLA-C	Exon 2	-	chr6:31271604-31271629	CUGCGCGGCUACUACAACCAGAGCG	1992
3107_2_39	HLA-C	Exon 2	-	chr6:31271624-31271649	ACCGAGUGAGCCUGCGGAACCUGCG	1993
3107_2_40	HLA-C	Exon 2	-	chr6:31271635-31271660	GGCACAGGCUGACCGAGUGAGCCUG	1994
3107_2_41	HLA-C	Exon 2	-	chr6:31271655-31271680	ACACAGAAGUACAAGCGCCAGGCAC	1995
3107_2_42	HLA-C	Exon 2	-	chr6:31271661-31271686	CGGGAGACACAGAAGUACAAGCGCC	1996
3107_2_43	HLA-C	Exon 2	-	chr6:31271685-31271710	CAGGAGGGGCCGGAGUAUUGGGACC	1997
3107_2_44	HLA-C	Exon 2	-	chr6:31271686-31271711	GCAGGAGGGGCCGGAGUAUUGGGAC	1998
3107_2_45	HLA-C	Exon 2	-	chr6:31271691-31271716	GUGGAGCAGGAGGGGCCGGAGUAUU	1999
3107_2_46	HLA-C	Exon 2	-	chr6:31271692-31271717	GGUGGAGCAGGAGGGGCCGGAGUAU	2000
3107_2_47	HLA-C	Exon 2	-	chr6:31271700-31271725	GCGCCGUGGGUGGAGCAGGAGGGGC	2001
3107_2_48	HLA-C	Exon 2	-	chr6:31271704-31271729	GCGGGCGCCGUGGGUGGAGCAGGAG	2002
3107_2_49	HLA-C	Exon 2	-	chr6:31271705-31271730	CGCGGGCGCCGUGGGUGGAGCAGGA	2003
3107_2_50	HLA-C	Exon 2	-	chr6:31271706-31271731	CCGCGGGCGCCGUGGGUGGAGCAGG	2004
3107_2_51	HLA-C	Exon 2	-	chr6:31271709-31271734	GAGCCGCGGGCGCCGUGGGUGGAGC	2005
3107_2_52	HLA-C	Exon 2	-	chr6:31271715-31271740	AGAGGGGAGCCGCGGGCGCCGUGGG	2006
3107_2_53	HLA-C	Exon 2	-	chr6:31271718-31271743	CCGAGAGGGGAGCCGCGGGCGCCGU	2007
3107_2_54	HLA-C	Exon 2	-	chr6:31271719-31271744	UCCGAGAGGGGAGCCGCGGGCGCCG	2008
3107_2_55	HLA-C	Exon 2	-	chr6:31271727-31271752	GCCGCGAGUCCGAGAGGGGAGCCGC	2009
3107_2_56	HLA-C	Exon 2	-	chr6:31271728-31271753	CGCCGCGAGUCCGAGAGGGGAGCCG	2010

3107_2_57	HLA-C	Exon 2	-	chr6:31271736-31271761	GACAGCGACGCCGCGAGUCCGAGAG	2011
3107_2_58	HLA-C	Exon 2	-	chr6:31271737-31271762	CGACAGCGACGCCGCGAGUCCGAGA	2012
3107_2_59	HLA-C	Exon 2	-	chr6:31271738-31271763	UCGACAGCGACGCCGCGAGUCCGAG	2013
3107_2_60	HLA-C	Exon 2	-	chr6:31271767-31271792	CUACGUGGACGACACGCAGUUCGUG	2014
3107_2_61	HLA-C	Exon 2	-	chr6:31271787-31271812	CCCCGCUUCAUCUCAGUGGGCUACG	2015
3107_2_62	HLA-C	Exon 2	-	chr6:31271795-31271820	GCGGAGAGCCCCGCUUCAUCUCAGU	2016
3107_2_63	HLA-C	Exon 2	-	chr6:31271796-31271821	CGCGGAGAGCCCCGCUUCAUCUCAG	2017
3107_2_64	HLA-C	Exon 2	-	chr6:31271819-31271844	ACACCGCCGUGUCCCGGCCCGGCCG	2018
3107_2_65	HLA-C	Exon 2	-	chr6:31271825-31271850	AUUUCGACACCGCCGUGUCCCGGCC	2019
3107_2_66	HLA-C	Exon 2	-	chr6:31271830-31271855	GAGGUAUUUCGACACCGCCGUGUCC	2020
3107_2_67	HLA-C	Exon 2	-	chr6:31271854-31271879	CUCGCCCCCAGGCUCCCACUCCAUG	2021
3107_1_1	HLA-C	Exon 1	+	chr6:31271973-31271998	GCUUCCCUCCCAACCCCGCACUCAC	2022
3107_1_2	HLA-C	Exon 1	+	chr6:31271979-31272004	CUCCCAACCCCGCACUCACAGGCCC	2023
3107_1_3	HLA-C	Exon 1	+	chr6:31271985-31272010	ACCCCGCACUCACAGGCCCAGGUCU	2024
3107_1_4	HLA-C	Exon 1	+	chr6:31271990-31272015	GCACUCACAGGCCCAGGUCUCGGUC	2025
3107_1_5	HLA-C	Exon 1	+	chr6:31271991-31272016	CACUCACAGGCCCAGGUCUCGGUCA	2026
3107_1_6	HLA-C	Exon 1	+	chr6:31271996-31272021	ACAGGCCCAGGUCUCGGUCAGGGCC	2027
3107_1_7	HLA-C	Exon 1	+	chr6:31272014-31272039	CAGGGCCAGGCCUCCCGAGAGCAGC	2028
3107_1_8	HLA-C	Exon 1	+	chr6:31272017-31272042	GGCCAGGCCUCCCGAGAGCAGCAGG	2029
3107_1_9	HLA-C	Exon 1	+	chr6:31272020-31272045	CAGGCCUCCCGAGAGCAGCAGGAGG	2030
3107_1_10	HLA-C	Exon 1	+	chr6:31272021-31272046	AGGCCUCCCGAGAGCAGCAGGAGGA	2031
3107_1_11	HLA-C	Exon 1	+	chr6:31272026-31272051	UCCCGAGAGCAGCAGGAGGAGGGCU	2032
3107_1_12	HLA-C	Exon 1	+	chr6:31272027-31272052	CCCGAGAGCAGCAGGAGGAGGGCUC	2033
3107_1_13	HLA-C	Exon 1	+	chr6:31272028-31272053	CCGAGAGCAGCAGGAGGAGGGCUCG	2034
3107_1_14	HLA-C	Exon 1	+	chr6:31272048-31272073	GCUCGGGGCGCCAUGACCCGCAUCU	2035

3107_1_15	HLA-C	Exon 1	+	chr6:31272055-31272080	GCGCCAUGACCCGCAUCUCGGCCUC	2036
3107_1_16	HLA-C	Exon 1	+	chr6:31272056-31272081	CGCCAUGACCCGCAUCUCGGCCUCU	2037
3107_1_17	HLA-C	Exon 1	+	chr6:31272057-31272082	GCCAUGACCCGCAUCUCGGCCUCUG	2038
3107_1_18	HLA-C	Exon 1	+	chr6:31272072-31272097	UCGGCCUCUGGGGAGAAUGUGAGUC	2039
3107_1_19	HLA-C	Exon 1	+	chr6:31272073-31272098	CGGCCUCUGGGGAGAAUGUGAGUCC	2040
3107_1_20	HLA-C	Exon 1	+	chr6:31272076-31272101	CCUCUGGGGAGAAUGUGAGUCCGGG	2041
3107_1_21	HLA-C	Exon 1	+	chr6:31272077-31272102	CUCUGGGGAGAAUGUGAGUCCGGGU	2042
3107_1_22	HLA-C	Exon 1	+	chr6:31272084-31272109	GAGAAUGUGAGUCCGGGUGGGUGAC	2043
3107_1_23	HLA-C	Exon 1	+	chr6:31272085-31272110	AGAAUGUGAGUCCGGGUGGGUGACU	2044
3107_1_24	HLA-C	Exon 1	+	chr6:31272086-31272111	GAAUGUGAGUCCGGGUGGGUGACUG	2045
3107_1_25	HLA-C	Exon 1	+	chr6:31272099-31272124	GGUGGGUGACUGGGGACUUUAGAAC	2046
3107_1_26	HLA-C	Exon 1	+	chr6:31272100-31272125	GUGGGUGACUGGGGACUUUAGAACC	2047
3107_1_27	HLA-C	Exon 1	+	chr6:31272107-31272132	ACUGGGGACUUUAGAACCGGGACUG	2048
3107_1_28	HLA-C	Exon 1	+	chr6:31272120-31272145	GAACCGGGACUGCGGAGACGCUGAU	2049
3107_1_29	HLA-C	Exon 1	-	chr6:31271980-31272005	UGGGCCUGUGAGUGCGGGGUUGGGA	2050
3107_1_30	HLA-C	Exon 1	-	chr6:31271981-31272006	CUGGGCCUGUGAGUGCGGGGUUGGG	2051
3107_1_31	HLA-C	Exon 1	-	chr6:31271984-31272009	GACCUGGGCCUGUGAGUGCGGGGUU	2052
3107_1_32	HLA-C	Exon 1	-	chr6:31271985-31272010	AGACCUGGGCCUGUGAGUGCGGGGU	2053
3107_1_33	HLA-C	Exon 1	-	chr6:31271989-31272014	ACCGAGACCUGGGCCUGUGAGUGCG	2054
3107_1_34	HLA-C	Exon 1	-	chr6:31271990-31272015	GACCGAGACCUGGGCCUGUGAGUGC	2055
3107_1_35	HLA-C	Exon 1	-	chr6:31271991-31272016	UGACCGAGACCUGGGCCUGUGAGUG	2056
3107_1_36	HLA-C	Exon 1	-	chr6:31272004-31272029	GGAGGCCUGGCCCUGACCGAGACCU	2057
3107_1_37	HLA-C	Exon 1	-	chr6:31272005-31272030	GGGAGGCCUGGCCCUGACCGAGACC	2058
3107_1_38	HLA-C	Exon 1	-	chr6:31272022-31272047	CUCCUCCUGCUGCUCUCGGGAGGCC	2059
3107_1_39	HLA-C	Exon 1	-	chr6:31272027-31272052	GAGCCCUCCUCCUGCUGCUCUCGGG	2060

3107_1_40	HLA-C	Exon 1	-	chr6:31272030-31272055	CCCGAGCCCUCCUCCUGCUGCUCUC	2061
3107_1_41	HLA-C	Exon 1	-	chr6:31272031-31272056	CCCCGAGCCCUCCUCCUGCUGCUCU	2062
3107_1_42	HLA-C	Exon 1	-	chr6:31272061-31272086	UCCCCAGAGGCCGAGAUGCGGGUCA	2063
3107_1_43	HLA-C	Exon 1	-	chr6:31272067-31272092	ACAUUCUCCCCAGAGGCCGAGAUGC	2064
3107_1_44	HLA-C	Exon 1	-	chr6:31272068-31272093	CACAUUCUCCCCAGAGGCCGAGAUG	2065
3107_1_45	HLA-C	Exon 1	-	chr6:31272079-31272104	CCACCCGGACUCACAUUCUCCCCAG	2066
3107_1_46	HLA-C	Exon 1	-	chr6:31272099-31272124	GUUCUAAAGUCCCCAGUCACCCACC	2067
3107_1_47	HLA-C	Exon 1	-	chr6:31272126-31272151	AAGCCAAUCAGCGUCUCCGCAGUCC	2068
2908_11_1	NR3C1	Exon 11	+	chr5:143277948-143277973	UUUUAUUAUGAUGUUUCUCCAUAUU	2069
2908_11_2	NR3C1	Exon 11	+	chr5:143277963-143277988	UCUCCAUAUUUGGCAUUGCUGUAAA	2070
2908_11_3	NR3C1	Exon 11	+	chr5:143277985-143278010	AAAUGGCUAACAUUUACUGCCAAUU	2071
2908_11_4	NR3C1	Exon 11	+	chr5:143277998-143278023	UUACUGCCAAUUCGGUACAAAUGUG	2072
2908_11_5	NR3C1	Exon 11	+	chr5:143278003-143278028	GCCAAUUCGGUACAAAUGUGUGGUU	2073
2908_11_6	NR3C1	Exon 11	+	chr5:143278061-143278086	AAUAAAAGUUAAACAUUUCCACACA	2074
2908_11_7	NR3C1	Exon 11	+	chr5:143278090-143278115	UUUACAGUCUGACAUUUCACUGCGU	2075
2908_11_8	NR3C1	Exon 11	+	chr5:143278167-143278192	AAAACUACAACUUUUAUUUUUAAAC	2076
2908_11_9	NR3C1	Exon 11	+	chr5:143278176-143278201	ACUUUUAUUUUUAAACAGGAGUCAC	2077
2908_11_10	NR3C1	Exon 11	+	chr5:143278346-143278371	UAUAUGUAGUUAAGCAAGUUAUUUG	2078
2908_11_11	NR3C1	Exon 11	+	chr5:143278349-143278374	AUGUAGUUAAGCAAGUUAUUUGAGG	2079
2908_11_12	NR3C1	Exon 11	+	chr5:143278350-143278375	UGUAGUUAAGCAAGUUAUUUGAGGA	2080
2908_11_13	NR3C1	Exon 11	+	chr5:143278433-143278458	AGAAGCAAAUCCUUUCCUGAAAACC	2081
2908_11_14	NR3C1	Exon 11	+	chr5:143278446-143278471	UUCCUGAAAACCUGGUCACUAAUCC	2082
2908_11_15	NR3C1	Exon 11	+	chr5:143278447-143278472	UCCUGAAAACCUGGUCACUAAUCCU	2083
2908_11_16	NR3C1	Exon 11	+	chr5:143278450-143278475	UGAAAACCUGGUCACUAAUCCUGGG	2084
2908_11_17	NR3C1	Exon 11	+	chr5:143278456-143278481	CCUGGUCACUAAUCCUGGGUGGACC	2085

2908_11_18	NR3C1	Exon 11	+	chr5:143278475-143278500	UGGACCAGGUUGCUUGAAAAUAGUC	2086
2908_11_19	NR3C1	Exon 11	+	chr5:143278476-143278501	GGACCAGGUUGCUUGAAAAUAGUCU	2087
2908_11_20	NR3C1	Exon 11	+	chr5:143278500-143278525	UGGGAAAUUACGAAACUCCACCCAA	2088
2908_11_21	NR3C1	Exon 11	+	chr5:143278501-143278526	GGGAAAUUACGAAACUCCACCCAAA	2089
2908_11_22	NR3C1	Exon 11	+	chr5:143278594-143278619	AACACAUUCACCUACAGCUACAGUC	2090
2908_11_23	NR3C1	Exon 11	+	chr5:143278595-143278620	ACACAUUCACCUACAGCUACAGUCA	2091
2908_11_24	NR3C1	Exon 11	+	chr5:143278613-143278638	ACAGUCAGGGAGUGACCAGCCAAGA	2092
2908_11_25	NR3C1	Exon 11	+	chr5:143278628-143278653	CCAGCCAAGAUGGAAAUCUCACUGA	2093
2908_11_26	NR3C1	Exon 11	+	chr5:143278637-143278662	AUGGAAAUCUCACUGAAGGCUACCA	2094
2908_11_27	NR3C1	Exon 11	+	chr5:143278643-143278668	AUCUCACUGAAGGCUACCAUGGUUC	2095
2908_11_28	NR3C1	Exon 11	+	chr5:143278691-143278716	UUGUAUAACAAUAUUUUUCAUUCCA	2096
2908_11_29	NR3C1	Exon 11	+	chr5:143278707-143278732	UUCAUUCCAUGGUGAUGUAGUUUUC	2097
2908_11_30	NR3C1	Exon 11	+	chr5:143278708-143278733	UCAUUCCAUGGUGAUGUAGUUUUCA	2098
2908_11_31	NR3C1	Exon 11	+	chr5:143278719-143278744	UGAUGUAGUUUUCAGGGUUUUUAAA	2099
2908_11_32	NR3C1	Exon 11	+	chr5:143278720-143278745	GAUGUAGUUUUCAGGGUUUUUAAAA	2100
2908_11_33	NR3C1	Exon 11	+	chr5:143278742-143278767	AAAGGGAACUAAAAUUAUGAGACUU	2101
2908_11_34	NR3C1	Exon 11	+	chr5:143278751-143278776	UAAAAUUAUGAGACUUAGGUGAAAC	2102
2908_11_35	NR3C1	Exon 11	+	chr5:143278780-143278805	AUUGCUCCCUGCCUCUGAAUUCUGA	2103
2908_11_36	NR3C1	Exon 11	+	chr5:143278781-143278806	UUGCUCCCUGCCUCUGAAUUCUGAA	2104
2908_11_37	NR3C1	Exon 11	+	chr5:143278788-143278813	CUGCCUCUGAAUUCUGAAGGGAGCG	2105
2908_11_38	NR3C1	Exon 11	+	chr5:143278801-143278826	CUGAAGGGAGCGUGGCUUUCCUUCA	2106
2908_11_39	NR3C1	Exon 11	+	chr5:143278873-143278898	ACACAAAUCAUGUUAGUUUUCCUUU	2107
2908_11_40	NR3C1	Exon 11	+	chr5:143278874-143278899	CACAAAUCAUGUUAGUUUUCCUUUU	2108
2908_11_41	NR3C1	Exon 11	+	chr5:143278875-143278900	ACAAAUCAUGUUAGUUUUCCUUUUG	2109
2908_11_42	NR3C1	Exon 11	+	chr5:143278878-143278903	AAUCAUGUUAGUUUCCUUUUGGGG	2110

2908_11_43	NR3C1	Exon 11	+	chr5:143278884-143278909	GUUAGUUUUCCUUUUGGGGUGGCCA	2111
2908_11_44	NR3C1	Exon 11	+	chr5:143278904-143278929	GGCCAAGGUUUCCUCCCAUAGUUUU	2112
2908_11_45	NR3C1	Exon 11	+	chr5:143278911-143278936	GUUUCCUCCCAUAGUUUUAGGCAUU	2113
2908_11_46	NR3C1	Exon 11	+	chr5:143279007-143279032	CCUACAAACACUAAAAAUACUUUUC	2114
2908_11_47	NR3C1	Exon 11	+	chr5:143279062-143279087	GAAGUUACUACAAACUUCAACAGUU	2115
2908_11_48	NR3C1	Exon 11	+	chr5:143279063-143279088	AAGUUACUACAAACUUCAACAGUUU	2116
2908_11_49	NR3C1	Exon 11	+	chr5:143279067-143279092	UACUACAAACUUCAACAGUUUGGGU	2117
2908_11_50	NR3C1	Exon 11	+	chr5:143279068-143279093	ACUACAAACUUCAACAGUUUGGGUU	2118
2908_11_51	NR3C1	Exon 11	+	chr5:143279072-143279097	CAAACUUCAACAGUUUGGGUUGGGA	2119
2908_11_52	NR3C1	Exon 11	+	chr5:143279092-143279117	UGGGAUGGCCAGAUAACACAUACAU	2120
2908_11_53	NR3C1	Exon 11	+	chr5:143279190-143279215	UUUCUUUUCCCCCACGUAUCCUAAA	2121
2908_11_54	NR3C1	Exon 11	+	chr5:143279191-143279216	UUCUUUUCCCCCACGUAUCCUAAAA	2122
2908_11_55	NR3C1	Exon 11	+	chr5:143279327-143279352	UCUAUUUUUUGAGCGCCAAGAUUGU	2123
2908_11_56	NR3C1	Exon 11	+	chr5:143279328-143279353	CUAUUUUUUGAGCGCCAAGAUUGUU	2124
2908_11_57	NR3C1	Exon 11	+	chr5:143279365-143279390	AGAUUAAUGUGUGAGAUGUGCUUUC	2125
2908_11_58	NR3C1	Exon 11	+	chr5:143279392-143279417	GUUUUAACCACAUAACAUUCUAUAA	2126
2908_11_59	NR3C1	Exon 11	+	chr5:143279471-143279496	AUAAGAAUAUUCAAGCAGUUUUCUU	2127
2908_11_60	NR3C1	Exon 11	+	chr5:143279493-143279518	CUUAGGCACCAAAAAUUUAUCCAGC	2128
2908_11_61	NR3C1	Exon 11	+	chr5:143279494-143279519	UUAGGCACCAAAAAUUUAUCCAGCC	2129
2908_11_62	NR3C1	Exon 11	+	chr5:143279651-143279676	AACAAAAACAUGUCCUCAUUUUAUU	2130
2908_11_63	NR3C1	Exon 11	+	chr5:143279671-143279696	UUAUUUGGAAAUAAACUCUUGUUGU	2131
2908_11_64	NR3C1	Exon 11	+	chr5:143279680-143279705	AAUAAACUCUUGUUGUAGGAUAGAA	2132
2908_11_65	NR3C1	Exon 11	+	chr5:143279697-143279722	GGAUAGAAAGGAAUUAGUGUAUUAU	2133
2908_11_66	NR3C1	Exon 11	+	chr5:143279734-143279759	AGAUUCUGCACUAUUUACAUAUUGC	2134
2908_11_67	NR3C1	Exon 11	+	chr5:143279792-143279817	GAAGCUUCUGUUGUCAUUCAACUGC	2135

2908_11_68	NR3C1	Exon 11	+	chr5:143279793-143279818	AAGCUUCUGUUGUCAUUCAACUGCU	2136
2908_11_69	NR3C1	Exon 11	+	chr5:143279794-143279819	AGCUUCUGUUGUCAUUCAACUGCUG	2137
2908_11_70	NR3C1	Exon 11	+	chr5:143279795-143279820	GCUUCUGUUGUCAUUCAACUGCUGG	2138
2908_11_71	NR3C1	Exon 11	+	chr5:143279798-143279823	UCUGUUGUCAUUCAACUGCUGGGGG	2139
2908_11_72	NR3C1	Exon 11	+	chr5:143279799-143279824	CUGUUGUCAUUCAACUGCUGGGGGA	2140
2908_11_73	NR3C1	Exon 11	+	chr5:143279830-143279855	UAUGUGAAAGUAACCCGCUAUUAGA	2141
2908_11_74	NR3C1	Exon 11	+	chr5:143279841-143279866	AACCCGCUAUUAGAUGGUGCCUUUA	2142
2908_11_75	NR3C1	Exon 11	+	chr5:143279898-143279923	UACAUACUUUACAUACUUUAGUGCA	2143
2908_11_76	NR3C1	Exon 11	+	chr5:143279899-143279924	ACAUACUUUACAUACUUUAGUGCAA	2144
2908_11_77	NR3C1	Exon 11	+	chr5:143279900-143279925	CAUACUUUACAUACUUUAGUGCAAG	2145
2908_11_78	NR3C1	Exon 11	+	chr5:143279942-143279967	AAACCUGCGCUGACAGACUCACUGU	2146
2908_11_79	NR3C1	Exon 11	+	chr5:143279952-143279977	UGACAGACUCACUGUUGGAAUGAGA	2147
2908_11_80	NR3C1	Exon 11	+	chr5:143279953-143279978	GACAGACUCACUGUUGGAAUGAGAA	2148
2908_11_81	NR3C1	Exon 11	+	chr5:143279956-143279981	AGACUCACUGUUGGAAUGAGAAGGG	2149
2908_11_82	NR3C1	Exon 11	+	chr5:143279965-143279990	GUUGGAAUGAGAAGGGUGGUCAGAA	2150
2908_11_83	NR3C1	Exon 11	+	chr5:143279966-143279991	UUGGAAUGAGAAGGGUGGUCAGAAU	2151
2908_11_84	NR3C1	Exon 11	+	chr5:143279969-143279994	GAAUGAGAAGGGUGGUCAGAAUGGG	2152
2908_11_85	NR3C1	Exon 11	+	chr5:143279975-143280000	GAAGGGUGGUCAGAAUGGGAGGCAG	2153
2908_11_86	NR3C1	Exon 11	+	chr5:143280000-143280025	AGGAUAACUUCCUCUGUAAUCUCAC	2154
2908_11_87	NR3C1	Exon 11	+	chr5:143280001-143280026	GGAUAACUUCCUCUGUAAUCUCACU	2155
2908_11_88	NR3C1	Exon 11	+	chr5:143280033-143280058	AGCCUCAGCAACCUUCACUGCACAC	2156
2908_11_89	NR3C1	Exon 11	+	chr5:143280075-143280100	CCCUCUUCCCCUAGAGCAAACUGUU	2157
2908_11_90	NR3C1	Exon 11	+	chr5:143280131-143280156	UGCAUGUACAAACUAUAAAUCAUAU	2158
2908_11_91	NR3C1	Exon 11	+	chr5:143280404-143280429	UCAGUUUUCUAUUACACAAAUAAUU	2159
2908_11_92	NR3C1	Exon 11	+	chr5:143280435-143280460	CCUUGAAUAGAAAUCAAAUUUCUUG	2160

2908_11_93	NR3C1	Exon 11	+	chr5:143280475-143280500	GUUAAGUUUUGAGUUUACAGAAAGU	2161
2908_11_94	NR3C1	Exon 11	+	chr5:143280480-143280505	GUUUUGAGUUUACAGAAAGUUGGUA	2162
2908_11_95	NR3C1	Exon 11	+	chr5:143280494-143280519	GAAAGUUGGUAAGGUGCACACAGAA	2163
2908_11_96	NR3C1	Exon 11	+	chr5:143280495-143280520	AAAGUUGGUAAGGUGCACACAGAAA	2164
2908_11_97	NR3C1	Exon 11	+	chr5:143280551-143280576	AAUUUUCAACAGUGAAGAAAUUCAC	2165
2908_11_98	NR3C1	Exon 11	+	chr5:143280571-143280596	UUCACAGGACUUGUGUUAAACUCUA	2166
2908_11_99	NR3C1	Exon 11	+	chr5:143280582-143280607	UGUGUUAAACUCUAUGGCACACAUU	2167
2908_11_100	NR3C1	Exon 11	+	chr5:143280583-143280608	GUGUUAAACUCUAUGGCACACAUUA	2168
2908_11_101	NR3C1	Exon 11	+	chr5:143280605-143280630	UUAGGGAUGUGUAGUUUUACAAACA	2169
2908_11_102	NR3C1	Exon 11	+	chr5:143280666-143280691	AGUAGCUGAGCUUUCCUGUACCAUC	2170
2908_11_103	NR3C1	Exon 11	+	chr5:143280683-143280708	GUACCAUCAGGAAAGAUUAACCAAU	2171
2908_11_104	NR3C1	Exon 11	+	chr5:143280693-143280718	GAAAGAUUAACCAAUUGGUGACAGA	2172
2908_11_105	NR3C1	Exon 11	+	chr5:143280694-143280719	AAAGAUUAACCAAUUGGUGACAGAU	2173
2908_11_106	NR3C1	Exon 11	+	chr5:143280707-143280732	UUGGUGACAGAUGGGAAUGUGAAAA	2174
2908_11_107	NR3C1	Exon 11	+	chr5:143280708-143280733	UGGUGACAGAUGGGAAUGUGAAAAU	2175
2908_11_108	NR3C1	Exon 11	+	chr5:143280748-143280773	UUUGCCAUAUUAGAGAUUUAGUUUU	2176
2908_11_109	NR3C1	Exon 11	+	chr5:143280749-143280774	UUGCCAUAUUAGAGAUUUAGUUUUU	2177
2908_11_110	NR3C1	Exon 11	+	chr5:143280766-143280791	UAGUUUUUGGGUAAAGUUUAGUGAG	2178
2908_11_111	NR3C1	Exon 11	+	chr5:143280811-143280836	AAAAGUCUCUCAGCUGUGUUACAGC	2179
2908_11_112	NR3C1	Exon 11	+	chr5:143280819-143280844	CUCAGCUGUGUUACAGCUGGUUAUC	2180
2908_11_113	NR3C1	Exon 11	+	chr5:143280860-143280885	AAGAAGUUAUACAAACUACUUCAAA	2181
2908_11_114	NR3C1	Exon 11	+	chr5:143280917-143280942	CUUGCCAUAUAGCCAUUGCAAAAAU	2182
2908_11_115	NR3C1	Exon 11	+	chr5:143280918-143280943	UUGCCAUAUAGCCAUUGCAAAAAUA	2183
2908_11_116	NR3C1	Exon 11	+	chr5:143280925-143280950	AUAGCCAUUGCAAAAAUAGGGCGUU	2184
2908_11_117	NR3C1	Exon 11	+	chr5:143280935-143280960	CAAAAAUAGGGCGUUAGGUACAGAC	2185

2908_11_118	NR3C1	Exon 11	+	chr5:143280936-143280961	AAAAAUAGGGCGUUAGGUACAGACA	2186
2908_11_119	NR3C1	Exon 11	+	chr5:143280944-143280969	GGCGUUAGGUACAGACAGGGCCUCU	2187
2908_11_120	NR3C1	Exon 11	+	chr5:143280999-143281024	AACCAUCAUCCACAGUUUACCCAGC	2188
2908_11_121	NR3C1	Exon 11	+	chr5:143281006-143281031	AUCCACAGUUUACCCAGCAGGUCAC	2189
2908_11_122	NR3C1	Exon 11	+	chr5:143281012-143281037	AGUUUACCCAGCAGGUCACUGGACU	2190
2908_11_123	NR3C1	Exon 11	+	chr5:143281030-143281055	CUGGACUAGGUGCUCUAUACCAGUU	2191
2908_11_124	NR3C1	Exon 11	+	chr5:143281123-143281148	UUUUUUUUUUUUUUGACAAGAAUAC	2192
2908_11_125	NR3C1	Exon 11	+	chr5:143281145-143281170	UACUGGAGAUUUGAGUCAAUUUUUG	2193
2908_11_126	NR3C1	Exon 11	+	chr5:143281171-143281196	GGUCUUCUGAUAGCUAAGUGCCAUC	2194
2908_11_127	NR3C1	Exon 11	+	chr5:143281229-143281254	GAUUGAUUAAUGUUUAGAGUUUAUU	2195
2908_11_128	NR3C1	Exon 11	+	chr5:143281230-143281255	AUUGAUUAAUGUUUAGAGUUUAUUU	2196
2908_11_129	NR3C1	Exon 11	+	chr5:143281331-143281356	AGCAAGCGUAGUUCACUAAAUAUAA	2197
2908_11_130	NR3C1	Exon 11	+	chr5:143281367-143281392	AAAACCAGACAGUAAUAGCUAUAAA	2198
2908_11_131	NR3C1	Exon 11	+	chr5:143281412-143281437	GAUAUACACUUGUAAACUUUUUUUC	2199
2908_11_132	NR3C1	Exon 11	+	chr5:143281453-143281478	AUCAAAAAUGCUAUCCUAACUAUAC	2200
2908_11_133	NR3C1	Exon 11	+	chr5:143281454-143281479	UCAAAAAUGCUAUCCUAACUAUACA	2201
2908_11_134	NR3C1	Exon 11	+	chr5:143281455-143281480	CAAAAAUGCUAUCCUAACUAUACAG	2202
2908_11_135	NR3C1	Exon 11	+	chr5:143281456-143281481	AAAAAUGCUAUCCUAACUAUACAGG	2203
2908_11_136	NR3C1	Exon 11	+	chr5:143281457-143281482	AAAAUGCUAUCCUAACUAUACAGGG	2204
2908_11_137	NR3C1	Exon 11	+	chr5:143281458-143281483	AAAUGCUAUCCUAACUAUACAGGGG	2205
2908_11_138	NR3C1	Exon 11	+	chr5:143281459-143281484	AAUGCUAUCCUAACUAUACAGGGGG	2206
2908_11_139	NR3C1	Exon 11	+	chr5:143281543-143281568	AAGAGAAAGUUCAUCACACAGACUU	2207
2908_11_140	NR3C1	Exon 11	+	chr5:143281544-143281569	AGAGAAAGUUCAUCACACAGACUUU	2208
2908_11_141	NR3C1	Exon 11	+	chr5:143281550-143281575	AGUUCAUCACACAGACUUUGGGCAC	2209
2908_11_142	NR3C1	Exon 11	+	chr5:143281553-143281578	UCAUCACACAGACUUUGGGCACUGG	2210

2908_11_143	NR3C1	Exon 11	+	chr5:143281559-143281584	CACAGACUUUGGGCACUGGUGGUUU	2211
2908_11_144	NR3C1	Exon 11	+	chr5:143281581-143281606	UUUAGGUGCCAUCCUUCUUUGACUG	2212
2908_11_145	NR3C1	Exon 11	+	chr5:143281603-143281628	CUGUGGAGAUUACGUCCACAUAUUA	2213
2908_11_146	NR3C1	Exon 11	+	chr5:143281617-143281642	UCCACAUAUUAAGGUUUCUAAUUUC	2214
2908_11_147	NR3C1	Exon 11	+	chr5:143281618-143281643	CCACAUAUUAAGGUUUCUAAUUUCU	2215
2908_11_148	NR3C1	Exon 11	+	chr5:143281703-143281728	CUCAACUGCUUCUGUUGCCAAGUCU	2216
2908_11_149	NR3C1	Exon 11	+	chr5:143281788-143281813	AAAAAUAAAACAACAAAACCUCUAC	2217
2908_11_150	NR3C1	Exon 11	+	chr5:143281839-143281864	AAAGCUAUUAAUUCGACUUUCUUUA	2218
2908_11_151	NR3C1	Exon 11	+	chr5:143281857-143281882	UUCUUUAAGGCAACCAUUCUUAUUA	2219
2908_11_152	NR3C1	Exon 11	+	chr5:143281911-143281936	UUUUGAUAUUUCCAUUUGAAUAUUU	2220
2908_11_153	NR3C1	Exon 11	+	chr5:143281922-143281947	CCAUUUGAAUAUUUUGGUAUCUGAU	2221
2908_11_154	NR3C1	Exon 11	+	chr5:143281946-143281971	UUGGUGAUGAUUUCAGCUAACAUCU	2222
2908_11_155	NR3C1	Exon 11	+	chr5:143281947-143281972	UGGUGAUGAUUUCAGCUAACAUCUC	2223
2908_11_156	NR3C1	Exon 11	+	chr5:143281948-143281973	GGUGAUGAUUUCAGCUAACAUCUCG	2224
2908_11_157	NR3C1	Exon 11	+	chr5:143281964-143281989	AACAUCUCGGGGAAUUCAAUACUCA	2225
2908_11_158	NR3C1	Exon 11	+	chr5:143281984-143282009	ACUCAUGGUCUUAUCCAAAAAUGUU	2226
2908_11_159	NR3C1	Exon 11	+	chr5:143281999-143282024	CAAAAAUGUUUGGAAGCAAUAGUUA	2227
2908_11_160	NR3C1	Exon 11	+	chr5:143282031-143282056	UUUCAACCACCUGCAAGAGAAGAUA	2228
2908_11_161	NR3C1	Exon 11	-	chr5:143277969-143277994	UAGCCAUUUACAGCAAUGCCAAAUA	2229
2908_11_162	NR3C1	Exon 11	-	chr5:143278007-143278032	ACCAAACCACACAUUUGUACCGAAU	2230
2908_11_163	NR3C1	Exon 11	-	chr5:143278039-143278064	AUUUUUUCAUUUAAAUUUGCUGUUC	2231
2908_11_164	NR3C1	Exon 11	-	chr5:143278082-143278107	AAAUGUCAGACUGUAAAACCUUGUG	2232
2908_11_165	NR3C1	Exon 11	-	chr5:143278271-143278296	GGACAAAUCUAUAUUAUACUGUGUA	2233
2908_11_166	NR3C1	Exon 11	-	chr5:143278297-143278322	UUUGUAUAUUAAAUGCUAUAUAAUG	2234
2908_11_167	NR3C1	Exon 11	-	chr5:143278298-143278323	UUUUGUAUAUUAAAUGCUAUAUAAU	2235

2908_11_168	NR3C1	Exon 11	-	chr5:143278299-143278324	AUUUUGUAUAUUAAAUGCUAUAUAA	2236
2908_11_169	NR3C1	Exon 11	-	chr5:143278394-143278419	UGAAAGGAUUUUAUUUUCUGAUGAA	2237
2908_11_170	NR3C1	Exon 11	-	chr5:143278415-143278440	UGCUUCUCUCUAGAAAAUGUCUGAA	2238
2908_11_171	NR3C1	Exon 11	-	chr5:143278446-143278471	GGAUUAGUGACCAGGUUUUCAGGAA	2239
2908_11_172	NR3C1	Exon 11	-	chr5:143278451-143278476	ACCCAGGAUUAGUGACCAGGUUUUC	2240
2908_11_173	NR3C1	Exon 11	-	chr5:143278459-143278484	CCUGGUCCACCCAGGAUUAGUGACC	2241
2908_11_174	NR3C1	Exon 11	-	chr5:143278472-143278497	UAUUUUCAAGCAACCUGGUCCACCC	2242
2908_11_175	NR3C1	Exon 11	-	chr5:143278482-143278507	UUUCCCAGACUAUUUUCAAGCAACC	2243
2908_11_176	NR3C1	Exon 11	-	chr5:143278520-143278545	AGGAGGACACUUUAAACCCUUUGGG	2244
2908_11_177	NR3C1	Exon 11	-	chr5:143278523-143278548	GUAAGGAGGACACUUUAAACCCUUU	2245
2908_11_178	NR3C1	Exon 11	-	chr5:143278524-143278549	UGUAAGGAGGACACUUUAAACCCUU	2246
2908_11_179	NR3C1	Exon 11	-	chr5:143278542-143278567	UCAGAAGGGAAAUAAAAGUGUAAGG	2247
2908_11_180	NR3C1	Exon 11	-	chr5:143278545-143278570	GUGUCAGAAGGGAAAUAAAAGUGUA	2248
2908_11_181	NR3C1	Exon 11	-	chr5:143278561-143278586	ACACACAGACGUUUUAGUGUCAGAA	2249
2908_11_182	NR3C1	Exon 11	-	chr5:143278562-143278587	CACACACAGACGUUUUAGUGUCAGA	2250
2908_11_183	NR3C1	Exon 11	-	chr5:143278607-143278632	CUGGUCACUCCCUGACUGUAGCUGU	2251
2908_11_184	NR3C1	Exon 11	-	chr5:143278631-143278656	CCUUCAGUGAGAUUUCCAUCUUGGC	2252
2908_11_185	NR3C1	Exon 11	-	chr5:143278635-143278660	GUAGCCUUCAGUGAGAUUUCCAUCU	2253
2908_11_186	NR3C1	Exon 11	-	chr5:143278662-143278687	UUGAUCUGUCAAACUUCCAGAACCA	2254
2908_11_187	NR3C1	Exon 11	-	chr5:143278716-143278741	AAAAACCCUGAAAACUACAUCACCA	2255
2908_11_188	NR3C1	Exon 11	-	chr5:143278789-143278814	ACGCUCCCUUCAGAAUUCAGAGGCA	2256
2908_11_189	NR3C1	Exon 11	-	chr5:143278790-143278815	CACGCUCCCUUCAGAAUUCAGAGGC	2257
2908_11_190	NR3C1	Exon 11	-	chr5:143278794-143278819	AAGCCACGCUCCCUUCAGAAUUCAG	2258
2908_11_191	NR3C1	Exon 11	-	chr5:143278823-143278848	GGGAUGAGCUCUGGGCAUGCCAUGA	2259
2908_11_192	NR3C1	Exon 11	-	chr5:143278836-143278861	GGAUAAUUAGCAUGGGAUGAGCUCU	2260

2908_11_193	NR3C1	Exon 11	-	chr5:143278837-143278862	UGGAUAAUUAGCAUGGGAUGAGCUC	2261
2908_11_194	NR3C1	Exon 11	-	chr5:143278848-143278873	CUAUGAAGUGCUGGAUAAUUAGCAU	2262
2908_11_195	NR3C1	Exon 11	-	chr5:143278849-143278874	UCUAUGAAGUGCUGGAUAAUUAGCA	2263
2908_11_196	NR3C1	Exon 11	-	chr5:143278862-143278887	AACAUGAUUUGUGUCUAUGAAGUGC	2264
2908_11_197	NR3C1	Exon 11	-	chr5:143278896-143278921	GGGAGGAAACCUUGGCCACCCCAAA	2265
2908_11_198	NR3C1	Exon 11	-	chr5:143278909-143278934	UGCCUAAAACUAUGGGAGGAAACCU	2266
2908_11_199	NR3C1	Exon 11	-	chr5:143278918-143278943	AUAUCCAAAUGCCUAAAACUAUGGG	2267
2908_11_200	NR3C1	Exon 11	-	chr5:143278921-143278946	UAUAUAUCCAAAUGCCUAAAACUAU	2268
2908_11_201	NR3C1	Exon 11	-	chr5:143278922-143278947	AUAUAUAUCCAAAUGCCUAAAACUA	2269
2908_11_202	NR3C1	Exon 11	-	chr5:143278951-143278976	AGGCACUUAGGACAUAACACUUUUG	2270
2908_11_203	NR3C1	Exon 11	-	chr5:143278952-143278977	GAGGCACUUAGGACAUAACACUUUU	2271
2908_11_204	NR3C1	Exon 11	-	chr5:143278953-143278978	UGAGGCACUUAGGACAUAACACUUU	2272
2908_11_205	NR3C1	Exon 11	-	chr5:143278968-143278993	CUAUACAAGCAGAACUGAGGCACUU	2273
2908_11_206	NR3C1	Exon 11	-	chr5:143278976-143279001	GUGGGAUACUAUACAAGCAGAACUG	2274
2908_11_207	NR3C1	Exon 11	-	chr5:143278999-143279024	UUUUUAGUGUUUGUAGGUAUUCUGU	2275
2908_11_208	NR3C1	Exon 11	-	chr5:143279000-143279025	AUUUUUAGUGUUUGUAGGUAUUCUG	2276
2908_11_209	NR3C1	Exon 11	-	chr5:143279010-143279035	CCUGAAAAGUAUUUUUAGUGUUUGU	2277
2908_11_210	NR3C1	Exon 11	-	chr5:143279053-143279078	AGUUUGUAGUAACUUCAGUGAGAGU	2278
2908_11_211	NR3C1	Exon 11	-	chr5:143279103-143279128	AUUUAUUUCCUAUGUAUGUGUUAUC	2279
2908_11_212	NR3C1	Exon 11	-	chr5:143279147-143279172	AAUUGUGGAUUUAAGUGCUAUAUGG	2280
2908_11_213	NR3C1	Exon 11	-	chr5:143279150-143279175	UUUAAUUGUGGAUUUAAGUGCUAUA	2281
2908_11_214	NR3C1	Exon 11	-	chr5:143279167-143279192	AAGUCAUCUUAAUUAUGUUUAAUUG	2282
2908_11_215	NR3C1	Exon 11	-	chr5:143279201-143279226	AGCUGUGCCCUUUUAGGAUACGUGG	2283
2908_11_216	NR3C1	Exon 11	-	chr5:143279202-143279227	AAGCUGUGCCCUUUUAGGAUACGUG	2284
2908_11_217	NR3C1	Exon 11	-	chr5:143279203-143279228	GAAGCUGUGCCCUUUUAGGAUACGU	2285

2908_11_218	NR3C1	Exon 11	-	chr5:143279204-143279229	AGAAGCUGUGCCCUUUUAGGAUACG	2286
2908_11_219	NR3C1	Exon 11	-	chr5:143279212-143279237	AUGGGAAAAGAAGCUGUGCCCUUUU	2287
2908_11_220	NR3C1	Exon 11	-	chr5:143279235-143279260	AACUAUAGGAGGCUUUUCAUUAAAU	2288
2908_11_221	NR3C1	Exon 11	-	chr5:143279236-143279261	CAACUAUAGGAGGCUUUUCAUUAAA	2289
2908_11_222	NR3C1	Exon 11	-	chr5:143279251-143279276	ACUGAUGCUCAUCGACAACUAUAGG	2290
2908_11_223	NR3C1	Exon 11	-	chr5:143279254-143279279	UCAACUGAUGCUCAUCGACAACUAU	2291
2908_11_224	NR3C1	Exon 11	-	chr5:143279345-143279370	AAUCUGAUUUUCAUCCCAACAAUCU	2292
2908_11_225	NR3C1	Exon 11	-	chr5:143279402-143279427	UAUCAUUCCUUUAUAGAAUGUUAUG	2293
2908_11_226	NR3C1	Exon 11	-	chr5:143279504-143279529	UGUGUAACCCGGCUGGAUAAAUUUU	2294
2908_11_227	NR3C1	Exon 11	-	chr5:143279516-143279541	AUUUUAAGAUGGUGUGUAACCCGGC	2295
2908_11_228	NR3C1	Exon 11	-	chr5:143279520-143279545	UAAUAUUUUAAGAUGGUGUGUAACC	2296
2908_11_229	NR3C1	Exon 11	-	chr5:143279532-143279557	UAAAAGGGAAUGUAAUAUUUUAAGA	2297
2908_11_230	NR3C1	Exon 11	-	chr5:143279552-143279577	UUUGCUUUUUGAAUGCUCUCUAAAA	2298
2908_11_231	NR3C1	Exon 11	-	chr5:143279553-143279578	AUUUGCUUUUUGAAUGCUCUCUAAA	2299
2908_11_232	NR3C1	Exon 11	-	chr5:143279607-143279632	AUGUUAUUUGUUAUUUUCAGUAUUU	2300
2908_11_233	NR3C1	Exon 11	-	chr5:143279667-143279692	CAAGAGUUUAUUUCCAAAUAAAAUG	2301
2908_11_234	NR3C1	Exon 11	-	chr5:143279731-143279756	AUAUGUAAAUAGUGCAGAAUCUCAU	2302
2908_11_235	NR3C1	Exon 11	-	chr5:143279767-143279792	AGAAGUUUGGCAAUAGUUUGCAUAG	2303
2908_11_236	NR3C1	Exon 11	-	chr5:143279785-143279810	AAUGACAACAGAAGCUUCAGAAGUU	2304
2908_11_237	NR3C1	Exon 11	-	chr5:143279846-143279871	AUCCUUAAAGGCACCAUCUAAUAGC	2305
2908_11_238	NR3C1	Exon 11	-	chr5:143279847-143279872	CAUCCUUAAAGGCACCAUCUAAUAG	2306
2908_11_239	NR3C1	Exon 11	-	chr5:143279863-143279888	AGGAAGGUGGUGCUUACAUCCUUAA	2307
2908_11_240	NR3C1	Exon 11	-	chr5:143279881-143279906	AGUAUGUAAACAGGAGACAGGAAGG	2308
2908_11_241	NR3C1	Exon 11	-	chr5:143279884-143279909	UAAAGUAUGUAAACAGGAGACAGGA	2309
2908_11_242	NR3C1	Exon 11	-	chr5:143279888-143279913	UAUGUAAAGUAUGUAAACAGGAGAC	2310

2908_11_243	NR3C1	Exon 11	-	chr5:143279895-143279920	ACUAAAGUAUGUAAAGUAUGUAAAC	2311
2908_11_244	NR3C1	Exon 11	-	chr5:143279948-143279973	AUUCCAACAGUGAGUCUGUCAGCGC	2312
2908_11_245	NR3C1	Exon 11	-	chr5:143280013-143280038	AGGCUCUGACCCAGUGAGAUUACAG	2313
2908_11_246	NR3C1	Exon 11	-	chr5:143280038-143280063	GUCCUGUGUGCAGUGAAGGUUGCUG	2314
2908_11_247	NR3C1	Exon 11	-	chr5:143280047-143280072	UGGAGACUGGUCCUGUGUGCAGUGA	2315
2908_11_248	NR3C1	Exon 11	-	chr5:143280065-143280090	UCUAGGGGAAGAGGGAGAUGGAGAC	2316
2908_11_249	NR3C1	Exon 11	-	chr5:143280072-143280097	AGUUUGCUCUAGGGGAAGAGGGAGA	2317
2908_11_250	NR3C1	Exon 11	-	chr5:143280078-143280103	CCAAACAGUUUGCUCUAGGGGAAGA	2318
2908_11_251	NR3C1	Exon 11	-	chr5:143280079-143280104	ACCAAACAGUUUGCUCUAGGGGAAG	2319
2908_11_252	NR3C1	Exon 11	-	chr5:143280085-143280110	UCAGAAACCAAACAGUUUGCUCUAG	2320
2908_11_253	NR3C1	Exon 11	-	chr5:143280086-143280111	CUCAGAAACCAAACAGUUUGCUCUA	2321
2908_11_254	NR3C1	Exon 11	-	chr5:143280087-143280112	UCUCAGAAACCAAACAGUUUGCUCU	2322
2908_11_255	NR3C1	Exon 11	-	chr5:143280115-143280140	GUACAUGCAUUCAUACAGGCAGCGA	2323
2908_11_256	NR3C1	Exon 11	-	chr5:143280124-143280149	UUAUAGUUUGUACAUGCAUUCAUAC	2324
2908_11_257	NR3C1	Exon 11	-	chr5:143280166-143280191	UUUGUAGGGGUCAAAGAAAUGCUGA	2325
2908_11_258	NR3C1	Exon 11	-	chr5:143280184-143280209	AUGACAUGUUAUAUAUUUUUUGUAG	2326
2908_11_259	NR3C1	Exon 11	-	chr5:143280185-143280210	CAUGACAUGUUAUAUAUUUUUUGUA	2327
2908_11_260	NR3C1	Exon 11	-	chr5:143280186-143280211	UCAUGACAUGUUAUAUAUUUUUUGU	2328
2908_11_261	NR3C1	Exon 11	-	chr5:143280305-143280330	CCAUAACACUAAUCUGGGAAGGGAA	2329
2908_11_262	NR3C1	Exon 11	-	chr5:143280306-143280331	ACCAUAACACUAAUCUGGGAAGGGA	2330
2908_11_263	NR3C1	Exon 11	-	chr5:143280310-143280335	UAUAACCAUAACACUAAUCUGGGAA	2331
2908_11_264	NR3C1	Exon 11	-	chr5:143280311-143280336	GUAUAACCAUAACACUAAUCUGGGA	2332
2908_11_265	NR3C1	Exon 11	-	chr5:143280315-143280340	UAUAGUAUAACCAUAACACUAAUCU	2333
2908_11_266	NR3C1	Exon 11	-	chr5:143280316-143280341	AUAUAGUAUAACCAUAACACUAAUC	2334
2908_11_267	NR3C1	Exon 11	-	chr5:143280385-143280410	AACUGAAAAUCUAAUAUUAAAAAUA	2335

2908_11_268	NR3C1	Exon 11	-	chr5:143280435-143280460	CAAGAAAUUUGAUUUCUAUUCAAGG	2336
2908_11_269	NR3C1	Exon 11	-	chr5:143280438-143280463	CCACAAGAAAUUUGAUUUCUAUUCA	2337
2908_11_270	NR3C1	Exon 11	-	chr5:143280683-143280708	AUUGGUUAAUCUUUCCUGAUGGUAC	2338
2908_11_271	NR3C1	Exon 11	-	chr5:143280689-143280714	UCACCAAUUGGUUAAUCUUUCCUGA	2339
2908_11_272	NR3C1	Exon 11	-	chr5:143280706-143280731	UUUCACAUUCCCAUCUGUCACCAAU	2340
2908_11_273	NR3C1	Exon 11	-	chr5:143280746-143280771	AACUAAAUCUCUAAUAUGGCAAAAA	2341
2908_11_274	NR3C1	Exon 11	-	chr5:143280755-143280780	UUACCCAAAAACUAAAUCUCUAAUA	2342
2908_11_275	NR3C1	Exon 11	-	chr5:143280892-143280917	AAAGCUGGUAAACUAUUUGUCUUUC	2343
2908_11_276	NR3C1	Exon 11	-	chr5:143280912-143280937	UGCAAUGGCUAUAUGGCAAGAAAGC	2344
2908_11_277	NR3C1	Exon 11	-	chr5:143280924-143280949	ACGCCCUAUUUUUGCAAUGGCUAUA	2345
2908_11_278	NR3C1	Exon 11	-	chr5:143280932-143280957	UGUACCUAACGCCCUAUUUUUGCAA	2346
2908_11_279	NR3C1	Exon 11	-	chr5:143280967-143280992	ACUAAUUUAAAAAAUAACUACCAAG	2347
2908_11_280	NR3C1	Exon 11	-	chr5:143281004-143281029	GACCUGCUGGGUAAACUGUGGAUGA	2348
2908_11_281	NR3C1	Exon 11	-	chr5:143281011-143281036	GUCCAGUGACCUGCUGGGUAAACUG	2349
2908_11_282	NR3C1	Exon 11	-	chr5:143281021-143281046	AGAGCACCUAGUCCAGUGACCUGCU	2350
2908_11_283	NR3C1	Exon 11	-	chr5:143281022-143281047	UAGAGCACCUAGUCCAGUGACCUGC	2351
2908_11_284	NR3C1	Exon 11	-	chr5:143281052-143281077	GGUUGUGCAAAUUAACAGUCCUAAC	2352
2908_11_285	NR3C1	Exon 11	-	chr5:143281078-143281103	UAUCUGCUUCAGUGGAGAAUUAUAU	2353
2908_11_286	NR3C1	Exon 11	-	chr5:143281091-143281116	CAUAUUUUGUAUAUAUCUGCUUCAG	2354
2908_11_287	NR3C1	Exon 11	-	chr5:143281194-143281219	AAAUGGGUUGGUGCUUCUAACCUGA	2355
2908_11_288	NR3C1	Exon 11	-	chr5:143281211-143281236	AUCAAUCAUCUGUGUGAAAAUGGGU	2356
2908_11_289	NR3C1	Exon 11	-	chr5:143281215-143281240	AUUAAUCAAUCAUCUGUGUGAAAAU	2357
2908_11_290	NR3C1	Exon 11	-	chr5:143281216-143281241	CAUUAAUCAAUCAUCUGUGUGAAAA	2358
2908_11_291	NR3C1	Exon 11	-	chr5:143281279-143281304	AAGUUAUUGUACAGCUGUUUAAGAU	2359
2908_11_292	NR3C1	Exon 11	-	chr5:143281280-143281305	CAAGUUAUUGUACAGCUGUUUAAGA	2360

2908_11_293	NR3C1	Exon 11	-	chr5:143281374-143281399	UGUGCCUUUUAUAGCUAUUACUGUC	2361
2908_11_294	NR3C1	Exon 11	-	chr5:143281406-143281431	AAGUUUACAAGUGUAUAUCAGAAAA	2362
2908_11_295	NR3C1	Exon 11	-	chr5:143281407-143281432	AAAGUUUACAAGUGUAUAUCAGAAA	2363
2908_11_296	NR3C1	Exon 11	-	chr5:143281446-143281471	UAGGAUAGCAUUUUUGAUUUAUGCA	2364
2908_11_297	NR3C1	Exon 11	-	chr5:143281470-143281495	UGGUGUAUCCCCCCCCUGUAUAGUU	2365
2908_11_298	NR3C1	Exon 11	-	chr5:143281495-143281520	GGAUGAAAUUUUCUAGACUUUCUGU	2366
2908_11_299	NR3C1	Exon 11	-	chr5:143281521-143281546	CUUCAUACUUUUUUUCACAGUUGGC	2367
2908_11_300	NR3C1	Exon 11	-	chr5:143281525-143281550	UUCUCUUCAUACUUUUUUCACAGU	2368
2908_11_301	NR3C1	Exon 11	-	chr5:143281592-143281617	CGUAAUCUCCACAGUCAAAGAAGGA	2369
2908_11_302	NR3C1	Exon 11	-	chr5:143281596-143281621	UGGACGUAAUCUCCACAGUCAAAGA	2370
2908_11_303	NR3C1	Exon 11	-	chr5:143281621-143281646	CCCAGAAAUUAGAAACCUUAAUAUG	2371
2908_11_304	NR3C1	Exon 11	-	chr5:143281671-143281696	CACUUUUCAGUGAUGGGAGAGUAGA	2372
2908_11_305	NR3C1	Exon 11	-	chr5:143281682-143281707	UGAGUCGUCAUCACUUUUCAGUGAU	2373
2908_11_306	NR3C1	Exon 11	-	chr5:143281683-143281708	UUGAGUCGUCAUCACUUUUCAGUGA	2374
2908_11_307	NR3C1	Exon 11	-	chr5:143281723-143281748	AUGUGGUUUAUAGAGGGCCAAGACU	2375
2908_11_308	NR3C1	Exon 11	-	chr5:143281734-143281759	AUACGCACUACAUGUGGUUUAUAGA	2376
2908_11_309	NR3C1	Exon 11	-	chr5:143281735-143281760	AAUACGCACUACAUGUGGUUUAUAG	2377
2908_11_310	NR3C1	Exon 11	-	chr5:143281745-143281770	UUUUGUUUUAAAUACGCACUACAUG	2378
2908_11_311	NR3C1	Exon 11	-	chr5:143281809-143281834	UAUAAACUAUCAGUUUGUCCUGUAG	2379
2908_11_312	NR3C1	Exon 11	-	chr5:143281873-143281898	UCAAAAGUGACUGCCUUAAUAAGAA	2380
2908_11_313	NR3C1	Exon 11	-	chr5:143281925-143281950	CCAAUCAGAUACCAAAAUAUUCAAA	2381
2908_11_314	NR3C1	Exon 11	-	chr5:143282001-143282026	CUUAACUAUUGCUUCCAAACAUUUU	2382
2908_11_315	NR3C1	Exon 11	-	chr5:143282040-143282065	UCAUUACCAUAUCUUCUCUUGCAGG	2383
2908_10_1	NR3C1	Exon 10	+	chr5:143282594-143282619	CAGUUGAUAAAACCGCUGCCAGUUC	2384
2908_10_2	NR3C1	Exon 10	+	chr5:143282598-143282623	UGAUAAAACCGCUGCCAGUUCUGGC	2385

2908_10_3	NR3C1	Exon 10	+	chr5:143282622-143282647	CUGGAGUUUCCUUCCCUCUUGACAA	2386
2908_10_4	NR3C1	Exon 10	+	chr5:143282646-143282671	AUGGCUUUUCCUAGCUCUUUGAUGU	2387
2908_10_5	NR3C1	Exon 10	+	chr5:143282675-143282700	CAUUCUAAUUUCAUCAAAUAGCUCU	2388
2908_10_6	NR3C1	Exon 10	+	chr5:143282695-143282720	GCUCUUGGCUCUUCAGACCGUCCUU	2389
2908_10_7	NR3C1	Exon 10	+	chr5:143282705-143282730	CUUCAGACCGUCCUUAGGAACUAAA	2390
2908_10_8	NR3C1	Exon 10	-	chr5:143282584-143282609	CGGUUUUAUCAACUGACAAAACUCU	2391
2908_10_9	NR3C1	Exon 10	-	chr5:143282609-143282634	AGGAAACUCCAGCCAGAACUGGCAG	2392
2908_10_10	NR3C1	Exon 10	-	chr5:143282615-143282640	GAGGGAAGGAAACUCCAGCCAGAAC	2393
2908_10_11	NR3C1	Exon 10	-	chr5:143282634-143282659	UAGGAAAAGCCAUUGUCAAGAGGGA	2394
2908_10_12	NR3C1	Exon 10	-	chr5:143282638-143282663	GAGCUAGGAAAAGCCAUUGUCAAGA	2395
2908_10_13	NR3C1	Exon 10	-	chr5:143282639-143282664	AGAGCUAGGAAAAGCCAUUGUCAAG	2396
2908_10_14	NR3C1	Exon 10	-	chr5:143282658-143282683	UUAGAAUGACCUACAUCAAAGAGCU	2397
2908_10_15	NR3C1	Exon 10	-	chr5:143282715-143282740	AUCUUAACCUUUUAGUUCCUAAGGA	2398
2908_10_16	NR3C1	Exon 10	-	chr5:143282719-143282744	CUUCAUCUUAACCUUUUAGUUCCUA	2399
2908_9_1	NR3C1	Exon 9	+	chr5:143293879-143293904	UAAACAAGUAAAGUUGUUAGUAUCC	2400
2908_9_2	NR3C1	Exon 9	+	chr5:143293900-143293925	AUCCAGGCACUGAAUUAUACCUUCA	2401
2908_9_3	NR3C1	Exon 9	+	chr5:143293972-143293997	ACUUCUUUAACAAGUGUACCGCUAC	2402
2908_9_4	NR3C1	Exon 9	+	chr5:143294007-143294032	AAACGUCUCUAGCAAUGAUCUUUAU	2403
2908_9_5	NR3C1	Exon 9	+	chr5:143294008-143294033	AACGUCUCUAGCAAUGAUCUUUAUC	2404
2908_9_6	NR3C1	Exon 9	+	chr5:143294119-143294144	AAAACAUUAAGAUGAAUGUGCGCUU	2405
2908_9_7	NR3C1	Exon 9	+	chr5:143294194-143294219	GCAACAUCCAUAGCUUACAGUUAUU	2406
2908_9_8	NR3C1	Exon 9	+	chr5:143294221-143294246	GCAACUAUGAAACCACAGUUACUAA	2407
2908_9_9	NR3C1	Exon 9	+	chr5:143294273-143294298	AAAUGUACUUAUUUGUAUAUGAAAG	2408
2908_9_10	NR3C1	Exon 9	+	chr5:143294332-143294357	AUUGAUAUGUAAUUUUUACUUGAAA	2409
2908_9_11	NR3C1	Exon 9	+	chr5:143294339-143294364	UGUAAUUUUUACUUGAAAUGGCCUA	2410

2908_9_12	NR3C1	Exon 9	+	chr5:143295014-143295039	AAUAGUAAUUAAGCACACCUUUUCU	2411
2908_9_13	NR3C1	Exon 9	+	chr5:143295063-143295088	UUUCUCAUACAUGCUAAUACUCAUU	2412
2908_9_14	NR3C1	Exon 9	+	chr5:143295098-143295123	AAUUUUUAACCAAAUAACAGUGUAG	2413
2908_9_15	NR3C1	Exon 9	+	chr5:143295157-143295182	AUGUCUUCCCAUGAUCAAAGAUCAA	2414
2908_9_16	NR3C1	Exon 9	+	chr5:143295161-143295186	CUUCCCAUGAUCAAAGAUCAAAGGA	2415
2908_9_17	NR3C1	Exon 9	+	chr5:143295165-143295190	CCAUGAUCAAAGAUCAAAGGAAGGA	2416
2908_9_18	NR3C1	Exon 9	+	chr5:143295261-143295286	CCAUACCUAUUUGUCUUAUUAAUCU	2417
2908_9_19	NR3C1	Exon 9	+	chr5:143295319-143295344	CAUUCAUAAAAAUCAUCUGACUAGU	2418
2908_9_20	NR3C1	Exon 9	+	chr5:143295337-143295362	GACUAGUAGGAAAUAAUAGUAGACU	2419
2908_9_21	NR3C1	Exon 9	+	chr5:143295382-143295407	UGUAUAUAAAUUAACCUUUGUUUCU	2420
2908_9_22	NR3C1	Exon 9	+	chr5:143295411-143295436	CUUCAUAUUUCAUGCUUUUGACAUA	2421
2908_9_23	NR3C1	Exon 9	+	chr5:143295419-143295444	UUCAUGCUUUUGACAUAAGGUGAAA	2422
2908_9_24	NR3C1	Exon 9	+	chr5:143295452-143295477	UACCAACCUGAAGAGAGAAGCAGUA	2423
2908_9_25	NR3C1	Exon 9	+	chr5:143295506-143295531	GAUACCUGAAGCCUGUGUAACUCAG	2424
2908_9_26	NR3C1	Exon 9	+	chr5:143295532-143295557	GGAAACAUACAGCAUGUGUUUACAU	2425
2908_9_27	NR3C1	Exon 9	+	chr5:143295545-143295570	AUGUGUUUACAUUGGUCGUACAUGC	2426
2908_9_28	NR3C1	Exon 9	+	chr5:143295546-143295571	UGUGUUUACAUUGGUCGUACAUGCA	2427
2908_9_29	NR3C1	Exon 9	+	chr5:143295583-143295608	UCUCUGCCUGUGAAAGAUAAAUAGC	2428
2908_9_30	NR3C1	Exon 9	+	chr5:143295584-143295609	CUCUGCCUGUGAAAGAUAAAUAGCA	2429
2908_9_31	NR3C1	Exon 9	-	chr5:143293861-143293886	UUGUUUUUUUUUUUUUUUUUCUU	2430
2908_9_32	NR3C1	Exon 9	-	chr5:143293905-143293930	UACCAUGAAGGUAUAAUUCAGUGCC	2431
2908_9_33	NR3C1	Exon 9	-	chr5:143293922-143293947	AUCAUAGCUUUGAUUGAUACCAUGA	2432
2908_9_34	NR3C1	Exon 9	-	chr5:143293993-143294018	UAGAGACGUUUAAUGUUACCUGUAG	2433
2908_9_35	NR3C1	Exon 9	-	chr5:143294047-143294072	AGAAGUAUUAAUAAUAUUUCAGUCA	2434
2908_9_36	NR3C1	Exon 9	-	chr5:143294080-143294105	UCAACAAAAAGUUAUUUUAUGUUAA	2435

2908_9_37	NR3C1	Exon 9	-	chr5:143294204-143294229	AUAGUUGCCAAAUAACUGUAAGCUA	2436
2908_9_38	NR3C1	Exon 9	-	chr5:143294236-143294261	AAAGUCUUAAUUCCAUUAGUAACUG	2437
2908_9_39	NR3C1	Exon 9	-	chr5:143294363-143294388	UGAACUAGUUGGUAUUAUAAACCUU	2438
2908_9_40	NR3C1	Exon 9	-	chr5:143294379-143294404	AAAUUUUAAAGCUCUAUGAACUAGU	2439
2908_9_41	NR3C1	Exon 9	-	chr5:143294957-143294982	UGUCAGAGAUUCAUUAUCUAGAAAA	2440
2908_9_42	NR3C1	Exon 9	-	chr5:143294987-143295012	GGAUUGGUUAACAUAGCAUGGGAGC	2441
2908_9_43	NR3C1	Exon 9	-	chr5:143294993-143295018	UAUUGGGGAUUGGUUAACAUAGCAU	2442
2908_9_44	NR3C1	Exon 9	-	chr5:143294994-143295019	CUAUUGGGGAUUGGUUAACAUAGCA	2443
2908_9_45	NR3C1	Exon 9	-	chr5:143295008-143295033	GGUGUGCUUAAUUACUAUUGGGGAU	2444
2908_9_46	NR3C1	Exon 9	-	chr5:143295013-143295038	GAAAAGGUGUGCUUAAUUACUAUUG	2445
2908_9_47	NR3C1	Exon 9	-	chr5:143295014-143295039	AGAAAAGGUGUGCUUAAUUACUAUU	2446
2908_9_48	NR3C1	Exon 9	-	chr5:143295015-143295040	UAGAAAAGGUGUGCUUAAUUACUAU	2447
2908_9_49	NR3C1	Exon 9	-	chr5:143295034-143295059	GGGAGAAAAAGGCGCAUCCUAGAAA	2448
2908_9_50	NR3C1	Exon 9	-	chr5:143295050-143295075	AUGUAUGAGAAAUUAUGGGAGAAAA	2449
2908_9_51	NR3C1	Exon 9	-	chr5:143295059-143295084	AGUAUUAGCAUGUAUGAGAAAUUAU	2450
2908_9_52	NR3C1	Exon 9	-	chr5:143295060-143295085	GAGUAUUAGCAUGUAUGAGAAAUUA	2451
2908_9_53	NR3C1	Exon 9	-	chr5:143295110-143295135	UGAUUUUGUCCACUACACUGUUAUU	2452
2908_9_54	NR3C1	Exon 9	-	chr5:143295158-143295183	UUUGAUCUUUGAUCAUGGGAAGACA	2453
2908_9_55	NR3C1	Exon 9	-	chr5:143295167-143295192	CUUCCUUCCUUUGAUCUUUGAUCAU	2454
2908_9_56	NR3C1	Exon 9	-	chr5:143295168-143295193	CCUUCCUUCCUUUGAUCUUUGAUCA	2455
2908_9_57	NR3C1	Exon 9	-	chr5:143295232-143295257	AACAGAGAGGUAUAUGAGCUGCAUA	2456
2908_9_58	NR3C1	Exon 9	-	chr5:143295233-143295258	AAACAGAGAGGUAUAUGAGCUGCAU	2457
2908_9_59	NR3C1	Exon 9	-	chr5:143295250-143295275	ACAAAUAGGUAUGGCAGAAACAGAG	2458
2908_9_60	NR3C1	Exon 9	-	chr5:143295264-143295289	CCAAGAUUAAUAAGACAAAUAGGUA	2459
2908_9_61	NR3C1	Exon 9	-	chr5:143295269-143295294	UGACACCAAGAUUAAUAAGACAAAU	2460

2908_9_62	NR3C1	Exon 9	-	chr5:143295306-143295331	UUUUUAUGAAUGUAAAAUAUUAGAA	2461
2908_9_63	NR3C1	Exon 9	-	chr5:143295399-143295424	AUGAAAUAUGAAGGCCUAGAAACAA	2462
2908_9_64	NR3C1	Exon 9	-	chr5:143295413-143295438	CUUAUGUCAAAAGCAUGAAAUAUGA	2463
2908_9_65	NR3C1	Exon 9	-	chr5:143295457-143295482	AACCUUACUGCUUCUCUCUUCAGGU	2464
2908_9_66	NR3C1	Exon 9	-	chr5:143295461-143295486	UGAAAACCUUACUGCUUCUCUCUUC	2465
2908_9_67	NR3C1	Exon 9	-	chr5:143295513-143295538	GUUUCCUCUGAGUUACACAGGCUUC	2466
2908_9_68	NR3C1	Exon 9	-	chr5:143295520-143295545	GCUGUAUGUUUCCUCUGAGUUACAC	2467
2908_8_1	NR3C1	Exon 8	+	chr5:143298659-143298684	CAACUUACUCAUUAAUAAUCAGAUC	2468
2908_8_2	NR3C1	Exon 8	+	chr5:143298675-143298700	AAUCAGAUCAGGAGCAAAACACAGC	2469
2908_8_3	NR3C1	Exon 8	+	chr5:143298736-143298761	AGAGCAAAUGCCAUAAGAAACAUCC	2470
2908_8_4	NR3C1	Exon 8	+	chr5:143298750-143298775	AAGAAACAUCCAGGAGUACUGCAGU	2471
2908_8_5	NR3C1	Exon 8	+	chr5:143298751-143298776	AGAAACAUCCAGGAGUACUGCAGUA	2472
2908_8_6	NR3C1	Exon 8	+	chr5:143298759-143298784	CCAGGAGUACUGCAGUAGGGUCAUU	2473
2908_8_7	NR3C1	Exon 8	+	chr5:143298768-143298793	CUGCAGUAGGGUCAUUUGGUCAUCC	2474
2908_8_8	NR3C1	Exon 8	+	chr5:143298805-143298830	CUGAAACCUGAAUUAAGAGAAAUAA	2475
2908_8_9	NR3C1	Exon 8	-	chr5:143298732-143298757	GUUUCUUAUGGCAUUUGCUCUGGGG	2476
2908_8_10	NR3C1	Exon 8	-	chr5:143298735-143298760	GAUGUUUCUUAUGGCAUUUGCUCUG	2477
2908_8_11	NR3C1	Exon 8	-	chr5:143298736-143298761	GGAUGUUUCUUAUGGCAUUUGCUCU	2478
2908_8_12	NR3C1	Exon 8	-	chr5:143298737-143298762	UGGAUGUUUCUUAUGGCAUUUGCUC	2479
2908_8_13	NR3C1	Exon 8	-	chr5:143298749-143298774	CUGCAGUACUCCUGGAUGUUUCUUA	2480
2908_8_14	NR3C1	Exon 8	-	chr5:143298762-143298787	CCAAAUGACCCUACUGCAGUACUCC	2481
2908_8_15	NR3C1	Exon 8	-	chr5:143298794-143298819	AAUUCAGGUUUCAGGAACUUACACC	2482
2908_8_16	NR3C1	Exon 8	-	chr5:143298807-143298832	CUUUAUUUCUCUUAAUUCAGGUUUC	2483
2908_7_1	NR3C1	Exon 7	+	chr5:143300460-143300485	GCUCUUUUAUGUUUUGCAUCUUACC	2484
2908_7_2	NR3C1	Exon 7	+	chr5:143300547-143300572	UAGUCAUGAUCCUCCAAGUUGAGUC	2485

2908_7_3	NR3C1	Exon 7	+	chr5:143300583-143300608	UAUCAUAUCCUGCAUAUAACACUUC	2486
2908_7_4	NR3C1	Exon 7	+	chr5:143300611-143300636	UUCAAUAACCUCCAACAGUGACACC	2487
2908_7_5	NR3C1	Exon 7	+	chr5:143300612-143300637	UCAAUAACCUCCAACAGUGACACCA	2488
2908_7_6	NR3C1	Exon 7	+	chr5:143300616-143300641	UAACCUCCAACAGUGACACCAGGGU	2489
2908_7_7	NR3C1	Exon 7	+	chr5:143300617-143300642	AACCUCCAACAGUGACACCAGGGUA	2490
2908_7_8	NR3C1	Exon 7	+	chr5:143300618-143300643	ACCUCCAACAGUGACACCAGGGUAG	2491
2908_7_9	NR3C1	Exon 7	+	chr5:143300628-143300653	GUGACACCAGGGUAGGGGUGAGUUG	2492
2908_7_10	NR3C1	Exon 7	+	chr5:143300640-143300665	UAGGGGUGAGUUGUGGUAACGUUGC	2493
2908_7_11	NR3C1	Exon 7	+	chr5:143300661-143300686	UUGCAGGAACUAUUGUUUUGUUACC	2494
2908_7_12	NR3C1	Exon 7	+	chr5:143300672-143300697	AUUGUUUUGUUACCAGGAUUUUCAG	2495
2908_7_13	NR3C1	Exon 7	+	chr5:143300696-143300721	GAGGUUUCUUGUGAGACUCCUGUAG	2496
2908_7_14	NR3C1	Exon 7	+	chr5:143300741-143300766	AUUUUUUUCUUUGUUUUUCGAGCUG	2497
2908_7_15	NR3C1	Exon 7	+	chr5:143300742-143300767	UUUUUUUCUUUGUUUUUCGAGCUGU	2498
2908_7_16	NR3C1	Exon 7	-	chr5:143300486-143300511	CAGUGAAAUGGGCAAAGGCAAUACC	2499
2908_7_17	NR3C1	Exon 7	-	chr5:143300496-143300521	GUGAUUGCAGCAGUGAAAUGGGCAA	2500
2908_7_18	NR3C1	Exon 7	-	chr5:143300502-143300527	CGGCAAGUGAUUGCAGCAGUGAAAU	2501
2908_7_19	NR3C1	Exon 7	-	chr5:143300503-143300528	GCGGCAAGUGAUUGCAGCAGUGAAA	2502
2908_7_20	NR3C1	Exon 7	-	chr5:143300527-143300552	GACUACGCUCAACAUGUUAGGAGGG	2503
2908_7_21	NR3C1	Exon 7	-	chr5:143300530-143300555	CAUGACUACGCUCAACAUGUUAGGA	2504
2908_7_22	NR3C1	Exon 7	-	chr5:143300531-143300556	UCAUGACUACGCUCAACAUGUUAGG	2505
2908_7_23	NR3C1	Exon 7	-	chr5:143300534-143300559	GGAUCAUGACUACGCUCAACAUGUU	2506
2908_7_24	NR3C1	Exon 7	-	chr5:143300560-143300585	UAGCUCUGUUCCAGACUCAACUUGG	2507
2908_7_25	NR3C1	Exon 7	-	chr5:143300563-143300588	UGAUAGCUCUGUUCCAGACUCAACU	2508
2908_7_26	NR3C1	Exon 7	-	chr5:143300594-143300619	UUAUUGAACCUGAAGUGUUAUAUGC	2509
2908_7_27	NR3C1	Exon 7	-	chr5:143300622-143300647	ACCCCUACCCUGGUGUCACUGUUGG	2510

2908_7_28	NR3C1	Exon 7	-	chr5:143300625-143300650	CUCACCCCUACCCUGGUGUCACUGU	2511
2908_7_29	NR3C1	Exon 7	-	chr5:143300637-143300662	ACGUUACCACAACUCACCCCUACCC	2512
2908_7_30	NR3C1	Exon 7	-	chr5:143300687-143300712	UCUCACAAGAAACCUCUGAAAAUCC	2513
2908_7_31	NR3C1	Exon 7	-	chr5:143300717-143300742	UAAAAGGAAUUCAGCAGGCCACUAC	2514
2908_7_32	NR3C1	Exon 7	-	chr5:143300727-143300752	AAGAAAAAAAUAAAAGGAAUUCAGC	2515
2908_7_33	NR3C1	Exon 7	-	chr5:143300738-143300763	CUCGAAAAACAAAGAAAAAAAUAAA	2516
2908_6_1	NR3C1	Exon 6	+	chr5:143310076-143310101	CUUUCAGAUAUUUAUAUUACCUUCC	2517
2908_6_2	NR3C1	Exon 6	+	chr5:143310109-143310134	UCCAGCCUGAAGACAUUUUCGAUAG	2518
2908_6_3	NR3C1	Exon 6	+	chr5:143310117-143310142	GAAGACAUUUUCGAUAGCGGCAUGC	2519
2908_6_4	NR3C1	Exon 6	+	chr5:143310118-143310143	AAGACAUUUUCGAUAGCGGCAUGCU	2520
2908_6_5	NR3C1	Exon 6	+	chr5:143310172-143310197	GAUGCAAUCAUUCCUUCCAGCACAU	2521
2908_6_6	NR3C1	Exon 6	+	chr5:143310193-143310218	ACAUAGGUAAUUGUGCUGUCCUAUA	2522
2908_6_7	NR3C1	Exon 6	+	chr5:143310202-143310227	AUUGUGCUGUCCUAUAUGGAAUAAA	2523
2908_6_8	NR3C1	Exon 6	-	chr5:143310098-143310123	GUCUUCAGGCUGGAAUGAACCUGGA	2524
2908_6_9	NR3C1	Exon 6	-	chr5:143310102-143310127	AAAUGUCUUCAGGCUGGAAUGAACC	2525
2908_6_10	NR3C1	Exon 6	-	chr5:143310113-143310138	GCCGCUAUCGAAAAUGUCUUCAGGC	2526
2908_6_11	NR3C1	Exon 6	-	chr5:143310117-143310142	GCAUGCCGCUAUCGAAAAUGUCUUC	2527
2908_6_12	NR3C1	Exon 6	-	chr5:143310187-143310212	ACAGCACAAUUACCUAUGUGCUGGA	2528
2908_6_13	NR3C1	Exon 6	-	chr5:143310191-143310216	UAGGACAGCACAAUUACCUAUGUGC	2529
2908_5_1	NR3C1	Exon 5	+	chr5:143314062-143314087	UCCUGAAGCUUCAUCAGAGCACACC	2530
2908_5_2	NR3C1	Exon 5	+	chr5:143314072-143314097	UCAUCAGAGCACACCAGGCAGAGUU	2531
2908_5_3	NR3C1	Exon 5	+	chr5:143314073-143314098	CAUCAGAGCACACCAGGCAGAGUUU	2532
2908_5_4	NR3C1	Exon 5	+	chr5:143314076-143314101	CAGAGCACACCAGGCAGAGUUUGGG	2533
2908_5_5	NR3C1	Exon 5	+	chr5:143314079-143314104	AGCACACCAGGCAGAGUUUGGGAGG	2534
2908_5_6	NR3C1	Exon 5	+	chr5:143314099-143314124	GGAGGUGGUCCUGUUGUUGCUGUUG	2535

2908_5_7	NR3C1	Exon 5	+	chr5:143314105-143314130	GGUCCUGUUGUUGCUGUUGAGGAGC	2536
2908_5_8	NR3C1	Exon 5	+	chr5:143314109-143314134	CUGUUGUUGCUGUUGAGGAGCUGGA	2537
2908_5_9	NR3C1	Exon 5	+	chr5:143314112-143314137	UUGUUGCUGUUGAGGAGCUGGAUGG	2538
2908_5_10	NR3C1	Exon 5	+	chr5:143314127-143314152	AGCUGGAUGGAGGAGAGCUUACAUC	2539
2908_5_11	NR3C1	Exon 5	+	chr5:143314138-143314163	GGAGAGCUUACAUCUGGUCUCAUGC	2540
2908_5_12	NR3C1	Exon 5	+	chr5:143314139-143314164	GAGAGCUUACAUCUGGUCUCAUGCU	2541
2908_5_13	NR3C1	Exon 5	+	chr5:143314140-143314165	AGAGCUUACAUCUGGUCUCAUGCUG	2542
2908_5_14	NR3C1	Exon 5	+	chr5:143314150-143314175	UCUGGUCUCAUGCUGGGGCUAAAGA	2543
2908_5_15	NR3C1	Exon 5	+	chr5:143314151-143314176	CUGGUCUCAUGCUGGGGCUAAAGAA	2544
2908_5_16	NR3C1	Exon 5	+	chr5:143314152-143314177	UGGUCUCAUGCUGGGGCUAAAGAAG	2545
2908_5_17	NR3C1	Exon 5	-	chr5:143314003-143314028	AAGUUUUCUUCAAAAGAGCAGUGGA	2546
2908_5_18	NR3C1	Exon 5	-	chr5:143314007-143314032	UGUAAAGUUUUCUUCAAAAGAGCAG	2547
2908_5_19	NR3C1	Exon 5	-	chr5:143314039-143314064	GAUGUCAUUAUGGAGUCUUAACUUG	2548
2908_5_20	NR3C1	Exon 5	-	chr5:143314054-143314079	CUGAUGAAGCUUCAGGAUGUCAUUA	2549
2908_5_21	NR3C1	Exon 5	-	chr5:143314066-143314091	GCCUGGUGUGCUCUGAUGAAGCUUC	2550
2908_5_22	NR3C1	Exon 5	-	chr5:143314088-143314113	ACAGGACCACCUCCCAAACUCUGCC	2551
2908_5_23	NR3C1	Exon 5	-	chr5:143314111-143314136	CAUCCAGCUCCUCAACAGCAACAAC	2552
2908_4_1	NR3C1	Exon 4	+	chr5:143399662-143399687	AGCCAUUAGAAAAAACUGUUCGACC	2553
2908_4_2	NR3C1	Exon 4	+	chr5:143399663-143399688	GCCAUUAGAAAAAACUGUUCGACCA	2554
2908_4_3	NR3C1	Exon 4	+	chr5:143399711-143399736	AGUCAAGUUGUCAUCUCCAGAUCCU	2555
2908_4_4	NR3C1	Exon 4	+	chr5:143399730-143399755	GAUCCUUGGCACCUAUUCCAAUUUU	2556
2908_4_5	NR3C1	Exon 4	+	chr5:143399739-143399764	CACCUAUUCCAAUUUUCGGAACCAA	2557
2908_4_6	NR3C1	Exon 4	+	chr5:143399740-143399765	ACCUAUUCCAAUUUUCGGAACCAAC	2558
2908_4_7	NR3C1	Exon 4	+	chr5:143399746-143399771	UCCAAUUUUCGGAACCAACGGGAAU	2559
2908_4_8	NR3C1	Exon 4	+	chr5:143399749-143399774	AAUUUUCGGAACCAACGGGAAUUGG	2560

2908_4_9	NR3C1	Exon 4	+	chr5:143399767-143399792	GAAUUGGUGGAAUGACAUUAAAAAU	2561
2908_4_10	NR3C1	Exon 4	+	chr5:143399792-143399817	AGGCUUCUGAUCCUGCUGUUGAGAA	2562
2908_4_11	NR3C1	Exon 4	+	chr5:143399793-143399818	GGCUUCUGAUCCUGCUGUUGAGAAA	2563
2908_4_12	NR3C1	Exon 4	+	chr5:143399816-143399841	AAGGGAUGCUGUAUUCAUGUCAUAG	2564
2908_4_13	NR3C1	Exon 4	+	chr5:143399835-143399860	UCAUAGUGGUACAUCUGUCCUCCAG	2565
2908_4_14	NR3C1	Exon 4	+	chr5:143399859-143399884	GAGGUACUCACACCAUGAACAGAAA	2566
2908_4_15	NR3C1	Exon 4	+	chr5:143399893-143399918	UUUUAUUACCAAUUAUAUUUGCUCC	2567
2908_4_16	NR3C1	Exon 4	+	chr5:143399947-143399972	CCAGUUUCUCUUGCUUAAUUACCCC	2568
2908_4_17	NR3C1	Exon 4	+	chr5:143399948-143399973	CAGUUUCUCUUGCUUAAUUACCCCA	2569
2908_4_18	NR3C1	Exon 4	+	chr5:143399949-143399974	AGUUUCUCUUGCUUAAUUACCCCAG	2570
2908_4_19	NR3C1	Exon 4	+	chr5:143399990-143400015	GAAAUCUUCUUUUUCUGUUUUUCACU	2571
2908_4_20	NR3C1	Exon 4	+	chr5:143399991-143400016	AAAUCUUCUUUUUCUGUUUUCACUU	2572
2908_4_21	NR3C1	Exon 4	+	chr5:143399992-143400017	AAUCUUCUUUUUCUGUUUUCACUUG	2573
2908_4_22	NR3C1	Exon 4	+	chr5:143400009-143400034	UUCACUUGGGGCAGUGUUACAUUAC	2574
2908_4_23	NR3C1	Exon 4	+	chr5:143400010-143400035	UCACUUGGGGCAGUGUUACAUUACU	2575
2908_4_24	NR3C1	Exon 4	+	chr5:143400011-143400036	CACUUGGGGCAGUGUUACAUUACUG	2576
2908_4_25	NR3C1	Exon 4	+	chr5:143400048-143400073	ACCAGAUCUCCAUUAUCCUUAAUUU	2577
2908_4_26	NR3C1	Exon 4	+	chr5:143400049-143400074	CCAGAUCUCCAUUAUCCUUAAUUUU	2578
2908_4_27	NR3C1	Exon 4	+	chr5:143400061-143400086	UAUCCUUAAUUUUGGGUUUAGUGUC	2579
2908_4_28	NR3C1	Exon 4	+	chr5:143400073-143400098	UGGGUUUAGUGUCCGGUAAAAUGAG	2580
2908_4_29	NR3C1	Exon 4	+	chr5:143400107-143400132	GUCCUCAUUCGAGUUUCCUUCCAAA	2581
2908_4_30	NR3C1	Exon 4	+	chr5:143400133-143400158	GGAAUGAAUCGUCUUCUCCCGCCAG	2582
2908_4_31	NR3C1	Exon 4	+	chr5:143400164-143400189	AAGCAAACAGUUUUCAUCUAUCAAC	2583
2908_4_32	NR3C1	Exon 4	+	chr5:143400178-143400203	CAUCUAUCAACAGGUCUGAUCUCCA	2584
2908_4_33	NR3C1	Exon 4	+	chr5:143400202-143400227	AAGGACUCUCAUUCGUCUCUUUACC	2585

2908_4_34	NR3C1	Exon 4	+	chr5:143400203-143400228	AGGACUCUCAUUCGUCUCUUUACCU	2586
2908_4_35	NR3C1	Exon 4	+	chr5:143400204-143400229	GGACUCUCAUUCGUCUCUUUACCUG	2587
2908_4_36	NR3C1	Exon 4	+	chr5:143400243-143400268	AACUCCAAAUCCUGCAAAAUGUCAA	2588
2908_4_37	NR3C1	Exon 4	+	chr5:143400251-143400276	AUCCUGCAAAAUGUCAAAGGUGCUU	2589
2908_4_38	NR3C1	Exon 4	+	chr5:143400258-143400283	AAAAUGUCAAAGGUGCUUUGGUCUG	2590
2908_4_39	NR3C1	Exon 4	+	chr5:143400285-143400310	GUAUACAAUUUCACAUUGCCACCGU	2591
2908_4_40	NR3C1	Exon 4	+	chr5:143400296-143400321	CACAUUGCCACCGUUGGUGCCAGUC	2592
2908_4_41	NR3C1	Exon 4	+	chr5:143400343-143400368	CUGAAGAUACAUCAGAGUGAGUUUU	2593
2908_4_42	NR3C1	Exon 4	+	chr5:143400360-143400385	UGAGUUUUUGGAAACUCCUUCUCUG	2594
2908_4_43	NR3C1	Exon 4	+	chr5:143400361-143400386	GAGUUUUUGGAAACUCCUUCUCUGU	2595
2908_4_44	NR3C1	Exon 4	+	chr5:143400362-143400387	AGUUUUUGGAAACUCCUUCUCUGUG	2596
2908_4_45	NR3C1	Exon 4	+	chr5:143400363-143400388	GUUUUUGGAAACUCCUUCUCUGUGG	2597
2908_4_46	NR3C1	Exon 4	+	chr5:143400381-143400406	UCUGUGGGGGCAGCAGACACAGCAG	2598
2908_4_47	NR3C1	Exon 4	+	chr5:143400396-143400421	GACACAGCAGUGGAUGCUGAACUCU	2599
2908_4_48	NR3C1	Exon 4	+	chr5:143400397-143400422	ACACAGCAGUGGAUGCUGAACUCUU	2600
2908_4_49	NR3C1	Exon 4	+	chr5:143400398-143400423	CACAGCAGUGGAUGCUGAACUCUUG	2601
2908_4_50	NR3C1	Exon 4	+	chr5:143400406-143400431	UGGAUGCUGAACUCUUGGGGUUCUC	2602
2908_4_51	NR3C1	Exon 4	+	chr5:143400414-143400439	GAACUCUUGGGGUUCUCUGGAACAC	2603
2908_4_52	NR3C1	Exon 4	+	chr5:143400428-143400453	CUCUGGAACACUGGUCGACCUAUUG	2604
2908_4_53	NR3C1	Exon 4	+	chr5:143400474-143400499	AAAAGCUUUAAGUCUGUUUCCCCCG	2605
2908_4_54	NR3C1	Exon 4	+	chr5:143400479-143400504	CUUUAAGUCUGUUUCCCCCGAGGAA	2606
2908_4_55	NR3C1	Exon 4	+	chr5:143400488-143400513	UGUUUCCCCCGAGGAAAGGCUGAUU	2607
2908_4_56	NR3C1	Exon 4	+	chr5:143400499-143400524	AGGAAAGGCUGAUUUGGCCCUGCUG	2608
2908_4_57	NR3C1	Exon 4	+	chr5:143400500-143400525	GGAAAGGCUGAUUUGGCCCUGCUGU	2609
2908_4_58	NR3C1	Exon 4	+	chr5:143400509-143400534	GAUUUGGCCCUGCUGUGGGAAUCCC	2610

2908_4_59	NR3C1	Exon 4	+	chr5:143400576-143400601	AGUCCCAUUGAGAGUGAAACUGCUU	2611
2908_4_60	NR3C1	Exon 4	+	chr5:143400586-143400611	AGAGUGAAACUGCUUUGGACAGAUC	2612
2908_4_61	NR3C1	Exon 4	+	chr5:143400616-143400641	GCUGCGCAUUGCUUACUGAGCCUUU	2613
2908_4_62	NR3C1	Exon 4	+	chr5:143400645-143400670	AAAUCAACCAAAAGUCUUCGCUGCU	2614
2908_4_63	NR3C1	Exon 4	+	chr5:143400675-143400700	UCUGAUUGAGAAGCGACAGCCAGUG	2615
2908_4_64	NR3C1	Exon 4	+	chr5:143400676-143400701	CUGAUUGAGAAGCGACAGCCAGUGA	2616
2908_4_65	NR3C1	Exon 4	+	chr5:143400716-143400741	AACCUUCACAGUAGCUCCUCCUCUU	2617
2908_4_66	NR3C1	Exon 4	+	chr5:143400717-143400742	ACCUUCACAGUAGCUCCUCCUCUUA	2618
2908_4_67	NR3C1	Exon 4	+	chr5:143400768-143400793	CCCCUCUCCUGAGCAAGCACACUGC	2619
2908_4_68	NR3C1	Exon 4	+	chr5:143400769-143400794	CCCUCUCCUGAGCAAGCACACUGCU	2620
2908_4_69	NR3C1	Exon 4	+	chr5:143400770-143400795	CCUCUCCUGAGCAAGCACACUGCUG	2621
2908_4_70	NR3C1	Exon 4	+	chr5:143400787-143400812	CACUGCUGGGGUUUUCUUCUCUACC	2622
2908_4_71	NR3C1	Exon 4	+	chr5:143400804-143400829	UCUCUACCAGGAGUUAAUGAUUCUU	2623
2908_4_72	NR3C1	Exon 4	+	chr5:143400848-143400873	UCAACUACAAAACAAAAAACAAAAA	2624
2908_4_73	NR3C1	Exon 4	+	chr5:143400849-143400874	CAACUACAAAACAAAAACAAAAAC	2625
2908_4_74	NR3C1	Exon 4	-	chr5:143399657-143399682	AACAGUUUUUUCUAAUGGCUAUUCA	2626
2908_4_75	NR3C1	Exon 4	-	chr5:143399667-143399692	UCCCUGGUCGAACAGUUUUUUCUAA	2627
2908_4_76	NR3C1	Exon 4	-	chr5:143399688-143399713	CUUCUCUGGGGACUCUGAACUUCCC	2628
2908_4_77	NR3C1	Exon 4	-	chr5:143399705-143399730	UGGAGAUGACAACUUGACUUCUCUG	2629
2908_4_78	NR3C1	Exon 4	-	chr5:143399706-143399731	CUGGAGAUGACAACUUGACUUCUCU	2630
2908_4_79	NR3C1	Exon 4	-	chr5:143399707-143399732	UCUGGAGAUGACAACUUGACUUCUC	2631
2908_4_80	NR3C1	Exon 4	-	chr5:143399730-143399755	AAAAUUGGAAUAGGUGCCAAGGAUC	2632
2908_4_81	NR3C1	Exon 4	-	chr5:143399736-143399761	GUUCCGAAAAUUGGAAUAGGUGCCA	2633
2908_4_82	NR3C1	Exon 4	-	chr5:143399744-143399769	UCCCGUUGGUUCCGAAAAUUGGAAU	2634
2908_4_83	NR3C1	Exon 4	-	chr5:143399750-143399775	ACCAAUUCCCGUUGGUUCCGAAAAU	2635

2908_4_84	NR3C1	Exon 4	-	chr5:143399763-143399788	UUAAUGUCAUUCCACCAAUUCCCGU	2636
2908_4_85	NR3C1	Exon 4	-	chr5:143399806-143399831	AAUACAGCAUCCCUUUCUCAACAGC	2637
2908_4_86	NR3C1	Exon 4	-	chr5:143399856-143399881	CUGUUCAUGGUGUGAGUACCUCUGG	2638
2908_4_87	NR3C1	Exon 4	-	chr5:143399859-143399884	UUUCUGUUCAUGGUGUGAGUACCUC	2639
2908_4_88	NR3C1	Exon 4	-	chr5:143399874-143399899	AUAAAAUGUCUGCCAUUUCUGUUCA	2640
2908_4_89	NR3C1	Exon 4	-	chr5:143399904-143399929	CAAGCUUUCCUGGAGCAAAUAUAAU	2641
2908_4_90	NR3C1	Exon 4	-	chr5:143399919-143399944	CAGUUUACUGUCAGGCAAGCUUUCC	2642
2908_4_91	NR3C1	Exon 4	-	chr5:143399932-143399957	GAGAAACUGGGCACAGUUUACUGUC	2643
2908_4_92	NR3C1	Exon 4	-	chr5:143399949-143399974	CUGGGGUAAUUAAGCAAGAGAAACU	2644
2908_4_93	NR3C1	Exon 4	-	chr5:143399950-143399975	CCUGGGGUAAUUAAGCAAGAGAAAC	2645
2908_4_94	NR3C1	Exon 4	-	chr5:143399971-143399996	GAUUUCAUCGAACUCUGCACCCCUG	2646
2908_4_95	NR3C1	Exon 4	-	chr5:143399972-143399997	AGAUUUCAUCGAACUCUGCACCCCU	2647
2908_4_96	NR3C1	Exon 4	-	chr5:143399973-143399998	AAGAUUUCAUCGAACUCUGCACCCC	2648
2908_4_97	NR3C1	Exon 4	-	chr5:143400052-143400077	CCCAAAAUUAAGGAUAAUGGAGAUC	2649
2908_4_98	NR3C1	Exon 4	-	chr5:143400060-143400085	ACACUAAACCCAAAAUUAAGGAUAA	2650
2908_4_99	NR3C1	Exon 4	-	chr5:143400067-143400092	UUACCGGACACUAAACCCAAAAUUA	2651
2908_4_100	NR3C1	Exon 4	-	chr5:143400088-143400113	GAGGACUGCAAGCCUCUCAUUUUAC	2652
2908_4_101	NR3C1	Exon 4	-	chr5:143400112-143400137	UUCCUUUUGGAAGGAAACUCGAAUG	2653
2908_4_102	NR3C1	Exon 4	-	chr5:143400126-143400151	GAGAAGACGAUUCAUUCCUUUUGGA	2654
2908_4_103	NR3C1	Exon 4	-	chr5:143400130-143400155	GCGGGAGAAGACGAUUCAUUCCUUU	2655
2908_4_104	NR3C1	Exon 4	-	chr5:143400153-143400178	AAAACUGUUUGCUUUCUCCUCUGGC	2656
2908_4_105	NR3C1	Exon 4	-	chr5:143400154-143400179	GAAAACUGUUUGCUUUCUCCUCUGG	2657
2908_4_106	NR3C1	Exon 4	-	chr5:143400157-143400182	GAUGAAAACUGUUUGCUUUCUCCUC	2658
2908_4_107	NR3C1	Exon 4	-	chr5:143400203-143400228	AGGUAAAGAGACGAAUGAGAGUCCU	2659
2908_4_108	NR3C1	Exon 4	-	chr5:143400228-143400253	AUUUGGAGUUUUCUUCUGGGUCCCC	2660

2908_4_109	NR3C1	Exon 4	-	chr5:143400236-143400261	UUUGCAGGAUUUGGAGUUUUCUUCU	2661
2908_4_110	NR3C1	Exon 4	-	chr5:143400237-143400262	UUUUGCAGGAUUUGGAGUUUUCUUC	2662
2908_4_111	NR3C1	Exon 4	-	chr5:143400250-143400275	AGCACCUUUGACAUUUUGCAGGAUU	2663
2908_4_112	NR3C1	Exon 4	-	chr5:143400256-143400281	GACCAAAGCACCUUUGACAUUUUGC	2664
2908_4_113	NR3C1	Exon 4	-	chr5:143400306-143400331	UGAAGGGCCAGACUGGCACCAACGG	2665
2908_4_114	NR3C1	Exon 4	-	chr5:143400309-143400334	AUUUGAAGGGCCAGACUGGCACCAA	2666
2908_4_115	NR3C1	Exon 4	-	chr5:143400318-143400343	AACAGCAACAUUUGAAGGGCCAGAC	2667
2908_4_116	NR3C1	Exon 4	-	chr5:143400327-143400352	UAUCUUCAGAACAGCAACAUUUGAA	2668
2908_4_117	NR3C1	Exon 4	-	chr5:143400328-143400353	GUAUCUUCAGAACAGCAACAUUUGA	2669
2908_4_118	NR3C1	Exon 4	-	chr5:143400379-143400404	GCUGUGUCUGCUGCCCCACAGAGA	2670
2908_4_119	NR3C1	Exon 4	-	chr5:143400449-143400474	GGAAGAAAGCAUUGCAAACCUCAAU	2671
2908_4_120	NR3C1	Exon 4	-	chr5:143400475-143400500	UCGGGGGAAACAGACUUAAAGCUUU	2672
2908_4_121	NR3C1	Exon 4	-	chr5:143400496-143400521	CAGGGCCAAAUCAGCCUUUCCUCGG	2673
2908_4_122	NR3C1	Exon 4	-	chr5:143400497-143400522	GCAGGGCCAAAUCAGCCUUUCCUCG	2674
2908_4_123	NR3C1	Exon 4	-	chr5:143400498-143400523	AGCAGGGCCAAAUCAGCCUUUCCUC	2675
2908_4_124	NR3C1	Exon 4	-	chr5:143400499-143400524	CAGCAGGGCCAAAUCAGCCUUUCCU	2676
2908_4_125	NR3C1	Exon 4	-	chr5:143400519-143400544	GAAAUGACCUGGGAUUCCCACAGCA	2677
2908_4_126	NR3C1	Exon 4	-	chr5:143400520-143400545	GGAAAUGACCUGGGAUUCCCACAGC	2678
2908_4_127	NR3C1	Exon 4	-	chr5:143400534-143400559	AAACAAAAGUGAUGGGAAAUGACCU	2679
2908_4_128	NR3C1	Exon 4	-	chr5:143400535-143400560	GAAACAAAAGUGAUGGGAAAUGACC	2680
2908_4_129	NR3C1	Exon 4	-	chr5:143400546-143400571	UGGGAGAGACAGAAACAAAAGUGAU	2681
2908_4_130	NR3C1	Exon 4	-	chr5:143400547-143400572	AUGGGAGAGACAGAAACAAAAGUGA	2682
2908_4_131	NR3C1	Exon 4	-	chr5:143400570-143400595	UUUCACUCUCAAUGGGACUGUAUAU	2683
2908_4_132	NR3C1	Exon 4	-	chr5:143400571-143400596	GUUUCACUCUCAAUGGGACUGUAUA	2684
2908_4_133	NR3C1	Exon 4	-	chr5:143400582-143400607	UGUCCAAAGCAGUUUCACUCUCAAU	2685

2908_4_134	NR3C1	Exon 4	-	chr5:143400583-143400608	CUGUCCAAAGCAGUUUCACUCUCAA	2686
2908_4_135	NR3C1	Exon 4	-	chr5:143400639-143400664	GAAGACUUUUGGUUGAUUUUCCAAA	2687
2908_4_136	NR3C1	Exon 4	-	chr5:143400655-143400680	UCAGACUCCAAGCAGCGAAGACUUU	2688
2908_4_137	NR3C1	Exon 4	-	chr5:143400697-143400722	AAGGUUUCUGCGUCUUCACCCUCAC	2689
2908_4_138	NR3C1	Exon 4	-	chr5:143400721-143400746	ACCCUAAGAGGAGGAGCUACUGUGA	2690
2908_4_139	NR3C1	Exon 4	-	chr5:143400735-143400760	UGGACUUCUAUAAAACCCUAAGAGG	2691
2908_4_140	NR3C1	Exon 4	-	chr5:143400738-143400763	UGAUGGACUUCUAUAAAACCCUAAG	2692
2908_4_141	NR3C1	Exon 4	-	chr5:143400760-143400785	CUUGCUCAGGAGAGGGGAGAUGUGA	2693
2908_4_142	NR3C1	Exon 4	-	chr5:143400771-143400796	CCAGCAGUGUGCUUGCUCAGGAGAG	2694
2908_4_143	NR3C1	Exon 4	-	chr5:143400772-143400797	CCCAGCAGUGUGCUUGCUCAGGAGA	2695
2908_4_144	NR3C1	Exon 4	-	chr5:143400773-143400798	CCCCAGCAGUGUGCUUGCUCAGGAG	2696
2908_4_145	NR3C1	Exon 4	-	chr5:143400778-143400803	GAAAACCCCAGCAGUGUGCUUGCUC	2697
2908_4_146	NR3C1	Exon 4	-	chr5:143400813-143400838	UGGACUCCAAAGAAUCAUUAACUCC	2698
2908_4_147	NR3C1	Exon 4	-	chr5:143400838-143400863	UUGUUUUGUAGUUGAUAUUCACUGA	2699
2908_3_1	NR3C1	Exon 3	+	chr5:143403188-143403213	CCCCUCCCGCCUCGCUUCUUACCUC	2700
2908_3_2	NR3C1	Exon 3	+	chr5:143403194-143403219	CCGCCUCGCUUCUUACCUCUGGCAG	2701
2908_3_3	NR3C1	Exon 3	+	chr5:143403267-143403292	AAACAACUUAGCUUGUGAACGCAGA	2702
2908_3_4	NR3C1	Exon 3	+	chr5:143403273-143403298	CUUAGCUUGUGAACGCAGAAGGAGC	2703
2908_3_5	NR3C1	Exon 3	+	chr5:143403276-143403301	AGCUUGUGAACGCAGAAGGAGCAGG	2704
2908_3_6	NR3C1	Exon 3	+	chr5:143403277-143403302	GCUUGUGAACGCAGAAGGAGCAGGA	2705
2908_3_7	NR3C1	Exon 3	+	chr5:143403305-143403330	AAAUAUAUUUUUUUUUCUAAAAAA	2706
2908_3_8	NR3C1	Exon 3	+	chr5:143403333-143403358	AAGUAAACAGCCGCCCCUUUCUCCA	2707
2908_3_9	NR3C1	Exon 3	+	chr5:143403334-143403359	AGUAAACAGCCGCCCCUUUCUCCAU	2708
2908_3_10	NR3C1	Exon 3	+	chr5:143403337-143403362	AAACAGCCGCCCCUUUCUCCAUGGG	2709
2908_3_11	NR3C1	Exon 3	+	chr5:143403338-143403363	AACAGCCGCCCCUUUCUCCAUGGGU	2710

2908_3_12	NR3C1	Exon 3	+	chr5:143403339-143403364	ACAGCCGCCCCUUUCUCCAUGGGUG	2711
2908_3_13	NR3C1	Exon 3	+	chr5:143403340-143403365	CAGCCGCCCCUUUCUCCAUGGGUGG	2712
2908_3_14	NR3C1	Exon 3	+	chr5:143403341-143403366	AGCCGCCCCUUUCUCCAUGGGUGGG	2713
2908_3_15	NR3C1	Exon 3	+	chr5:143403406-143403431	GACAAGCCAGCCCUCCGCCCCGCGC	2714
2908_3_16	NR3C1	Exon 3	+	chr5:143403407-143403432	ACAAGCCAGCCCUCCGCCCCGCGCC	2715
2908_3_17	NR3C1	Exon 3	+	chr5:143403415-143403440	GCCCUCCGCCCCGCGCCGGGCUCCG	2716
2908_3_18	NR3C1	Exon 3	+	chr5:143403416-143403441	CCCUCCGCCCCGCGCCGGGCUCCGC	2717
2908_3_19	NR3C1	Exon 3	+	chr5:143403422-143403447	GCCCCGCGCCGGGCUCCGCGGGUCG	2718
2908_3_20	NR3C1	Exon 3	+	chr5:143403428-143403453	CGCCGGGCUCCGCGGGUCGAGGUUC	2719
2908_3_21	NR3C1	Exon 3	+	chr5:143403429-143403454	GCCGGGCUCCGCGGGUCGAGGUUCC	2720
2908_3_22	NR3C1	Exon 3	+	chr5:143403448-143403473	GGUUCCGGGCGCGCGUGCCCCGUCC	2721
2908_3_23	NR3C1	Exon 3	+	chr5:143403463-143403488	UGCCCCGUCCCGGUCCCAGCUGCUU	2722
2908_3_24	NR3C1	Exon 3	+	chr5:143403472-143403497	CCGGUCCCAGCUGCUUCGGCCGCUC	2723
2908_3_25	NR3C1	Exon 3	+	chr5:143403478-143403503	CCAGCUGCUUCGGCCGCUCCGGCUG	2724
2908_3_26	NR3C1	Exon 3	+	chr5:143403513-143403538	UUCCACCCACAGAAUCCGUCCCCGA	2725
2908_3_27	NR3C1	Exon 3	+	chr5:143403514-143403539	UCCACCCACAGAAUCCGUCCCCGAC	2726
2908_3_28	NR3C1	Exon 3	+	chr5:143403518-143403543	CCCACAGAAUCCGUCCCCGACGGGC	2727
2908_3_29	NR3C1	Exon 3	+	chr5:143403521-143403546	ACAGAAUCCGUCCCCGACGGGCAGG	2728
2908_3_30	NR3C1	Exon 3	+	chr5:143403529-143403554	CGUCCCCGACGGGCAGGCGGUGACU	2729
2908_3_31	NR3C1	Exon 3	+	chr5:143403530-143403555	GUCCCCGACGGGCAGGCGGUGACUC	2730
2908_3_32	NR3C1	Exon 3	+	chr5:143403561-143403586	CCGUCACAGACACGAGCUCGCAAAA	2731
2908_3_33	NR3C1	Exon 3	+	chr5:143403564-143403589	UCACAGACACGAGCUCGCAAAAUGG	2732
2908_3_34	NR3C1	Exon 3	+	chr5:143403567-143403592	CAGACACGAGCUCGCAAAAUGGAGG	2733
2908_3_35	NR3C1	Exon 3	+	chr5:143403570-143403595	ACACGAGCUCGCAAAAUGGAGGAGG	2734
2908_3_36	NR3C1	Exon 3	+	chr5:143403573-143403598	CGAGCUCGCAAAAUGGAGGAGGCGG	2735

2908_3_37	NR3C1	Exon 3	+	chr5:143403576-143403601	GCUCGCAAAAUGGAGGAGGCGGCGG	2736
2908_3_38	NR3C1	Exon 3	+	chr5:143403579-143403604	CGCAAAAUGGAGGAGGCGGCGGCGG	2737
2908_3_39	NR3C1	Exon 3	+	chr5:143403580-143403605	GCAAAAUGGAGGAGGCGGCGGCGGA	2738
2908_3_40	NR3C1	Exon 3	+	chr5:143403592-143403617	AGGCGGCGGCGGAGGGAAGAGAGCG	2739
2908_3_41	NR3C1	Exon 3	+	chr5:143403604-143403629	AGGGAAGAGAGCGCGGACACGCGAA	2740
2908_3_42	NR3C1	Exon 3	+	chr5:143403605-143403630	GGGAAGAGAGCGCGGACACGCGAAA	2741
2908_3_43	NR3C1	Exon 3	+	chr5:143403613-143403638	AGCGCGGACACGCGAAAGGGCAGCC	2742
2908_3_44	NR3C1	Exon 3	+	chr5:143403618-143403643	GGACACGCGAAAGGGCAGCCCGGCC	2743
2908_3_45	NR3C1	Exon 3	+	chr5:143403619-143403644	GACACGCGAAAGGGCAGCCCGGCCU	2744
2908_3_46	NR3C1	Exon 3	+	chr5:143403630-143403655	GGGCAGCCCGGCCUGGGCGAGCGAG	2745
2908_3_47	NR3C1	Exon 3	+	chr5:143403631-143403656	GGCAGCCCGGCCUGGGCGAGCGAGC	2746
2908_3_48	NR3C1	Exon 3	+	chr5:143403640-143403665	GCCUGGGCGAGCGAGCGGGACCGAG	2747
2908_3_49	NR3C1	Exon 3	+	chr5:143403641-143403666	CCUGGGCGAGCGAGCGGGACCGAGC	2748
2908_3_50	NR3C1	Exon 3	+	chr5:143403642-143403667	CUGGGCGAGCGAGCGGGACCGAGCG	2749
2908_3_51	NR3C1	Exon 3	+	chr5:143403647-143403672	CGAGCGAGCGGGACCGAGCGGGGAG	2750
2908_3_52	NR3C1	Exon 3	+	chr5:143403648-143403673	GAGCGAGCGGGACCGAGCGGGGAGC	2751
2908_3_53	NR3C1	Exon 3	+	chr5:143403651-143403676	CGAGCGGGACCGAGCGGGGAGCGGG	2752
2908_3_54	NR3C1	Exon 3	+	chr5:143403654-143403679	GCGGGACCGAGCGGGGAGCGGGUGG	2753
2908_3_55	NR3C1	Exon 3	+	chr5:143403657-143403682	GGACCGAGCGGGGAGCGGGUGGAGG	2754
2908_3_56	NR3C1	Exon 3	+	chr5:143403665-143403690	CGGGGAGCGGGUGGAGGCGGCGCCA	2755
2908_3_57	NR3C1	Exon 3	-	chr5:143403190-143403215	CAGAGGUAAGAAGCGAGGCGGGAGG	2756
2908_3_58	NR3C1	Exon 3	-	chr5:143403191-143403216	CCAGAGGUAAGAAGCGAGGCGGGAG	2757
2908_3_59	NR3C1	Exon 3	-	chr5:143403192-143403217	GCCAGAGGUAAGAAGCGAGGCGGGA	2758
2908_3_60	NR3C1	Exon 3	-	chr5:143403193-143403218	UGCCAGAGGUAAGAAGCGAGGCGGG	2759
2908_3_61	NR3C1	Exon 3	-	chr5:143403196-143403221	CUCUGCCAGAGGUAAGAAGCGAGGC	2760

2908_3_62	NR3C1	Exon 3	-	chr5:143403197-143403222	CCUCUGCCAGAGGUAAGAAGCGAGG	2761
2908_3_63	NR3C1	Exon 3	-	chr5:143403200-143403225	GCUCCUCUGCCAGAGGUAAGAAGCG	2762
2908_3_64	NR3C1	Exon 3	-	chr5:143403212-143403237	GGCGGGCGAGCGGCUCCUCUGCCAG	2763
2908_3_65	NR3C1	Exon 3	-	chr5:143403227-143403252	GGAACUGCGGACGGUGGCGGGCGAG	2764
2908_3_66	NR3C1	Exon 3	-	chr5:143403234-143403259	UGCGGCGGGAACUGCGGACGGUGGC	2765
2908_3_67	NR3C1	Exon 3	-	chr5:143403235-143403260	CUGCGGCGGGAACUGCGGACGGUGG	2766
2908_3_68	NR3C1	Exon 3	-	chr5:143403238-143403263	CGGCUGCGGCGGGAACUGCGGACGG	2767
2908_3_69	NR3C1	Exon 3	-	chr5:143403241-143403266	UCUCGGCUGCGGCGGGAACUGCGGA	2768
2908_3_70	NR3C1	Exon 3	-	chr5:143403245-143403270	UUUAUCUCGGCUGCGGCGGGAACUG	2769
2908_3_71	NR3C1	Exon 3	-	chr5:143403253-143403278	CUAAGUUGUUUAUCUCGGCUGCGGC	2770
2908_3_72	NR3C1	Exon 3	-	chr5:143403254-143403279	GCUAAGUUGUUUAUCUCGGCUGCGG	2771
2908_3_73	NR3C1	Exon 3	-	chr5:143403257-143403282	CAAGCUAAGUUGUUUAUCUCGGCUG	2772
2908_3_74	NR3C1	Exon 3	-	chr5:143403263-143403288	CGUUCACAAGCUAAGUUGUUUAUCU	2773
2908_3_75	NR3C1	Exon 3	-	chr5:143403346-143403371	CUCCCCCCACCCAUGGAGAAAGGGG	2774
2908_3_76	NR3C1	Exon 3	-	chr5:143403349-143403374	GCUCUCCCCCCACCCAUGGAGAAAG	2775
2908_3_77	NR3C1	Exon 3	-	chr5:143403350-143403375	GGCUCUCCCCCCACCCAUGGAGAAA	2776
2908_3_78	NR3C1	Exon 3	-	chr5:143403351-143403376	GGGCUCUCCCCCCACCCAUGGAGAA	2777
2908_3_79	NR3C1	Exon 3	-	chr5:143403358-143403383	UAAAUAGGGGCUCUCCCCCACCCA	2778
2908_3_80	NR3C1	Exon 3	-	chr5:143403376-143403401	GGCAAUGGGAGACUUUCUUAAAUAG	2779
2908_3_81	NR3C1	Exon 3	-	chr5:143403377-143403402	GGGCAAUGGGAGACUUUCUUAAAUA	2780
2908_3_82	NR3C1	Exon 3	-	chr5:143403378-143403403	UGGGCAAUGGGAGACUUUCUUAAAU	2781
2908_3_83	NR3C1	Exon 3	-	chr5:143403395-143403420	AGGGCUGGCUUGUCAGCUGGGCAAU	2782
2908_3_84	NR3C1	Exon 3	-	chr5:143403396-143403421	GAGGGCUGGCUUGUCAGCUGGGCAA	2783
2908_3_85	NR3C1	Exon 3	-	chr5:143403402-143403427	GGGGCGGAGGGCUGGCUUGUCAGCU	2784
2908_3_86	NR3C1	Exon 3	-	chr5:143403403-143403428	CGGGGCGGAGGGCUGGCUUGUCAGC	2785

2908_3_87	NR3C1	Exon 3	-	chr5:143403415-143403440	CGGAGCCCGGCGCGGGGCGGAGGGC	2786
2908_3_88	NR3C1	Exon 3	-	chr5:143403419-143403444	CCCGCGGAGCCCGGCGCGGGGCGGA	2787
2908_3_89	NR3C1	Exon 3	-	chr5:143403420-143403445	ACCCGCGGAGCCCGGCGCGGGGCGG	2788
2908_3_90	NR3C1	Exon 3	-	chr5:143403423-143403448	UCGACCCGCGGAGCCCGGCGCGGGG	2789
2908_3_91	NR3C1	Exon 3	-	chr5:143403426-143403451	ACCUCGACCCGCGGAGCCCGGCGCG	2790
2908_3_92	NR3C1	Exon 3	-	chr5:143403427-143403452	AACCUCGACCCGCGGAGCCCGGCGC	2791
2908_3_93	NR3C1	Exon 3	-	chr5:143403428-143403453	GAACCUCGACCCGCGGAGCCCGGCG	2792
2908_3_94	NR3C1	Exon 3	-	chr5:143403433-143403458	GCCCGGAACCUCGACCCGCGGAGCC	2793
2908_3_95	NR3C1	Exon 3	-	chr5:143403440-143403465	CACGCGCGCCCGGAACCUCGACCCG	2794
2908_3_96	NR3C1	Exon 3	-	chr5:143403455-143403480	GGGACCGGGACGGGGCACGCGCGCC	2795
2908_3_97	NR3C1	Exon 3	-	chr5:143403468-143403493	GGCCGAAGCAGCUGGGACCGGGACG	2796
2908_3_98	NR3C1	Exon 3	-	chr5:143403469-143403494	CGGCCGAAGCAGCUGGGACCGGGAC	2797
2908_3_99	NR3C1	Exon 3	-	chr5:143403470-143403495	GCGGCCGAAGCAGCUGGGACCGGGA	2798
2908_3_100	NR3C1	Exon 3	-	chr5:143403474-143403499	CGGAGCGGCCGAAGCAGCUGGGACC	2799
2908_3_101	NR3C1	Exon 3	-	chr5:143403475-143403500	CCGGAGCGGCCGAAGCAGCUGGGAC	2800
2908_3_102	NR3C1	Exon 3	-	chr5:143403480-143403505	CGCAGCCGGAGCGGCCGAAGCAGCU	2801
2908_3_103	NR3C1	Exon 3	-	chr5:143403481-143403506	CCGCAGCCGGAGCGGCCGAAGCAGC	2802
2908_3_104	NR3C1	Exon 3	-	chr5:143403494-143403519	GUGGAAGGAGACGCCGCAGCCGGAG	2803
2908_3_105	NR3C1	Exon 3	-	chr5:143403499-143403524	UGUGGGUGGAAGGAGACGCCGCAGC	2804
2908_3_106	NR3C1	Exon 3	-	chr5:143403514-143403539	GUCGGGGACGGAUUCUGUGGGUGGA	2805
2908_3_107	NR3C1	Exon 3	-	chr5:143403518-143403543	GCCCGUCGGGGACGGAUUCUGUGGG	2806
2908_3_108	NR3C1	Exon 3	-	chr5:143403521-143403546	CCUGCCCGUCGGGGACGGAUUCUGU	2807
2908_3_109	NR3C1	Exon 3	-	chr5:143403522-143403547	GCCUGCCCGUCGGGGACGGAUUCUG	2808
2908_3_110	NR3C1	Exon 3	-	chr5:143403531-143403556	CGAGUCACCGCCUGCCCGUCGGGGA	2809
2908_3_111	NR3C1	Exon 3	-	chr5:143403535-143403560	AGCCCGAGUCACCGCCUGCCCGUCG	2810

2908_3_112	NR3C1	Exon 3	-	chr5:143403536-143403561	GAGCCCGAGUCACCGCCUGCCCGUC	2811
2908_3_113	NR3C1	Exon 3	-	chr5:143403537-143403562	GGAGCCCGAGUCACCGCCUGCCCGU	2812
2908_3_114	NR3C1	Exon 3	-	chr5:143403563-143403588	CAUUUUGCGAGCUCGUGUCUGUGAC	2813
2908_3_115	NR3C1	Exon 3	-	chr5:143403564-143403589	CCAUUUUGCGAGCUCGUGUCUGUGA	2814
2908_3_116	NR3C1	Exon 3	-	chr5:143403639-143403664	UCGGUCCCGCUCGCUCGCCCAGGCC	2815
2908_3_117	NR3C1	Exon 3	-	chr5:143403640-143403665	CUCGGUCCCGCUCGCUCGCCCAGGC	2816
2908_3_118	NR3C1	Exon 3	-	chr5:143403644-143403669	CCCGCUCGGUCCCGCUCGCUCGCCC	2817
2908_3_119	NR3C1	Exon 3	-	chr5:143403663-143403688	GCGCCGCCUCCACCCGCUCCCCGCU	2818
2908_2_1	NR3C1	Exon 2	+	chr5:143404352-143404377	AGCGGGGGUCGGCGCAUACGUACUU	2819
2908_2_2	NR3C1	Exon 2	+	chr5:143404353-143404378	GCGGGGGUCGGCGCAUACGUACUUU	2820
2908_2_3	NR3C1	Exon 2	+	chr5:143404358-143404383	GGUCGGCGCAUACGUACUUUGGGCC	2821
2908_2_4	NR3C1	Exon 2	+	chr5:143404359-143404384	GUCGGCGCAUACGUACUUUGGGCCC	2822
2908_2_5	NR3C1	Exon 2	+	chr5:143404360-143404385	UCGGCGCAUACGUACUUUGGGCCCG	2823
2908_2_6	NR3C1	Exon 2	+	chr5:143404361-143404386	CGGCGCAUACGUACUUUGGGCCCGG	2824
2908_2_7	NR3C1	Exon 2	+	chr5:143404362-143404387	GGCGCAUACGUACUUUGGGCCCGGG	2825
2908_2_8	NR3C1	Exon 2	+	chr5:143404375-143404400	UUUGGGCCCGGGGGGAGUCGCGUGC	2826
2908_2_9	NR3C1	Exon 2	+	chr5:143404379-143404404	GGCCCGGGGGGAGUCGCGUGCCGGC	2827
2908_2_10	NR3C1	Exon 2	+	chr5:143404402-143404427	GCAGGUCCCCCACCACCGCAUCAUC	2828
2908_2_11	NR3C1	Exon 2	+	chr5:143404403-143404428	CAGGUCCCCCACCACCGCAUCAUCU	2829
2908_2_12	NR3C1	Exon 2	+	chr5:143404406-143404431	GUCCCCCACCACCGCAUCAUCUGGG	2830
2908_2_13	NR3C1	Exon 2	+	chr5:143404410-143404435	CCCACCACCGCAUCAUCUGGGCGGC	2831
2908_2_14	NR3C1	Exon 2	+	chr5:143404411-143404436	CCACCACCGCAUCAUCUGGGCGGCC	2832
2908_2_15	NR3C1	Exon 2	+	chr5:143404444-143404469	AGCUGCCGCCGCCGCGCUCUCGCAC	2833
2908_2_16	NR3C1	Exon 2	+	chr5:143404445-143404470	GCUGCCGCCGCCGCGCUCUCGCACU	2834
2908_2_17	NR3C1	Exon 2	-	chr5:143404384-143404409	GACCUGCCGGCACGCGACUCCCCCC	2835

2908_2_18	NR3C1	Exon 2	-	chr5:143404385-143404410	GGACCUGCCGGCACGCGACUCCCCC	2836
2908_2_19	NR3C1	Exon 2	-	chr5:143404402-143404427	GAUGAUGCGGUGGUGGGGGACCUGC	2837
2908_2_20	NR3C1	Exon 2	-	chr5:143404411-143404436	GGCCGCCCAGAUGAUGCGGUGGUGG	2838
2908_2_21	NR3C1	Exon 2	-	chr5:143404412-143404437	CGGCCGCCCAGAUGAUGCGGUGGUG	2839
2908_2_22	NR3C1	Exon 2	-	chr5:143404413-143404438	CCGGCCGCCCAGAUGAUGCGGUGGU	2840
2908_2_23	NR3C1	Exon 2	-	chr5:143404414-143404439	CCCGGCCGCCCAGAUGAUGCGGUGG	2841
2908_2_24	NR3C1	Exon 2	-	chr5:143404417-143404442	AGACCCGGCCGCCCAGAUGAUGCGG	2842
2908_2_25	NR3C1	Exon 2	-	chr5:143404420-143404445	UGAAGACCCGGCCGCCCAGAUGAUG	2843
2908_2_26	NR3C1	Exon 2	-	chr5:143404437-143404462	AGCGCGGCGGCGGCAGCUGAAGACC	2844
2908_2_27	NR3C1	Exon 2	-	chr5:143404452-143404477	CUCUCCCAGUGCGAGAGCGCGGCGG	2845
2908_2_28	NR3C1	Exon 2	-	chr5:143404455-143404480	CUUCUCUCCCAGUGCGAGAGCGCGG	2846
2908_2_29	NR3C1	Exon 2	-	chr5:143404458-143404483	CAACUUCUCUCCCAGUGCGAGAGCG	2847
2908_1_1	NR3C1	Exon 1	+	chr5:143434553-143434578	GAAGCAAAGUCUUCUUUGUUCUUUG	2848
2908_1_2	NR3C1	Exon 1	+	chr5:143434558-143434583	AAAGUCUUCUUUGUUCUUUGAGGAA	2849
2908_1_3	NR3C1	Exon 1	+	chr5:143434565-143434590	UCUUUGUUCUUUGAGGAAAGGAGCC	2850
2908_1_4	NR3C1	Exon 1	+	chr5:143434590-143434615	AGGCAGAUGAAAAUUCCUGUUAUUA	2851
2908_1_5	NR3C1	Exon 1	+	chr5:143434608-143434633	GUUAUUAAGGUACAACUAAAGCCCG	2852
2908_1_6	NR3C1	Exon 1	+	chr5:143434611-143434636	AUUAAGGUACAACUAAAGCCCGAGG	2853
2908_1_7	NR3C1	Exon 1	+	chr5:143434612-143434637	UUAAGGUACAACUAAAGCCCGAGGA	2854
2908_1_8	NR3C1	Exon 1	+	chr5:143434616-143434641	GGUACAACUAAAGCCCGAGGAGGGU	2855
2908_1_9	NR3C1	Exon 1	+	chr5:143434655-143434680	GUUCCUCCCCAUUCUCGCACAGAGA	2856
2908_1_10	NR3C1	Exon 1	+	chr5:143434691-143434716	AAGUGCUUAUCAAAGUUAAUAUCUG	2857
2908_1_11	NR3C1	Exon 1	+	chr5:143434736-143434761	CCUCUGCAGCAGUCGUCACAGAAGC	2858
2908_1_12	NR3C1	Exon 1	+	chr5:143434748-143434773	UCGUCACAGAAGCUGGCCCCUUUCC	2859
2908_1_13	NR3C1	Exon 1	+	chr5:143434749-143434774	CGUCACAGAAGCUGGCCCCUUUCCU	2860

2908_1_14	NR3C1	Exon 1	+	chr5:143434923-143434948	UUUCAGAUCAGAAGAUCCUGUCUCU	2861
2908_1_15	NR3C1	Exon 1	+	chr5:143434924-143434949	UUCAGAUCAGAAGAUCCUGUCUCUC	2862
2908_1_16	NR3C1	Exon 1	+	chr5:143434944-143434969	CUCUCGGGUAUAACUUUUUUUUUUU	2863
2908_1_17	NR3C1	Exon 1	+	chr5:143434974-143434999	AGAAAUACAGUGACUCUCCUAAUUA	2864
2908_1_18	NR3C1	Exon 1	+	chr5:143435026-143435051	CCACUGAUUCAGCAGAUAUUCCCCC	2865
2908_1_19	NR3C1	Exon 1	+	chr5:143435039-143435064	AGAUAUUCCCCCAGGCAGAUCCUAA	2866
2908_1_20	NR3C1	Exon 1	+	chr5:143435055-143435080	AGAUCCUAAUGGAAACCAACAUGUG	2867
2908_1_21	NR3C1	Exon 1	+	chr5:143435066-143435091	GAAACCAACAUGUGAGGUCUGAUGC	2868
2908_1_22	NR3C1	Exon 1	+	chr5:143435067-143435092	AAACCAACAUGUGAGGUCUGAUGCU	2869
2908_1_23	NR3C1	Exon 1	+	chr5:143435089-143435114	GCUGGGAAUUUUAUCAUGCUCAACA	2870
2908_1_24	NR3C1	Exon 1	+	chr5:143435226-143435251	CCCACUCAUGCCCCAGUGCUUCCGU	2871
2908_1_25	NR3C1	Exon 1	+	chr5:143435245-143435270	UUCCGUUGGACACAUGCGCAUUUUA	2872
2908_1_26	NR3C1	Exon 1	+	chr5:143435254-143435279	ACACAUGCGCAUUUUACGGUCCUGC	2873
2908_1_27	NR3C1	Exon 1	+	chr5:143435255-143435280	CACAUGCGCAUUUUACGGUCCUGCA	2874
2908_1_28	NR3C1	Exon 1	+	chr5:143435281-143435306	GGCUUGAAAGAUUUCUGACCUUCUA	2875
2908_1_29	NR3C1	Exon 1	+	chr5:143435294-143435319	UCUGACCUUCUAAGGUCCAGUGAUU	2876
2908_1_30	NR3C1	Exon 1	+	chr5:143435458-143435483	AGAAGAGGAAGAGGUACCUUUUGAA	2877
2908_1_31	NR3C1	Exon 1	+	chr5:143435459-143435484	GAAGAGGAAGAGGUACCUUUUGAAU	2878
2908_1_32	NR3C1	Exon 1	+	chr5:143435460-143435485	AAGAGGAAGAGGUACCUUUUGAAUG	2879
2908_1_33	NR3C1	Exon 1	+	chr5:143435498-143435523	CCCUUACAUAACCUGACCACACAAU	2880
2908_1_34	NR3C1	Exon 1	+	chr5:143435501-143435526	UUACAUAACCUGACCACACAAUAGG	2881
2908_1_35	NR3C1	Exon 1	-	chr5:143434537-143434562	CUUUGCUUCAUUAAAGUGUCUGAGA	2882
2908_1_36	NR3C1	Exon 1	-	chr5:143434591-143434616	UUAAUAACAGGAAUUUUCAUCUGCC	2883
2908_1_37	NR3C1	Exon 1	-	chr5:143434608-143434633	CGGGCUUUAGUUGUACCUUAAUAAC	2884
2908_1_38	NR3C1	Exon 1	-	chr5:143434632-143434657	ACAAAAUGCAGCUCCUACCCUCCUC	2885

2908_1_39	NR3C1	Exon 1	-	chr5:143434633-143434658	AACAAAAUGCAGCUCCUACCCUCCU	2886
2908_1_40	NR3C1	Exon 1	-	chr5:143434661-143434686	GUGCCUUCUCUGUGCGAGAAUGGGG	2887
2908_1_41	NR3C1	Exon 1	-	chr5:143434664-143434689	UGAGUGCCUUCUCUGUGCGAGAAUG	2888
2908_1_42	NR3C1	Exon 1	-	chr5:143434665-143434690	AUGAGUGCCUUCUCUGUGCGAGAAU	2889
2908_1_43	NR3C1	Exon 1	-	chr5:143434666-143434691	AAUGAGUGCCUUCUCUGUGCGAGAA	2890
2908_1_44	NR3C1	Exon 1	-	chr5:143434735-143434760	CUUCUGUGACGACUGCUGCAGAGGC	2891
2908_1_45	NR3C1	Exon 1	-	chr5:143434739-143434764	CCAGCUUCUGUGACGACUGCUGCAG	2892
2908_1_46	NR3C1	Exon 1	-	chr5:143434767-143434792	UCUCAGAGCAGUUAGCCCAGGAAAG	2893
2908_1_47	NR3C1	Exon 1	-	chr5:143434768-143434793	CUCUCAGAGCAGUUAGCCCAGGAAA	2894
2908_1_48	NR3C1	Exon 1	-	chr5:143434769-143434794	GCUCUCAGAGCAGUUAGCCCAGGAA	2895
2908_1_49	NR3C1	Exon 1	-	chr5:143434774-143434799	CUGGUGCUCUCAGAGCAGUUAGCCC	2896
2908_1_50	NR3C1	Exon 1	-	chr5:143434798-143434823	GUCAUAUCUAAGUCAGAUUUCAUUC	2897
2908_1_51	NR3C1	Exon 1	-	chr5:143434833-143434858	UGUGUAGCUGGCUUCUUCUGAAAAA	2898
2908_1_52	NR3C1	Exon 1	-	chr5:143434850-143434875	AUUUGUUCAUCAAGAGUUGUGUAGC	2899
2908_1_53	NR3C1	Exon 1	-	chr5:143434883-143434908	AAAUUCUCUGGUUUGUGCUCAUCGU	2900
2908_1_54	NR3C1	Exon 1	-	chr5:143434900-143434925	AAUUUUCUUCACUUCUGAAAUUCUC	2901
2908_1_55	NR3C1	Exon 1	-	chr5:143434942-143434967	AAAAAAAAAGUUAUACCCGAGAGAC	2902
2908_1_56	NR3C1	Exon 1	-	chr5:143434994-143435019	CUGAACUAGGAAAUUCACCAUAAUU	2903
2908_1_57	NR3C1	Exon 1	-	chr5:143435012-143435037	UGAAUCAGUGGCUCUGAGCUGAACU	2904
2908_1_58	NR3C1	Exon 1	-	chr5:143435029-143435054	CCUGGGGGAAUAUCUGCUGAAUCAG	2905
2908_1_59	NR3C1	Exon 1	-	chr5:143435049-143435074	UUGGUUUCCAUUAGGAUCUGCCUGG	2906
2908_1_60	NR3C1	Exon 1	-	chr5:143435050-143435075	GUUGGUUUCCAUUAGGAUCUGCCUG	2907
2908_1_61	NR3C1	Exon 1	-	chr5:143435051-143435076	UGUUGGUUUCCAUUAGGAUCUGCCU	2908
2908_1_62	NR3C1	Exon 1	-	chr5:143435052-143435077	AUGUUGGUUUCCAUUAGGAUCUGCC	2909
2908_1_63	NR3C1	Exon 1	-	chr5:143435062-143435087	CAGACCUCACAUGUUGGUUUCCAUU	2910

2908_1_64	NR3C1	Exon 1	-	chr5:143435073-143435098	AUUCCCAGCAUCAGACCUCACAUGU	2911
2908_1_65	NR3C1	Exon 1	-	chr5:143435166-143435191	AAAAGGGAAAGUGGUGAAGGCAGGG	2912
2908_1_66	NR3C1	Exon 1	-	chr5:143435169-143435194	GAAAAAAGGGAAAGUGGUGAAGGCA	2913
2908_1_67	NR3C1	Exon 1	-	chr5:143435170-143435195	AGAAAAAAGGGAAAGUGGUGAAGGC	2914
2908_1_68	NR3C1	Exon 1	-	chr5:143435174-143435199	GAGAAGAAAAAAGGGAAAGUGGGUGA	2915
2908_1_69	NR3C1	Exon 1	-	chr5:143435180-143435205	GGGUAAGAGAAGAAAAAAGGGAAAG	2916
2908_1_70	NR3C1	Exon 1	-	chr5:143435187-143435212	AGAAAGAGGGUAAGAGAAGAAAAAA	2917
2908_1_71	NR3C1	Exon 1	-	chr5:143435188-143435213	CAGAAAGAGGGUAAGAGAAGAAAAA	2918
2908_1_72	NR3C1	Exon 1	-	chr5:143435205-143435230	UGGGGAAGGAAUAGAAACAGAAAGA	2919
2908_1_73	NR3C1	Exon 1	-	chr5:143435206-143435231	GUGGGGAAGGAAUAGAAACAGAAAG	2920
2908_1_74	NR3C1	Exon 1	-	chr5:143435224-143435249	GGAAGCACUGGGGCAUGAGUGGGGA	2921
2908_1_75	NR3C1	Exon 1	-	chr5:143435228-143435253	CAACGGAAGCACUGGGGCAUGAGUG	2922
2908_1_76	NR3C1	Exon 1	-	chr5:143435229-143435254	CCAACGGAAGCACUGGGGCAUGAGU	2923
2908_1_77	NR3C1	Exon 1	-	chr5:143435230-143435255	UCCAACGGAAGCACUGGGGCAUGAG	2924
2908_1_78	NR3C1	Exon 1	-	chr5:143435239-143435264	GCGCAUGUGUCCAACGGAAGCACUG	2925
2908_1_79	NR3C1	Exon 1	-	chr5:143435240-143435265	UGCGCAUGUGUCCAACGGAAGCACU	2926
2908_1_80	NR3C1	Exon 1	-	chr5:143435241-143435266	AUGCGCAUGUGUCCAACGGAAGCAC	2927
2908_1_81	NR3C1	Exon 1	-	chr5:143435250-143435275	GACCGUAAAAUGCGCAUGUGUCCAA	2928
2908_1_82	NR3C1	Exon 1	-	chr5:143435277-143435302	AGGUCAGAAAUCUUUCAAGCCCUGC	2929
2908_1_83	NR3C1	Exon 1	-	chr5:143435302-143435327	UGAUACCAAAUCACUGGACCUUAGA	2930
2908_1_84	NR3C1	Exon 1	-	chr5:143435313-143435338	CUUAGAUCUUCUGAUACCAAAUCAC	2931
2908_1_85	NR3C1	Exon 1	-	chr5:143435347-143435372	CACGCUUCUUUAAAUGGCAGAGAGA	2932
2908_1_86	NR3C1	Exon 1	-	chr5:143435358-143435383	GGAAAUUGCAACACGCUUCUUUAAA	2933
2908_1_87	NR3C1	Exon 1	-	chr5:143435384-143435409	AGGCGAAUCACUUUCACUUCUGCUG	2934
2908_1_88	NR3C1	Exon 1	-	chr5:143435385-143435410	GAGGCGAAUCACUUUCACUUCUGCU	2935

2908_1_89	NR3C1	Exon 1	-	chr5:143435386-143435411	AGAGGCGAAUCACUUUCACUUCUGC	2936
2908_1_90	NR3C1	Exon 1	-	chr5:143435409-143435434	ACACGGAAUGCAGACAUUUGAGUAG	2937
2908_1_91	NR3C1	Exon 1	-	chr5:143435477-143435502	AGGGUUUGCUUUCACCCCAUUCAAA	2938
2908_1_92	NR3C1	Exon 1	-	chr5:143435501-143435526	CCUAUUGUGUGGUCAGGUUAUGUAA	2939
2908_1_93	NR3C1	Exon 1	-	chr5:143435502-143435527	UCCUAUUGUGUGGUCAGGUUAUGUA	2940
2908_1_94	NR3C1	Exon 1	-	chr5:143435512-143435537	UUUCAUUUCCUCCUAUUGUGUGGUC	2941
1633_1_1	DCK	Exon 1	+	chr4:70993523-70993548	CCCGGCCUUCACGUGACCUGGCGUG	5278
1633_1_2	DCK	Exon 1	+	chr4:70993536-70993561	UGACCUGGCGUGCGGAGCGCGCACG	5279
1633_1_3	DCK	Exon 1	+	chr4:70993537-70993562	GACCUGGCGUGCGGAGCGCGCACGC	5280
1633_1_4	DCK	Exon 1	+	chr4:70993549-70993574	GGAGCGCGCACGCGGGAACCCGCGC	5281
1633_1_5	DCK	Exon 1	+	chr4:70993552-70993577	GCGCGCACGCGGGAACCCGCGCUGG	5282
1633_1_6	DCK	Exon 1	+	chr4:70993555-70993580	CGCACGCGGGAACCCGCGCUGGAGG	5283
1633_1_7	DCK	Exon 1	+	chr4:70993556-70993581	GCACGCGGGAACCCGCGCUGGAGGC	5284
1633_1_8	DCK	Exon 1	+	chr4:70993561-70993586	CGGGAACCCGCGCUGGAGGCGGGCG	5285
1633_1_9	DCK	Exon 1	+	chr4:70993562-70993587	GGGAACCCGCGCUGGAGGCGGGCGA	5286
1633_1_10	DCK	Exon 1	+	chr4:70993568-70993593	CCGCGCUGGAGGCGGGCGAGGGCCG	5287
1633_1_11	DCK	Exon 1	+	chr4:70993569-70993594	CGCGCUGGAGGCGGGCGAGGGCCGA	5288
1633_1_12	DCK	Exon 1	+	chr4:70993570-70993595	GCGCUGGAGGCGGGCGAGGGCCGAG	5289
1633_1_13	DCK	Exon 1	+	chr4:70993578-70993603	GGCGGGCGAGGGCCGAGGGGCAGCU	5290
1633_1_14	DCK	Exon 1	+	chr4:70993579-70993604	GCGGGCGAGGGCCGAGGGGCAGCUA	5291
1633_1_15	DCK	Exon 1	+	chr4:70993586-70993611	AGGGCCGAGGGGCAGCUAGGGAGCG	5292
1633_1_16	DCK	Exon 1	+	chr4:70993593-70993618	AGGGGCAGCUAGGGAGCGCGGCUUG	5293
1633_1_17	DCK	Exon 1	+	chr4:70993596-70993621	GGCAGCUAGGGAGCGCGGCUUGAGG	5294
1633_1_18	DCK	Exon 1	+	chr4:70993597-70993622	GCAGCUAGGGAGCGCGGCUUGAGGA	5295
1633_1_19	DCK	Exon 1	+	chr4:70993600-70993625	GCUAGGGAGCGCGGCUUGAGGAGGG	5296

1633_1_20	DCK	Exon 1	+	chr4:70993601-70993626	CUAGGGAGCGCGGCUUGAGGAGGGC	5297
1633_1_21	DCK	Exon 1	+	chr4:70993602-70993627	UAGGGAGCGCGGCUUGAGGAGGGCG	5298
1633_1_22	DCK	Exon 1	+	chr4:70993614-70993639	CUUGAGGAGGGCGGGGCCGCCCCGC	5299
1633_1_23	DCK	Exon 1	+	chr4:70993671-70993696	GCCAAAGUCAAACCCCGACACCCGC	5300
1633_1_24	DCK	Exon 1	+	chr4:70993674-70993699	AAAGUCAAACCCCGACACCCGCCGG	5301
1633_1_25	DCK	Exon 1	+	chr4:70993675-70993700	AAGUCAAACCCCGACACCCGCCGGC	5302
1633_1_26	DCK	Exon 1	+	chr4:70993679-70993704	CAAACCCCGACACCCGCCGGCGGGC	5303
1633_1_27	DCK	Exon 1	+	chr4:70993700-70993725	GGGCCGGUGAGCUCACUAGCUGACC	5304
1633_1_28	DCK	Exon 1	+	chr4:70993704-70993729	CGGUGAGCUCACUAGCUGACCCGGC	5305
1633_1_29	DCK	Exon 1	+	chr4:70993709-70993734	AGCUCACUAGCUGACCCGGCAGGUC	5306
1633_1_30	DCK	Exon 1	+	chr4:70993715-70993740	CUAGCUGACCCGGCAGGUCAGGAUC	5307
1633_1_31	DCK	Exon 1	+	chr4:70993723-70993748	CCCGGCAGGUCAGGAUCUGGCUUAG	5308
1633_1_32	DCK	Exon 1	+	chr4:70993753-70993778	CCGCGAGCUCCAGUGCGCGCACCCG	5309
1633_1_33	DCK	Exon 1	+	chr4:70993777-70993802	GUGGCCGCCUCCCAGCCCUCUUUGC	5310
1633_1_34	DCK	Exon 1	+	chr4:70993788-70993813	CCAGCCCUCUUUGCCGGACGAGCUC	5311
1633_1_35	DCK	Exon 1	+	chr4:70993789-70993814	CAGCCCUCUUUGCCGGACGAGCUCU	5312
1633_1_36	DCK	Exon 1	+	chr4:70993806-70993831	CGAGCUCUGGGCCGCCACAAGACUA	5313
1633_1_37	DCK	Exon 1	+	chr4:70993811-70993836	UCUGGGCCGCCACAAGACUAAGGAA	5314
1633_1_38	DCK	Exon 1	+	chr4:70993859-70993884	UGCCCGUCUUUCUCAGCCAGCUCUG	5315
1633_1_39	DCK	Exon 1	+	chr4:70993860-70993885	GCCCGUCUUUCUCAGCCAGCUCUGA	5316
1633_1_40	DCK	Exon 1	+	chr4:70993861-70993886	CCCGUCUUUCUCAGCCAGCUCUGAG	5317
1633_1_41	DCK	Exon 1	+	chr4:70993890-70993915	CCCGCAUCAAGAAAAUCUCCAUCGA	5318
1633_1_42	DCK	Exon 1	+	chr4:70993891-70993916	CCGCAUCAAGAAAAUCUCCAUCGAA	5319
1633_1_43	DCK	Exon 1	+	chr4:70993899-70993924	AGAAAAUCUCCAUCGAAGGGAACAU	5320
1633_1_44	DCK	Exon 1	+	chr4:70993904-70993929	AUCUCCAUCGAAGGGAACAUCGGUA	5321

1633_1_45	DCK	Exon 1	+	chr4:70993913-70993938	GAAGGGAACAUCGGUAAGGAGCCUC	5322
1633_1_46	DCK	Exon 1	+	chr4:70993921-70993946	CAUCGGUAAGGAGCCUCCGGAAAUG	5323
1633_1_47	DCK	Exon 1	+	chr4:70993922-70993947	AUCGGUAAGGAGCCUCCGGAAAUGU	5324
1633_1_48	DCK	Exon 1	-	chr4:70993525-70993550	CGCACGCCAGGUCACGUGAAGGCCG	5325
1633_1_49	DCK	Exon 1	-	chr4:70993526-70993551	CCGCACGCCAGGUCACGUGAAGGCC	5326
1633_1_50	DCK	Exon 1	-	chr4:70993527-70993552	UCCGCACGCCAGGUCACGUGAAGGC	5327
1633_1_51	DCK	Exon 1	-	chr4:70993531-70993556	GCGCUCCGCACGCCAGGUCACGUGA	5328
1633_1_52	DCK	Exon 1	-	chr4:70993542-70993567	UUCCCGCGUGCGCGCUCCGCACGCC	5329
1633_1_53	DCK	Exon 1	-	chr4:70993570-70993595	CUCGGCCCUCGCCCGCCUCCAGCGC	5330
1633_1_54	DCK	Exon 1	-	chr4:70993571-70993596	CCUCGGCCCUCGCCCGCCUCCAGCG	5331
1633_1_55	DCK	Exon 1	-	chr4:70993593-70993618	CAAGCCGCGCUCCCUAGCUGCCCCU	5332
1633_1_56	DCK	Exon 1	-	chr4:70993633-70993658	UGAGGACACUGGCGGGCCUGCGGGG	5333
1633_1_57	DCK	Exon 1	-	chr4:70993636-70993661	AGCUGAGGACACUGGCGGGCCUGCG	5334
1633_1_58	DCK	Exon 1	-	chr4:70993637-70993662	CAGCUGAGGACACUGGCGGGCCUGC	5335
1633_1_59	DCK	Exon 1	-	chr4:70993638-70993663	GCAGCUGAGGACACUGGCGGGCCUG	5336
1633_1_60	DCK	Exon 1	-	chr4:70993645-70993670	CGCGGAGGCAGCUGAGGACACUGGC	5337
1633_1_61	DCK	Exon 1	-	chr4:70993646-70993671	GCGCGGAGGCAGCUGAGGACACUGG	5338
1633_1_62	DCK	Exon 1	-	chr4:70993649-70993674	GGCGCGCGGAGGCAGCUGAGGACAC	5339
1633_1_63	DCK	Exon 1	-	chr4:70993656-70993681	UGACUUUGGCGCGCGGAGGCAGCUG	5340
1633_1_64	DCK	Exon 1	-	chr4:70993665-70993690	GUCGGGGUUUGACUUUGGCGCGCGG	5341
1633_1_65	DCK	Exon 1	-	chr4:70993668-70993693	GGUGUCGGGGUUUGACUUUGGCGCG	5342
1633_1_66	DCK	Exon 1	-	chr4:70993675-70993700	GCCGGCGGGUGUCGGGGUUUGACUU	5343
1633_1_67	DCK	Exon 1	-	chr4:70993686-70993711	CUCACCGGCCCGCCGGCGGGUGUCG	5344
1633_1_68	DCK	Exon 1	-	chr4:70993687-70993712	GCUCACCGGCCCGCCGGCGGGUGUC	5345
1633_1_69	DCK	Exon 1	-	chr4:70993688-70993713	AGCUCACCGGCCCGCCGGCGGGUGU	5346

1633_1_70	DCK	Exon 1	-	chr4:70993694-70993719	CUAGUGAGCUCACCGGCCCGCCGGC	5347
1633_1_71	DCK	Exon 1	-	chr4:70993695-70993720	GCUAGUGAGCUCACCGGCCCGCCGG	5348
1633_1_72	DCK	Exon 1	-	chr4:70993698-70993723	UCAGCUAGUGAGCUCACCGGCCCGC	5349
1633_1_73	DCK	Exon 1	-	chr4:70993706-70993731	CUGCCGGGUCAGCUAGUGAGCUCAC	5350
1633_1_74	DCK	Exon 1	-	chr4:70993726-70993751	CCGCUAAGCCAGAUCCUGACCUGCC	5351
1633_1_75	DCK	Exon 1	-	chr4:70993727-70993752	GCCGCUAAGCCAGAUCCUGACCUGC	5352
1633_1_76	DCK	Exon 1	-	chr4:70993756-70993781	CCACGGGUGCGCGCACUGGAGCUCG	5353
1633_1_77	DCK	Exon 1	-	chr4:70993765-70993790	GGGAGGCGGCCACGGGUGCGCGCAC	5354
1633_1_78	DCK	Exon 1	-	chr4:70993777-70993802	GCAAAGAGGGCUGGGAGGCGGCCAC	5355
1633_1_79	DCK	Exon 1	-	chr4:70993778-70993803	GGCAAAGAGGGCUGGGAGGCGGCCA	5356
1633_1_80	DCK	Exon 1	-	chr4:70993784-70993809	UCGUCCGGCAAAGAGGGCUGGGAGG	5357
1633_1_81	DCK	Exon 1	-	chr4:70993787-70993812	AGCUCGUCCGGCAAAGAGGGCUGGG	5358
1633_1_82	DCK	Exon 1	-	chr4:70993790-70993815	CAGAGCUCGUCCGGCAAAGAGGGCU	5359
1633_1_83	DCK	Exon 1	-	chr4:70993791-70993816	CCAGAGCUCGUCCGGCAAAGAGGGC	5360
1633_1_84	DCK	Exon 1	-	chr4:70993795-70993820	CGGCCCAGAGCUCGUCCGGCAAAGA	5361
1633_1_85	DCK	Exon 1	-	chr4:70993796-70993821	GCGGCCCAGAGCUCGUCCGGCAAAG	5362
1633_1_86	DCK	Exon 1	-	chr4:70993804-70993829	GUCUUGUGGCGGCCCAGAGCUCGUC	5363
1633_1_87	DCK	Exon 1	-	chr4:70993820-70993845	GGGUGGCCAUUCCUUAGUCUUGUGG	5364
1633_1_88	DCK	Exon 1	-	chr4:70993823-70993848	GCGGGGUGGCCAUUCCUUAGUCUUG	5365
1633_1_89	DCK	Exon 1	-	chr4:70993842-70993867	GACGGGCAGCUUCUCUUGGGCGGGG	5366
1633_1_90	DCK	Exon 1	-	chr4:70993845-70993870	AAAGACGGGCAGCUUCUCUUGGGCG	5367
1633_1_91	DCK	Exon 1	-	chr4:70993846-70993871	GAAAGACGGGCAGCUUCUCUUGGGC	5368
1633_1_92	DCK	Exon 1	-	chr4:70993847-70993872	AGAAAGACGGGCAGCUUCUCUUGGG	5369
1633_1_93	DCK	Exon 1	-	chr4:70993850-70993875	CUGAGAAAGACGGGCAGCUUCUCUU	5370
1633_1_94	DCK	Exon 1	-	chr4:70993851-70993876	GCUGAGAAAGACGGGCAGCUUCUCU	5371

1633_1_95	DCK	Exon 1	-	chr4:70993864-70993889	CCCCUCAGAGCUGGCUGAGAAAGAC	5372
1633_1_96	DCK	Exon 1	-	chr4:70993865-70993890	UCCCCUCAGAGCUGGCUGAGAAAGA	5373
1633_1_97	DCK	Exon 1	-	chr4:70993878-70993903	UUCUUGAUGCGGGUCCCCUCAGAGC	5374
1633_1_98	DCK	Exon 1	-	chr4:70993893-70993918	CCUUCGAUGGAGAUUUUCUUGAUGC	5375
1633_1_99	DCK	Exon 1	-	chr4:70993894-70993919	CCCUUCGAUGGAGAUUUUCUUGAUG	5376
1633_1_100	DCK	Exon 1	-	chr4:70993911-70993936	GGCUCCUUACCGAUGUUCCCUUCGA	5377
1633_2_1	DCK	Exon 2	+	chr4:70998045-70998070	UUUUAUCUUUCCUCACAACAGCUGC	5378
1633_2_2	DCK	Exon 2	+	chr4:70998046-70998071	UUUAUCUUUCCUCACAACAGCUGCA	5379
1633_2_3	DCK	Exon 2	+	chr4:70998091-70998116	UAUCCUUAAACAAUUGUGUGAAGAU	5380
1633_2_4	DCK	Exon 2	+	chr4:70998092-70998117	AUCCUUAAACAAUUGUGUGAAGAUU	5381
1633_2_5	DCK	Exon 2	+	chr4:70998098-70998123	AAACAAUUGUGUGAAGAUUGGGAAG	5382
1633_2_6	DCK	Exon 2	+	chr4:70998121-70998146	AGUGGUUCCUGAACCUGUUGCCAGA	5383
1633_2_7	DCK	Exon 2	+	chr4:70998155-70998180	GUUCAAAGUACUCAAGAUGAAUUUG	5384
1633_2_8	DCK	Exon 2	-	chr4:70998058-70998083	UGUUGACUUCCCUGCAGCUGUUGUG	5385
1633_2_9	DCK	Exon 2	-	chr4:70998097-70998122	UUCCCAAUCUUCACACAAUUGUUUA	5386
1633_2_10	DCK	Exon 2	-	chr4:70998131-70998156	CAUUGCACCAUCUGGCAACAGGUUC	5387
1633_2_11	DCK	Exon 2	-	chr4:70998137-70998162	UUUGAACAUUGCACCAUCUGGCAAC	5388
1633_2_12	DCK	Exon 2	-	chr4:70998144-70998169	UGAGUACUUUGAACAUUGCACCAUC	5389
1633_3_1	DCK	Exon 3	+	chr4:71022364-71022389	AGGAACUUACAAUGUCUCAGAAAAA	5390
1633_3_2	DCK	Exon 3	+	chr4:71022367-71022392	AACUUACAAUGUCUCAGAAAAAUGG	5391
1633_3_3	DCK	Exon 3	+	chr4:71022368-71022393	ACUUACAAUGUCUCAGAAAAAUGGU	5392
1633_3_4	DCK	Exon 3	+	chr4:71022407-71022432	GAUGAUGUAUGAGAAACCUGAACGA	5393
1633_3_5	DCK	Exon 3	+	chr4:71022472-71022497	UAAGAGCUCAGCUUGCCUCUCUGAA	5394
1633_3_6	DCK	Exon 3	+	chr4:71022533-71022558	UUUUGAACGAUCUGUGUAUAGUGAC	5395
1633_3_7	DCK	Exon 3	+	chr4:71022546-71022571	GUGUAUAGUGACAGGUAUGUAUAAA	5396

1633_3_8	DCK	Exon 3	+	chr4:71022557-71022582	CAGGUAUGUAUAAAUGGCUUGUACG	5397
1633_3_9	DCK	Exon 3	-	chr4:71022426-71022451	UUUGGAAGGUAAAAGACCAUCGUUC	5398
1633_3_10	DCK	Exon 3	-	chr4:71022445-71022470	CGACUGAGACAGGCAUAUGUUUGGA	5399
1633_3_11	DCK	Exon 3	-	chr4:71022449-71022474	UAUUCGACUGAGACAGGCAUAUGUU	5400
1633_3_12	DCK	Exon 3	-	chr4:71022460-71022485	AGCUGAGCUCUUAUUCGACUGAGAC	5401
1633_3_13	DCK	Exon 3	-	chr4:71022490-71022515	GCAUCUUUGAGCUUGCCAUUCAGAG	5402
1633_3_14	DCK	Exon 3	-	chr4:71022525-71022550	ACACAGAUCGUUCAAAAAAUAAUAC	5403
1633_4_1	DCK	Exon 4	+	chr4:71023585-71023610	AUCUGAAUGCAUGAAUGAGACAGAG	5404
1633_4_2	DCK	Exon 4	+	chr4:71023603-71023628	GACAGAGUGGACAAUUUAUCAAGAC	5405
1633_4_3	DCK	Exon 4	+	chr4:71023612-71023637	GACAAUUUAUCAAGACUGGCAUGAC	5406
1633_4_4	DCK	Exon 4	+	chr4:71023629-71023654	GGCAUGACUGGAUGAAUAACCAAUU	5407
1633_4_5	DCK	Exon 4	+	chr4:71023646-71023671	AACCAAUUUGGCCAAAGCCUUGAAU	5408
1633_4_6	DCK	Exon 4	+	chr4:71023650-71023675	AAUUUGGCCAAAGCCUUGAAUUGGA	5409
1633_4_7	DCK	Exon 4	+	chr4:71023679-71023704	AUCAUUUAUCUUCAAGCCACUCCAG	5410
1633_4_8	DCK	Exon 4	-	chr4:71023651-71023676	AUCCAAUUCAAGGCUUUGGCCAAAU	5411
1633_4_9	DCK	Exon 4	-	chr4:71023660-71023685	AAUGAUUCCAUCCAAUUCAAGGCUU	5412
1633_4_10	DCK	Exon 4	-	chr4:71023666-71023691	AAGAUAAAUGAUUCCAUCCAAUUCA	5413
1633_4_11	DCK	Exon 4	-	chr4:71023698-71023723	UUUUUAUUGGGUUUUACCUCUGGAG	5414
1633_4_12	DCK	Exon 4	-	chr4:71023703-71023728	ACACAUUUUUAUUGGGUUUUACCUC	5415
1633_5_1	DCK	Exon 5	+	chr4:71025814-71025839	GACAUGCUUACAUAGAAUAUAUUUA	5416
1633_5_2	DCK	Exon 5	+	chr4:71025815-71025840	ACAUGCUUACAUAGAAUAUAUUUAC	5417
1633_5_3	DCK	Exon 5	+	chr4:71025816-71025841	CAUGCUUACAUAGAAUAUAUUUACG	5418
1633_5_4	DCK	Exon 5	+	chr4:71025834-71025859	AUUUACGGGGAAGAAAUGAAGAGCA	5419
1633_5_5	DCK	Exon 5	+	chr4:71025883-71025908	GAAGCUUCAUUAUAAACAUGAAAGC	5420
1633_5_6	DCK	Exon 5	+	chr4:71025895-71025920	UAAACAUGAAAGCUGGCUCCUGCAU	5421

1633_5_7	DCK	Exon 5	-	chr4:71025794-71025819	AUGUCUAAAAGCAAGUAAUAAGAGA	5422
1633_5_8	DCK	Exon 5	-	chr4:71025869-71025894	AAUGAAGCUUCUCUAAAUAUUCAAG	5423
1633_5_9	DCK	Exon 5	-	chr4:71025916-71025941	UAAGUCUUACUUCAGUGUCCUAUGC	5424
1633_6_1	DCK	Exon 6	+	chr4:71026662-71026687	AGAACCAACUUCGAUUAUCUUCAAG	5425
1633_6_2	DCK	Exon 6	+	chr4:71026680-71026705	CUUCAAGAGGUGCCUAUCUUAACAC	5426
1633_6_3	DCK	Exon 6	+	chr4:71026719-71026744	GACUUUAAAGACAAAUAUGAAAGUC	5427
1633_6_4	DCK	Exon 6	+	chr4:71026728-71026753	GACAAAUAUGAAAGUCUGGUUGAAA	5428
1633_6_5	DCK	Exon 6	-	chr4:71026669-71026694	GGCACCUCUUGAAGAUAAUCGAAGU	5429
1633_6_6	DCK	Exon 6	-	chr4:71026695-71026720	CUUCAUUAACAUCCAGUGUUAAGAU	5430
1633_7_1	DCK	Exon 7	+	chr4:71029369-71029394	ACUUUGUGAUCUUGCUGAAGACUAC	5431
1633_7_2	DCK	Exon 7	+	chr4:71029380-71029405	UUGCUGAAGACUACAGGCAGCCAAA	5432
1633_7_3	DCK	Exon 7	+	chr4:71029473-71029498	CAAGUUUUUAAUCGUUUUUGUUUUA	5433
1633_7_4	DCK	Exon 7	+	chr4:71029705-71029730	UCCUCAGCAGGUUGGCUUUUUUCCC	5434
1633_7_5	DCK	Exon 7	+	chr4:71029723-71029748	UUUUCCCUGGUGCCUCUCACUUCGU	5435
1633_7_6	DCK	Exon 7	+	chr4:71029769-71029794	GAAAGCUUUAAUGUUACAUAGUAAA	5436
1633_7_7	DCK	Exon 7	+	chr4:71029817-71029842	AGUGUACCUAUUAAAAGUUGCAAAG	5437
1633_7_8	DCK	Exon 7	+	chr4:71029826-71029851	AUUAAAAGUUGCAAAGUGGAAUUAA	5438
1633_7_9	DCK	Exon 7	+	chr4:71029842-71029867	UGGAAUUAAAGGAAUCCCUAGAAUA	5439
1633_7_10	DCK	Exon 7	+	chr4:71029932-71029957	GCCUCAGUCUGCUUUCUCUACUGUC	5440
1633_7_11	DCK	Exon 7	+	chr4:71029942-71029967	GCUUUCUCUACUGUCUGGAUUAAUU	5441
1633_7_12	DCK	Exon 7	+	chr4:71030131-71030156	CUGAAAGCAUUAUUUUUUGUUGAAU	5442
1633_7_13	DCK	Exon 7	+	chr4:71030155-71030180	UAGGAAAUAAAAUUAAUGAAGACAG	5443
1633_7_14	DCK	Exon 7	+	chr4:71030241-71030266	UGUGAAUAUUUGUAAAAAUAAUGAA	5444
1633_7_15	DCK	Exon 7	+	chr4:71030296-71030321	AUUUUCUUUCUAGUUUGUUUAGUUA	5445
1633_7_16	DCK	Exon 7	+	chr4:71030370-71030395	AGAAAAUUUUAUGUAUUUUAAAAUA	5446

1633_7_17	DCK	Exon 7	+	chr4:71030371-71030396	GAAAAUUUUAUGUAUUUUAAAAUAA	5447
1633_7_18	DCK	Exon 7	+	chr4:71030372-71030397	AAAAUUUUAUGUAUUUUAAAAUAAG	5448
1633_7_19	DCK	Exon 7	+	chr4:71030430-71030455	UUUCUUUCCAAGUCAUUUUUGUUUU	5449
1633_7_20	DCK	Exon 7	+	chr4:71030459-71030484	UUCUUAUUCAAAGAUGAUAAUUUAG	5450
1633_7_21	DCK	Exon 7	+	chr4:71030494-71030519	AGUCCAGACGCACUGAUCUUUGCAA	5451
1633_7_22	DCK	Exon 7	+	chr4:71030575-71030600	UGCAUUUUUUUAGUUUGUUUUUGUU	5452
1633_7_23	DCK	Exon 7	+	chr4:71030633-71030658	UAAGUAUAAACCUUAUGAACUACAG	5453
1633_7_24	DCK	Exon 7	+	chr4:71030734-71030759	CUUUUAAAUAAAUUAUGAAUAUUAA	5454
1633_7_25	DCK	Exon 7	+	chr4:71030773-71030798	UAAAUUACUUUGAUUCCAUUUUAAG	5455
1633_7_26	DCK	Exon 7	+	chr4:71030901-71030926	UCAUGACUCAAAAGUUGUCUCAGUG	5456
1633_7_27	DCK	Exon 7	+	chr4:71030904-71030929	UGACUCAAAAGUUGUCUCAGUGUGG	5457
1633_7_28	DCK	Exon 7	-	chr4:71029343-71029368	CUCAAAAACUCUUUGACCUGAGGAA	5458
1633_7_29	DCK	Exon 7	-	chr4:71029348-71029373	AAGUACUCAAAAACUCUUUGACCUG	5459
1633_7_30	DCK	Exon 7	-	chr4:71029403-71029428	CAAAGCUGAAGUAUCUGGAACCAUU	5460
1633_7_31	DCK	Exon 7	-	chr4:71029413-71029438	CGAAGAUACACAAAGCUGAAGUAUC	5461
1633_7_32	DCK	Exon 7	-	chr4:71029474-71029499	UUAAAACAAAAACGAUUAAAAACUU	5462
1633_7_33	DCK	Exon 7	-	chr4:71029475-71029500	CUUAAAACAAAAACGAUUAAAAACU	5463
1633_7_34	DCK	Exon 7	-	chr4:71029545-71029570	UUUUUUUUUUGUUUUCUUUCUUUC	5464
1633_7_35	DCK	Exon 7	-	chr4:71029730-71029755	GUCACCAACGAAGUGAGAGGCACCA	5465
1633_7_36	DCK	Exon 7	-	chr4:71029731-71029756	GGUCACCAACGAAGUGAGAGGCACC	5466
1633_7_37	DCK	Exon 7	-	chr4:71029738-71029763	AGAAACUGGUCACCAACGAAGUGAG	5467
1633_7_38	DCK	Exon 7	-	chr4:71029757-71029782	CAUUAAAGCUUUCAGUUUAAGAAAC	5468
1633_7_39	DCK	Exon 7	-	chr4:71029808-71029833	UUUUAAUAGGUACACUAAUUUACAC	5469
1633_7_40	DCK	Exon 7	-	chr4:71029826-71029851	UUAAUUCCACUUUGCAACUUUUAAU	5470
1633_7_41	DCK	Exon 7	-	chr4:71029860-71029885	AUAAAACUUCAGAAUCCUUAUUCUA	5471

1633_7_42	DCK	Exon 7	-	chr4:71029861-71029886	AAUAAAACUUCAGAAUCCUUAUUCU	5472
1633_7_43	DCK	Exon 7	-	chr4:71029918-71029943	CAGACUGAGGCAGGAAGUAAGAGGU	5473
1633_7_44	DCK	Exon 7	-	chr4:71029919-71029944	GCAGACUGAGGCAGGAAGUAAGAGG	5474
1633_7_45	DCK	Exon 7	-	chr4:71029922-71029947	AAAGCAGACUGAGGCAGGAAGUAAG	5475
1633_7_46	DCK	Exon 7	-	chr4:71029932-71029957	GACAGUAGAGAAAGCAGACUGAGGC	5476
1633_7_47	DCK	Exon 7	-	chr4:71029936-71029961	UCCAGACAGUAGAGAAAGCAGACUG	5477
1633_7_48	DCK	Exon 7	-	chr4:71029976-71030001	AAAUGUGUGACUUUAACUUUAUAGC	5478
1633_7_49	DCK	Exon 7	-	chr4:71030133-71030158	CUAUUCAACAAAAAAUAAUGCUUUC	5479
1633_7_50	DCK	Exon 7	-	chr4:71030197-71030222	UAGUUAAGUGUGUCUCAUUAAUUAA	5480
1633_7_51	DCK	Exon 7	-	chr4:71030237-71030262	UUAUUUUUACAAAUAUUCACAUAGA	5481
1633_7_52	DCK	Exon 7	-	chr4:71030341-71030366	CGUAAAAUGGAAAGGUUUAAUACAC	5482
1633_7_53	DCK	Exon 7	-	chr4:71030354-71030379	AAAUUUUCUAAAACGUAAAAUGGAA	5483
1633_7_54	DCK	Exon 7	-	chr4:71030359-71030384	ACAUAAAAUUUUCUAAAACGUAAAA	5484
1633_7_55	DCK	Exon 7	-	chr4:71030440-71030465	UAAGAAACCAAAAACAAAAAUGACU	5485
1633_7_56	DCK	Exon 7	-	chr4:71030495-71030520	UUUGCAAAGAUCAGUGCGUCUGGAC	5486
1633_7_57	DCK	Exon 7	-	chr4:71030500-71030525	UCUCCUUUGCAAAGAUCAGUGCGUC	5487
1633_7_58	DCK	Exon 7	-	chr4:71030550-71030575	UACGUAUAAUGAGACAGUUUAUGUA	5488
1633_7_59	DCK	Exon 7	-	chr4:71030646-71030671	GAGUGUAGCUCCACUGUAGUUCAUA	5489
1633_7_60	DCK	Exon 7	-	chr4:71030791-71030816	CACUGAAAUAUGUCUCCACUUAAAA	5490
1633_7_61	DCK	Exon 7	-	chr4:71030830-71030855	UUUAAAAGUCAUUAUACAUUUUUAA	5491
TRAC-1a	TRAC	EXON-1	+		UCUCAAACAAAUGUGUCACAAAGUA	5816
TRAC-2a	TRAC	EXON-1	+		CACAGACAAAACUGUGCUAGACAUG	5817
TRAC-3a	TRAC	EXON-1	+		AAAACUGUGCUAGACAUGAGGUCUA	5818
TRAC-4a	TRAC	EXON-1	+		AUGGACUUCAAGAGCAACAGUGCUG	5819
TRAC-5a	TRAC	EXON-1	+		CUUCAAGAGCAACAGUGCUGUGGCC	5820

TRAC-6a	TRAC	EXON-1	-		CUGGGCUGGGGAAGAAGGUGUCUUC	5821
TRAC-7a	TRAC	EXON-1	-		UCUUCUGGAAUAAUGCUGUUGUUGA	5822
TRAC-8a	TRAC	EXON-1	-		CAUGCAAAGUCAGAUUUGUUGCUCC	5823
TRAC-9a	TRAC	EXON-1	-		GACACAUUUGUUUGAGAAUCAAAAU	5824
TRAC-10a	TRAC	EXON-1	-		UGUUUGAGAAUCAAAAUCGGUGAAU	5825
TRAC-11	TRAC	EXON-1	-		GUGAAUAGGCAGACAGACUUGUCAC	5826
TRAC-12	TRAC	EXON-1	-		GUCACUGGAUUUAGAGUCUCUCAGC	5827
TRAC-13	TRAC	EXON-1	-		GAUUUAGAGUCUCUCAGCUGGUACA	5828
TRAC-14	TRAC	EXON-1	-		UAGAGUCUCUCAGCUGGUACACGGC	5829
TRAC-15	TRAC	EXON-1	-		AGAGUCUCUCAGCUGGUACACGGCA	5830
TRAC-16	TRAC	EXON-1	-		CUCUCAGCUGGUACACGGCAGGGUC	5831
TRAC-17	TRAC	EXON-1	-		UCUCAGCUGGUACACGGCAGGGUCA	5832
TRAC-18	TRAC	EXON-1	-		CUGGUACACGGCAGGGUCAGGGUUC	5833
TRAC-19	TRAC	EXON-1	-		GCAGGGUCAGGGUUCUGGAUAUCUG	5834
TRAC-20	TRAC	EXON-1	-		CAGGGUCAGGGUUCUGGAUAUCUGU	5835
TRAC-21	TRAC	EXON-1	-		GGGUUCUGGAUAUCUGUGGGACAAG	5836
TRAC-22	TRAC	EXON-1	-		UGGAUAUCUGUGGGACAAGAGGAUC	5837
TRAC-23	TRAC	EXON-1	-		GGAUAUCUGUGGGACAAGAGGAUCA	5838
TRAC-24	TRAC	EXON-1	-		UCUGUGGGACAAGAGGAUCAGGGUU	5839
TRAC-25	TRAC	EXON-2	+		UUAGAAAGUUCCUGUGAUGUCAAGC	5840
TRAC-26	TRAC	EXON-2	+		AGCUGGUCGAGAAAAGCUUUGAAAC	5841
TRAC-27	TRAC	EXON-2	+		AGAAAAGCUUUGAAACAGGUAAGAC	5842
TRAC-28	TRAC	EXON-2	+		GAAAAGCUUUGAAACAGGUAAGACA	5843
TRAC-29	TRAC	EXON-2	+		AAAAGCUUUGAAACAGGUAAGACAG	5844
TRAC-30	TRAC	EXON-2	+		AAACAGGUAAGACAGGGGUCUAGCC	5845

TRAC-31	TRAC	EXON-2	+		AACAGGUAAGACAGGGGUCUAGCCU	5846
TRAC-32	TRAC	EXON-2	-		CUUUUCUCGACCAGCUUGACAUCAC	5847
TRAC-33	TRAC	EXON-2	-		CUUGACAUCACAGGAACUUUCUAAA	5848
TRAC-34	TRAC	EXON-3	+		UAAACUUUCAAAACCUGUCAGUGAU	5849
TRAC-35	TRAC	EXON-3	+		AAACUUUCAAAACCUGUCAGUGAUU	5850
TRAC-36	TRAC	EXON-3	+		GGGUUCCGAAUCCUCCUCCUGAAAG	5851
TRAC-37	TRAC	EXON-3	+		UCCGAAUCCUCCUCCUGAAAGUGGC	5852
TRAC-38	TRAC	EXON-3	+		CCGAAUCCUCCUCCUGAAAGUGGCC	5853
TRAC-39	TRAC	EXON-3	+		CGGGUUUAAUCUGCUCAUGACGCUG	5854
TRAC-40	TRAC	EXON-3	+		UAAUCUGCUCAUGACGCUGCGGCUG	5855
TRAC-41	TRAC	EXON-3	+		UGACGCUGCGGCUGUGGUCCAGCUG	5856
TRAC-42	TRAC	EXON-3	+		CUGCGGCUGUGGUCCAGCUGAGGUG	5857
TRAC-43	TRAC	EXON-3	+		UGCGGCUGUGGUCCAGCUGAGGUGA	5858
TRAC-44	TRAC	EXON-3	+		GCGGCUGUGGUCCAGCUGAGGUGAG	5859
TRAC-45	TRAC	EXON-3	+		CAGCUGAGGUGAGGGGCCUUGAAGC	5860
TRAC-46	TRAC	EXON-3	+		AGCUGAGGUGAGGGGCCUUGAAGCU	5861
TRAC-47	TRAC	EXON-3	-		CAGCUUCAAGGCCCCUCACCUCAGC	5862
TRAC-48	TRAC	EXON-3	-		CGCAGCGUCAUGAGCAGAUUAAACC	5863
TRAC-49	TRAC	EXON-3	-		GAGCAGAUUAAACCCGGCCACUUUC	5864
TRAC-50	TRAC	EXON-3	-		CAGAUUAAACCCGGCCACUUUCAGG	5865
TRAC-51	TRAC	EXON-3	-		AUUAAACCCGGCCACUUUCAGGAGG	5866
TRAC-52	TRAC	EXON-3	-		CCCGGCCACUUUCAGGAGGAGGAUU	5867
TRAC-53	TRAC	EXON-3	-		GAGGAUUCGGAACCCAAUCACUGAC	5868
TRAC-54	TRAC	EXON-3	-		AAUCACUGACAGGUUUUGAAAGUUU	5869
TRAC-55	TRAC	EXON-3	-		UUAGGUUCGUAUCUGUAAAACCAAG	5870

TRAC-56	TRAC	EXON-3	-		UAUCUGUAAAACCAAGAGGCCACAG	5871
TRAC-57	TRAC	EXON-4	+		GCCCCUCUUCUCCCUCUCCAAACAG	5872
TRAC-58	TRAC	EXON-4	+		CCCCUCUUCUCCCUCUCCAAACAGA	5873
TRAC-59	TRAC	EXON-4	+		AACAGAGGGAACUCUCCUACCCCCA	5874
TRAC-60	TRAC	EXON-4	+		AGAGGGAACUCUCCUACCCCCAAGG	5875
TRAC-61	TRAC	EXON-4	+		AGCUGCUACCACCUCUGUGCCCCCC	5876
TRAC-62	TRAC	EXON-4	+		GUGCCCCCCCGGCAAUGCCACCAAC	5877
TRAC-63	TRAC	EXON-4	+		GCUGCUUGUCACUGCCUGACAUUCA	5878
TRAC-64	TRAC	EXON-4	+		UGUCACUGCCUGACAUUCACGGCAG	5879
TRAC-65	TRAC	EXON-4	+		CUGCCUGACAUUCACGGCAGAGGCA	5880
TRAC-66	TRAC	EXON-4	+		GAGGCAAGGCUGCUGCAGCCUCCCC	5881
TRAC-67	TRAC	EXON-4	+		ACUGCCUCCGCCAUCCCACAGAUGA	5882
TRAC-68	TRAC	EXON-4	+		CAUCCCACAGAUGAUGGAUCUUCAG	5883
TRAC-69	TRAC	EXON-4	+		AUCCCACAGAUGAUGGAUCUUCAGU	5884
TRAC-70	TRAC	EXON-4	+		AUGAUGGAUCUUCAGUGGGUUCUCU	5885
TRAC-71	TRAC	EXON-4	+		UGAUGGAUCUUCAGUGGGUUCUCUU	5886
TRAC-72	TRAC	EXON-4	+		UCUUCAGUGGGUUCUCUUGGGCUCU	5887
TRAC-73	TRAC	EXON-4	+		GCUCUAGGUCCUGCAGAAUGUUGUG	5888
TRAC-74	TRAC	EXON-4	+		CUCUAGGUCCUGCAGAAUGUUGUGA	5889
TRAC-75	TRAC	EXON-4	+		UCUAGGUCCUGCAGAAUGUUGUGAG	5890
TRAC-76	TRAC	EXON-4	+		ACAUAGUAUUCUUCUUCUCAAGACG	5891
TRAC-77	TRAC	EXON-4	+		CAUAGUAUUCUUCUUCUCAAGACGU	5892
TRAC-78	TRAC	EXON-4	+		AUAGUAUUCUUCUUCUCAAGACGUG	5893
TRAC-79	TRAC	EXON-4	+		UAGUAUUCUUCUUCUCAAGACGUGG	5894
TRAC-80	TRAC	EXON-4	+		AGUAUUCUUCUUCUCAAGACGUGGG	5895

TRAC-81	TRAC	EXON-4	+		GUGGGGGGAAAUUAUCUCAUUAUCG	5896
TRAC-82	TRAC	EXON-4	+		UCGAGGCCCUGCUAUGCUGUGUAUC	5897
TRAC-83	TRAC	EXON-4	+		CGAGGCCCUGCUAUGCUGUGUAUCU	5898
TRAC-84	TRAC	EXON-4	+		UGCCGAUGCCUUCAUUAAAAUGAUU	5899
TRAC-85	TRAC	EXON-4	+		AGCAGAGACUGUGCCUCUGUUUGAC	5900
TRAC-86	TRAC	EXON-4	+		GCAGAGACUGUGCCUCUGUUUGACU	5901
TRAC-87	TRAC	EXON-4	+		GACUGUGCCUCUGUUUGACUGGGUU	5902
TRAC-88	TRAC	EXON-4	+		GUGCCUCUGUUUGACUGGGUUUGGU	5903
TRAC-89	TRAC	EXON-4	-		ACUCCUACCAAACCCAGUCAAACAG	5904
TRAC-90	TRAC	EXON-4	-		CUGCUCUUCCAAAUCAUUUUAAUGA	5905
TRAC-91	TRAC	EXON-4	-		UUCCAAAUCAUUUUAAUGAAGGCAU	5906
TRAC-92	TRAC	EXON-4	-		UCAUUUUAAUGAAGGCAUCGGCAGC	5907
TRAC-93	TRAC	EXON-4	-		AACACGCCCAGAUACACAGCAUAGC	5908
TRAC-94	TRAC	EXON-4	-		ACACGCCCAGAUACACAGCAUAGCA	5909
TRAC-95	TRAC	EXON-4	-		AAAUAAACCCCUCACAACAUUCUGC	5910
TRAC-96	TRAC	EXON-4	-		GAACCCACUGAAGAUCCAUCAUCUG	5911
TRAC-97	TRAC	EXON-4	-		AACCCACUGAAGAUCCAUCAUCUGU	5912
TRAC-98	TRAC	EXON-4	-		CACUGAAGAUCCAUCAUCUGUGGGA	5913
TRAC-99	TRAC	EXON-4	-		UGAAGAUCCAUCAUCUGUGGGAUGG	5914
TRAC-100	TRAC	EXON-4	-		AGAUCCAUCAUCUGUGGGAUGGCGG	5915
TRAC-101	TRAC	EXON-4	-		UCUGUGGGAUGGCGGAGGCAGUCUC	5916
TRAC-102	TRAC	EXON-4	-		CUGUGGGAUGGCGGAGGCAGUCUCU	5917
TRAC-103	TRAC	EXON-4	-		UGUGGGAUGGCGGAGGCAGUCUCUG	5918
TRAC-104	TRAC	EXON-4	-		AUGGCGGAGGCAGUCUCUGGGGAGC	5919
TRAC-105	TRAC	EXON-4	-		GCGGAGGCAGUCUCUGGGGAGCAGG	5920

TRAC-106	TRAC	EXON-4	-		CGGAGGCAGUCUCUGGGGAGCAGGA	5921
TRAC-107	TRAC	EXON-4	-		GGAGCAGGAGGGAAUGUGCACAGCC	5922
TRAC-108	TRAC	EXON-4	-		GAGCAGGAGGGAAUGUGCACAGCCA	5923
TRAC-109	TRAC	EXON-4	-		AGCAGGAGGGAAUGUGCACAGCCAG	5924
TRAC-110	TRAC	EXON-4	-		AGGAGGGAAUGUGCACAGCCAGGGG	5925
TRAC-111	TRAC	EXON-4	-		CAGCCUUGCCUCUGCCGUGAAUGUC	5926
TRAC-112	TRAC	EXON-4	-		UGUCAGGCAGUGACAAGCAGCAAUA	5927
TRAC-113	TRAC	EXON-4	-		GUCAGGCAGUGACAAGCAGCAAUAA	5928
TRAC-114	TRAC	EXON-4	-		GUGACAAGCAGCAAUAAGGGAACAG	5929
TRAC-115	TRAC	EXON-4	-		UGACAAGCAGCAAUAAGGGAACAGA	5930
TRAC-116	TRAC	EXON-4	-		GACAAGCAGCAAUAAGGGAACAGAG	5931
TRAC-117	TRAC	EXON-4	-		ACAAGCAGCAAUAAGGGAACAGAGG	5932
TRAC-118	TRAC	EXON-4	-		AGCAGCAAUAAGGGAACAGAGGGGG	5933
TRAC-119	TRAC	EXON-4	-		GAACAGAGGGGGUGGCAGCAGUGUU	5934
TRAC-120	TRAC	EXON-4	-		UCUUCAGCAAUCUUAAUCAUAAAUU	5935
TRAC-121	TRAC	EXON-4	-		CUUCAGCAAUCUUAAUCAUAAAUUC	5936
TRAC-122	TRAC	EXON-4	-		AGCAAUCUUAAUCAUAAAUUCGGGU	5937
TRAC-123	TRAC	EXON-4	-		AUCAUAAAUUCGGGUAGGAUCCAGU	5938
TRAC-124	TRAC	EXON-4	-		AUAAAUUCGGGUAGGAUCCAGUUGG	5939
TRAC-125	TRAC	EXON-4	-		GGUAGGAUCCAGUUGGUGGCAUUGC	5940
TRAC-126	TRAC	EXON-4	-		GUAGGAUCCAGUUGGUGGCAUUGCC	5941
TRAC-127	TRAC	EXON-4	-		UAGGAUCCAGUUGGUGGCAUUGCCG	5942
TRAC-128	TRAC	EXON-4	-		AGGAUCCAGUUGGUGGCAUUGCCGG	5943
TRAC-129	TRAC	EXON-4	-		GGAUCCAGUUGGUGGCAUUGCCGGG	5944
TRAC-130	TRAC	EXON-4	-		GAUCCAGUUGGUGGCAUUGCCGGGG	5945

TRAC-131	TRAC	EXON-4	-		UGGUGGCAUUGCCGGGGGGGCACAG	5946
TRAC-132	TRAC	EXON-4	-		UGGCAUUGCCGGGGGGGCACAGAGG	5947
TRAC-133	TRAC	EXON-4	-		GAGGUGGUAGCAGCUUUCACCUCCU	5948
TRAC-134	TRAC	EXON-4	-		AGGUGGUAGCAGCUUUCACCUCCUU	5949
TRAC-135	TRAC	EXON-4	-		GGUGGUAGCAGCUUUCACCUCCUUG	5950
TRAC-136	TRAC	EXON-4	-		GUGGUAGCAGCUUUCACCUCCUUGG	5951
TRAC-137	TRAC	EXON-4	-		UAGCAGCUUUCACCUCCUUGGGGGU	5952
TRAC-138	TRAC	EXON-4	-		UGGGGGUAGGAGAGUUCCCUCUGUU	5953
TRAC-139	TRAC	EXON-4	-		GUAGGAGAGUUCCCUCUGUUUGGAG	5954
TRAC-140	TRAC	EXON-4	-		UAGGAGAGUUCCCUCUGUUUGGAGA	5955
TRAC-141	TRAC	EXON-4	-		UUCCCUCUGUUUGGAGAGGGAGAAG	5956
TRAC-142	TRAC	EXON-4	-		UCCCUCUGUUUGGAGAGGGAGAAGA	5957
TRAC-143	TRAC	EXON-4	-		CCCUCUGUUUGGAGAGGGAGAAGAG	5958
TRAC-144	TRAC	EXON-4	-		GAGAGGGAGAAGAGGGGCAAUGCAG	5959
TRAC-145	TRAC	EXON-4	-		GGGAGAAGAGGGGCAAUGCAGAGGA	5960
TRAC-146	TRAC	EXON-4	-		GAGGGGCAAUGCAGAGGAAGGAGCG	5961
TRAC-147	TRAC	EXON-4	-		AGGGGCAAUGCAGAGGAAGGAGCGA	5962
TRAC-148	TRAC	EXON-4	-		UGCAGAGGAAGGAGCGAGGGAGCAC	5963
TRAC-149	TRAC	EXON-4	-		AGGCUGUCUUACAAUCUUGCAGAUC	5964
TRAC-150	TRAC	EXON-4	-		CUUACAAUCUUGCAGAUCUGGAAUG	5965
TRBC1-1	TRBC	EXON-1	+		CUUCCCUUUCCAGAGGACCUGAACA	5966
TRBC1-2	TRBC	EXON-1	+		GACCUGAACAAGGUGUUCCCACCCG	5967
TRBC1-3	TRBC	EXON-1	+		GAAGCAGAGAUCUCCCACACCCAAA	5968
TRBC1-4	TRBC	EXON-1	+		AUCUCCCACACCCAAAAGGCCACAC	5969
TRBC1-5	TRBC	EXON-1	+		ACCCAAAAGGCCACACUGGUGUGCC	5970

TRBC1-6	TRBC	EXON-1	+		AGGCCACACUGGUGUGCCUGGCCAC	5971
TRBC1-7	TRBC	EXON-1	+		GCCACAGGCUUCUUCCCCGACCACG	5972
TRBC1-8	TRBC	EXON-1	+		CUUCCCCGACCACGUGGAGCUGAGC	5973
TRBC1-9	TRBC	EXON-1	+		CCCCGACCACGUGGAGCUGAGCUGG	5974
TRBC1-10	TRBC	EXON-1	+		CCCGACCACGUGGAGCUGAGCUGGU	5975
TRBC1-11	TRBC	EXON-1	+		ACGUGGAGCUGAGCUGGUGGGUGAA	5976
TRBC1-12	TRBC	EXON-1	+		CGUGGAGCUGAGCUGGUGGGUGAAU	5977
TRBC1-13	TRBC	EXON-1	+		GAGCUGAGCUGGUGGGUGAAUGGGA	5978
TRBC1-14	TRBC	EXON-1	+		CUGAGCUGGUGGGUGAAUGGGAAGG	5979
TRBC1-15	TRBC	EXON-1	+		GGGUGAAUGGGAAGGAGGUGCACAG	5980
TRBC1-16	TRBC	EXON-1	+		GGUGAAUGGGAAGGAGGUGCACAGU	5981
TRBC1-17	TRBC	EXON-1	+		GUGAAUGGGAAGGAGGUGCACAGUG	5982
TRBC1-18	TRBC	EXON-1	+		GUCAGCACAGACCCGCAGCCCCUCA	5983
TRBC1-19	TRBC	EXON-1	+		CAGAUACUGCCUGAGCAGCCGCCUG	5984
TRBC1-20	TRBC	EXON-1	+		AGAUACUGCCUGAGCAGCCGCCUGA	5985
TRBC1-21	TRBC	EXON-1	+		UGCCUGAGCAGCCGCCUGAGGGUCU	5986
TRBC1-22	TRBC	EXON-1	+		CCGCCUGAGGGUCUCGGCCACCUUC	5987
TRBC1-23	TRBC	EXON-1	+		ACUUCCGCUGUCAAGUCCAGUUCUA	5988
TRBC1-24	TRBC	EXON-1	+		CUUCCGCUGUCAAGUCCAGUUCUAC	5989
TRBC1-25	TRBC	EXON-1	+		UGUCAAGUCCAGUUCUACGGGCUCU	5990
TRBC1-26	TRBC	EXON-1	+		CUACGGGCUCUCGGAGAAUGACGAG	5991
TRBC1-27	TRBC	EXON-1	+		CUCUCGGAGAAUGACGAGUGGACCC	5992
TRBC1-28	TRBC	EXON-1	+		GGAGAAUGACGAGUGGACCCAGGAU	5993
TRBC1-29	TRBC	EXON-1	+		GAGAAUGACGAGUGGACCCAGGAUA	5994
TRBC1-30	TRBC	EXON-1	+		CCCGUCACCCAGAUCGUCAGCGCCG	5995

TRBC1-31	TRBC	EXON-1	+		CACCCAGAUCGUCAGCGCCGAGGCC	5996
TRBC1-32	TRBC	EXON-1	+		ACCCAGAUCGUCAGCGCCGAGGCCU	5997
TRBC1-33	TRBC	EXON-1	+		CCCAGAUCGUCAGCGCCGAGGCCUG	5998
TRBC1-34	TRBC	EXON-1	+		UCAGCGCCGAGGCCUGGGGUAGAGC	5999
TRBC1-35	TRBC	EXON-1	+		CGAGGCCUGGGGUAGAGCAGGUGAG	6000
TRBC1-36	TRBC	EXON-1	+		GAGGCCUGGGGUAGAGCAGGUGAGU	6001
TRBC1-37	TRBC	EXON-1	+		AGGCCUGGGGUAGAGCAGGUGAGUG	6002
TRBC1-38	TRBC	EXON-1	+		UGGGGUAGAGCAGGUGAGUGGGGCC	6003
TRBC1-39	TRBC	EXON-1	+		GGGGUAGAGCAGGUGAGUGGGGCCU	6004
TRBC1-40	TRBC	EXON-1	+		GGGUAGAGCAGGUGAGUGGGGCCUG	6005
TRAC1-41	TRBC	EXON-1	-		AGGCCCCACUCACCUGCUCUACCCC	6006
TRAC1-42	TRBC	EXON-1	-		CACUCACCUGCUCUACCCCAGGCCU	6007
TRAC1-43	TRBC	EXON-1	-		ACCCCAGGCCUCGGCGCUGACGAUC	6008
TRAC1-44	TRBC	EXON-1	-		CCCCAGGCCUCGGCGCUGACGAUCU	6009
TRAC1-45	TRBC	EXON-1	-		GCCUCGGCGCUGACGAUCUGGGUGA	6010
TRAC1-46	TRBC	EXON-1	-		CCUCGGCGCUGACGAUCUGGGUGAC	6011
TRAC1-47	TRBC	EXON-1	-		GCGCUGACGAUCUGGGUGACGGGUU	6012
TRAC1-48	TRBC	EXON-1	-		CUGGGUGACGGGUUUGGCCCUAUCC	6013
TRAC1-49	TRBC	EXON-1	-		UGGGUGACGGGUUUGGCCCUAUCCU	6014
TRAC1-50	TRBC	EXON-1	-		GUCAUUCUCCGAGAGCCCGUAGAAC	6015
TRAC1-51	TRBC	EXON-1	-		GAGCCCGUAGAACUGGACUUGACAG	6016
TRAC1-52	TRBC	EXON-1	-		GUAGAACUGGACUUGACAGCGGAAG	6017
TRAC1-53	TRBC	EXON-1	-		CUGGACUUGACAGCGGAAGUGGUUG	6018
TRAC1-54	TRBC	EXON-1	-		UGGACUUGACAGCGGAAGUGGUUGC	6019
TRAC1-55	TRBC	EXON-1	-		GGACUUGACAGCGGAAGUGGUUGCG	6020

TRAC1-56	TRBC	EXON-1	-		GACUUGACAGCGGAAGUGGUUGCGG	6021
TRAC1-57	TRBC	EXON-1	-		AAGUGGUUGCGGGGGUUCUGCCAGA	6022
TRAC1-58	TRBC	EXON-1	-		UGGUUGCGGGGGUUCUGCCAGAAGG	6023
TRAC1-59	TRBC	EXON-1	-		CUGCCAGAAGGUGGCCGAGACCCUC	6024
TRAC1-60	TRBC	EXON-1	-		CCAGAAGGUGGCCGAGACCCUCAGG	6025
TRAC1-61	TRBC	EXON-1	-		GGCCGAGACCCUCAGGCGGCUGCUC	6026
TRAC1-62	TRBC	EXON-1	-		CUCAGGCGGCUGCUCAGGCAGUAUC	6027
TRAC1-63	TRBC	EXON-1	-		GCUCAGGCAGUAUCUGGAGUCAUUG	6028
TRAC1-64	TRBC	EXON-1	-		CUCAGGCAGUAUCUGGAGUCAUUGA	6029
TRAC1-65	TRBC	EXON-1	-		AGGCAGUAUCUGGAGUCAUUGAGGG	6030
TRAC1-66	TRBC	EXON-1	-		GGCAGUAUCUGGAGUCAUUGAGGGC	6031
TRAC1-67	TRBC	EXON-1	-		GUCAUUGAGGGCGGGCUGCUCCUUG	6032
TRAC1-68	TRBC	EXON-1	-		UCAUUGAGGGCGGGCUGCUCCUUGA	6033
TRAC1-69	TRBC	EXON-1	-		CAUUGAGGGCGGGCUGCUCCUUGAG	6034
TRAC1-70	TRBC	EXON-1	-		GGGCGGGCUGCUCCUUGAGGGGCUG	6035
TRAC1-71	TRBC	EXON-1	-		GGCGGGCUGCUCCUUGAGGGGCUGC	6036
TRAC1-72	TRBC	EXON-1	-		AUUCACCCACCAGCUCAGCUCCACG	6037
TRAC1-73	TRBC	EXON-1	-		ACCCACCAGCUCAGCUCCACGUGGU	6038
TRAC1-74	TRBC	EXON-1	-		CCCACCAGCUCAGCUCCACGUGGUC	6039
TRAC1-75	TRBC	EXON-1	-		CCACCAGCUCAGCUCCACGUGGUCG	6040
TRAC1-76	TRBC	EXON-1	-		UCCACGUGGUCGGGGAAGAAGCCUG	6041
TRAC1-77	TRBC	EXON-1	-		GUGGUCGGGGAAGAAGCCUGUGGCC	6042
TRAC1-78	TRBC	EXON-1	-		AAGCCUGUGGCCAGGCACACCAGUG	6043
TRAC1-79	TRBC	EXON-1	-		GGCCAGGCACACCAGUGUGGCCUUU	6044
TRAC1-80	TRBC	EXON-1	-		GCCAGGCACACCAGUGUGGCCUUUU	6045

TRAC1-81	TRBC	EXON-1	-		GCACACCAGUGUGGCCUUUUGGGUG	6046
TRAC1-82	TRBC	EXON-1	-		CACACCAGUGUGGCCUUUUGGGUGU	6047
TRAC1-83	TRBC	EXON-1	-		GGGUGUGGGAGAUCUCUGCUUCUGA	6048
TRAC1-84	TRBC	EXON-1	-		UCUGAUGGCUCAAACACAGCGACCU	6049
TRAC1-85	TRBC	EXON-1	-		CUGAUGGCUCAAACACAGCGACCUC	6050
TRAC1-86	TRBC	EXON-1	-		AUGGCUCAAACACAGCGACCUCGGG	6051
TRAC1-87	TRBC	EXON-1	-		UGGCUCAAACACAGCGACCUCGGGU	6052
TRAC1-88	TRBC	EXON-1	-		GACCUCGGGUGGGAACACCUUGUUC	6053
TRAC1-89	TRBC	EXON-1	-		GUGGGAACACCUUGUUCAGGUCCUC	6054
TRAC1-90	TRBC	EXON-1	-		AACACCUUGUUCAGGUCCUCUGGAA	6055
TRAC1-91	TRBC	EXON-1	-		ACACCUUGUUCAGGUCCUCUGGAAA	6056
TRAC1-92	TRBC	EXON-1	-		UGUUCAGGUCCUCUGGAAAGGGAAG	6057
TRAC1-93	TRBC	EXON-1	-		GUUCAGGUCCUCUGGAAAGGGAAGA	6058
TRAC1-94	TRBC	EXON-1	-		UUCAGGUCCUCUGGAAAGGGAAGAG	6059
TRBC1-95	TRBC	EXON-2	+		UUUCUUUCAGACUGUGGCUUUACCU	6060
TRBC1-96	TRBC	EXON-2	+		UUCUUUCAGACUGUGGCUUUACCUC	6061
TRAC1-97	TRBC	EXON-2	-		GUAAAGCCACAGUCUGAAAGAAAGC	6062
TRAC1-98	TRBC	EXON-2	-		UAAAGCCACAGUCUGAAAGAAAGCA	6063
TRBC1-99	TRBC	EXON-3	+		CCGUGCCAACAGUGUCCUACCAGCA	6064
TRBC1-100	TRBC	EXON-3	+		CGUGCCAACAGUGUCCUACCAGCAA	6065
TRBC1-101	TRBC	EXON-3	+		GUGCCAACAGUGUCCUACCAGCAAG	6066
TRBC1-102	TRBC	EXON-3	+		CCACCAUCCUCUAUGAGAUCCUGCU	6067
TRBC1-103	TRBC	EXON-3	+		CACCAUCCUCUAUGAGAUCCUGCUA	6068
TRBC1-104	TRBC	EXON-3	+		AUCCUCUAUGAGAUCCUGCUAGGGA	6069
TRBC1-105	TRBC	EXON-3	+		GGGAAGGCCACCCUGUAUGCUGUGC	6070

TRBC1-106	TRBC	EXON-3	+		GUGCUGGUCAGCGCCCUUGUGUUGA	6071
TRBC1-107	TRBC	EXON-3	+		GUCAGCGCCCUUGUGUUGAUGGCCA	6072
TRBC1-108	TRBC	EXON-3	+		CCUUGUGUUGAUGGCCAUGGUAAGC	6073
TRBC1-109	TRBC	EXON-3	+		UGUGUUGAUGGCCAUGGUAAGCAGG	6074
TRBC1-110	TRBC	EXON-3	+		GUGUUGAUGGCCAUGGUAAGCAGGA	6075
TRBC1-111	TRBC	EXON-3	+		UGAUGGCCAUGGUAAGCAGGAGGGC	6076
TRBC1-112	TRBC	EXON-3	+		GGCCAUGGUAAGCAGGAGGGCAGGA	6077
TRBC1-113	TRBC	EXON-3	+		GCCAUGGUAAGCAGGAGGGCAGGAU	6078
TRBC1-114	TRBC	EXON-3	+		CCAUGGUAAGCAGGAGGGCAGGAUG	6079
TRAC1-115	TRBC	EXON-3	-		CCCCAUCCUGCCCUCCUGCUUACCA	6080
TRAC1-116	TRBC	EXON-3	-		CCUGCUUACCAUGGCCAUCAACACA	6081
TRAC1-117	TRBC	EXON-3	-		CUGCUUACCAUGGCCAUCAACACAA	6082
TRAC1-118	TRBC	EXON-3	-		AAGGGCGCUGACCAGCACAGCAUAC	6083
TRAC1-119	TRBC	EXON-3	-		AGGGCGCUGACCAGCACAGCAUACA	6084
TRAC1-120	TRBC	EXON-3	-		GCGCUGACCAGCACAGCAUACAGGG	6085
TRAC1-121	TRBC	EXON-3	-		AGCAUACAGGGUGGCCUUCCCUAGC	6086
TRAC1-122	TRBC	EXON-3	-		GGCCUUCCCUAGCAGGAUCUCAUAG	6087
TRAC1-123	TRBC	EXON-3	-		UUCCCUAGCAGGAUCUCAUAGAGGA	6088
TRAC1-124	TRBC	EXON-3	-		CCUAGCAGGAUCUCAUAGAGGAUGG	6089
TRAC1-125	TRBC	EXON-3	-		GAUCUCAUAGAGGAUGGUGGCAGAC	6090
TRAC1-126	TRBC	EXON-3	-		GAUGGUGGCAGACAGGACCCCUUGC	6091
TRAC1-127	TRBC	EXON-3	-		GUGGCAGACAGGACCCCUUGCUGGU	6092
TRAC1-128	TRBC	EXON-3	-		GGACCCCUUGCUGGUAGGACACUGU	6093
TRAC1-129	TRBC	EXON-3	-		CCUUGCUGGUAGGACACUGUUGGCA	6094
TRAC1-130	TRBC	EXON-3	-		UGCUGGUAGGACACUGUUGGCACGG	6095

TRBC1-131	TRBC	EXON-4	+		GCAGGUCAAGAGAAAGGAUUUCUGA	6096
TRBC1-132	TRBC	EXON-4	+		GAGAAAGGAUUUCUGAAGGCAGCCC	6097
TRBC2-1	TRBC2	EXON-1	+		GACCUGAAAAACGUGUUCCCACCCG	6098
TRBC2-2	TRBC2	EXON-1	+		GAAGCAGAGAUCUCCCACACCCAAA	6099
TRBC2-3	TRBC2	EXON-1	+		AUCUCCCACACCCAAAAGGCCACAC	6100
TRBC2-4	TRBC2	EXON-1	+		ACCCAAAAGGCCACACUGGUAUGCC	6101
TRBC2-5	TRBC2	EXON-1	+		AGGCCACACUGGUAUGCCUGGCCAC	6102
TRBC2-6	TRBC2	EXON-1	+		GCCACAGGCUUCUACCCCGACCACG	6103
TRBC2-7	TRBC2	EXON-1	+		CUACCCCGACCACGUGGAGCUGAGC	6104
TRBC2-8	TRBC2	EXON-1	+		CCCCGACCACGUGGAGCUGAGCUGG	6105
TRBC2-9	TRBC2	EXON-1	+		CCCGACCACGUGGAGCUGAGCUGGU	6106
TRBC2-10	TRBC2	EXON-1	+		ACGUGGAGCUGAGCUGGUGGGUGAA	6107
TRBC2-11	TRBC2	EXON-1	+		CGUGGAGCUGAGCUGGUGGGUGAAU	6108
TRBC2-12	TRBC2	EXON-1	+		GAGCUGAGCUGGUGGGUGAAUGGGA	6109
TRBC2-13	TRBC2	EXON-1	+		CUGAGCUGGUGGGUGAAUGGGAAGG	6110
TRBC2-14	TRBC2	EXON-1	+		GGGUGAAUGGGAAGGAGGUGCACAG	6111
TRBC2-15	TRBC2	EXON-1	+		GGUGAAUGGGAAGGAGGUGCACAGU	6112
TRBC2-16	TRBC2	EXON-1	+		GUGAAUGGGAAGGAGGUGCACAGUG	6113
TRBC2-17	TRBC2	EXON-1	+		GUCAGCACAGACCCGCAGCCCCUCA	6114
TRBC2-18	TRBC2	EXON-1	+		CAGAUACUGCCUGAGCAGCCGCCUG	6115
TRBC2-19	TRBC2	EXON-1	+		AGAUACUGCCUGAGCAGCCGCCUGA	6116
TRBC2-20	TRBC2	EXON-1	+		UGCCUGAGCAGCCGCCUGAGGGUCU	6117
TRBC2-21	TRBC2	EXON-1	+		CCGCCUGAGGGUCUCGGCCACCUUC	6118
TRBC2-22	TRBC2	EXON-1	+		ACUUCCGCUGUCAAGUCCAGUUCUA	6119
TRBC2-23	TRBC2	EXON-1	+		CUUCCGCUGUCAAGUCCAGUUCUAC	6120

TRBC2-24	TRBC2	EXON-1	+		UGUCAAGUCCAGUUCUACGGGCUCU	6121
TRBC2-25	TRBC2	EXON-1	+		CUACGGGCUCUCGGAGAAUGACGAG	6122
TRBC2-26	TRBC2	EXON-1	+		CUCUCGGAGAAUGACGAGUGGACCC	6123
TRBC2-27	TRBC2	EXON-1	+		GGAGAAUGACGAGUGGACCCAGGAU	6124
TRBC2-28	TRBC2	EXON-1	+		GAGAAUGACGAGUGGACCCAGGAUA	6125
TRBC2-29	TRBC2	EXON-1	+		CCCGUCACCCAGAUCGUCAGCGCCG	6126
TRBC2-30	TRBC2	EXON-1	+		CACCCAGAUCGUCAGCGCCGAGGCC	6127
TRBC2-31	TRBC2	EXON-1	+		ACCCAGAUCGUCAGCGCCGAGGCCU	6128
TRBC2-32	TRBC2	EXON-1	+		CCCAGAUCGUCAGCGCCGAGGCCUG	6129
TRBC2-33	TRBC2	EXON-1	+		UCAGCGCCGAGGCCUGGGGUAGAGC	6130
TRBC2-34	TRBC2	EXON-1	+		CGAGGCCUGGGGUAGAGCAGGUGAG	6131
TRBC2-35	TRBC2	EXON-1	+		GAGGCCUGGGGUAGAGCAGGUGAGU	6132
TRBC2-36	TRBC2	EXON-1	+		AGGCCUGGGGUAGAGCAGGUGAGUG	6133
TRBC2-37	TRBC2	EXON-1	+		UGGGGUAGAGCAGGUGAGUGGGGCC	6134
TRBC2-38	TRBC2	EXON-1	+		GGGGUAGAGCAGGUGAGUGGGGCCU	6135
TRBC2-39	TRBC2	EXON-1	+		GGGUAGAGCAGGUGAGUGGGGCCUG	6136
TRAC2-40	TRBC2	EXON-1	-		AGGCCCCACUCACCUGCUCUACCCC	6137
TRAC2-41	TRBC2	EXON-1	-		CACUCACCUGCUCUACCCCAGGCCU	6138
TRAC2-42	TRBC2	EXON-1	-		ACCCCAGGCCUCGGCGCUGACGAUC	6139
TRAC2-43	TRBC2	EXON-1	-		CCCCAGGCCUCGGCGCUGACGAUCU	6140
TRAC2-44	TRBC2	EXON-1	-		GCCUCGGCGCUGACGAUCUGGGUGA	6141
TRAC2-45	TRBC2	EXON-1	-		CCUCGGCGCUGACGAUCUGGGUGAC	6142
TRAC2-46	TRBC2	EXON-1	-		GCGCUGACGAUCUGGGUGACGGGUU	6143
TRAC2-47	TRBC2	EXON-1	-		CUGGGUGACGGGUUUGGCCCUAUCC	6144
TRAC2-48	TRBC2	EXON-1	-		UGGGUGACGGGUUUGGCCCUAUCCU	6145

TRAC2-49	TRBC2	EXON-1	-		GUCAUUCUCCGAGAGCCCGUAGAAC	6146
TRAC2-50	TRBC2	EXON-1	-		GAGCCCGUAGAACUGGACUUGACAG	6147
TRAC2-51	TRBC2	EXON-1	-		GUAGAACUGGACUUGACAGCGGAAG	6148
TRAC2-52	TRBC2	EXON-1	-		CUGGACUUGACAGCGGAAGUGGUUG	6149
TRAC2-53	TRBC2	EXON-1	-		UGGACUUGACAGCGGAAGUGGUUGC	6150
TRAC2-54	TRBC2	EXON-1	-		GGACUUGACAGCGGAAGUGGUUGCG	6151
TRAC2-55	TRBC2	EXON-1	-		GACUUGACAGCGGAAGUGGUUGCGG	6152
TRAC2-56	TRBC2	EXON-1	-		AAGUGGUUGCGGGGGUUCUGCCAGA	6153
TRAC2-57	TRBC2	EXON-1	-		UGGUUGCGGGGGUUCUGCCAGAAGG	6154
TRAC2-58	TRBC2	EXON-1	-		CUGCCAGAAGGUGGCCGAGACCCUC	6155
TRAC2-59	TRBC2	EXON-1	-		CCAGAAGGUGGCCGAGACCCUCAGG	6156
TRAC2-60	TRBC2	EXON-1	-		GGCCGAGACCCUCAGGCGGCUGCUC	6157
TRAC2-61	TRBC2	EXON-1	-		CUCAGGCGGCUGCUCAGGCAGUAUC	6158
TRAC2-62	TRBC2	EXON-1	-		GCUCAGGCAGUAUCUGGAGUCAUUG	6159
TRAC2-63	TRBC2	EXON-1	-		CUCAGGCAGUAUCUGGAGUCAUUGA	6160
TRAC2-64	TRBC2	EXON-1	-		AGGCAGUAUCUGGAGUCAUUGAGGG	6161
TRAC2-65	TRBC2	EXON-1	-		GGCAGUAUCUGGAGUCAUUGAGGGC	6162
TRAC2-66	TRBC2	EXON-1	-		GUCAUUGAGGGCGGGCUGCUCCUUG	6163
TRAC2-67	TRBC2	EXON-1	-		UCAUUGAGGGCGGGCUGCUCCUUGA	6164
TRAC2-68	TRBC2	EXON-1	-		CAUUGAGGGCGGGCUGCUCCUUGAG	6165
TRAC2-69	TRBC2	EXON-1	-		GGGCGGGCUGCUCCUUGAGGGGCUG	6166
TRAC2-70	TRBC2	EXON-1	-		GGCGGGCUGCUCCUUGAGGGGCUGC	6167
TRAC2-71	TRBC2	EXON-1	-		AUUCACCCACCAGCUCAGCUCCACG	6168
TRAC2-72	TRBC2	EXON-1	-		ACCCACCAGCUCAGCUCCACGUGGU	6169
TRAC2-73	TRBC2	EXON-1	-		CCCACCAGCUCAGCUCCACGUGGUC	6170

TRAC2-74	TRBC2	EXON-1	-		CCACCAGCUCAGCUCCACGUGGUCG	6171
TRAC2-75	TRBC2	EXON-1	-		UCCACGUGGUCGGGGUAGAAGCCUG	6172
TRAC2-76	TRBC2	EXON-1	-		GUGGUCGGGGUAGAAGCCUGUGGCC	6173
TRAC2-77	TRBC2	EXON-1	-		AAGCCUGUGGCCAGGCAUACCAGUG	6174
TRAC2-78	TRBC2	EXON-1	-		GGCCAGGCAUACCAGUGUGGCCUUU	6175
TRAC2-79	TRBC2	EXON-1	-		GCCAGGCAUACCAGUGUGGCCUUUU	6176
TRAC2-80	TRBC2	EXON-1	-		GCAUACCAGUGUGGCCUUUUGGGUG	6177
TRAC2-81	TRBC2	EXON-1	-		CAUACCAGUGUGGCCUUUUGGGUGU	6178
TRAC2-82	TRBC2	EXON-1	-		GGGUGUGGGAGAUCUCUGCUUCUGA	6179
TRAC2-83	TRBC2	EXON-1	-		UCUGAUGGCUCAAACACAGCGACCU	6180
TRAC2-84	TRBC2	EXON-1	-		CUGAUGGCUCAAACACAGCGACCUC	6181
TRAC2-85	TRBC2	EXON-1	-		AUGGCUCAAACACAGCGACCUCGGG	6182
TRAC2-86	TRBC2	EXON-1	-		UGGCUCAAACACAGCGACCUCGGGU	6183
TRAC2-87	TRBC2	EXON-1	-		GACCUCGGGUGGGAACACGUUUUUC	6184
TRAC2-88	TRBC2	EXON-1	-		GUGGGAACACGUUUUUCAGGUCCUC	6185
TRAC2-89	TRBC2	EXON-1	-		AACACGUUUUUCAGGUCCUCUGGAA	6186
TRAC2-90	TRBC2	EXON-1	-		ACACGUUUUUCAGGUCCUCUGGAAA	6187
TRAC2-91	TRBC2	EXON-1	-		UUUUCAGGUCCUCUGGAAAGGGAAG	6188
TRAC2-92	TRBC2	EXON-1	-		GGUCCUCUGGAAAGGGAAGAGGUAA	6189
TRAC2-93	TRBC2	EXON-1	-		GUCCUCUGGAAAGGGAAGAGGUAAU	6190
TRAC2-94	TRBC2	EXON-1	-		UCCUCUGGAAAGGGAAGAGGUAAUG	6191
TRBC2-95	TRBC2	EXON-2	+		UUCUUUCAGACUGUGGCUUCACCUC	6192
TRAC2-96	TRBC2	EXON-2	-		GUGAAGCCACAGUCUGAAAGAAAAC	6193
TRAC2-97	TRBC2	EXON-2	-		UGAAGCCACAGUCUGAAAGAAAACA	6194
TRAC2-98	TRBC2	EXON-2	-		GAAGCCACAGUCUGAAAGAAAACAG	6195

TRBC2-99	TRBC 2	EXON-3	+		UCUUGUCAACAGAG UCUUACCAGCA	6196
TRBC2-100	TRBC 2	EXON-3	+		CUUGUCAACAGAGU CUUACCAGCAA	6197
TRBC2-101	TRBC 2	EXON-3	+		UUGUCAACAGAGUC UUACCAGCAAG	6198
TRBC2-102	TRBC 2	EXON-3	+		CCACCAUCCUCUAU GAGAUCUUGCU	6199
TRBC2-103	TRBC 2	EXON-3	+		CACCAUCCUCUAUG AGAUCUUGCUA	6200
TRBC2-104	TRBC 2	EXON-3	+		AUCCUCUAUGAGAU CUUGCUAGGGA	6201
TRBC2-105	TRBC 2	EXON-3	+		GGGAAGGCCACCUU GUAUGCCGUGC	6202
TRBC2-106	TRBC 2	EXON-3	+		GUGCUGGUCAGUGC CCUCGUGCUGA	6203
TRBC2-107	TRBC 2	EXON-3	+		GUCAGUGCCCUCGU GCUGAUGGCCA	6204
TRBC2-108	TRBC 2	EXON-3	+		UGCCCUCGUGCUGA UGGCCAUGGUA	6205
TRBC2-109	TRBC 2	EXON-3	+		CCUCGUGCUGAUGG CCAUGGUAAGG	6206
TRBC2-110	TRBC 2	EXON-3	+		CGUGCUGAUGGCCA UGGUAAGGAGG	6207
TRBC2-111	TRBC 2	EXON-3	+		GUGCUGAUGGCCAU GGUAAGGAGGA	6208
TRBC2-112	TRBC 2	EXON-3	+		CUGAUGGCCAUGGU AAGGAGGAGGG	6209
TRBC2-113	TRBC 2	EXON-3	+		UGAUGGCCAUGGUA AGGAGGAGGGU	6210
TRBC2-114	TRBC 2	EXON-3	+		GCCAUGGUAAGGAG GAGGGUGGGAU	6211
TRBC2-115	TRBC 2	EXON-3	+		CCAUGGUAAGGAGG AGGGUGGGAUA	6212
TRAC2-116	TRBC 2	EXON-3	-		CCCUAUCCCACCCU CCUCCUUACCA	6213
TRAC2-117	TRBC 2	EXON-3	-		CCUCCUUACCAUGG CCAUCAGCACG	6214
TRAC2-118	TRBC 2	EXON-3	-		CUCCUUACCAUGGC CAUCAGCACGA	6215
TRAC2-119	TRBC 2	EXON-3	-		AUCAGCACGAGGGC ACUGACCAGCA	6216
TRAC2-120	TRBC 2	EXON-3	-		AGGGCACUGACCAG CACGGCAUACA	6217
TRAC2-121	TRBC 2	EXON-3	-		GCACUGACCAGCAC GGCAUACAAGG	6218
TRAC2-122	TRBC 2	EXON-3	-		GGCCUUCCCUAGCA AGAUCUCAUAG	6219
TRAC2-123	TRBC 2	EXON-3	-		UUCCCUAGCAAGAU CUCAUAGAGGA	6220

TRAC2-124	TRBC2	EXON-3	-		CCUAGCAAGAUCUCAUAGAGGAUGG	6221
TRAC2-125	TRBC2	EXON-3	-		GAUCUCAUAGAGGAUGGUGGCAGAC	6222
TRAC2-126	TRBC2	EXON-3	-		GAUGGUGGCAGACAGGACCCCUUGC	6223
TRBC2-127	TRBC2	EXON-4	+		UUCUCUCUUCCACAGGUCAAGAGAA	6224
TRBC2-128	TRBC2	EXON-4	+		CACAGGUCAAGAGAAAGGAUUCCAG	6225
TRAC2-129	TRBC2	EXON-4	-		CUCUGGAAUCCUUUCUCUUGACCUG	6226
CD52-1	CD52	EXON-1	+		UUCCUCCUACUCACCAUCAGCCUCC	6227
CD52-2	CD52	EXON-1	+		CUACUCACCAUCAGCCUCCUGGUUA	6228
CD52-3	CD52	EXON-1	+		ACCAUCAGCCUCCUGGUUAUGGUAC	6229
CD52-4	CD52	EXON-1	+		UUAUGGUACAGGUAAGAGCAACGCC	6230
CD52-5	CD52	EXON-1	-		CGUUGCUCUUACCUGUACCAUAACC	6231
CD52-6	CD52	EXON-1	-		UGCUCUUACCUGUACCAUAACCAGG	6232
CD52-7	CD52	EXON-1	-		ACCUGUACCAUAACCAGGAGGCUGA	6233
CD52-8	CD52	EXON-1	-		CAUAACCAGGAGGCUGAUGGUGAGU	6234
CD52-9	CD52	EXON-1	-		AACCAGGAGGCUGAUGGUGAGUAGG	6235
CD52-10	CD52	EXON-1	-		GAGGCUGAUGGUGAGUAGGAGGAAG	6236
CD52-11	CD52	EXON-1	-		AGGAGGAAGAGGAAGCGCUUCAUUU	6237
CD52-12	CD52	EXON-1	-		GGAAGAGGAAGCGCUUCAUUUUGGU	6238
CD52-13	CD52	EXON-1	-		GCGCUUCAUUUUGGUAGGAUCUUCG	6239
CD52-14	CD52	EXON-1	-		UUUGGUAGGAUCUUCGUGGCUGUCU	6240
CD52-15	CD52	EXON-1	-		GUGGCUGUCUUGGUAGCAGCUUUUU	6241
CD52-16	CD52	EXON-1	-		UGGUAGCAGCUUUUUAGGUGAUCUC	6242
CD52-17	CD52	EXON-1	-		GGUAGCAGCUUUUUAGGUGAUCUCA	6243
CD52-18	CD52	EXON-1	-		CUUUUUAGGUGAUCUCAGGGCUGUC	6244
CD52-19	CD52	EXON-1	-		UUUAGGUGAUCUCAGGGCUGUCUGG	6245

CD52-20	CD52	EXON-1	-		CUCAGGGCUGUCUGGAGGCUUCUUU	6246
CD52-21	CD52	EXON-1	-		CUUUUGGUUUAGCUGCUUUUGAACC	6247
CD52-22	CD52	EXON-1	-		UUGGUUUAGCUGCUUUUGAACCAGG	6248
CD52-23	CD52	EXON-1	-		UAGCUGCUUUUGAACCAGGAGGCAG	6249
CD52-24	CD52	EXON-1	-		CUGCUUUUGAACCAGGAGGCAGAGG	6250
CD52-25	CD52	EXON-1	-		CUUUUGAACCAGGAGGCAGAGGAGG	6251
CD52-26	CD52	EXON-2	+		CACUUCUCCUCCUACAGAUACAAAC	6252
CD52-27	CD52	EXON-2	+		UCCUACAGAUACAAACUGGACUCUC	6253
CD52-28	CD52	EXON-2	+		GCCCCUCAGCAUCCAGCAACAUAAG	6254
CD52-29	CD52	EXON-2	+		CCUCAGCAUCCAGCAACAUAAGCGG	6255
CD52-30	CD52	EXON-2	+		AGCGGAGGCAUUUUCCUUUUCUUCG	6256
CD52-31	CD52	EXON-2	+		UAAUCCACCUCUUCUGCUUCAGUUG	6257
CD52-32	CD52	EXON-2	+		CUCGCAAGAGAAUCCCCUCCAUCUU	6258
CD52-33	CD52	EXON-2	+		UCGCAAGAGAAUCCCCUCCAUCUUU	6259
CD52-34	CD52	EXON-2	+		CAAGAGAAUCCCCUCCAUCUUUGGG	6260
CD52-35	CD52	EXON-2	+		AAGAGAAUCCCCUCCAUCUUUGGGA	6261
CD52-36	CD52	EXON-2	+		AGAGAAUCCCCUCCAUCUUUGGGAG	6262
CD52-37	CD52	EXON-2	+		GGAGGGGUUGAUGCCAGACAUCACC	6263
CD52-38	CD52	EXON-2	+		ACAUCACCAGGUUGUAGAAGUUGAC	6264
CD52-39	CD52	EXON-2	+		UUGUAGAAGUUGACAGGCAGUGCCA	6265
CD52-40	CD52	EXON-2	+		UGUAGAAGUUGACAGGCAGUGCCAU	6266
CD52-41	CD52	EXON-2	+		GUAGAAGUUGACAGGCAGUGCCAUG	6267
CD52-42	CD52	EXON-2	+		UAGAAGUUGACAGGCAGUGCCAUGG	6268
CD52-43	CD52	EXON-2	+		GUGCCAUGGGGGCAACAGCCAAAAU	6269
CD52-44	CD52	EXON-2	+		UGCCAUGGGGGCAACAGCCAAAAUA	6270

CD52-45	CD52	EXON-2	+		GCCAUGGGGGCAACAGCCAAAAUAG	6271
CD52-46	CD52	EXON-2	+		CCAUGGGGGCAACAGCCAAAAUAGG	6272
CD52-47	CD52	EXON-2	+		CAUGGGGGCAACAGCCAAAAUAGGG	6273
CD52-48	CD52	EXON-2	+		AGCCAAAAUAGGGGGGUAAUGAUGU	6274
CD52-49	CD52	EXON-2	+		GCCAAAAUAGGGGGGUAAUGAUGUA	6275
CD52-50	CD52	EXON-2	+		CCAAAAUAGGGGGGUAAUGAUGUAG	6276
CD52-51	CD52	EXON-2	+		AUGUAGGGGCCAAGCAGUGCCCAGC	6277
CD52-52	CD52	EXON-2	+		UGUAGGGGCCAAGCAGUGCCCAGCU	6278
CD52-53	CD52	EXON-2	+		GUAGGGGCCAAGCAGUGCCCAGCUG	6279
CD52-54	CD52	EXON-2	+		UAGGGGCCAAGCAGUGCCCAGCUGG	6280
CD52-55	CD52	EXON-2	+		AAUAAAGUUACCCUUGUACUUGCAG	6281
CD52-56	CD52	EXON-2	+		AUAAAGUUACCCUUGUACUUGCAGU	6282
CD52-57	CD52	EXON-2	+		UAAAGUUACCCUUGUACUUGCAGUG	6283
CD52-58	CD52	EXON-2	+		UGUACUUGCAGUGGGGUCCUGCUUG	6284
CD52-59	CD52	EXON-2	+		GCAGUGGGGUCCUGCUUGUGGUUAC	6285
CD52-60	CD52	EXON-2	-		GUAGGGAUGUCCAGUAACCACAAGC	6286
CD52-61	CD52	EXON-2	-		CAAGCAGGACCCCACUGCAAGUACA	6287
CD52-62	CD52	EXON-2	-		AAGCAGGACCCCACUGCAAGUACAA	6288
CD52-63	CD52	EXON-2	-		AAGGGUAACUUUAUUGACCCCCAGC	6289
CD52-64	CD52	EXON-2	-		AGGGUAACUUUAUUGACCCCCAGCU	6290
CD52-65	CD52	EXON-2	-		UAUUGACCCCCAGCUGGGCACUGCU	6291
CD52-66	CD52	EXON-2	-		CCCCUACAUCAUUACCCCCCUAUUU	6292
CD52-67	CD52	EXON-2	-		CCCCCUAUUUUGGCUGUUGCCCCCA	6293
CD52-68	CD52	EXON-2	-		GCACUGCCUGUCAACUUCUACAACC	6294
CD52-69	CD52	EXON-2	-		UCAACUUCUACAACCUGGUGAUGUC	6295

CD52-70	CD52	EXON-2	-		GUCUGGCAUCAACCCCUCCCAAAGA	6296
CD52-71	CD52	EXON-2	-		UGGCAUCAACCCCUCCCAAAGAUGG	6297
CD52-72	CD52	EXON-2	-		GGCAUCAACCCCUCCCAAAGAUGGA	6298
CD52-73	CD52	EXON-2	-		GCAUCAACCCCUCCCAAAGAUGGAG	6299
CD52-74	CD52	EXON-2	-		AUGGAGGGGAUUCUCUUGCGAGUGA	6300
CD52-75	CD52	EXON-2	-		GAGGGGAUUCUCUUGCGAGUGAUGG	6301
CD52-76	CD52	EXON-2	-		UGCGAGUGAUGGUGGCAGCUGUUUC	6302
CD52-77	CD52	EXON-2	-		GCGAGUGAUGGUGGCAGCUGUUUCA	6303
CD52-78	CD52	EXON-2	-		CGAGUGAUGGUGGCAGCUGUUUCAG	6304
CD52-79	CD52	EXON-2	-		GAGUGAUGGUGGCAGCUGUUUCAGG	6305
CD52-80	CD52	EXON-2	-		UGGUGGCAGCUGUUUCAGGGGGCAC	6306
CD52-81	CD52	EXON-2	-		GGUGGCAGCUGUUUCAGGGGGCACA	6307
CD52-82	CD52	EXON-2	-		AGCUGUUUCAGGGGGCACAGGGCUA	6308
CD52-83	CD52	EXON-2	-		CGUGUCACCUCAACUGAAGCAGAAG	6309
CD52-84	CD52	EXON-2	-		GUCACCUCAACUGAAGCAGAAGAGG	6310
CD52-85	CD52	EXON-2	-		CAACUGAAGCAGAAGAGGUGGAUUA	6311
CD52-86	CD52	EXON-2	-		AAGCAGAAGAGGUGGAUUAUGGCAU	6312
CD52-87	CD52	EXON-2	-		GAUUAUGGCAUUGGCCACGAAGAAA	6313
CD52-88	CD52	EXON-2	-		AGGAAAAUGCCUCCGCUUAUGUUGC	6314
CD52-89	CD52	EXON-2	-		CCUCCGCUUAUGUUGCUGGAUGCUG	6315
CD52-90	CD52	EXON-2	-		CUCCGCUUAUGUUGCUGGAUGCUGA	6316
CD52-91	CD52	EXON-2	-		UCCGCUUAUGUUGCUGGAUGCUGAG	6317
CD52-92	CD52	EXON-2	-		AUGUUGCUGGAUGCUGAGGGGCUGC	6318
CD52-93	CD52	EXON-2	-		GCUGGAUGCUGAGGGGCUGCUGGUU	6319
CD52-94	CD52	EXON-2	-		GAUGCUGAGGGGCUGCUGGUUUGGC	6320

CD52-95	CD52	EXON-2	-		UCCUGAGAGUCCAGUUUGUAUCUGU	6321
CD52-96	CD52	EXON-2	-		UGAGAGUCCAGUUUGUAUCUGUAGG	6322
CD52-97	CD52	EXON-2	-		CAGUUUGUAUCUGUAGGAGGAGAAG	6323
CD52-98	CD52	EXON-2	-		AGUUUGUAUCUGUAGGAGGAGAAGU	6324
FKBP1A-1	FKBP1A	EXON-1	+		CGCGCGCCGUGUGGGGCGCGCACGC	6325
FKBP1A-2	FKBP1A	EXON-1	+		GCGCGCCGUGUGGGGCGCGCACGCA	6326
FKBP1A-3	FKBP1A	EXON-1	+		GCCGUGUGGGGCGCGCACGCAGGGC	6327
FKBP1A-4	FKBP1A	EXON-1	+		CCGUGUGGGGCGCGCACGCAGGGCU	6328
FKBP1A-5	FKBP1A	EXON-1	+		GGGCGCGCACGCAGGGCUGGGCGUG	6329
FKBP1A-6	FKBP1A	EXON-1	+		GGCGCGCACGCAGGGCUGGGCGUGA	6330
FKBP1A-7	FKBP1A	EXON-1	+		GCGCGCACGCAGGGCUGGGCGUGAG	6331
FKBP1A-8	FKBP1A	EXON-1	+		CGCGCACGCAGGGCUGGGCGUGAGG	6332
FKBP1A-9	FKBP1A	EXON-1	+		GGCGUGAGGGGGCGUGCGCGUGCGC	6333
FKBP1A-10	FKBP1A	EXON-1	+		GUGCGCGUGCGCAGGCGACGCGCCG	6334
FKBP1A-11	FKBP1A	EXON-1	+		UGCGCAGGCGACGCGCCGAGGUACU	6335
FKBP1A-12	FKBP1A	EXON-1	+		CGCGCCGAGGUACUAGGCAGAGCCG	6336
FKBP1A-13	FKBP1A	EXON-1	+		UAGGCAGAGCCGUGGAACCGCCGCC	6337
FKBP1A-14	FKBP1A	EXON-1	+		CGUGGAACCGCCGCCAGGUCGCUGU	6338
FKBP1A-15	FKBP1A	EXON-1	+		GCCCGCUCAGCGUCCGCCGCCGCCA	6339
FKBP1A-16	FKBP1A	EXON-1	+		CCCGCUCAGCGUCCGCCGCCGCCAU	6340
FKBP1A-17	FKBP1A	EXON-1	+		GCGUCCGCCGCCGCCAUGGGAGUGC	6341
FKBP1A-18	FKBP1A	EXON-1	+		UCCGCCGCCGCCAUGGGAGUGCAGG	6342
FKBP1A-19	FKBP1A	EXON-1	+		GAGUGCAGGUGGAAACCAUCUCCCC	6343
FKBP1A-20	FKBP1A	EXON-1	+		AGGUGGAAACCAUCUCCCCAGGAGA	6344
FKBP1A-21	FKBP1A	EXON-1	+		CAUCUCCCCAGGAGACGGUGAGUAG	6345

FKBP1A-22	FKBP1A	EXON-1	+		CCAGGAGACGGUGAGUAGUGGCGCG	6346
FKBP1A-23	FKBP1A	EXON-1	+		GGAGACGGUGAGUAGUGGCGCGCGG	6347
FKBP1A-24	FKBP1A	EXON-1	-		CCGCGCGCCACUACUCACCGUCUCC	6348
FKBP1A-25	FKBP1A	EXON-1	-		CGCGCGCCACUACUCACCGUCUCCU	6349
FKBP1A-26	FKBP1A	EXON-1	-		GCGCGCCACUACUCACCGUCUCCUG	6350
FKBP1A-27	FKBP1A	EXON-1	-		CACUACUCACCGUCUCCUGGGGAGA	6351
FKBP1A-28	FKBP1A	EXON-1	-		GAGAUGGUUUCCACCUGCACUCCCA	6352
FKBP1A-29	FKBP1A	EXON-1	-		AUGGUUUCCACCUGCACUCCCAUGG	6353
FKBP1A-30	FKBP1A	EXON-1	-		GUUUCCACCUGCACUCCCAUGGCGG	6354
FKBP1A-31	FKBP1A	EXON-1	-		UCCACCUGCACUCCCAUGGCGGCGG	6355
FKBP1A-32	FKBP1A	EXON-1	-		UCCCAUGGCGGCGGCGGACGCUGAG	6356
FKBP1A-33	FKBP1A	EXON-1	-		CCCAUGGCGGCGGCGGACGCUGAGC	6357
FKBP1A-34	FKBP1A	EXON-1	-		AUGGCGGCGGCGGACGCUGAGCGGG	6358
FKBP1A-35	FKBP1A	EXON-1	-		UGGCGGCGGCGGACGCUGAGCGGGC	6359
FKBP1A-36	FKBP1A	EXON-1	-		CGGCGGCGGACGCUGAGCGGGCGGG	6360
FKBP1A-37	FKBP1A	EXON-1	-		GACGCUGAGCGGGCGGGCGGCGCGA	6361
FKBP1A-38	FKBP1A	EXON-1	-		ACGCUGAGCGGGCGGGCGGCGCGAC	6362
FKBP1A-39	FKBP1A	EXON-1	-		CUGAGCGGGCGGGCGGCGCGACGGG	6363
FKBP1A-40	FKBP1A	EXON-1	-		CGGGCGGGCGGCGCGACGGGCGGCG	6364
FKBP1A-41	FKBP1A	EXON-1	-		CGGGCGGCGUGGACCAACAGCGACC	6365
FKBP1A-42	FKBP1A	EXON-1	-		GCGGCGUGGACCAACAGCGACCUGG	6366
FKBP1A-43	FKBP1A	EXON-1	-		GCGUGGACCAACAGCGACCUGGCGG	6367
FKBP1A-44	FKBP1A	EXON-1	-		CAACAGCGACCUGGCGGCGGUUCCA	6368
FKBP1A-45	FKBP1A	EXON-1	-		GGUUCCACGGCUCUGCCUAGUACCU	6369
FKBP1A-46	FKBP1A	EXON-1	-		CCCAGCCCUGCGUGCGCGCCCCACA	6370

FKBP1A-47	FKBP1A	EXON-2	+		CCUCAGGGCGCACCUUCCCCAAGCG	6371
FKBP1A-48	FKBP1A	EXON-2	+		UUCCCCAAGCGCGGCCAGACCUGCG	6372
FKBP1A-49	FKBP1A	EXON-2	+		GCCAGACCUGCGUGGUGCACUACAC	6373
FKBP1A-50	FKBP1A	EXON-2	+		UGCGUGGUGCACUACACCGGUGAGU	6374
FKBP1A-51	FKBP1A	EXON-2	+		GCGUGGUGCACUACACCGGUGAGUC	6375
FKBP1A-52	FKBP1A	EXON-2	+		CGUGGUGCACUACACCGGUGAGUCG	6376
FKBP1A-53	FKBP1A	EXON-2	+		GUGGUGCACUACACCGGUGAGUCGG	6377
FKBP1A-54	FKBP1A	EXON-2	+		CUACACCGGUGAGUCGGGGGCCCAG	6378
FKBP1A-55	FKBP1A	EXON-2	+		UACACCGGUGAGUCGGGGGCCCAGC	6379
FKBP1A-56	FKBP1A	EXON-2	+		ACACCGGUGAGUCGGGGGCCCAGCG	6380
FKBP1A-57	FKBP1A	EXON-2	+		CCGGUGAGUCGGGGGCCCAGCGGGG	6381
FKBP1A-58	FKBP1A	EXON-2	-		GACUCACCGGUGUAGUGCACCACGC	6382
FKBP1A-59	FKBP1A	EXON-2	-		ACCGGUGUAGUGCACCACGCAGGUC	6383
FKBP1A-60	FKBP1A	EXON-2	-		UGCACCACGCAGGUCUGGCCGCGCU	6384
FKBP1A-61	FKBP1A	EXON-2	-		GCACCACGCAGGUCUGGCCGCGCUU	6385
FKBP1A-62	FKBP1A	EXON-2	-		CACCACGCAGGUCUGGCCGCGCUUG	6386
FKBP1A-63	FKBP1A	EXON-2	-		ACGCAGGUCUGGCCGCGCUUGGGGA	6387
FKBP1A-64	FKBP1A	EXON-2	-		CCGCGCUUGGGGAAGGUGCGCCCUG	6388
FKBP1A-65	FKBP1A	EXON-2	-		AAGGUGCGCCCUGAGGAGACAGAGA	6389
FKBP1A-66	FKBP1A	EXON-2	-		AGGUGCGCCCUGAGGAGACAGAGAC	6390
FKBP1A-67	FKBP1A	EXON-3	+		UCUUUUUCACAGGGAUGCUUGAAGA	6391
FKBP1A-68	FKBP1A	EXON-3	+		AGAUGGAAAGAAAUUUGAUUCCUCC	6392
FKBP1A-69	FKBP1A	EXON-3	+		GAUGGAAAGAAAUUUGAUUCCUCCC	6393
FKBP1A-70	FKBP1A	EXON-3	+		GAAACAAGCCCUUUAAGUUUAUGCU	6394
FKBP1A-71	FKBP1A	EXON-3	+		CCCUUUAAGUUUAUGCUAGGCAAGC	6395

FKBP1A-72	FKBP1A	EXON-3	+		UUUAAGUUUAUGCUAGGCAAGCAGG	6396
FKBP1A-73	FKBP1A	EXON-3	+		UGCUAGGCAAGCAGGAGGUGAUCCG	6397
FKBP1A-74	FKBP1A	EXON-3	+		AGGCAAGCAGGAGGUGAUCCGAGGC	6398
FKBP1A-75	FKBP1A	EXON-3	+		GGCAAGCAGGAGGUGAUCCGAGGCU	6399
FKBP1A-76	FKBP1A	EXON-3	+		AGGAGGUGAUCCGAGGCUGGGAAGA	6400
FKBP1A-77	FKBP1A	EXON-3	+		GGAGGUGAUCCGAGGCUGGGAAGAA	6401
FKBP1A-78	FKBP1A	EXON-3	+		GAGGUGAUCCGAGGCUGGGAAGAAG	6402
FKBP1A-79	FKBP1A	EXON-3	+		CGAGGCUGGGAAGAAGGGGUUGCCC	6403
FKBP1A-80	FKBP1A	EXON-3	-		AACAAAACAAAUGAGAGAGCAUACC	6404
FKBP1A-81	FKBP1A	EXON-3	-		ACAAAACAAAUGAGAGAGCAUACCU	6405
FKBP1A-82	FKBP1A	EXON-3	-		CUGGGCAACCCCUUCUUCCCAGCCU	6406
FKBP1A-83	FKBP1A	EXON-3	-		UCCUGCUUGCCUAGCAUAAACUUAA	6407
FKBP1A-84	FKBP1A	EXON-3	-		CCUGCUUGCCUAGCAUAAACUUAAA	6408
FKBP1A-85	FKBP1A	EXON-3	-		AAACUUAAAGGGCUUGUUUCUGUCC	6409
FKBP1A-86	FKBP1A	EXON-3	-		AACUUAAAGGGCUUGUUUCUGUCCC	6410
FKBP1A-87	FKBP1A	EXON-3	-		UUAAAGGGCUUGUUUCUGUCCCGGG	6411
FKBP1A-88	FKBP1A	EXON-4	+		UCCUUGUUCUUUUCACAGAUGAGUG	6412
FKBP1A-89	FKBP1A	EXON-4	+		CCUUGUUCUUUUCACAGAUGAGUGU	6413
FKBP1A-90	FKBP1A	EXON-4	+		UGACUAUAUCUCCAGAUUAUGCCUA	6414
FKBP1A-91	FKBP1A	EXON-4	+		CUCCAGAUUAUGCCUAUGGUGCCAC	6415
FKBP1A-92	FKBP1A	EXON-4	+		UCCAGAUUAUGCCUAUGGUGCCACU	6416
FKBP1A-93	FKBP1A	EXON-4	+		AUGCCUAUGGUGCCACUGGGCACCC	6417
FKBP1A-94	FKBP1A	EXON-4	+		CCACAUGCCACUCUCGUCUUCGAUG	6418
FKBP1A-95	FKBP1A	EXON-4	+		GUCUUCGAUGUGGAGCUUCUAAAAC	6419
FKBP1A-96	FKBP1A	EXON-4	+		GUGGAGCUUCUAAAACUGGAAUGAC	6420

FKBP1A-97	FKBP1A	EXON-4	+		GCUUCUAAAACUGGAAUGACAGGAA	6421
FKBP1A-98	FKBP1A	EXON-4	+		GCCUCCUCCCUUAGCUCCCUGUUCU	6422
FKBP1A-99	FKBP1A	EXON-4	+		CCUCCUCCCUUAGCUCCCUGUUCUU	6423
FKBP1A-100	FKBP1A	EXON-4	+		UCCCUUAGCUCCCUGUUCUUGGGUA	6424
FKBP1A-101	FKBP1A	EXON-4	+		AGCUCCCUGUUCUUGGGUAAGGAAA	6425
FKBP1A-102	FKBP1A	EXON-4	+		CUUGGGUAAGGAAAUGGAAUACUGA	6426
FKBP1A-103	FKBP1A	EXON-4	+		UUGGGUAAGGAAAUGGAAUACUGAA	6427
FKBP1A-104	FKBP1A	EXON-4	-		GUAUUCCAUUUCCUUACCCAAGAAC	6428
FKBP1A-105	FKBP1A	EXON-4	-		UAUUCCAUUUCCUUACCCAAGAACA	6429
FKBP1A-106	FKBP1A	EXON-4	-		UUCCUUACCCAAGAACAGGGAGCUA	6430
FKBP1A-107	FKBP1A	EXON-4	-		UCCUUACCCAAGAACAGGGAGCUAA	6431
FKBP1A-108	FKBP1A	EXON-4	-		UUACCCAAGAACAGGGAGCUAAGGG	6432
FKBP1A-109	FKBP1A	EXON-4	-		CCCAAGAACAGGGAGCUAAGGGAGG	6433
FKBP1A-110	FKBP1A	EXON-4	-		AGAAGCUCCACAUCGAAGACGAGAG	6434
FKBP1A-111	FKBP1A	EXON-4	-		CCACAUCGAAGACGAGAGUGGCAUG	6435
FKBP1A-112	FKBP1A	EXON-4	-		CAUCGAAGACGAGAGUGGCAUGUGG	6436
FKBP1A-113	FKBP1A	EXON-4	-		AUCGAAGACGAGAGUGGCAUGUGGU	6437
FKBP1A-114	FKBP1A	EXON-4	-		GAGUGGCAUGUGGUGGGAUGAUGCC	6438
FKBP1A-115	FKBP1A	EXON-4	-		AGUGGCAUGUGGUGGGAUGAUGCCU	6439
FKBP1A-116	FKBP1A	EXON-4	-		GGUGGGAUGAUGCCUGGGUGCCCAG	6440
FKBP1A-117	FKBP1A	EXON-4	-		AUGCCUGGGUGCCCAGUGGCACCAU	6441
FKBP1A-118	FKBP1A	EXON-4	-		GCCCAGUGGCACCAUAGGCAUAAUC	6442
FKBP1A-119	FKBP1A	EXON-4	-		GCAUAAUCUGGAGAUAUAGUCAGUU	6443
FKBP1A-120	FKBP1A	EXON-4	-		CCCACACUCAUCUGUGAAAAGAACA	6444
FKBP1A-121	FKBP1A	EXON-5	+		UUUUCUGUCCCCAACAGAUCUGCCA	6445

FKBP1A-122	FKBP1A	EXON-5	+		UCUGUCCCCAACAGAUCUGCCAUGG	6446
FKBP1A-123	FKBP1A	EXON-5	+		CUGUCCCCAACAGAUCUGCCAUGGA	6447
FKBP1A-124	FKBP1A	EXON-5	+		CCAACAGAUCUGCCAUGGAGGGAUC	6448
FKBP1A-125	FKBP1A	EXON-5	+		CCAGACAUGUGCACAUGAAUCCAUA	6449
FKBP1A-126	FKBP1A	EXON-5	+		UAUUCAUUUUAUUUUGUUUUUCAUUU	6450
FKBP1A-127	FKBP1A	EXON-5	+		AUUCAUUUUAUUUUGUUUUCAUUUU	6451
FKBP1A-128	FKBP1A	EXON-5	+		UUCAUUUUAUUUUGUUUUCAUUUUG	6452
FKBP1A-129	FKBP1A	EXON-5	+		GGGUGAAGAUUCAGUUUCAGUCUUU	6453
FKBP1A-130	FKBP1A	EXON-5	+		GAUUCAGUUUCAGUCUUUUGGAUAU	6454
FKBP1A-131	FKBP1A	EXON-5	+		GGAUAUAGGUUUCCAAUUAAGUACA	6455
FKBP1A-132	FKBP1A	EXON-5	+		CAUGGUCAAGUAUUAACAGCACAAG	6456
FKBP1A-133	FKBP1A	EXON-5	+		GUCAAGUAUUAACAGCACAAGUGGU	6457
FKBP1A-134	FKBP1A	EXON-5	+		ACAAGUGGUAGGUUAACAUUAGAAU	6458
FKBP1A-135	FKBP1A	EXON-5	+		GGUAGGUUAACAUUAGAAUAGGAAU	6459
FKBP1A-136	FKBP1A	EXON-5	+		UUAACAUUAGAAUAGGAAUUGGUGU	6460
FKBP1A-137	FKBP1A	EXON-5	+		UAACAUUAGAAUAGGAAUUGGUGUU	6461
FKBP1A-138	FKBP1A	EXON-5	+		AACAUUAGAAUAGGAAUUGGUGUUG	6462
FKBP1A-139	FKBP1A	EXON-5	+		ACAUUAGAAUAGGAAUUGGUGUUGG	6463
FKBP1A-140	FKBP1A	EXON-5	+		CAUUAGAAUAGGAAUUGGUGUUGGG	6464
FKBP1A-141	FKBP1A	EXON-5	+		AUUAGAAUAGGAAUUGGUGUUGGGG	6465
FKBP1A-142	FKBP1A	EXON-5	+		UUAGAAUAGGAAUUGGUGUUGGGGG	6466
FKBP1A-143	FKBP1A	EXON-5	+		UAGAAUAGGAAUUGGUGUUGGGGGG	6467
FKBP1A-144	FKBP1A	EXON-5	+		AGAAUAGGAAUUGGUGUUGGGGGG	6468
FKBP1A-145	FKBP1A	EXON-5	+		GCAAGAAUAUUUUAUUUUAAUUUUU	6469
FKBP1A-146	FKBP1A	EXON-5	+		GCGCUGCAAAGCCAUAGCAGAUUUG	6470

FKBP1A-147	FKBP1A	EXON-5	+		CCAUAGCAGAUUUGAGGCGCUGUUG	6471
FKBP1A-148	FKBP1A	EXON-5	+		UACUCUCCAAGUUGAGAGAUGUCUU	6472
FKBP1A-149	FKBP1A	EXON-5	+		ACUCUCCAAGUUGAGAGAUGUCUUU	6473
FKBP1A-150	FKBP1A	EXON-5	+		AAAUUAAAAGCCCUACCUAAAACUG	6474
FKBP1A-151	FKBP1A	EXON-5	+		UUAAAAGCCCUACCUAAAACUGAGG	6475
FKBP1A-152	FKBP1A	EXON-5	+		UAAAAGCCCUACCUAAAACUGAGGU	6476
FKBP1A-153	FKBP1A	EXON-5	+		AAAAGCCCUACCUAAAACUGAGGUG	6477
FKBP1A-154	FKBP1A	EXON-5	+		GCCCUACCUAAAACUGAGGUGGGGA	6478
FKBP1A-155	FKBP1A	EXON-5	+		CCCUACCUAAAACUGAGGUGGGGAU	6479
FKBP1A-156	FKBP1A	EXON-5	+		CCUACCUAAAACUGAGGUGGGGAUG	6480
FKBP1A-157	FKBP1A	EXON-5	+		AAGUAGAUCAUGUUCACUGCAAUGC	6481
FKBP1A-158	FKBP1A	EXON-5	+		UGUUCACUGCAAUGCUGGACACUAC	6482
FKBP1A-159	FKBP1A	EXON-5	+		GCUGGACACUACAGGUAUCUGUCCC	6483
FKBP1A-160	FKBP1A	EXON-5	+		CUGGACACUACAGGUAUCUGUCCCU	6484
FKBP1A-161	FKBP1A	EXON-5	+		UACAGGUAUCUGUCCCUGGGCCAGC	6485
FKBP1A-162	FKBP1A	EXON-5	+		ACAGGUAUCUGUCCCUGGGCCAGCA	6486
FKBP1A-163	FKBP1A	EXON-5	+		GCAGGGACCUCUGAAGCCUUCUUUG	6487
FKBP1A-164	FKBP1A	EXON-5	+		GUGGCCUUUUUUUUUUUUCAUCCUG	6488
FKBP1A-165	FKBP1A	EXON-5	+		UUUUUUCAUCCUGUGGUUUUUCUAA	6489
FKBP1A-166	FKBP1A	EXON-5	+		CCUGUGGUUUUUCUAAUGGACUUUC	6490
FKBP1A-167	FKBP1A	EXON-5	+		AACUUUAAUUGACAGUUUCAAUUGA	6491
FKBP1A-168	FKBP1A	EXON-5	+		GAAUGUUCUCUUAAGAAAAUGAUGC	6492
FKBP1A-169	FKBP1A	EXON-5	+		UCAGCAUCUCCUGUUUUUUGAUGCU	6493
FKBP1A-170	FKBP1A	EXON-5	+		GCUCCCUCUGCUGAUCUCAGUUUCC	6494
FKBP1A-171	FKBP1A	EXON-5	+		CCCUUUGCUGUCCUGUGUAGUGAUU	6495

FKBP1A-172	FKBP1A	EXON-5	+		UUAUUGCAAUAAAAGUGCUUUAUGC	6496
FKBP1A-173	FKBP1A	EXON-5	+		GCCGGCUUUUCUCAGCUCUGUGUCA	6497
FKBP1A-174	FKBP1A	EXON-5	+		GGCUUUUCUCAGCUCUGUGUCAUGG	6498
FKBP1A-175	FKBP1A	EXON-5	+		GCUCUGUGUCAUGGUGGUUAUUUUC	6499
FKBP1A-176	FKBP1A	EXON-5	+		AUUUUCAGGUGCCUCCCCUGCCAUU	6500
FKBP1A-177	FKBP1A	EXON-5	-		ACCAUGACACAGAGCUGAGAAAAGC	6501
FKBP1A-178	FKBP1A	EXON-5	-		AAUAAUAAAACUUGAGACUCAUAAA	6502
FKBP1A-179	FKBP1A	EXON-5	-		AAAACUUGAGACUCAUAAAUGGUGC	6503
FKBP1A-180	FKBP1A	EXON-5	-		AAACUUGAGACUCAUAAAUGGUGCU	6504
FKBP1A-181	FKBP1A	EXON-5	-		AACUUGAGACUCAUAAAUGGUGCUG	6505
FKBP1A-182	FKBP1A	EXON-5	-		ACUUGAGACUCAUAAAUGGUGCUGG	6506
FKBP1A-183	FKBP1A	EXON-5	-		GAGACUCAUAAAUGGUGCUGGGGGA	6507
FKBP1A-184	FKBP1A	EXON-5	-		AGACUCAUAAAUGGUGCUGGGGGAA	6508
FKBP1A-185	FKBP1A	EXON-5	-		ACGAUUUCUCACCAAAUCACUACAC	6509
FKBP1A-186	FKBP1A	EXON-5	-		ACCAAAUCACUACACAGGACAGCAA	6510
FKBP1A-187	FKBP1A	EXON-5	-		CCAAAUCACUACACAGGACAGCAAA	6511
FKBP1A-188	FKBP1A	EXON-5	-		CAAAUCACUACACAGGACAGCAAAG	6512
FKBP1A-189	FKBP1A	EXON-5	-		UACACAGGACAGCAAAGGGGUGAGA	6513
FKBP1A-190	FKBP1A	EXON-5	-		ACACAGGACAGCAAAGGGGUGAGAA	6514
FKBP1A-191	FKBP1A	EXON-5	-		CACAGGACAGCAAAGGGGUGAGAAG	6515
FKBP1A-192	FKBP1A	EXON-5	-		ACAGCAAAGGGGUGAGAAGGGGCUG	6516
FKBP1A-193	FKBP1A	EXON-5	-		CAGCAAAGGGGUGAGAAGGGGCUGA	6517
FKBP1A-194	FKBP1A	EXON-5	-		CAAAGGGGUGAGAAGGGGCUGAGGG	6518
FKBP1A-195	FKBP1A	EXON-5	-		AGAAGGGGCUGAGGGAGGAAAAGCC	6519
FKBP1A-196	FKBP1A	EXON-5	-		AAAGCCAGGAAACUGAGAUCAGCAG	6520

FKBP1A-197	FKBP1A	EXON-5	-		AAGCCAGGAAACUGAGAUCAGCAGA	6521
FKBP1A-198	FKBP1A	EXON-5	-		CAGAGGGAGCCAAGCAUCAAAAAAC	6522
FKBP1A-199	FKBP1A	EXON-5	-		CAUCAUUUUCUUAAGAGAACAUUCA	6523
FKBP1A-200	FKBP1A	EXON-5	-		GAGAACAUUCAAGGAUUUGUCAUGA	6524
FKBP1A-201	FKBP1A	EXON-5	-		ACAUUCAAGGAUUUGUCAUGAUGGC	6525
FKBP1A-202	FKBP1A	EXON-5	-		CAUUCAAGGAUUUGUCAUGAUGGCU	6526
FKBP1A-203	FKBP1A	EXON-5	-		UUUGUCAUGAUGGCUGGGCUUUCAC	6527
FKBP1A-204	FKBP1A	EXON-5	-		UUGUCAUGAUGGCUGGGCUUUCACU	6528
FKBP1A-205	FKBP1A	EXON-5	-		CUGUCAAUUAAAGUUCUUAAGAUUU	6529
FKBP1A-206	FKBP1A	EXON-5	-		AUUAAAGUUCUUAAGAUUUAGGAAG	6530
FKBP1A-207	FKBP1A	EXON-5	-		AAAGUUCUUAAGAUUUAGGAAGUGG	6531
FKBP1A-208	FKBP1A	EXON-5	-		UUAAGAUUUAGGAAGUGGUGGAGCU	6532
FKBP1A-209	FKBP1A	EXON-5	-		CCUGAAAGUCCAUUAGAAAAACCAC	6533
FKBP1A-210	FKBP1A	EXON-5	-		AAAACCACAGGAUGAAAAAAAAAAA	6534
FKBP1A-211	FKBP1A	EXON-5	-		UGAAAAAAAAAAAAGGCCACAAAGA	6535
FKBP1A-212	FKBP1A	EXON-5	-		AAAAAGGCCACAAAGAAGGCUUCAG	6536
FKBP1A-213	FKBP1A	EXON-5	-		CAAAGAAGGCUUCAGAGGUCCCUGC	6537
FKBP1A-214	FKBP1A	EXON-5	-		AGGCUUCAGAGGUCCCUGCUGGCCC	6538
FKBP1A-215	FKBP1A	EXON-5	-		GGCUUCAGAGGUCCCUGCUGGCCCA	6539
FKBP1A-216	FKBP1A	EXON-5	-		UGCAGUGAACAUGAUCUACUUUCAA	6540
FKBP1A-217	FKBP1A	EXON-5	-		GAACAUGAUCUACUUUCAAAGGCAG	6541
FKBP1A-218	FKBP1A	EXON-5	-		AACAUGAUCUACUUUCAAAGGCAGA	6542
FKBP1A-219	FKBP1A	EXON-5	-		UCUACUUUCAAAGGCAGAGGGUUUA	6543
FKBP1A-220	FKBP1A	EXON-5	-		CUACUUUCAAAGGCAGAGGGUUUAA	6544
FKBP1A-221	FKBP1A	EXON-5	-		UACUUUCAAAGGCAGAGGGUUUAAG	6545

FKBP1A-222	FKBP1A	EXON-5	-		UUUCAAAGGCAGAGGGUUUAAGGGG	6546
FKBP1A-223	FKBP1A	EXON-5	-		UUCAAAGGCAGAGGGUUUAAGGGGA	6547
FKBP1A-224	FKBP1A	EXON-5	-		AAAGGCAGAGGGUUUAAGGGGAGGG	6548
FKBP1A-225	FKBP1A	EXON-5	-		AAGGCAGAGGGUUUAAGGGGAGGGU	6549
FKBP1A-226	FKBP1A	EXON-5	-		GCAGAGGGUUUAAGGGGAGGGUGGG	6550
FKBP1A-227	FKBP1A	EXON-5	-		CAGAGGGUUUAAGGGGAGGGUGGGU	6551
FKBP1A-228	FKBP1A	EXON-5	-		GGUUUAAGGGGAGGGUGGGUGGGAA	6552
FKBP1A-229	FKBP1A	EXON-5	-		UUAAGGGGAGGGUGGGUGGGAAUGG	6553
FKBP1A-230	FKBP1A	EXON-5	-		AGGGGAGGGUGGGUGGGAAUGGUGG	6554
FKBP1A-231	FKBP1A	EXON-5	-		GGGUGGGUGGGAAUGGUGGAGGCAA	6555
FKBP1A-232	FKBP1A	EXON-5	-		CUCUCCCCAUCCCCACCUCAGUUUU	6556
FKBP1A-233	FKBP1A	EXON-5	-		CCCCAUCCCCACCUCAGUUUUAGGU	6557
FKBP1A-234	FKBP1A	EXON-5	-		CCCAUCCCCACCUCAGUUUUAGGUA	6558
FKBP1A-235	FKBP1A	EXON-5	-		UUUAACCCAAAGACAUCUCUCAACU	6559
FKBP1A-236	FKBP1A	EXON-5	-		CCUCAACAGCGCCUCAAAUCUGCUA	6560
FKBP1A-237	FKBP1A	EXON-5	-		GUUAAUACUUGACCAUGUACUUAAU	6561
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FKBP1A-239	FKBP1A	EXON-5	-		AAUAAAAUGAAUAACUUGAGGUUUA	6563
FKBP1A-240	FKBP1A	EXON-5	-		ACUUGAGGUUUAUGGCAUAUAGUUU	6564
FKBP1A-241	FKBP1A	EXON-5	-		UAUAGUUUAGGUAAACACACAUACG	6565
FKBP1A-242	FKBP1A	EXON-5	-		UAGGUAAACACACAUACGAGGAGAA	6566
FKBP1A-243	FKBP1A	EXON-5	-		AGGUAAACACACAUACGAGGAGAAA	6567
FKBP1A-244	FKBP1A	EXON-5	-		GGUAAACACACAUACGAGGAGAAAG	6568
FKBP1A-245	FKBP1A	EXON-5	-		CACACAUACGAGGAGAAAGGGGAAG	6569
FKBP1A-246	FKBP1A	EXON-5	-		GAGGAGAAAGGGGAAGAGGAAACAG	6570

FKBP1A-247	FKBP1A	EXON-5	-		AAAGGGGAAGAGGAAACAGAGGUGU	6571
FKBP1A-248	FKBP1A	EXON-5	-		GCUGAGUGACAGAACACAUUCAGUC	6572
FKBP1A-249	FKBP1A	EXON-5	-		CUGAGUGACAGAACACAUUCAGUCA	6573
FKBP1A-250	FKBP1A	EXON-5	-		AGUCAGGGCAGAUGUCUAUACAAAG	6574
FKBP1A-251	FKBP1A	EXON-5	-		GGGCAGAUGUCUAUACAAAGUGGAG	6575
FKBP1A-252	FKBP1A	EXON-5	-		UCUAUACAAAGUGGAGUGGAACAUC	6576
FKBP1A-253	FKBP1A	EXON-5	-		GUGGAACAUCAGGAAAAGCUCCAUA	6577
FKBP1A-254	FKBP1A	EXON-5	-		CCAUAUGGAUUCAUGUGCACAUGUC	6578
FKBP1A-255	FKBP1A	EXON-5	-		UAUGGAUUCAUGUGCACAUGUCUGG	6579
FKBP1A-256	FKBP1A	EXON-5	-		UGUCUGGAGGCACCAGAUCCCUCCA	6580
FKBP1A-257	FKBP1A	EXON-5	-		CCAGAUCCCUCCAUGGCAGAUCUGU	6581
FKBP1A-258	FKBP1A	EXON-5	-		CAGAUCCCUCCAUGGCAGAUCUGUU	6582
FKBP1A-259	FKBP1A	EXON-5	-		AGAUCCCUCCAUGGCAGAUCUGUUG	6583
4261_1_3	CIITA	1	+	chr16_10877214_10877239	GUGAUGAGGCUGUGUGCUUCUGAGC	6750
4261_1_4	CIITA	1	+	chr16_10877215_10877240	UGAUGAGGCUGUGUGCUUCUGAGCU	6751
4261_1_6	CIITA	1	+	chr16_10877225_10877250	GUGUGCUUCUGAGCUGGGCAUCCGA	6752
4261_1_9	CIITA	1	+	chr16_10877234_10877259	UGAGCUGGGCAUCCGAAGGCAUCCU	6753
4261_1_12	CIITA	1	+	chr16_10877235_10877260	GAGCUGGGCAUCCGAAGGCAUCCUU	6754
4261_1_14	CIITA	1	+	chr16_10877236_10877261	AGCUGGGCAUCCGAAGGCAUCCUUG	6755
4261_1_17	CIITA	1	+	chr16_10877245_10877270	UCCGAAGGCAUCCUUGGGGAAGCUG	6756
4261_1_18	CIITA	1	+	chr16_10877246_10877271	CCGAAGGCAUCCUUGGGGAAGCUGA	6757
4261_1_21	CIITA	1	+	chr16_10877253_10877278	CAUCCUUGGGGAAGCUGAGGGCACG	6758
4261_1_25	CIITA	1	+	chr16_10877256_10877281	CCUUGGGGAAGCUGAGGGCACGAGG	6759
4261_1_26	CIITA	1	+	chr16_10877257_10877282	CUUGGGGAAGCUGAGGGCACGAGGA	6760
4261_1_27	CIITA	1	+	chr16_10877258_10877283	UUGGGGAAGCUGAGGGCACGAGGAG	6761

4261_1_30	CIITA	1	+	chr16_10877272_10877297	GGCACGAGGAGGGGCUGCCAGACUC	6762
4261_1_33	CIITA	1	+	chr16_10877273_10877298	GCACGAGGAGGGGCUGCCAGACUCC	6763
4261_1_34	CIITA	1	+	chr16_10877286_10877311	CUGCCAGACUCCGGGAGCUGCUGCC	6764
4261_1_37	CIITA	1	+	chr16_10877290_10877315	CAGACUCCGGGAGCUGCUGCCUGGC	6765
4261_1_38	CIITA	1	+	chr16_10877291_10877316	AGACUCCGGGAGCUGCUGCCUGGCU	6766
4261_1_39	CIITA	1	+	chr16_10877315_10877340	UGGGAUUCCUACACAAUGCGUUGCC	6767
4261_1_42	CIITA	1	+	chr16_10877331_10877356	UGCGUUGCCUGGCUCCACGCCCUGC	6768
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4261_4_21	CIITA	4	+	chr16_10898719_10898744	AAGGACAUUUUCAGUAAGUUUGUGG	6844
4261_4_22	CIITA	4	+	chr16_10898720_10898745	AGGACAUUUUCAGUAAGUUUGUGGU	6845
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4261_5_12	CIITA	5	+	chr16_10898935_10898960	CCAGAUGAAGUGAUCGGUGAGAGUA	6856
4261_5_16	CIITA	5	+	chr16_10898954_10898979	AGAGUAUGGAGAUGCCAGCAGAAGU	6857
4261_5_17	CIITA	5	+	chr16_10898955_10898980	GAGUAUGGAGAUGCCAGCAGAAGUU	6858
4261_5_29	CIITA	5	-	chr16_10898938_10898963	CCAUACUCUCACCGAUCACUUCAUC	6859
4261_5_34	CIITA	5	-	chr16_10898971_10898996	UCUGACUUUUCUGCCCAACUUCUGC	6860
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4261_8_19	CIITA	8	+	chr16_10902718_10902743	CCCCACCAUCUCCACUCUGCCCCAU	6916
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4261_9_4	CIITA	9	+	chr16_10903757_10903782	CCCCUCCCAGUGGAUUCACUGUCCA	6949
4261_9_6	CIITA	9	+	chr16_10903779_10903804	CCACGGCCUCCCAACAUCUCCAGAC	6950
4261_9_7	CIITA	9	+	chr16_10903784_10903809	GCCUCCCAACAUCUCCAGACCGGCC	6951
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4261_9_15	CIITA	9	+	chr16_10903883_10903908	CAAACAUGACAGGUAAGGACCCUUA	6955
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4261_9_21	CIITA	9	-	chr16_10903722_10903747	GGCCUGGGGCACCUCACCUACAUUG	6958
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4261_9_25	CIITA	9	-	chr16_10903724_10903749	CUGGCCUGGGGCACCUCACCUACAU	6960
4261_9_28	CIITA	9	-	chr16_10903741_10903766	UGGGAGGGGGUACUUGGCUGGCCUG	6961

4261_9_29	CIITA	9	-	chr16_10903742_10903767	CUGGGAGGGGGUACUUGGCUGGCCU	6962
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4261_9_33	CIITA	9	-	chr16_10903748_10903773	AAUCCACUGGGAGGGGGUACUUGGC	6964
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4261_9_45	CIITA	9	-	chr16_10903766_10903791	GGGAGGCCGUGGACAGUGAAUCCAC	6971
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4261_9_72	CIITA	9	-	chr16_10903834_10903859	CGUACGACCCGUCCAGUCUGGCUGA	6984
4261_9_75	CIITA	9	-	chr16_10903841_10903866	CCAAGUCCGUACGACCCGUCCAGUC	6985
4261_9_79	CIITA	9	-	chr16_10903880_10903905	GGGUCCUUACCUGUCAUGUUUGCUC	6986

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4261_10_4	CIITA	10	+	chr16_10904752_10904777	CGUCCCCCACCCAAUGCCCGGCAGC	6989
4261_10_7	CIITA	10	+	chr16_10904757_10904782	CCCACCCAAUGCCCGGCAGCUGGAG	6990
4261_10_8	CIITA	10	+	chr16_10904780_10904805	AGAGGUCUCCAACAAGCUUCCAAAA	6991
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4261_11_8	CIITA	11	+	chr16_10906513_10906538	UCUACCGCUCACUGCAGGACACGUA	7010
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4261_17_18	CIITA	17	+	chr16_10922215_10922240	GUGCUUCCGGACAUGGUGUCCCUCC	7507
4261_17_20	CIITA	17	+	chr16_10922221_10922246	CCGGACAUGGUGUCCCUCCGGGUGA	7508
4261_17_26	CIITA	17	+	chr16_10922232_10922257	GUCCCUCCGGGUGAUGGAGUGAGUG	7509
4261_17_28	CIITA	17	+	chr16_10922233_10922258	UCCCUCCGGGUGAUGGAGUGAGUGU	7510
4261_17_30	CIITA	17	+	chr16_10922240_10922265	GGGUGAUGGAGUGAGUGUGGGAGUC	7511

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4261_17_36	CIITA	17	-	chr16_10922162_10922187	CAGAUGCAGUUAUUGUACAAGCUGU	7514
4261_17_39	CIITA	17	-	chr16_10922201_10922226	UCCGGAAGCACACGAGCCAAGCUCU	7515
4261_17_41	CIITA	17	-	chr16_10922224_10922249	CCAUCACCCGGAGGGACACCAUGUC	7516
4261_17_44	CIITA	17	-	chr16_10922237_10922262	UCCCACACUCACUCCAUCACCCGGA	7517
4261_17_46	CIITA	17	-	chr16_10922238_10922263	CUCCCACACUCACUCCAUCACCCGG	7518
4261_17_48	CIITA	17	-	chr16_10922241_10922266	AGACUCCCACACUCACUCCAUCACC	7519
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4261_18_8	CIITA	18	+	chr16_10922409_10922434	CCAGUACAACAAGUUCACGGCUGCC	7522
4261_18_9	CIITA	18	+	chr16_10922410_10922435	CAGUACAACAAGUUCACGGCUGCCG	7523
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4261_18_14	CIITA	18	+	chr16_10922439_10922464	CCAGCAGCUCGCUGCCAGCCUUCGG	7525
4261_18_16	CIITA	18	+	chr16_10922452_10922477	GCCAGCCUUCGGAGGUGUCCUCAUG	7526
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4261_18_20	CIITA	18	+	chr16_10922473_10922498	CAUGUGGAGACGCUGGCGUAAGUCC	7528
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4261_18_27	CIITA	18	-	chr16_10922412_10922437	CCCGGCAGCCGUGAACUUGUUGUAC	7531
4261_18_30	CIITA	18	-	chr16_10922435_10922460	AGGCUGGCAGCGAGCUGCUGGGCCC	7532
4261_18_31	CIITA	18	-	chr16_10922441_10922466	CUCCGAAGGCUGGCAGCGAGCUGCU	7533
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4261_18_35	CIITA	18	-	chr16_10922456_10922481	UCCACAUGAGGACACCUCCGAAGGC	7535
4261_18_36	CIITA	18	-	chr16_10922460_10922485	CGUCUCCACAUGAGGACACCUCCGA	7536

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4261_19_7	CIITA	19	+	chr16_10923252_10923277	AGUGUCCAGGAACACCUGCAACAAC	7539
4261_19_9	CIITA	19	+	chr16_10923260_10923285	GGAACACCUGCAACAACAGGAUUCA	7540
4261_19_13	CIITA	19	+	chr16_10923292_10923317	GCCUGAGAUGAUCCCAGCUGUGCUC	7541
4261_19_15	CIITA	19	+	chr16_10923297_10923322	AGAUGAUCCCAGCUGUGCUCUGGAC	7542
4261_19_16	CIITA	19	+	chr16_10923298_10923323	GAUGAUCCCAGCUGUGCUCUGGACA	7543
4261_19_18	CIITA	19	+	chr16_10923306_10923331	CAGCUGUGCUCUGGACAGGGUAACC	7544
4261_19_19	CIITA	19	+	chr16_10923307_10923332	AGCUGUGCUCUGGACAGGGUAACCA	7545
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4261_19_22	CIITA	19	+	chr16_10923311_10923336	GUGCUCUGGACAGGGUAACCAGGGU	7547
4261_19_24	CIITA	19	+	chr16_10923316_10923341	CUGGACAGGGUAACCAGGGUGGGCU	7548
4261_19_25	CIITA	19	+	chr16_10923317_10923342	UGGACAGGGUAACCAGGGUGGGCUU	7549
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4261_19_28	CIITA	19	-	chr16_10923214_10923239	GGCGUCCACAUCCUGCAAGGGGGGA	7551
4261_19_30	CIITA	19	-	chr16_10923218_10923243	GGUGGGCGUCCACAUCCUGCAAGGG	7552
4261_19_32	CIITA	19	-	chr16_10923219_10923244	UGGUGGGCGUCCACAUCCUGCAAGG	7553
4261_19_33	CIITA	19	-	chr16_10923220_10923245	AUGGUGGGCGUCCACAUCCUGCAAG	7554
4261_19_36	CIITA	19	-	chr16_10923221_10923246	GAUGGUGGGCGUCCACAUCCUGCAA	7555
4261_19_37	CIITA	19	-	chr16_10923222_10923247	GGAUGGUGGGCGUCCACAUCCUGCA	7556
4261_19_41	CIITA	19	-	chr16_10923240_10923265	GUUCCUGGACACUGAAUGGGAUGGU	7557
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4261_19_44	CIITA	19	-	chr16_10923244_10923269	AGGUGUUCCUGGACACUGAAUGGGA	7559
4261_19_46	CIITA	19	-	chr16_10923248_10923273	UUGCAGGUGUUCCUGGACACUGAAU	7560
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4261_19_56	CIITA	19	-	chr16_10923296_10923321	UCCAGAGCACAGCUGGGAUCAUCUC	7564
4261_19_58	CIITA	19	-	chr16_10923307_10923332	UGGUUACCCUGUCCAGAGCACAGCU	7565
4261_19_60	CIITA	19	-	chr16_10923308_10923333	CUGGUUACCCUGUCCAGAGCACAGC	7566
4261_20_3	CIITA	20	+	chr16_10923863_10923888	UCCUCCCGCUACAGCAUGUUCUCUG	7567
4261_20_5	CIITA	20	+	chr16_10923879_10923904	UGUUCUCUGAGGACACUAACCACGC	7568
4261_20_9	CIITA	20	+	chr16_10923891_10923916	ACACUAACCACGCUGGACCUUGAAC	7569
4261_20_10	CIITA	20	+	chr16_10923892_10923917	CACUAACCACGCUGGACCUUGAACU	7570
4261_20_12	CIITA	20	+	chr16_10923901_10923926	CGCUGGACCUUGAACUGGGUACUUG	7571
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4261_20_18	CIITA	20	+	chr16_10923947_10923972	CUGUAUCCCAUGAGCCUCAGCAUCC	7573
4261_20_19	CIITA	20	+	chr16_10923954_10923979	CCAUGAGCCUCAGCAUCCUGGCACC	7574
4261_20_20	CIITA	20	+	chr16_10923964_10923989	CAGCAUCCUGGCACCCGGCCCCUGC	7575
4261_20_22	CIITA	20	+	chr16_10923970_10923995	CCUGGCACCCGGCCCCUGCUGGUUC	7576
4261_20_23	CIITA	20	+	chr16_10923971_10923996	CUGGCACCCGGCCCCUGCUGGUUCA	7577
4261_20_24	CIITA	20	+	chr16_10923975_10924000	CACCCGGCCCCUGCUGGUUCAGGGU	7578
4261_20_25	CIITA	20	+	chr16_10923986_10924011	UGCUGGUUCAGGGUUGGCCCCUGCC	7579
4261_20_27	CIITA	20	+	chr16_10923992_10924017	UUCAGGGUUGGCCCCUGCCCGGCUG	7580
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4261_20_35	CIITA	20	+	chr16_10924039_10924064	UGCUGACAGACACAGGCCCGGCUCC	7583
4261_20_37	CIITA	20	+	chr16_10924059_10924084	GCUCCAGGCUCCUUUAGCGCCCAGU	7584
4261_20_38	CIITA	20	+	chr16_10924060_10924085	CUCCAGGCUCCUUUAGCGCCCAGUU	7585
4261_20_40	CIITA	20	+	chr16_10924063_10924088	CAGGCUCCUUUAGCGCCCAGUUGGG	7586

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4261_20_51	CIITA	20	+	chr16_10924103_10924128	AGCUGCGGUCCACCCAGGAGCCCCG	7591
4261_20_54	CIITA	20	+	chr16_10924116_10924141	CCAGGAGCCCCGAGGCCUUCUCUGA	7592
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4261_20_57	CIITA	20	+	chr16_10924135_10924160	CUCUGAAGGACAUUGCGGACAGCCA	7594
4261_20_59	CIITA	20	+	chr16_10924140_10924165	AAGGACAUUGCGGACAGCCACGGCC	7595
4261_20_62	CIITA	20	+	chr16_10924147_10924172	UUGCGGACAGCCACGGCCAGGCCAG	7596
4261_20_65	CIITA	20	+	chr16_10924148_10924173	UGCGGACAGCCACGGCCAGGCCAGA	7597
4261_20_68	CIITA	20	+	chr16_10924159_10924184	ACGGCCAGGCCAGAGGGAGUGACAG	7598
4261_20_69	CIITA	20	+	chr16_10924182_10924207	AGAGGCAGCCCCAUUCUGCCUGCCC	7599
4261_20_71	CIITA	20	+	chr16_10924197_10924222	CUGCCUGCCCAGGCCCCUGCCACCC	7600
4261_20_73	CIITA	20	+	chr16_10924198_10924223	UGCCUGCCCAGGCCCCUGCCACCCU	7601
4261_20_77	CIITA	20	+	chr16_10924199_10924224	GCCUGCCCAGGCCCCUGCCACCCUG	7602
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4261_20_86	CIITA	20	+	chr16_10924555_10924580	UGCUCUCCGACCAGACACCUUGACA	7604
4261_20_88	CIITA	20	+	chr16_10924563_10924588	GACCAGACACCUUGACAGGGCACAC	7605
4261_20_89	CIITA	20	+	chr16_10924564_10924589	ACCAGACACCUUGACAGGGCACACC	7606
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4261_20_94	CIITA	20	+	chr16_10924585_10924610	CACCGGGCACUCAGAAGACACUGAU	7608
4261_20_95	CIITA	20	+	chr16_10924622_10924647	GCCUGCUAAUUCCCCAGAUUGCAAC	7609
4261_20_97	CIITA	20	+	chr16_10924626_10924651	GCUAAUUCCCCAGAUUGCAACAGGC	7610
4261_20_98	CIITA	20	+	chr16_10924627_10924652	CUAAUUCCCCAGAUUGCAACAGGCU	7611

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4261_20_105	CIITA	20	+	chr16_10924656_10924681	UUCAGUGGCAGCUGCUUUUGUCUAU	7614
4261_20_110	CIITA	20	+	chr16_10924679_10924704	AUGGGACUCAAUGCACUGACAUUGU	7615
4261_20_111	CIITA	20	+	chr16_10924696_10924721	GACAUUGUUGGCCAAAGCCAAAGCU	7616
4261_20_112	CIITA	20	+	chr16_10924701_10924726	UGUUGGCCAAAGCCAAAGCUAGGCC	7617
4261_20_116	CIITA	20	+	chr16_10924725_10924750	CUGGCCAGAUGCACCAGCCCUUAGC	7618
4261_20_118	CIITA	20	+	chr16_10924726_10924751	UGGCCAGAUGCACCAGCCCUUAGCA	7619
4261_20_122	CIITA	20	+	chr16_10924739_10924764	CAGCCCUUAGCAGGGAAACAGCUAA	7620
4261_20_123	CIITA	20	+	chr16_10924740_10924765	AGCCCUUAGCAGGGAAACAGCUAAU	7621
4261_20_126	CIITA	20	+	chr16_10924750_10924775	AGGGAAACAGCUAAUGGGACACUAA	7622
4261_20_128	CIITA	20	+	chr16_10924751_10924776	GGGAAACAGCUAAUGGGACACUAAU	7623
4261_20_129	CIITA	20	+	chr16_10924752_10924777	GGAAACAGCUAAUGGGACACUAAUG	7624
4261_20_130	CIITA	20	+	chr16_10924755_10924780	AACAGCUAAUGGGACACUAAUGGGG	7625
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4261_20_136	CIITA	20	+	chr16_10924763_10924788	AUGGGACACUAAUGGGGCGGUGAGA	7627
4261_20_138	CIITA	20	+	chr16_10924764_10924789	UGGGACACUAAUGGGGCGGUGAGAG	7628
4261_20_141	CIITA	20	+	chr16_10924774_10924799	AUGGGGCGGUGAGAGGGGAACAGAC	7629
4261_20_151	CIITA	20	+	chr16_10924838_10924863	AUUAUAAAUGUCUCUUUAAUGUCAC	7630
4261_20_152	CIITA	20	+	chr16_10924842_10924867	UAAAUGUCUCUUUAAUGUCACAGGC	7631
4261_20_155	CIITA	20	+	chr16_10924848_10924873	UCUCUUUAAUGUCACAGGCAGGUCC	7632
4261_20_156	CIITA	20	+	chr16_10924849_10924874	CUCUUUAAUGUCACAGGCAGGUCCA	7633
4261_20_162	CIITA	20	+	chr16_10924878_10924903	UUGAGUUCAUACCCUGUUACCAUUU	7634
4261_20_163	CIITA	20	+	chr16_10924879_10924904	UGAGUUCAUACCCUGUUACCAUUUU	7635
4261_20_165	CIITA	20	+	chr16_10924880_10924905	GAGUUCAUACCCUGUUACCAUUUUG	7636

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4261_20_176	CIITA	20	-	chr16_10923870_10923895	GUGUCCUCAGAGAACAUGCUGUAGC	7639
4261_20_179	CIITA	20	-	chr16_10923871_10923896	AGUGUCCUCAGAGAACAUGCUGUAG	7640
4261_20_186	CIITA	20	-	chr16_10923901_10923926	CAAGUACCCAGUUCAAGGUCCAGCG	7641
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4261_20_191	CIITA	20	-	chr16_10923945_10923970	AUGCUGAGGCUCAUGGGAUACAGCC	7643
4261_20_194	CIITA	20	-	chr16_10923956_10923981	CGGGUGCCAGGAUGCUGAGGCUCAU	7644
4261_20_195	CIITA	20	-	chr16_10923957_10923982	CCGGGUGCCAGGAUGCUGAGGCUCA	7645
4261_20_198	CIITA	20	-	chr16_10923964_10923989	GCAGGGGCCGGGUGCCAGGAUGCUG	7646
4261_20_200	CIITA	20	-	chr16_10923973_10923998	CCUGAACCAGCAGGGGCCGGGUGCC	7647
4261_20_202	CIITA	20	-	chr16_10923980_10924005	GGCCAACCCUGAACCAGCAGGGGCC	7648
4261_20_203	CIITA	20	-	chr16_10923981_10924006	GGGCCAACCCUGAACCAGCAGGGGC	7649
4261_20_205	CIITA	20	-	chr16_10923985_10924010	GCAGGGGCCAACCCUGAACCAGCAG	7650
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4261_20_214	CIITA	20	-	chr16_10924007_10924032	AUGUGGUUCAUUCCGCAGCCGGGCA	7654
4261_20_215	CIITA	20	-	chr16_10924008_10924033	GAUGUGGUUCAUUCCGCAGCCGGGC	7655
4261_20_218	CIITA	20	-	chr16_10924012_10924037	GCAAGAUGUGGUUCAUUCCGCAGCC	7656
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4261_20_221	CIITA	20	-	chr16_10924029_10924054	CUGUGUCUGUCAGCAGAGCAAGAUG	7658
4261_20_223	CIITA	20	-	chr16_10924058_10924083	CUGGGCGCUAAAGGAGCCUGGAGCC	7659
4261_20_224	CIITA	20	-	chr16_10924059_10924084	ACUGGGCGCUAAAGGAGCCUGGAGC	7660
4261_20_227	CIITA	20	-	chr16_10924065_10924090	CACCCAACUGGGCGCUAAAGGAGCC	7661

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4261_20_232	CIITA	20	-	chr16_10924081_10924106	GCUGCCACCAGGCAUCCACCCAACU	7663
4261_20_233	CIITA	20	-	chr16_10924082_10924107	AGCUGCCACCAGGCAUCCACCCAAC	7664
4261_20_235	CIITA	20	-	chr16_10924097_10924122	UCCUGGGUGGACCGCAGCUGCCACC	7665
4261_20_236	CIITA	20	-	chr16_10924115_10924140	CAGAGAAGGCCUCGGGGCUCCUGGG	7666
4261_20_239	CIITA	20	-	chr16_10924118_10924143	CUUCAGAGAAGGCCUCGGGGCUCCU	7667
4261_20_240	CIITA	20	-	chr16_10924119_10924144	CCUUCAGAGAAGGCCUCGGGGCUCC	7668
4261_20_242	CIITA	20	-	chr16_10924126_10924151	GCAAUGUCCUUCAGAGAAGGCCUCG	7669
4261_20_243	CIITA	20	-	chr16_10924127_10924152	CGCAAUGUCCUUCAGAGAAGGCCUC	7670
4261_20_245	CIITA	20	-	chr16_10924128_10924153	CCGCAAUGUCCUUCAGAGAAGGCCU	7671
4261_20_247	CIITA	20	-	chr16_10924134_10924159	GGCUGUCCGCAAUGUCCUUCAGAGA	7672
4261_20_251	CIITA	20	-	chr16_10924160_10924185	UCUGUCACUCCCUCUGGCCUGGCCG	7673
4261_20_252	CIITA	20	-	chr16_10924166_10924191	GCUGCCUCUGUCACUCCCUCUGGCC	7674
4261_20_253	CIITA	20	-	chr16_10924171_10924196	AUGGGGCUGCCUCUGUCACUCCCUC	7675
4261_20_254	CIITA	20	-	chr16_10924193_10924218	GGCAGGGGCCUGGGCAGGCAGAAUG	7676
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4261_20_260	CIITA	20	-	chr16_10924203_10924228	UCCCCAGGGUGGCAGGGGCCUGGGC	7679
4261_20_263	CIITA	20	-	chr16_10924207_10924232	UUUCUCCCCAGGGUGGCAGGGGCCU	7680
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4261_20_266	CIITA	20	-	chr16_10924213_10924238	UUGUACUUUCUCCCCAGGGUGGCAG	7682
4261_20_267	CIITA	20	-	chr16_10924214_10924239	CUUGUACUUUCUCCCCAGGGUGGCA	7683
4261_20_268	CIITA	20	-	chr16_10924215_10924240	UCUUGUACUUUCUCCCCAGGGUGGC	7684
4261_20_271	CIITA	20	-	chr16_10924219_10924244	UUUUUCUUGUACUUUCUCCCCAGGG	7685
4261_20_272	CIITA	20	-	chr16_10924222_10924247	UUUUUUUUCUUGUACUUUCUCCCCA	7686

4261_20_273	CIITA	20	-	chr16_10924223_10924248	UUUUUUUUUCUUGUACUUUCUCCCC	7687
4261_20_279	CIITA	20	-	chr16_10924552_10924577	CAAGGUGUCUGGUCGGAGAGCAGGG	7688
4261_20_282	CIITA	20	-	chr16_10924555_10924580	UGUCAAGGUGUCUGGUCGGAGAGCA	7689
4261_20_283	CIITA	20	-	chr16_10924556_10924581	CUGUCAAGGUGUCUGGUCGGAGAGC	7690
4261_20_286	CIITA	20	-	chr16_10924564_10924589	GGUGUGCCCUGUCAAGGUGUCUGGU	7691
4261_20_289	CIITA	20	-	chr16_10924568_10924593	GCCCGGUGUGCCCUGUCAAGGUGUC	7692
4261_20_291	CIITA	20	-	chr16_10924575_10924600	UCUGAGUGCCCGGUGUGCCCUGUCA	7693
4261_20_293	CIITA	20	-	chr16_10924590_10924615	UGCCCAUCAGUGUCUUCUGAGUGCC	7694
4261_20_296	CIITA	20	-	chr16_10924619_10924644	GCAAUCUGGGGAAUUAGCAGGCUGG	7695
4261_20_298	CIITA	20	-	chr16_10924620_10924645	UGCAAUCUGGGGAAUUAGCAGGCUG	7696
4261_20_299	CIITA	20	-	chr16_10924621_10924646	UUGCAAUCUGGGGAAUUAGCAGGCU	7697
4261_20_302	CIITA	20	-	chr16_10924622_10924647	GUUGCAAUCUGGGGAAUUAGCAGGC	7698
4261_20_304	CIITA	20	-	chr16_10924626_10924651	GCCUGUUGCAAUCUGGGGAAUUAGC	7699
4261_20_306	CIITA	20	-	chr16_10924636_10924661	CUGAAGCCCAGCCUGUUGCAAUCUG	7700
4261_20_307	CIITA	20	-	chr16_10924637_10924662	ACUGAAGCCCAGCCUGUUGCAAUCU	7701
4261_20_310	CIITA	20	-	chr16_10924638_10924663	CACUGAAGCCCAGCCUGUUGCAAUC	7702
4261_20_319	CIITA	20	-	chr16_10924710_10924735	AUCUGGCCAGGCCUAGCUUUGGCUU	7703
4261_20_320	CIITA	20	-	chr16_10924716_10924741	UGGUGCAUCUGGCCAGGCCUAGCUU	7704
4261_20_321	CIITA	20	-	chr16_10924727_10924752	CUGCUAAGGGCUGGUGCAUCUGGCC	7705
4261_20_324	CIITA	20	-	chr16_10924732_10924757	UUUCCCUGCUAAGGGCUGGUGCAUC	7706
4261_20_326	CIITA	20	-	chr16_10924741_10924766	CAUUAGCUGUUUCCCUGCUAAGGGC	7707
4261_20_327	CIITA	20	-	chr16_10924745_10924770	GUCCCAUUAGCUGUUUCCCUGCUAA	7708
4261_20_328	CIITA	20	-	chr16_10924746_10924771	UGUCCCAUUAGCUGUUUCCCUGCUA	7709
4261_20_336	CIITA	20	-	chr16_10924821_10924846	UUUAUAAUGUAGUGAAAAAAGACAC	7710
4261_20_342	CIITA	20	-	chr16_10924874_10924899	GGUAACAGGGUAUGAACUCAAACCC	7711

4261_20_345	CIITA	20	-	chr16_10924892_10924917	GUGUGGGUACCCCAAAAUGGUAACA	7712
4261_20_346	CIITA	20	-	chr16_10924893_10924918	CGUGUGGGUACCCCAAAAUGGUAAC	7713
4261_20_348	CIITA	20	-	chr16_10924900_10924925	UUGGUCUCGUGUGGGUACCCCAAAA	7714
4261_20_349	CIITA	20	-	chr16_10924913_10924938	AAUGUAUAAUCUAUUGGUCUCGUGU	7715
4261_20_350	CIITA	20	-	chr16_10924914_10924939	CAAUGUAUAAUCUAUUGGUCUCGUG	7716
84166_1_4	NLRC5	EXON	+	chr16:57017065-57017085	CCCCUUAGGAGUCUGCACUA	8622
84166_1_6	NLRC5	EXON	+	chr16:57017091-57017111	CAACCUGUCAAUCCAGCUCA	8623
84166_1_9	NLRC5	EXON	+	chr16:57017129-57017149	CACCCAUGAGACCCUCUCCG	8624
84166_1_11	NLRC5	EXON	+	chr16:57017130-57017150	ACCCAUGAGACCCUCUCCGU	8625
84166_1_13	NLRC5	EXON	+	chr16:57017131-57017151	CCCAUGAGACCCUCUCCGUG	8626
84166_1_19	NLRC5	EXON	+	chr16:57017158-57017178	UAGAGCACCUAUCAUGAACG	8627
84166_1_20	NLRC5	EXON	+	chr16:57017170-57017190	CAUGAACGAGGAGACCAAGU	8628
84166_1_21	NLRC5	EXON	-	chr16:57017056-57017076	CUCCUAAGGGGAGAGAAGAC	8629
84166_1_28	NLRC5	EXON	-	chr16:57017068-57017088	CCAUAGUGCAGACUCCUAAG	8630
84166_1_30	NLRC5	EXON	-	chr16:57017069-57017089	UCCAUAGUGCAGACUCCUAA	8631
84166_1_33	NLRC5	EXON	-	chr16:57017070-57017090	UUCCAUAGUGCAGACUCCUA	8632
84166_1_37	NLRC5	EXON	-	chr16:57017097-57017117	GUGCCUUGAGCUGGAUUGAC	8633
84166_1_38	NLRC5	EXON	-	chr16:57017106-57017126	GGGCUAUGUGUGCCUUGAGC	8634
84166_1_41	NLRC5	EXON	-	chr16:57017126-57017146	AGAGGGUCUCAUGGGUGUCU	8635
84166_1_42	NLRC5	EXON	-	chr16:57017127-57017147	GAGAGGGUCUCAUGGGUGUC	8636
84166_1_44	NLRC5	EXON	-	chr16:57017134-57017154	CCCCACGGAGAGGGUCUCAU	8637
84166_1_45	NLRC5	EXON	-	chr16:57017135-57017155	UCCCCACGGAGAGGGUCUCA	8638
84166_1_47	NLRC5	EXON	-	chr16:57017143-57017163	CUCUAGGGUCCCCACGGAGA	8639
84166_1_48	NLRC5	EXON	-	chr16:57017144-57017164	GCUCUAGGGUCCCCACGGAG	8640
84166_1_52	NLRC5	EXON	-	chr16:57017149-57017169	UAGGUGCUCUAGGGUCCCCA	8641

84166_1_55	NLRC5	EXON	-	chr16:57017158-57017178	CGUUCAUGAUAGGUGCUCUA	8642
84166_1_56	NLRC5	EXON	-	chr16:57017159-57017179	UCGUUCAUGAUAGGUGCUCU	8643
84166_1_59	NLRC5	EXON	-	chr16:57017168-57017188	UUGGUCUCCUCGUUCAUGAU	8644
84166_1_60	NLRC5	EXON	-	chr16:57017187-57017207	GGAGAGAAAAAUCACCUACU	8645
84166_2_1	NLRC5	EXON	+	chr16:57020683-57020703	CUUCCCUGUCCCUCCAGGGC	8646
84166_2_4	NLRC5	EXON	+	chr16:57020693-57020713	CCUCCAGGGCUGGCUCCUCA	8647
84166_2_5	NLRC5	EXON	+	chr16:57020703-57020723	UGGCUCCUCAUGGACCCCGU	8648
84166_2_6	NLRC5	EXON	+	chr16:57020715-57020735	GACCCCGUUGGCCUCCAGCU	8649
84166_2_11	NLRC5	EXON	+	chr16:57020731-57020751	AGCUCGGCAACAAGAACCUG	8650
84166_2_13	NLRC5	EXON	+	chr16:57020746-57020766	ACCUGUGGAGCUGUCUUGUG	8651
84166_2_17	NLRC5	EXON	+	chr16:57020770-57020790	UGCUCACCAAAGACCCAGAA	8652
84166_2_21	NLRC5	EXON	+	chr16:57020807-57020827	GAAGUUCUUCCUCCCCAACA	8653
84166_2_23	NLRC5	EXON	+	chr16:57020813-57020833	CUUCCUCCCCAACACGGACC	8654
84166_2_27	NLRC5	EXON	+	chr16:57020821-57020841	CCAACACGGACCUGGAUUCC	8655
84166_2_31	NLRC5	EXON	+	chr16:57020834-57020854	GGAUUCCAGGAACGAGACCU	8656
84166_2_38	NLRC5	EXON	+	chr16:57020882-57020902	ACUCAACAAGCUGCAUGUCC	8657
84166_2_39	NLRC5	EXON	+	chr16:57020883-57020903	CUCAACAAGCUGCAUGUCCA	8658
84166_2_41	NLRC5	EXON	+	chr16:57020888-57020908	CAAGCUGCAUGUCCAGGGUU	8659
84166_2_42	NLRC5	EXON	+	chr16:57020896-57020916	AUGUCCAGGGUUCGGACACC	8660
84166_2_49	NLRC5	EXON	+	chr16:57020973-57020993	GUGCUGCUGCUGAGUACUUU	8661
84166_2_50	NLRC5	EXON	+	chr16:57020985-57021005	AGUACUUUUGGCUAUGAUGA	8662
84166_2_52	NLRC5	EXON	+	chr16:57020990-57021010	UUUUGGCUAUGAUGAUGGUA	8663
84166_2_53	NLRC5	EXON	+	chr16:57020991-57021011	UUUGGCUAUGAUGAUGGUAA	8664
84166_2_57	NLRC5	EXON	+	chr16:57020995-57021015	GCUAUGAUGAUGGUAAGGGC	8665
84166_2_61	NLRC5	EXON	-	chr16:57020689-57020709	GAGCCAGCCCUGGAGGGACA	8666

84166_2_63	NLRC5	EXON	-	chr16:57020690-57020710	GGAGCCAGCCCUGGAGGGAC	8667
84166_2_65	NLRC5	EXON	-	chr16:57020695-57020715	CAUGAGGAGCCAGCCCUGGA	8668
84166_2_66	NLRC5	EXON	-	chr16:57020696-57020716	CCAUGAGGAGCCAGCCCUGG	8669
84166_2_69	NLRC5	EXON	-	chr16:57020699-57020719	GGUCCAUGAGGAGCCAGCCC	8670
84166_2_72	NLRC5	EXON	-	chr16:57020711-57020731	GGAGGCCAACGGGGUCCAUG	8671
84166_2_78	NLRC5	EXON	-	chr16:57020720-57020740	UGCCGAGCUGGAGGCCAACG	8672
84166_2_80	NLRC5	EXON	-	chr16:57020721-57020741	UUGCCGAGCUGGAGGCCAAC	8673
84166_2_82	NLRC5	EXON	-	chr16:57020722-57020742	GUUGCCGAGCUGGAGGCCAA	8674
84166_2_84	NLRC5	EXON	-	chr16:57020729-57020749	GGUUCUUGUUGCCGAGCUGG	8675
84166_2_86	NLRC5	EXON	-	chr16:57020732-57020752	ACAGGUUCUUGUUGCCGAGC	8676
84166_2_89	NLRC5	EXON	-	chr16:57020750-57020770	GCCUCACAAGACAGCUCCAC	8677
84166_2_96	NLRC5	EXON	-	chr16:57020779-57020799	GUUCAGCCAUUCUGGGUCUU	8678
84166_2_98	NLRC5	EXON	-	chr16:57020786-57020806	UCUUGGCGUUCAGCCAUUCU	8679
84166_2_99	NLRC5	EXON	-	chr16:57020787-57020807	AUCUUGGCGUUCAGCCAUUC	8680
84166_2_102	NLRC5	EXON	-	chr16:57020803-57020823	GGGGAGGAAGAACUUCAUCU	8681
84166_2_105	NLRC5	EXON	-	chr16:57020819-57020839	AAUCCAGGUCCGUGUUGGGG	8682
84166_2_109	NLRC5	EXON	-	chr16:57020822-57020842	UGGAAUCCAGGUCCGUGUUG	8683
84166_2_112	NLRC5	EXON	-	chr16:57020823-57020843	CUGGAAUCCAGGUCCGUGUU	8684
84166_2_114	NLRC5	EXON	-	chr16:57020824-57020844	CCUGGAAUCCAGGUCCGUGU	8685
84166_2_116	NLRC5	EXON	-	chr16:57020834-57020854	AGGUCUCGUUCCUGGAAUCC	8686
84166_2_118	NLRC5	EXON	-	chr16:57020842-57020862	AGGGUCCAAGGUCUCGUUCC	8687
84166_2_121	NLRC5	EXON	-	chr16:57020854-57020874	GACUCUCUGUUCAGGGUCCA	8688
84166_2_123	NLRC5	EXON	-	chr16:57020861-57020881	GCAGGAUGACUCUCUGUUCA	8689
84166_2_125	NLRC5	EXON	-	chr16:57020862-57020882	UGCAGGAUGACUCUCUGUUC	8690
84166_2_128	NLRC5	EXON	-	chr16:57020879-57020899	CAUGCAGCUUGUUGAGUUGC	8691

84166_2_131	NLRC5	EXON	-	chr16:57020903-57020923	ACUGCCAGGUGUCCGAACCC	8692
84166_2_134	NLRC5	EXON	-	chr16:57020917-57020937	ACAAUGAAUGAAAGACUGCC	8693
84166_3_2	NLRC5	EXON	+	chr16:57022250-57022270	UGCAGGGUUCACCAGCCAGC	8694
84166_3_5	NLRC5	EXON	+	chr16:57022251-57022271	GCAGGGUUCACCAGCCAGCU	8695
84166_3_10	NLRC5	EXON	+	chr16:57022259-57022279	CACCAGCCAGCUGGGAGCUG	8696
84166_3_12	NLRC5	EXON	+	chr16:57022260-57022280	ACCAGCCAGCUGGGAGCUGA	8697
84166_3_14	NLRC5	EXON	+	chr16:57022261-57022281	CCAGCCAGCUGGGAGCUGAG	8698
84166_3_17	NLRC5	EXON	+	chr16:57022293-57022313	CCUGAAUCUCAGCUCCACCA	8699
84166_3_20	NLRC5	EXON	+	chr16:57022298-57022318	AUCUCAGCUCCACCAUGGUG	8700
84166_3_23	NLRC5	EXON	+	chr16:57022303-57022323	AGCUCCACCAUGGUGAGGAC	8701
84166_3_26	NLRC5	EXON	+	chr16:57022309-57022329	ACCAUGGUGAGGACUGGAGU	8702
84166_3_28	NLRC5	EXON	+	chr16:57022310-57022330	CCAUGGUGAGGACUGGAGUU	8703
84166_3_29	NLRC5	EXON	+	chr16:57022311-57022331	CAUGGUGAGGACUGGAGUUG	8704
84166_3_30	NLRC5	EXON	+	chr16:57022312-57022332	AUGGUGAGGACUGGAGUUGG	8705
84166_3_32	NLRC5	EXON	-	chr16:57022244-57022264	UGGUGAACCCUGCAAGAGAG	8706
84166_3_35	NLRC5	EXON	-	chr16:57022245-57022265	CUGGUGAACCCUGCAAGAGA	8707
84166_3_36	NLRC5	EXON	-	chr16:57022246-57022266	GCUGGUGAACCCUGCAAGAG	8708
84166_3_45	NLRC5	EXON	-	chr16:57022264-57022284	CCCCUCAGCUCCCAGCUGGC	8709
84166_3_47	NLRC5	EXON	-	chr16:57022268-57022288	UUUUCCCCUCAGCUCCCAGC	8710
84166_3_49	NLRC5	EXON	-	chr16:57022292-57022312	GGUGGAGCUGAGAUUCAGGU	8711
84166_3_50	NLRC5	EXON	-	chr16:57022296-57022316	CCAUGGUGGAGCUGAGAUUC	8712
84166_3_53	NLRC5	EXON	-	chr16:57022310-57022330	AACUCCAGUCCUCACCAUGG	8713
84166_3_55	NLRC5	EXON	-	chr16:57022313-57022333	CCCAACUCCAGUCCUCACCA	8714
84166_4_11	NLRC5	EXON	+	chr16:57023789-57023809	AAGCGCCCACAUCAGAGCUG	8715
84166_4_12	NLRC5	EXON	+	chr16:57023790-57023810	AGCGCCCACAUCAGAGCUGU	8716

84166_4_15	NLRC5	EXON	+	chr16:57023805-57023825	GCUGUGGGUCCUCACCCCGC	8717
84166_4_17	NLRC5	EXON	+	chr16:57023831-57023851	CAGUGCAAGAAGCAGCAGCU	8718
84166_4_19	NLRC5	EXON	+	chr16:57023834-57023854	UGCAAGAAGCAGCAGCUAGG	8719
84166_4_20	NLRC5	EXON	+	chr16:57023835-57023855	GCAAGAAGCAGCAGCUAGGU	8720
84166_4_23	NLRC5	EXON	+	chr16:57023846-57023866	CAGCUAGGUGGGUACCAGUG	8721
84166_4_24	NLRC5	EXON	+	chr16:57023847-57023867	AGCUAGGUGGGUACCAGUGU	8722
84166_4_27	NLRC5	EXON	+	chr16:57023848-57023868	GCUAGGUGGGUACCAGUGUG	8723
84166_4_29	NLRC5	EXON	-	chr16:57023767-57023787	GGCCUGAAAAAGCAAAGGAA	8724
84166_4_30	NLRC5	EXON	-	chr16:57023768-57023788	AGGCCUGAAAAAGCAAAGGA	8725
84166_4_32	NLRC5	EXON	-	chr16:57023772-57023792	CUUCAGGCCUGAAAAAGCAA	8726
84166_4_36	NLRC5	EXON	-	chr16:57023788-57023808	AGCUCUGAUGUGGGCGCUUC	8727
84166_4_37	NLRC5	EXON	-	chr16:57023797-57023817	AGGACCCACAGCUCUGAUGU	8728
84166_4_38	NLRC5	EXON	-	chr16:57023798-57023818	GAGGACCCACAGCUCUGAUG	8729
84166_4_43	NLRC5	EXON	-	chr16:57023817-57023837	GCACUGCUUCCGGCGGGGUG	8730
84166_4_46	NLRC5	EXON	-	chr16:57023822-57023842	UUCUUGCACUGCUUCCGGCG	8731
84166_4_47	NLRC5	EXON	-	chr16:57023823-57023843	CUUCUUGCACUGCUUCCGGC	8732
84166_4_49	NLRC5	EXON	-	chr16:57023824-57023844	GCUUCUUGCACUGCUUCCGG	8733
84166_4_51	NLRC5	EXON	-	chr16:57023827-57023847	GCUGCUUCUUGCACUGCUUC	8734
84166_5_1	NLRC5	EXON	+	chr16:57025350-57025370	GUCCCUGCCCCUUGCAGAGU	8735
84166_5_6	NLRC5	EXON	+	chr16:57025376-57025396	AGAAGUACCUGCAGCUCCUG	8736
84166_5_9	NLRC5	EXON	+	chr16:57025400-57025420	CCUCUGCCCAGCAGCGCUAC	8737
84166_5_11	NLRC5	EXON	+	chr16:57025414-57025434	CGCUACAGGAGCCAAAUCCC	8738
84166_5_12	NLRC5	EXON	+	chr16:57025415-57025435	GCUACAGGAGCCAAAUCCCU	8739
84166_5_14	NLRC5	EXON	+	chr16:57025420-57025440	AGGAGCCAAAUCCCUGGGUC	8740
84166_5_15	NLRC5	EXON	+	chr16:57025421-57025441	GGAGCCAAAUCCCUGGGUCA	8741

84166_5_16	NLRC5	EXON	+	chr16:57025443-57025463	GCAGCCCCACGCCUUCCACC	8742
84166_5_19	NLRC5	EXON	+	chr16:57025469-57025489	AUGUCCCUCCAAUCCUGCGC	8743
84166_5_20	NLRC5	EXON	+	chr16:57025470-57025490	UGUCCCUCCAAUCCUGCGCC	8744
84166_5_22	NLRC5	EXON	+	chr16:57025494-57025514	CACAGCAUCCUUAGACACUC	8745
84166_5_26	NLRC5	EXON	+	chr16:57025497-57025517	AGCAUCCUUAGACACUCCGG	8746
84166_5_27	NLRC5	EXON	+	chr16:57025498-57025518	GCAUCCUUAGACACUCCGGA	8747
84166_5_29	NLRC5	EXON	+	chr16:57025499-57025519	CAUCCUUAGACACUCCGGAG	8748
84166_5_30	NLRC5	EXON	+	chr16:57025500-57025520	AUCCUUAGACACUCCGGAGG	8749
84166_5_34	NLRC5	EXON	+	chr16:57025509-57025529	CACUCCGGAGGGGGCCAUUA	8750
84166_5_35	NLRC5	EXON	+	chr16:57025510-57025530	ACUCCGGAGGGGGCCAUUAU	8751
84166_5_37	NLRC5	EXON	+	chr16:57025511-57025531	CUCCGGAGGGGGCCAUUAUG	8752
84166_5_39	NLRC5	EXON	+	chr16:57025512-57025532	UCCGGAGGGGGCCAUUAUGG	8753
84166_5_40	NLRC5	EXON	+	chr16:57025521-57025541	GGCCAUUAUGGGGGACGUCA	8754
84166_5_43	NLRC5	EXON	+	chr16:57025524-57025544	CAUUAUGGGGGACGUCAAGG	8755
84166_5_45	NLRC5	EXON	+	chr16:57025531-57025551	GGGGACGUCAAGGUGGAAGA	8756
84166_5_48	NLRC5	EXON	+	chr16:57025551-57025571	UGGUGCUGACGUGAGCAUCU	8757
84166_5_50	NLRC5	EXON	+	chr16:57025568-57025588	UCUCGGACCUCUUCAACACC	8758
84166_5_51	NLRC5	EXON	+	chr16:57025569-57025589	CUCGGACCUCUUCAACACCA	8759
84166_5_53	NLRC5	EXON	+	chr16:57025578-57025598	CUUCAACACCAGGGUUAACA	8760
84166_5_54	NLRC5	EXON	+	chr16:57025579-57025599	UUCAACACCAGGGUUAACAA	8761
84166_5_58	NLRC5	EXON	+	chr16:57025586-57025606	CCAGGGUUAACAAGGGCCCG	8762
84166_5_59	NLRC5	EXON	+	chr16:57025587-57025607	CAGGGUUAACAAGGGCCCGA	8763
84166_5_63	NLRC5	EXON	+	chr16:57025602-57025622	CCCGAGGGUGACCGUGCUUU	8764
84166_5_65	NLRC5	EXON	+	chr16:57025603-57025623	CCGAGGGUGACCGUGCUUUU	8765
84166_5_66	NLRC5	EXON	+	chr16:57025604-57025624	CGAGGGUGACCGUGCUUUUG	8766

84166_5_68	NLRC5	EXON	+	chr16:57025608-57025628	GGUGACCGUGCUUUUGGGGA	8767
84166_5_69	NLRC5	EXON	+	chr16:57025612-57025632	ACCGUGCUUUUGGGGAAGGC	8768
84166_5_71	NLRC5	EXON	+	chr16:57025617-57025637	GCUUUUGGGGAAGGCUGGCA	8769
84166_5_72	NLRC5	EXON	+	chr16:57025618-57025638	CUUUUGGGGAAGGCUGGCAU	8770
84166_5_76	NLRC5	EXON	+	chr16:57025632-57025652	UGGCAUGGGCAAGACCACGC	8771
84166_5_77	NLRC5	EXON	+	chr16:57025640-57025660	GCAAGACCACGCUGGCCCAC	8772
84166_5_80	NLRC5	EXON	+	chr16:57025655-57025675	CCCACCGGCUCUGCCAGAAG	8773
84166_5_81	NLRC5	EXON	+	chr16:57025656-57025676	CCACCGGCUCUGCCAGAAGU	8774
84166_5_84	NLRC5	EXON	+	chr16:57025662-57025682	GCUCUGCCAGAAGUGGGCAG	8775
84166_5_85	NLRC5	EXON	+	chr16:57025663-57025683	CUCUGCCAGAAGUGGGCAGA	8776
84166_5_87	NLRC5	EXON	+	chr16:57025683-57025703	GGGCCAUCUGAACUGUUUCC	8777
84166_5_98	NLRC5	EXON	+	chr16:57025727-57025747	GCCAGCUCAACUUGAUCACG	8778
84166_5_109	NLRC5	EXON	+	chr16:57025779-57025799	UCUGUACCUGAGCCCUGAAU	8779
84166_5_112	NLRC5	EXON	+	chr16:57025806-57025826	CGACACUGUCUUCCAGUACC	8780
84166_5_117	NLRC5	EXON	+	chr16:57025843-57025863	CAAGUCCUGCUGAUCUUUGA	8781
84166_5_118	NLRC5	EXON	+	chr16:57025844-57025864	AAGUCCUGCUGAUCUUUGAU	8782
84166_5_120	NLRC5	EXON	+	chr16:57025854-57025874	GAUCUUUGAUGGGCUAGAUG	8783
84166_5_124	NLRC5	EXON	+	chr16:57025869-57025889	AGAUGAGGCCCUCCAGCCUA	8784
84166_5_125	NLRC5	EXON	+	chr16:57025870-57025890	GAUGAGGCCCUCCAGCCUAU	8785
84166_5_126	NLRC5	EXON	+	chr16:57025879-57025899	CUCCAGCCUAUGGGUCCUGA	8786
84166_5_127	NLRC5	EXON	+	chr16:57025885-57025905	CCUAUGGGUCCUGAUGGCCC	8787
84166_5_129	NLRC5	EXON	+	chr16:57025921-57025941	CUUUUCUCCCAUCUCUGCAA	8788
84166_5_131	NLRC5	EXON	+	chr16:57025922-57025942	UUUUCUCCCAUCUCUGCAAU	8789
84166_5_136	NLRC5	EXON	+	chr16:57025995-57026015	GCCUGCCUGCCUGCCUGCAG	8790
84166_5_137	NLRC5	EXON	+	chr16:57026004-57026024	CCUGCCUGCAGAGGCAGCCA	8791

84166_5_139	NLRC5	EXON	+	chr16:57026016-57026036	GGCAGCCAUGGUCCACAUGU	8792
84166_5_140	NLRC5	EXON	+	chr16:57026017-57026037	GCAGCCAUGGUCCACAUGUU	8793
84166_5_142	NLRC5	EXON	+	chr16:57026026-57026046	GUCCACAUGUUGGGCUUUGA	8794
84166_5_143	NLRC5	EXON	+	chr16:57026027-57026047	UCCACAUGUUGGGCUUUGAU	8795
84166_5_145	NLRC5	EXON	+	chr16:57026033-57026053	UGUUGGGCUUUGAUGGGCCA	8796
84166_5_146	NLRC5	EXON	+	chr16:57026034-57026054	GUUGGGCUUUGAUGGGCCAC	8797
84166_5_149	NLRC5	EXON	+	chr16:57026037-57026057	GGGCUUUGAUGGGCCACGGG	8798
84166_5_158	NLRC5	EXON	+	chr16:57026078-57026098	UCUUCAGCGCCCAGCCAUCG	8799
84166_5_159	NLRC5	EXON	+	chr16:57026079-57026099	CUUCAGCGCCCAGCCAUCGC	8800
84166_5_163	NLRC5	EXON	+	chr16:57026082-57026102	CAGCGCCCAGCCAUCGCGGG	8801
84166_5_165	NLRC5	EXON	+	chr16:57026083-57026103	AGCGCCCAGCCAUCGCGGGA	8802
84166_5_168	NLRC5	EXON	+	chr16:57026084-57026104	GCGCCCAGCCAUCGCGGGAG	8803
84166_5_169	NLRC5	EXON	+	chr16:57026085-57026105	CGCCCAGCCAUCGCGGGAGG	8804
84166_5_170	NLRC5	EXON	+	chr16:57026091-57026111	GCCAUCGCGGGAGGGGGCCC	8805
84166_5_173	NLRC5	EXON	+	chr16:57026094-57026114	AUCGCGGGAGGGGGCCCUGG	8806
84166_5_175	NLRC5	EXON	+	chr16:57026110-57026130	CUGGUGGAGUUACAGACAAA	8807
84166_5_178	NLRC5	EXON	+	chr16:57026133-57026153	ACGUCUCCGAAGCCUGUGUG	8808
84166_5_179	NLRC5	EXON	+	chr16:57026197-57026217	CUGCUUCCUGACCACGCCCC	8809
84166_5_181	NLRC5	EXON	+	chr16:57026208-57026228	CCACGCCCCAGGCCAGUCUG	8810
84166_5_182	NLRC5	EXON	+	chr16:57026247-57026267	GACUCAGCUCUAUAUGCAGA	8811
84166_5_184	NLRC5	EXON	+	chr16:57026269-57026289	GUGCUCGCCCUCAGCCCCCC	8812
84166_5_185	NLRC5	EXON	+	chr16:57026270-57026290	UGCUCGCCCUCAGCCCCCU	8813
84166_5_187	NLRC5	EXON	+	chr16:57026295-57026315	CUUGCCCACCUCGUCCCUAC	8814
84166_5_191	NLRC5	EXON	+	chr16:57026301-57026321	CACCUCGUCCCUACUGGACC	8815
84166_5_193	NLRC5	EXON	+	chr16:57026302-57026322	ACCUCGUCCCUACUGGACCU	8816

84166_5_195	NLRC5	EXON	+	chr16:57026303-57026323	CCUCGUCCCUACUGGACCUG	8817
84166_5_197	NLRC5	EXON	+	chr16:57026304-57026324	CUCGUCCCUACUGGACCUGG	8818
84166_5_198	NLRC5	EXON	+	chr16:57026307-57026327	GUCCCUACUGGACCUGGGGG	8819
84166_5_199	NLRC5	EXON	+	chr16:57026310-57026330	CCUACUGGACCUGGGGGAGG	8820
84166_5_203	NLRC5	EXON	+	chr16:57026318-57026338	ACCUGGGGGAGGUGGCCCUG	8821
84166_5_204	NLRC5	EXON	+	chr16:57026319-57026339	CCUGGGGGAGGUGGCCCUGA	8822
84166_5_205	NLRC5	EXON	+	chr16:57026320-57026340	CUGGGGGAGGUGGCCCUGAG	8823
84166_5_208	NLRC5	EXON	+	chr16:57026325-57026345	GGAGGUGGCCCUGAGGGGCC	8824
84166_5_210	NLRC5	EXON	+	chr16:57026332-57026352	GCCCUGAGGGGCCUGGAGAC	8825
84166_5_212	NLRC5	EXON	+	chr16:57026333-57026353	CCCUGAGGGGCCUGGAGACA	8826
84166_5_214	NLRC5	EXON	+	chr16:57026337-57026357	GAGGGGCCUGGAGACAGGGA	8827
84166_5_218	NLRC5	EXON	+	chr16:57026383-57026403	GCUCCACCCUUGAUAGCUUU	8828
84166_5_220	NLRC5	EXON	+	chr16:57026384-57026404	CUCCACCCUUGAUAGCUUUU	8829
84166_5_222	NLRC5	EXON	+	chr16:57026385-57026405	UCCACCCUUGAUAGCUUUUG	8830
84166_5_227	NLRC5	EXON	+	chr16:57026425-57026445	ACUUCCUUCUGCGUCUGCAC	8831
84166_5_230	NLRC5	EXON	+	chr16:57026431-57026451	UUCUGCGUCUGCACAGGCCC	8832
84166_5_231	NLRC5	EXON	+	chr16:57026432-57026452	UCUGCGUCUGCACAGGCCCU	8833
84166_5_233	NLRC5	EXON	+	chr16:57026446-57026466	GGCCCUGGGCACCAGCAGAC	8834
84166_5_235	NLRC5	EXON	+	chr16:57026475-57026495	UUUCACCCACCUCAGCCUGC	8835
84166_5_239	NLRC5	EXON	+	chr16:57026502-57026522	UCUUGCUGCCCUGCACCUGA	8836
84166_5_243	NLRC5	EXON	+	chr16:57026514-57026534	GCACCUGAUGGCCAGCCCCA	8837
84166_5_247	NLRC5	EXON	+	chr16:57026561-57026581	AUGUUACCCUCCAUUCCCGC	8838
84166_5_248	NLRC5	EXON	+	chr16:57026562-57026582	UGUUACCCUCCAUUCCCGCU	8839
84166_5_251	NLRC5	EXON	+	chr16:57026570-57026590	UCCAUUCCCGCUGGGUACAG	8840
84166_5_254	NLRC5	EXON	+	chr16:57026586-57026606	ACAGCGGACCAAAGCUAGAC	8841

84166_5_255	NLRC5	EXON	+	chr16:57026587-57026607	CAGCGGACCAAAGCUAGACU	8842
84166_5_256	NLRC5	EXON	+	chr16:57026616-57026636	AGACCACCUCCCCACCUUCC	8843
84166_5_258	NLRC5	EXON	+	chr16:57026619-57026639	CCACCUCCCCACCUUCCUGG	8844
84166_5_259	NLRC5	EXON	+	chr16:57026620-57026640	CACCUCCCCACCUUCCUGGC	8845
84166_5_260	NLRC5	EXON	+	chr16:57026625-57026645	CCCCACCUUCCUGGCGGGCC	8846
84166_5_262	NLRC5	EXON	+	chr16:57026661-57026681	CCGCCCCUUCCUUAGCCACC	8847
84166_5_264	NLRC5	EXON	+	chr16:57026667-57026687	CUUCCUUAGCCACCUGGCGC	8848
84166_5_265	NLRC5	EXON	+	chr16:57026668-57026688	UUCCUUAGCCACCUGGCGCA	8849
84166_5_270	NLRC5	EXON	+	chr16:57026676-57026696	CCACCUGGCGCAGGGCAAUG	8850
84166_5_272	NLRC5	EXON	+	chr16:57026685-57026705	GCAGGGCAAUGAGGACUGUG	8851
84166_5_273	NLRC5	EXON	+	chr16:57026686-57026706	CAGGGCAAUGAGGACUGUGU	8852
84166_5_274	NLRC5	EXON	+	chr16:57026697-57026717	GGACUGUGUGGGUGCCAAGC	8853
84166_5_275	NLRC5	EXON	+	chr16:57026712-57026732	CAAGCAGGCUGCUGUAGUGC	8854
84166_5_278	NLRC5	EXON	+	chr16:57026727-57026747	AGUGCAGGUGUUGAAGAAGU	8855
84166_5_281	NLRC5	EXON	+	chr16:57026746-57026766	UUGGCCACCCGCAAGCUCAC	8856
84166_5_282	NLRC5	EXON	+	chr16:57026747-57026767	UGGCCACCCGCAAGCUCACA	8857
84166_5_284	NLRC5	EXON	+	chr16:57026754-57026774	CCGCAAGCUCACAGGGCCAA	8858
84166_5_287	NLRC5	EXON	+	chr16:57026778-57026798	UGUAGAGCUGUGUCACUGUG	8859
84166_5_291	NLRC5	EXON	+	chr16:57026790-57026810	UCACUGUGUGGAUGAGACAC	8860
84166_5_294	NLRC5	EXON	+	chr16:57026802-57026822	UGAGACACAGGAGCCUGAGC	8861
84166_5_296	NLRC5	EXON	+	chr16:57026874-57026894	CCCACUGACCUGCACCGACC	8862
84166_5_302	NLRC5	EXON	+	chr16:57026903-57026923	UGACCAACAUCCUAGAGCAC	8863
84166_5_303	NLRC5	EXON	+	chr16:57026904-57026924	GACCAACAUCCUAGAGCACA	8864
84166_5_305	NLRC5	EXON	+	chr16:57026907-57026927	CAACAUCCUAGAGCACAGGG	8865
84166_5_307	NLRC5	EXON	+	chr16:57026922-57026942	CAGGGAGGCCCCCAUCCACC	8866

84166_5_308	NLRC5	EXON	+	chr16:57026932-57026952	CCCAUCCACCUGGAUUUUGA	8867
84166_5_311	NLRC5	EXON	+	chr16:57026943-57026963	GGAUUUUGAUGGCUGUCCCC	8868
84166_5_316	NLRC5	EXON	+	chr16:57026961-57026981	CCUGGAGCCCCACUGCCCUG	8869
84166_5_317	NLRC5	EXON	+	chr16:57026967-57026987	GCCCCACUGCCCUGAGGCUC	8870
84166_5_318	NLRC5	EXON	+	chr16:57026971-57026991	CACUGCCCUGAGGCUCUGGU	8871
84166_5_320	NLRC5	EXON	+	chr16:57026977-57026997	CCUGAGGCUCUGGUAGGCUG	8872
84166_5_321	NLRC5	EXON	+	chr16:57026978-57026998	CUGAGGCUCUGGUAGGCUGU	8873
84166_5_325	NLRC5	EXON	+	chr16:57026996-57027016	GUGGGCAGAUAGAGAAUCUC	8874
84166_5_330	NLRC5	EXON	+	chr16:57027009-57027029	GAAUCUCAGGUGAGUAAGAG	8875
84166_5_333	NLRC5	EXON	+	chr16:57027012-57027032	UCUCAGGUGAGUAAGAGUGG	8876
84166_5_334	NLRC5	EXON	+	chr16:57027015-57027035	CAGGUGAGUAAGAGUGGAGG	8877
84166_5_337	NLRC5	EXON	-	chr16:57025355-57025375	GGCCAACUCUGCAAGGGGCA	8878
84166_5_338	NLRC5	EXON	-	chr16:57025356-57025376	UGGCCAACUCUGCAAGGGGC	8879
84166_5_341	NLRC5	EXON	-	chr16:57025360-57025380	UUCUUGGCCAACUCUGCAAG	8880
84166_5_342	NLRC5	EXON	-	chr16:57025361-57025381	CUUCUUGGCCAACUCUGCAA	8881
84166_5_344	NLRC5	EXON	-	chr16:57025362-57025382	ACUUCUUGGCCAACUCUGCA	8882
84166_5_346	NLRC5	EXON	-	chr16:57025376-57025396	CAGGAGCUGCAGGUACUUCU	8883
84166_5_347	NLRC5	EXON	-	chr16:57025386-57025406	CAGAGGUCCGCAGGAGCUGC	8884
84166_5_348	NLRC5	EXON	-	chr16:57025395-57025415	GCUGCUGGGCAGAGGUCCGC	8885
84166_5_351	NLRC5	EXON	-	chr16:57025403-57025423	CCUGUAGCGCUGCUGGGCAG	8886
84166_5_355	NLRC5	EXON	-	chr16:57025409-57025429	UUGGCUCCUGUAGCGCUGCU	8887
84166_5_356	NLRC5	EXON	-	chr16:57025410-57025430	UUUGGCUCCUGUAGCGCUGC	8888
84166_5_358	NLRC5	EXON	-	chr16:57025428-57025448	GCUGCCCUGACCCAGGGAUU	8889
84166_5_359	NLRC5	EXON	-	chr16:57025434-57025454	CGUGGGGCUGCCCUGACCCA	8890
84166_5_361	NLRC5	EXON	-	chr16:57025435-57025455	GCGUGGGGCUGCCCUGACCC	8891

84166_5_363	NLRC5	EXON	-	chr16:57025450-57025470	UAGACCUGGUGGAAGGCGUG	8892
84166_5_364	NLRC5	EXON	-	chr16:57025451-57025471	AUAGACCUGGUGGAAGGCGU	8893
84166_5_365	NLRC5	EXON	-	chr16:57025452-57025472	CAUAGACCUGGUGGAAGGCG	8894
84166_5_369	NLRC5	EXON	-	chr16:57025457-57025477	AGGGACAUAGACCUGGUGGA	8895
84166_5_370	NLRC5	EXON	-	chr16:57025461-57025481	UUGGAGGGACAUAGACCUGG	8896
84166_5_373	NLRC5	EXON	-	chr16:57025464-57025484	GGAUUGGAGGGACAUAGACC	8897
84166_5_374	NLRC5	EXON	-	chr16:57025476-57025496	UGGCCCGGCGCAGGAUUGGA	8898
84166_5_376	NLRC5	EXON	-	chr16:57025477-57025497	GUGGCCCGGCGCAGGAUUGG	8899
84166_5_378	NLRC5	EXON	-	chr16:57025480-57025500	GCUGUGGCCCGGCGCAGGAU	8900
84166_5_381	NLRC5	EXON	-	chr16:57025485-57025505	AGGAUGCUGUGGCCCGGCGC	8901
84166_5_383	NLRC5	EXON	-	chr16:57025491-57025511	UGUCUAAGGAUGCUGUGGCC	8902
84166_5_384	NLRC5	EXON	-	chr16:57025496-57025516	CGGAGUGUCUAAGGAUGCUG	8903
84166_5_385	NLRC5	EXON	-	chr16:57025505-57025525	GGCCCCCUCCGGAGUGUCUA	8904
84166_5_388	NLRC5	EXON	-	chr16:57025516-57025536	UCCCCCAUAAUGGCCCCCUC	8905
84166_5_392	NLRC5	EXON	-	chr16:57025526-57025546	CACCUUGACGUCCCCCAUAA	8906
84166_5_397	NLRC5	EXON	-	chr16:57025578-57025598	UGUUAACCCUGGUGUUGAAG	8907
84166_5_400	NLRC5	EXON	-	chr16:57025589-57025609	CCUCGGGCCCUUGUUAACCC	8908
84166_5_402	NLRC5	EXON	-	chr16:57025605-57025625	CCAAAAGCACGGUCACCCUC	8909
84166_5_403	NLRC5	EXON	-	chr16:57025606-57025626	CCCAAAAGCACGGUCACCCU	8910
84166_5_405	NLRC5	EXON	-	chr16:57025616-57025636	GCCAGCCUUCCCCAAAAGCA	8911
84166_5_408	NLRC5	EXON	-	chr16:57025649-57025669	GCAGAGCCGGUGGGCCAGCG	8912
84166_5_409	NLRC5	EXON	-	chr16:57025658-57025678	CCACUUCUGGCAGAGCCGGU	8913
84166_5_410	NLRC5	EXON	-	chr16:57025659-57025679	CCCACUUCUGGCAGAGCCGG	8914
84166_5_412	NLRC5	EXON	-	chr16:57025662-57025682	CUGCCCACUUCUGGCAGAGC	8915
84166_5_415	NLRC5	EXON	-	chr16:57025671-57025691	GAUGGCCCUCUGCCCACUUC	8916

84166_5_416	NLRC5	EXON	-	chr16:57025689-57025709	GGGCCUGGAAACAGUUCAGA	8917
84166_5_419	NLRC5	EXON	-	chr16:57025704-57025724	AUUCAAAAAGGAACAGGGCC	8918
84166_5_421	NLRC5	EXON	-	chr16:57025709-57025729	GCGGAAUUCAAAAAGGAACA	8919
84166_5_422	NLRC5	EXON	-	chr16:57025710-57025730	GGCGGAAUUCAAAAAGGAAC	8920
84166_5_426	NLRC5	EXON	-	chr16:57025716-57025736	UGAGCUGGCGGAAUUCAAAA	8921
84166_5_429	NLRC5	EXON	-	chr16:57025728-57025748	UCGUGAUCAAGUUGAGCUGG	8922
84166_5_431	NLRC5	EXON	-	chr16:57025731-57025751	ACCUCGUGAUCAAGUUGAGC	8923
84166_5_433	NLRC5	EXON	-	chr16:57025755-57025775	AAAGGAGCUCGGACGGUGUC	8924
84166_5_436	NLRC5	EXON	-	chr16:57025762-57025782	AGAUCAAAAAGGAGCUCGGA	8925
84166_5_437	NLRC5	EXON	-	chr16:57025766-57025786	GUACAGAUCAAAAAGGAGCU	8926
84166_5_440	NLRC5	EXON	-	chr16:57025773-57025793	GGCUCAGGUACAGAUCAAAA	8927
84166_5_443	NLRC5	EXON	-	chr16:57025788-57025808	CGUGGUCCGAUUCAGGGCUC	8928
84166_5_444	NLRC5	EXON	-	chr16:57025794-57025814	CAGUGUCGUGGUCCGAUUCA	8929
84166_5_445	NLRC5	EXON	-	chr16:57025795-57025815	ACAGUGUCGUGGUCCGAUUC	8930
84166_5_447	NLRC5	EXON	-	chr16:57025806-57025826	GGUACUGGAAGACAGUGUCG	8931
84166_5_451	NLRC5	EXON	-	chr16:57025821-57025841	CAGCGUUCUUCUCCAGGUAC	8932
84166_5_454	NLRC5	EXON	-	chr16:57025827-57025847	CUUGGUCAGCGUUCUUCUCC	8933
84166_5_455	NLRC5	EXON	-	chr16:57025845-57025865	CAUCAAAGAUCAGCAGGACU	8934
84166_5_456	NLRC5	EXON	-	chr16:57025851-57025871	CUAGCCCAUCAAAGAUCAGC	8935
84166_5_458	NLRC5	EXON	-	chr16:57025880-57025900	AUCAGGACCCAUAGGCUGGA	8936
84166_5_459	NLRC5	EXON	-	chr16:57025881-57025901	CAUCAGGACCCAUAGGCUGG	8937
84166_5_462	NLRC5	EXON	-	chr16:57025884-57025904	GGCCAUCAGGACCCAUAGGC	8938
84166_5_464	NLRC5	EXON	-	chr16:57025888-57025908	CCUGGGCCAUCAGGACCCAU	8939
84166_5_465	NLRC5	EXON	-	chr16:57025897-57025917	AGGACUGGGCCUGGGCCAUC	8940
84166_5_467	NLRC5	EXON	-	chr16:57025905-57025925	AAAGGGUGAGGACUGGGCCU	8941

84166_5_468	NLRC5	EXON	-	chr16:57025906-57025926	AAAAGGGUGAGGACUGGGCC	8942
84166_5_470	NLRC5	EXON	-	chr16:57025911-57025931	GGGAGAAAAGGGUGAGGACU	8943
84166_5_471	NLRC5	EXON	-	chr16:57025912-57025932	UGGGAGAAAAGGGUGAGGAC	8944
84166_5_474	NLRC5	EXON	-	chr16:57025917-57025937	AGAGAUGGGAGAAAAGGGUG	8945
84166_5_477	NLRC5	EXON	-	chr16:57025922-57025942	AUUGCAGAGAUGGGAGAAAA	8946
84166_5_478	NLRC5	EXON	-	chr16:57025923-57025943	CAUUGCAGAGAUGGGAGAAA	8947
84166_5_481	NLRC5	EXON	-	chr16:57025931-57025951	CUCCGUCCCAUUGCAGAGAU	8948
84166_5_483	NLRC5	EXON	-	chr16:57025932-57025952	CCUCCGUCCCAUUGCAGAGA	8949
84166_5_487	NLRC5	EXON	-	chr16:57026024-57026044	AAAGCCCAACAUGUGGACCA	8950
84166_5_488	NLRC5	EXON	-	chr16:57026031-57026051	GCCCAUCAAAGCCCAACAUG	8951
84166_5_493	NLRC5	EXON	-	chr16:57026053-57026073	UUCACAUAUUCUUCCACCCG	8952
84166_5_497	NLRC5	EXON	-	chr16:57026090-57026110	GGCCCCCUCCCGCGAUGGCU	8953
84166_5_498	NLRC5	EXON	-	chr16:57026091-57026111	GGGCCCCCUCCCGCGAUGGC	8954
84166_5_500	NLRC5	EXON	-	chr16:57026095-57026115	ACCAGGGCCCCCUCCCGCGA	8955
84166_5_503	NLRC5	EXON	-	chr16:57026111-57026131	AUUUGUCUGUAACUCCACCA	8956
84166_5_504	NLRC5	EXON	-	chr16:57026112-57026132	CAUUUGUCUGUAACUCCACC	8957
84166_5_508	NLRC5	EXON	-	chr16:57026142-57026162	CGGGCACCGCACACAGGCUU	8958
84166_5_511	NLRC5	EXON	-	chr16:57026148-57026168	ACAGUGCGGGCACCGCACAC	8959
84166_5_512	NLRC5	EXON	-	chr16:57026161-57026181	CAGGCGACUUGGCACAGUGC	8960
84166_5_513	NLRC5	EXON	-	chr16:57026162-57026182	ACAGGCGACUUGGCACAGUG	8961
84166_5_515	NLRC5	EXON	-	chr16:57026172-57026192	GGAGGCAGAGACAGGCGACU	8962
84166_5_516	NLRC5	EXON	-	chr16:57026180-57026200	CAGAUGGUGGAGGCAGAGAC	8963
84166_5_518	NLRC5	EXON	-	chr16:57026190-57026210	GGUCAGGAAGCAGAUGGUGG	8964
84166_5_520	NLRC5	EXON	-	chr16:57026193-57026213	CGUGGUCAGGAAGCAGAUGG	8965
84166_5_522	NLRC5	EXON	-	chr16:57026196-57026216	GGGCGUGGUCAGGAAGCAGA	8966

84166_5_523	NLRC5	EXON	-	chr16:57026206-57026226	GACUGGCCUGGGGCGUGGUC	8967
84166_5_526	NLRC5	EXON	-	chr16:57026211-57026231	CCACAGACUGGCCUGGGGCG	8968
84166_5_527	NLRC5	EXON	-	chr16:57026216-57026236	GAGGGCCACAGACUGGCCUG	8969
84166_5_528	NLRC5	EXON	-	chr16:57026217-57026237	GGAGGGCCACAGACUGGCCU	8970
84166_5_529	NLRC5	EXON	-	chr16:57026218-57026238	AGGAGGGCCACAGACUGGCC	8971
84166_5_533	NLRC5	EXON	-	chr16:57026223-57026243	UGGGCAGGAGGGCCACAGAC	8972
84166_5_534	NLRC5	EXON	-	chr16:57026234-57026254	CUGAGUCAUGUUGGGCAGGA	8973
84166_5_535	NLRC5	EXON	-	chr16:57026235-57026255	GCUGAGUCAUGUUGGGCAGG	8974
84166_5_537	NLRC5	EXON	-	chr16:57026238-57026258	AGAGCUGAGUCAUGUUGGGC	8975
84166_5_540	NLRC5	EXON	-	chr16:57026242-57026262	AUAUAGAGCUGAGUCAUGUU	8976
84166_5_541	NLRC5	EXON	-	chr16:57026243-57026263	CAUAUAGAGCUGAGUCAUGU	8977
84166_5_546	NLRC5	EXON	-	chr16:57026279-57026299	CAAGUGCCCAGGGGGGCUGA	8978
84166_5_547	NLRC5	EXON	-	chr16:57026280-57026300	GCAAGUGCCCAGGGGGGCUG	8979
84166_5_550	NLRC5	EXON	-	chr16:57026286-57026306	AGGUGGGCAAGUGCCCAGGG	8980
84166_5_551	NLRC5	EXON	-	chr16:57026287-57026307	GAGGUGGGCAAGUGCCCAGG	8981
84166_5_553	NLRC5	EXON	-	chr16:57026288-57026308	CGAGGUGGGCAAGUGCCCAG	8982
84166_5_555	NLRC5	EXON	-	chr16:57026289-57026309	ACGAGGUGGGCAAGUGCCCA	8983
84166_5_556	NLRC5	EXON	-	chr16:57026290-57026310	GACGAGGUGGGCAAGUGCCC	8984
84166_5_559	NLRC5	EXON	-	chr16:57026302-57026322	AGGUCCAGUAGGGACGAGGU	8985
84166_5_560	NLRC5	EXON	-	chr16:57026303-57026323	CAGGUCCAGUAGGGACGAGG	8986
84166_5_562	NLRC5	EXON	-	chr16:57026306-57026326	CCCCAGGUCCAGUAGGGACG	8987
84166_5_564	NLRC5	EXON	-	chr16:57026312-57026332	CACCUCCCCCAGGUCCAGUA	8988
84166_5_565	NLRC5	EXON	-	chr16:57026313-57026333	CCACCUCCCCCAGGUCCAGU	8989
84166_5_568	NLRC5	EXON	-	chr16:57026322-57026342	CCCUCAGGGCCACCUCCCCC	8990
84166_5_570	NLRC5	EXON	-	chr16:57026336-57026356	CCCUGUCUCCAGGCCCCUCA	8991

84166_5_571	NLRC5	EXON	-	chr16:57026337-57026357	UCCCUGUCUCCAGGCCCCUC	8992
84166_5_573	NLRC5	EXON	-	chr16:57026346-57026366	AGAUAACCUUCCCUGUCUCC	8993
84166_5_580	NLRC5	EXON	-	chr16:57026389-57026409	GCCCCAAAAGCUAUCAAGGG	8994
84166_5_582	NLRC5	EXON	-	chr16:57026392-57026412	GUGGCCCCAAAAGCUAUCAA	8995
84166_5_583	NLRC5	EXON	-	chr16:57026393-57026413	AGUGGCCCCAAAAGCUAUCA	8996
84166_5_585	NLRC5	EXON	-	chr16:57026411-57026431	GGAAGUCAGCAGGCUGUGAG	8997
84166_5_587	NLRC5	EXON	-	chr16:57026421-57026441	AGACGCAGAAGGAAGUCAGC	8998
84166_5_588	NLRC5	EXON	-	chr16:57026432-57026452	AGGGCCUGUGCAGACGCAGA	8999
84166_5_593	NLRC5	EXON	-	chr16:57026451-57026471	AGCCUGUCUGCUGGUGCCCA	9000
84166_5_594	NLRC5	EXON	-	chr16:57026452-57026472	UAGCCUGUCUGCUGGUGCCC	9001
84166_5_596	NLRC5	EXON	-	chr16:57026460-57026480	UGAAAGCAUAGCCUGUCUGC	9002
84166_5_598	NLRC5	EXON	-	chr16:57026483-57026503	AAACUCCUGCAGGCUGAGGU	9003
84166_5_599	NLRC5	EXON	-	chr16:57026484-57026504	GAAACUCCUGCAGGCUGAGG	9004
84166_5_601	NLRC5	EXON	-	chr16:57026487-57026507	CAAGAAACUCCUGCAGGCUG	9005
84166_5_603	NLRC5	EXON	-	chr16:57026493-57026513	GGGCAGCAAGAAACUCCUGC	9006
84166_5_606	NLRC5	EXON	-	chr16:57026513-57026533	GGGGCUGGCCAUCAGGUGCA	9007
84166_5_607	NLRC5	EXON	-	chr16:57026514-57026534	UGGGGCUGGCCAUCAGGUGC	9008
84166_5_612	NLRC5	EXON	-	chr16:57026520-57026540	UCACCUUGGGGCUGGCCAUC	9009
84166_5_613	NLRC5	EXON	-	chr16:57026528-57026548	GUCUUUGUUCACCUUGGGGC	9010
84166_5_614	NLRC5	EXON	-	chr16:57026532-57026552	GUGUGUCUUUGUUCACCUUG	9011
84166_5_615	NLRC5	EXON	-	chr16:57026533-57026553	AGUGUGUCUUUGUUCACCUU	9012
84166_5_616	NLRC5	EXON	-	chr16:57026534-57026554	AAGUGUGUCUUUGUUCACCU	9013
84166_5_619	NLRC5	EXON	-	chr16:57026558-57026578	GGAAUGGAGGGUAACAUACU	9014
84166_5_620	NLRC5	EXON	-	chr16:57026559-57026579	GGGAAUGGAGGGUAACAUAC	9015
84166_5_622	NLRC5	EXON	-	chr16:57026570-57026590	CUGUACCCAGCGGGAAUGGA	9016

84166_5_623	NLRC5	EXON	-	chr16:57026571-57026591	GCUGUACCCAGCGGGAAUGG	9017
84166_5_627	NLRC5	EXON	-	chr16:57026574-57026594	UCCGCUGUACCCAGCGGGAA	9018
84166_5_630	NLRC5	EXON	-	chr16:57026579-57026599	UUUGGUCCGCUGUACCCAGC	9019
84166_5_633	NLRC5	EXON	-	chr16:57026580-57026600	CUUUGGUCCGCUGUACCCAG	9020
84166_5_635	NLRC5	EXON	-	chr16:57026597-57026617	UGAGAGGCCCAGUCUAGCUU	9021
84166_5_636	NLRC5	EXON	-	chr16:57026613-57026633	AGGUGGGGAGGUGGUCUGAG	9022
84166_5_639	NLRC5	EXON	-	chr16:57026622-57026642	CCGCCAGGAAGGUGGGGAGG	9023
84166_5_640	NLRC5	EXON	-	chr16:57026625-57026645	GGCCCGCCAGGAAGGUGGGG	9024
84166_5_641	NLRC5	EXON	-	chr16:57026628-57026648	CCAGGCCCGCCAGGAAGGUG	9025
84166_5_643	NLRC5	EXON	-	chr16:57026629-57026649	GCCAGGCCCGCCAGGAAGGU	9026
84166_5_645	NLRC5	EXON	-	chr16:57026630-57026650	UGCCAGGCCCGCCAGGAAGG	9027
84166_5_648	NLRC5	EXON	-	chr16:57026633-57026653	GGAUGCCAGGCCCGCCAGGA	9028
84166_5_650	NLRC5	EXON	-	chr16:57026637-57026657	UGCAGGAUGCCAGGCCCGCC	9029
84166_5_652	NLRC5	EXON	-	chr16:57026646-57026666	GGCGGCAGGUGCAGGAUGCC	9030
84166_5_653	NLRC5	EXON	-	chr16:57026654-57026674	AAGGAAGGGGCGGCAGGUGC	9031
84166_5_655	NLRC5	EXON	-	chr16:57026660-57026680	GUGGCUAAGGAAGGGGCGGC	9032
84166_5_656	NLRC5	EXON	-	chr16:57026664-57026684	CCAGGUGGCUAAGGAAGGGG	9033
84166_5_657	NLRC5	EXON	-	chr16:57026667-57026687	GCGCCAGGUGGCUAAGGAAG	9034
84166_5_658	NLRC5	EXON	-	chr16:57026668-57026688	UGCGCCAGGUGGCUAAGGAA	9035
84166_5_660	NLRC5	EXON	-	chr16:57026669-57026689	CUGCGCCAGGUGGCUAAGGA	9036
84166_5_664	NLRC5	EXON	-	chr16:57026673-57026693	UGCCCUGCGCCAGGUGGCUA	9037
84166_5_666	NLRC5	EXON	-	chr16:57026679-57026699	CCUCAUUGCCCUGCGCCAGG	9038
84166_5_667	NLRC5	EXON	-	chr16:57026682-57026702	AGUCCUCAUUGCCCUGCGCC	9039
84166_5_669	NLRC5	EXON	-	chr16:57026714-57026734	CUGCACUACAGCAGCCUGCU	9040
84166_5_675	NLRC5	EXON	-	chr16:57026753-57026773	UGGCCCUGUGAGCUUGCGGG	9041

84166_5_676	NLRC5	EXON	-	chr16:57026756-57026776	CUUUGGCCCUGUGAGCUUGC	9042
84166_5_677	NLRC5	EXON	-	chr16:57026757-57026777	CCUUUGGCCCUGUGAGCUUG	9043
84166_5_680	NLRC5	EXON	-	chr16:57026773-57026793	UGACACAGCUCUACAACCUU	9044
84166_5_683	NLRC5	EXON	-	chr16:57026818-57026838	GCGGUGAGACUGGCCAGCUC	9045
84166_5_684	NLRC5	EXON	-	chr16:57026828-57026848	GAGGCUUUGUGCGGUGAGAC	9046
84166_5_687	NLRC5	EXON	-	chr16:57026837-57026857	UUGAUAGGGGAGGCUUUGUG	9047
84166_5_689	NLRC5	EXON	-	chr16:57026847-57026867	GGAAGGGCAGUUGAUAGGGG	9048
84166_5_691	NLRC5	EXON	-	chr16:57026850-57026870	UGUGGAAGGGCAGUUGAUAG	9049
84166_5_692	NLRC5	EXON	-	chr16:57026851-57026871	UUGUGGAAGGGCAGUUGAUA	9050
84166_5_695	NLRC5	EXON	-	chr16:57026852-57026872	AUUGUGGAAGGGCAGUUGAU	9051
84166_5_697	NLRC5	EXON	-	chr16:57026863-57026883	GUCAGUGGGAAAUUGUGGAA	9052
84166_5_698	NLRC5	EXON	-	chr16:57026864-57026884	GGUCAGUGGGAAAUUGUGGA	9053
84166_5_701	NLRC5	EXON	-	chr16:57026868-57026888	UGCAGGUCAGUGGGAAAUUG	9054
84166_5_704	NLRC5	EXON	-	chr16:57026877-57026897	CCAGGUCGGUGCAGGUCAGU	9055
84166_5_705	NLRC5	EXON	-	chr16:57026878-57026898	GCCAGGUCGGUGCAGGUCAG	9056
84166_5_709	NLRC5	EXON	-	chr16:57026885-57026905	CAGGGUGGCCAGGUCGGUGC	9057
84166_5_710	NLRC5	EXON	-	chr16:57026891-57026911	GUUGGUCAGGGUGGCCAGGU	9058
84166_5_711	NLRC5	EXON	-	chr16:57026895-57026915	GGAUGUUGGUCAGGGUGGCC	9059
84166_5_712	NLRC5	EXON	-	chr16:57026900-57026920	CUCUAGGAUGUUGGUCAGGG	9060
84166_5_713	NLRC5	EXON	-	chr16:57026903-57026923	GUGCUCUAGGAUGUUGGUCA	9061
84166_5_714	NLRC5	EXON	-	chr16:57026904-57026924	UGUGCUCUAGGAUGUUGGUC	9062
84166_5_716	NLRC5	EXON	-	chr16:57026909-57026929	CUCCCUGUGCUCUAGGAUGU	9063
84166_5_717	NLRC5	EXON	-	chr16:57026916-57026936	UGGGGGCCUCCCUGUGCUCU	9064
84166_5_719	NLRC5	EXON	-	chr16:57026933-57026953	AUCAAAAUCCAGGUGGAUGG	9065
84166_5_720	NLRC5	EXON	-	chr16:57026934-57026954	CAUCAAAAUCCAGGUGGAUG	9066

84166_5_721	NLRC5	EXON	-	chr16:57026935-57026955	CCAUCAAAAUCCAGGUGGAU	9067
84166_5_724	NLRC5	EXON	-	chr16:57026936-57026956	GCCAUCAAAAUCCAGGUGGA	9068
84166_5_726	NLRC5	EXON	-	chr16:57026940-57026960	GACAGCCAUCAAAAUCCAGG	9069
84166_5_728	NLRC5	EXON	-	chr16:57026943-57026963	GGGGACAGCCAUCAAAAUCC	9070
84166_5_729	NLRC5	EXON	-	chr16:57026962-57026982	UCAGGGCAGUGGGGCUCCAG	9071
84166_5_731	NLRC5	EXON	-	chr16:57026963-57026983	CUCAGGGCAGUGGGGCUCCA	9072
84166_5_732	NLRC5	EXON	-	chr16:57026964-57026984	CCUCAGGGCAGUGGGGCUCC	9073
84166_5_735	NLRC5	EXON	-	chr16:57026971-57026991	ACCAGAGCCUCAGGGCAGUG	9074
84166_5_736	NLRC5	EXON	-	chr16:57026972-57026992	UACCAGAGCCUCAGGGCAGU	9075
84166_5_738	NLRC5	EXON	-	chr16:57026973-57026993	CUACCAGAGCCUCAGGGCAG	9076
84166_5_740	NLRC5	EXON	-	chr16:57026979-57026999	CACAGCCUACCAGAGCCUCA	9077
84166_5_741	NLRC5	EXON	-	chr16:57026980-57027000	CCACAGCCUACCAGAGCCUC	9078
84166_6_5	NLRC5	EXON	+	chr16:57028061-57028081	CUUAUGGCAGCUUUAAGAGC	9079
84166_6_10	NLRC5	EXON	+	chr16:57028069-57028089	AGCUUUAAGAGCAGGAAGUG	9080
84166_6_13	NLRC5	EXON	+	chr16:57028070-57028090	GCUUUAAGAGCAGGAAGUGU	9081
84166_6_14	NLRC5	EXON	+	chr16:57028071-57028091	CUUUAAGAGCAGGAAGUGUG	9082
84166_6_19	NLRC5	EXON	+	chr16:57028097-57028117	CCUUUGCAGAAGCCCUCUCC	9083
84166_6_24	NLRC5	EXON	+	chr16:57028113-57028133	CUCCAGGAGCUUGCCGACAA	9084
84166_6_27	NLRC5	EXON	+	chr16:57028114-57028134	UCCAGGAGCUUGCCGACAAU	9085
84166_6_28	NLRC5	EXON	+	chr16:57028115-57028135	CCAGGAGCUUGCCGACAAUG	9086
84166_6_30	NLRC5	EXON	+	chr16:57028118-57028138	GGAGCUUGCCGACAAUGGGG	9087
84166_6_34	NLRC5	EXON	+	chr16:57028131-57028151	AAUGGGGAGGCUGCAGAUGC	9088
84166_6_35	NLRC5	EXON	+	chr16:57028132-57028152	AUGGGGAGGCUGCAGAUGCU	9089
84166_6_36	NLRC5	EXON	+	chr16:57028133-57028153	UGGGGAGGCUGCAGAUGCUG	9090
84166_6_38	NLRC5	EXON	+	chr16:57028142-57028162	UGCAGAUGCUGGGGUGAGCC	9091

84166_6_41	NLRC5	EXON	+	chr16:57028148-57028168	UGCUGGGGUGAGCCAGGCCU	9092
84166_6_50	NLRC5	EXON	-	chr16:57028100-57028120	CCUGGAGAGGGCUUCUGCAA	9093
84166_6_52	NLRC5	EXON	-	chr16:57028112-57028132	UGUCGGCAAGCUCCUGGAGA	9094
84166_6_53	NLRC5	EXON	-	chr16:57028113-57028133	UUGUCGGCAAGCUCCUGGAG	9095
84166_6_57	NLRC5	EXON	-	chr16:57028118-57028138	CCCCAUUGUCGGCAAGCUCC	9096
84166_6_59	NLRC5	EXON	-	chr16:57028129-57028149	AUCUGCAGCCUCCCCAUUGU	9097
84166_7_3	NLRC5	EXON	+	chr16:57028287-57028307	UGCUUACUCUGUAGGUUAGC	9098
84166_7_9	NLRC5	EXON	+	chr16:57028308-57028328	GGAAGUAAAAUCACUGCCCG	9099
84166_7_10	NLRC5	EXON	+	chr16:57028322-57028342	UGCCCGAGGCAUCAGCCACC	9100
84166_7_16	NLRC5	EXON	+	chr16:57028363-57028383	GUCCACAGCUGAAAGAAGUC	9101
84166_7_19	NLRC5	EXON	+	chr16:57028378-57028398	AAGUCAGGUGAGUGAUCUCC	9102
84166_7_22	NLRC5	EXON	+	chr16:57028381-57028401	UCAGGUGAGUGAUCUCCAGG	9103
84166_7_23	NLRC5	EXON	+	chr16:57028382-57028402	CAGGUGAGUGAUCUCCAGGA	9104
84166_7_31	NLRC5	EXON	-	chr16:57028327-57028347	CACCAGGUGGCUGAUGCCUC	9105
84166_7_32	NLRC5	EXON	-	chr16:57028328-57028348	UCACCAGGUGGCUGAUGCCU	9106
84166_7_34	NLRC5	EXON	-	chr16:57028340-57028360	GAGGCAAAGCUUUCACCAGG	9107
84166_7_35	NLRC5	EXON	-	chr16:57028343-57028363	AGAGAGGCAAAGCUUUCACC	9108
84166_7_39	NLRC5	EXON	-	chr16:57028359-57028379	UCUUUCAGCUGUGGACAGAG	9109
84166_7_42	NLRC5	EXON	-	chr16:57028368-57028388	CACCUGACUUCUUUCAGCUG	9110
84166_8_2	NLRC5	EXON	+	chr16:57029756-57029776	CUUGGUCUCCUCGCAGUUUU	9111
84166_8_4	NLRC5	EXON	+	chr16:57029757-57029777	UUGGUCUCCUCGCAGUUUUC	9112
84166_8_9	NLRC5	EXON	+	chr16:57029778-57029798	GGACAACCAGCUCAGUGACC	9113
84166_8_10	NLRC5	EXON	+	chr16:57029781-57029801	CAACCAGCUCAGUGACCAGG	9114
84166_8_13	NLRC5	EXON	+	chr16:57029796-57029816	CCAGGUGGUGCUGAACAUUG	9115
84166_8_15	NLRC5	EXON	+	chr16:57029799-57029819	GGUGGUGCUGAACAUUGUGG	9116

84166_8_17	NLRC5	EXON	+	chr16:57029819-57029839	AGGUUCUCCCUCACCUACCA	9117
84166_8_21	NLRC5	EXON	+	chr16:57029825-57029845	UCCCUCACCUACCACGGCUC	9118
84166_8_24	NLRC5	EXON	-	chr16:57029758-57029778	CGAAAACUGCGAGGAGACCA	9119
84166_8_26	NLRC5	EXON	-	chr16:57029767-57029787	UGGUUGUCCCGAAAACUGCG	9120
84166_8_31	NLRC5	EXON	-	chr16:57029787-57029807	GCACCACCUGGUCACUGAGC	9121
84166_8_33	NLRC5	EXON	-	chr16:57029799-57029819	CCACAAUGUUCAGCACCACC	9122
84166_8_38	NLRC5	EXON	-	chr16:57029829-57029849	UCCGGAGCCGUGGUAGGUGA	9123
84166_8_39	NLRC5	EXON	-	chr16:57029830-57029850	UUCCGGAGCCGUGGUAGGUG	9124
84166_8_44	NLRC5	EXON	-	chr16:57029835-57029855	CAAGCUUCCGGAGCCGUGGU	9125
84166_8_45	NLRC5	EXON	-	chr16:57029839-57029859	UACUCAAGCUUCCGGAGCCG	9126
84166_8_46	NLRC5	EXON	-	chr16:57029847-57029867	AGAUCACUUACUCAAGCUUC	9127
84166_9_5	NLRC5	EXON	+	chr16:57030015-57030035	CGUGUCAACCCUACUCUGCU	9128
84166_9_7	NLRC5	EXON	+	chr16:57030020-57030040	CAACCCUACUCUGCUUGGCA	9129
84166_9_8	NLRC5	EXON	+	chr16:57030021-57030041	AACCCUACUCUGCUUGGCAA	9130
84166_9_9	NLRC5	EXON	+	chr16:57030024-57030044	CCUACUCUGCUUGGCAAGGG	9131
84166_9_12	NLRC5	EXON	+	chr16:57030047-57030067	CAGUCACGUGUCCUACCGUC	9132
84166_9_13	NLRC5	EXON	+	chr16:57030057-57030077	UCCUACCGUCAGGAUGCUUC	9133
84166_9_14	NLRC5	EXON	+	chr16:57030062-57030082	CCGUCAGGAUGCUUCAGGCC	9134
84166_9_18	NLRC5	EXON	+	chr16:57030073-57030093	CUUCAGGCCAGGUGAGCAGA	9135
84166_9_22	NLRC5	EXON	+	chr16:57030078-57030098	GGCCAGGUGAGCAGAAGGAA	9136
84166_9_24	NLRC5	EXON	+	chr16:57030079-57030099	GCCAGGUGAGCAGAAGGAAA	9137
84166_9_25	NLRC5	EXON	-	chr16:57029977-57029997	AGGCUGCAAGAUUGUGGCAA	9138
84166_9_27	NLRC5	EXON	-	chr16:57029983-57030003	CUGCUCAGGCUGCAAGAUUG	9139
84166_9_29	NLRC5	EXON	-	chr16:57029997-57030017	CGCAGAUGCUGUUGCUGCUC	9140
84166_9_31	NLRC5	EXON	-	chr16:57030026-57030046	CACCCUUGCCAAGCAGAGUA	9141

84166_9_32	NLRC5	EXON	-	chr16:57030027-57030047	CCACCCUUGCCAAGCAGAGU	9142
84166_9_35	NLRC5	EXON	-	chr16:57030061-57030081	GCCUGAAGCAUCCUGACGGU	9143
84166_9_37	NLRC5	EXON	-	chr16:57030065-57030085	CCUGGCCUGAAGCAUCCUGA	9144
84166_9_42	NLRC5	EXON	-	chr16:57030083-57030103	UCCCUUUCCUUCUGCUCACC	9145
84166_10_1	NLRC5	EXON	+	chr16:57031385-57031405	UGGUAUCUGAUCCUGCAGGG	9146
84166_10_4	NLRC5	EXON	+	chr16:57031388-57031408	UAUCUGAUCCUGCAGGGAGG	9147
84166_10_11	NLRC5	EXON	+	chr16:57031441-57031461	AGACAACUGCAGAGCUACAA	9148
84166_10_14	NLRC5	EXON	+	chr16:57031456-57031476	UACAAAGGUAAGAAGCCAAG	9149
84166_10_15	NLRC5	EXON	+	chr16:57031459-57031479	AAAGGUAAGAAGCCAAGAGG	9150
84166_10_16	NLRC5	EXON	-	chr16:57031399-57031419	GAUGAGGUCCGCCUCCCUGC	9151
84166_10_18	NLRC5	EXON	-	chr16:57031415-57031435	GCGGGGAAAGAAGGAAGAUG	9152
84166_10_21	NLRC5	EXON	-	chr16:57031424-57031444	UCUCUGUGGGCGGGGAAAGA	9153
84166_10_27	NLRC5	EXON	-	chr16:57031432-57031452	UGCAGUUGUCUCUGUGGGCG	9154
84166_10_29	NLRC5	EXON	-	chr16:57031433-57031453	CUGCAGUUGUCUCUGUGGGC	9155
84166_10_31	NLRC5	EXON	-	chr16:57031434-57031454	UCUGCAGUUGUCUCUGUGGG	9156
84166_10_35	NLRC5	EXON	-	chr16:57031437-57031457	AGCUCUGCAGUUGUCUCUGU	9157
84166_10_36	NLRC5	EXON	-	chr16:57031438-57031458	UAGCUCUGCAGUUGUCUCUG	9158
84166_11_7	NLRC5	EXON	+	chr16:57033597-57033617	UGCCAGAGCUCCAGACCUGC	9159
84166_11_9	NLRC5	EXON	+	chr16:57033607-57033627	CCAGACCUGCAGGAAAGUGA	9160
84166_11_13	NLRC5	EXON	+	chr16:57033614-57033634	UGCAGGAAAGUGACGGCCAG	9161
84166_11_16	NLRC5	EXON	+	chr16:57033619-57033639	GAAAGUGACGGCCAGAGGAA	9162
84166_11_17	NLRC5	EXON	+	chr16:57033620-57033640	AAAGUGACGGCCAGAGGAAA	9163
84166_11_18	NLRC5	EXON	+	chr16:57033621-57033641	AAGUGACGGCCAGAGGAAAG	9164
84166_11_21	NLRC5	EXON	+	chr16:57033647-57033667	AGAGCAGAAGCUUGACGCUC	9165
84166_11_23	NLRC5	EXON	+	chr16:57033655-57033675	AGCUUGACGCUCAGGUACCU	9166

84166_11_27	NLRC5	EXON	+	chr16:57033658-57033678	UUGACGCUCAGGUACCUUGG	9167
84166_11_28	NLRC5	EXON	+	chr16:57033659-57033679	UGACGCUCAGGUACCUUGGA	9168
84166_11_34	NLRC5	EXON	-	chr16:57033602-57033622	UUCCUGCAGGUCUGGAGCUC	9169
84166_11_36	NLRC5	EXON	-	chr16:57033610-57033630	CCGUCACUUUCCUGCAGGUC	9170
84166_11_40	NLRC5	EXON	-	chr16:57033615-57033635	UCUGGCCGUCACUUUCCUGC	9171
84166_11_42	NLRC5	EXON	-	chr16:57033633-57033653	UGCUCUGAGCCCCUUUCCUC	9172
84166_12_2	NLRC5	EXON	+	chr16:57034167-57034187	GCUGCAGAAGUGUCAGCUCC	9173
84166_12_5	NLRC5	EXON	+	chr16:57034179-57034199	UCAGCUCCAGGUCCACGAUG	9174
84166_12_6	NLRC5	EXON	+	chr16:57034182-57034202	GCUCCAGGUCCACGAUGCGG	9175
84166_12_9	NLRC5	EXON	+	chr16:57034203-57034223	GGCCCUCAUAGCCCUGCUCC	9176
84166_12_10	NLRC5	EXON	+	chr16:57034207-57034227	CUCAUAGCCCUGCUCCAGGA	9177
84166_12_12	NLRC5	EXON	+	chr16:57034218-57034238	GCUCCAGGAAGGCCCUCACC	9178
84166_12_16	NLRC5	EXON	+	chr16:57034221-57034241	CCAGGAAGGCCCUCACCUGG	9179
84166_12_18	NLRC5	EXON	+	chr16:57034227-57034247	AGGCCCUCACCUGGAGGAAG	9180
84166_12_23	NLRC5	EXON	+	chr16:57034241-57034261	AGGAAGUGGAGUGAGUAUCA	9181
84166_12_24	NLRC5	EXON	+	chr16:57034242-57034262	GGAAGUGGAGUGAGUAUCAC	9182
84166_12_27	NLRC5	EXON	-	chr16:57034152-57034172	GCAGCCUUGGGUAGGAGUGG	9183
84166_12_28	NLRC5	EXON	-	chr16:57034153-57034173	UGCAGCCUUGGGUAGGAGUG	9184
84166_12_30	NLRC5	EXON	-	chr16:57034154-57034174	CUGCAGCCUUGGGUAGGAGU	9185
84166_12_33	NLRC5	EXON	-	chr16:57034155-57034175	UCUGCAGCCUUGGGUAGGAG	9186
84166_12_36	NLRC5	EXON	-	chr16:57034160-57034180	ACACUUCUGCAGCCUUGGGU	9187
84166_12_38	NLRC5	EXON	-	chr16:57034164-57034184	GCUGACACUUCUGCAGCCUU	9188
84166_12_39	NLRC5	EXON	-	chr16:57034165-57034185	AGCUGACACUUCUGCAGCCU	9189
84166_12_42	NLRC5	EXON	-	chr16:57034188-57034208	GGGCCUCCGCAUCGUGGACC	9190
84166_12_44	NLRC5	EXON	-	chr16:57034194-57034214	CUAUGAGGGCCUCCGCAUCG	9191

84166_12_47	NLRC5	EXON	-	chr16:57034208-57034228	UUCCUGGAGCAGGGCUAUGA	9192
84166_12_48	NLRC5	EXON	-	chr16:57034209-57034229	CUUCCUGGAGCAGGGCUAUG	9193
84166_12_51	NLRC5	EXON	-	chr16:57034217-57034237	GUGAGGGCCUUCCUGGAGCA	9194
84166_12_52	NLRC5	EXON	-	chr16:57034218-57034238	GGUGAGGGCCUUCCUGGAGC	9195
84166_12_55	NLRC5	EXON	-	chr16:57034224-57034244	CCUCCAGGUGAGGGCCUUCC	9196
84166_12_58	NLRC5	EXON	-	chr16:57034233-57034253	ACUCCACUUCCUCCAGGUGA	9197
84166_12_59	NLRC5	EXON	-	chr16:57034234-57034254	CACUCCACUUCCUCCAGGUG	9198
84166_12_62	NLRC5	EXON	-	chr16:57034239-57034259	AUACUCACUCCACUUCCUCC	9199
84166_13_4	NLRC5	EXON	+	chr16:57036085-57036105	GCCCCCCGUCUCAGCCUCUC	9200
84166_13_6	NLRC5	EXON	+	chr16:57036086-57036106	CCCCCCGUCUCAGCCUCUCA	9201
84166_13_9	NLRC5	EXON	+	chr16:57036096-57036116	CAGCCUCUCAGGGAACCAGC	9202
84166_13_11	NLRC5	EXON	+	chr16:57036106-57036126	GGGAACCAGCUGGAAGAUGA	9203
84166_13_12	NLRC5	EXON	+	chr16:57036113-57036133	AGCUGGAAGAUGAAGGCUGU	9204
84166_13_13	NLRC5	EXON	+	chr16:57036120-57036140	AGAUGAAGGCUGUCGGCUGA	9205
84166_13_15	NLRC5	EXON	+	chr16:57036126-57036146	AGGCUGUCGGCUGAUGGCAG	9206
84166_13_17	NLRC5	EXON	+	chr16:57036152-57036172	CAUCCCAGCUGCACAUCGCC	9207
84166_13_20	NLRC5	EXON	+	chr16:57036159-57036179	GCUGCACAUCGCCAGGAAGC	9208
84166_13_24	NLRC5	EXON	-	chr16:57036089-57036109	CCCUGAGAGGCUGAGACGGG	9209
84166_13_25	NLRC5	EXON	-	chr16:57036090-57036110	UCCCUGAGAGGCUGAGACGG	9210
84166_13_26	NLRC5	EXON	-	chr16:57036091-57036111	UUCCCUGAGAGGCUGAGACG	9211
84166_13_29	NLRC5	EXON	-	chr16:57036092-57036112	GUUCCCUGAGAGGCUGAGAC	9212
84166_13_30	NLRC5	EXON	-	chr16:57036093-57036113	GGUUCCCUGAGAGGCUGAGA	9213
84166_13_36	NLRC5	EXON	-	chr16:57036102-57036122	CUUCCAGCUGGUUCCCUGAG	9214
84166_13_39	NLRC5	EXON	-	chr16:57036114-57036134	GACAGCCUUCAUCUUCCAGC	9215
84166_13_41	NLRC5	EXON	-	chr16:57036158-57036178	CUUCCUGGCGAUGUGCAGCU	9216

84166_13_42	NLRC5	EXON	-	chr16:57036159-57036179	GCUUCCUGGCGAUGUGCAGC	9217
84166_13_45	NLRC5	EXON	-	chr16:57036173-57036193	GACAACUCACUCCAGCUUCC	9218
84166_14_3	NLRC5	EXON	+	chr16:57037186-57037206	CUCCACAGCCUCAGUAACAA	9219
84166_14_4	NLRC5	EXON	+	chr16:57037187-57037207	UCCACAGCCUCAGUAACAAC	9220
84166_14_5	NLRC5	EXON	+	chr16:57037197-57037217	CAGUAACAACGGGCUUUCUG	9221
84166_14_7	NLRC5	EXON	+	chr16:57037201-57037221	AACAACGGGCUUUCUGUGGC	9222
84166_14_9	NLRC5	EXON	+	chr16:57037202-57037222	ACAACGGGCUUUCUGUGGCC	9223
84166_14_10	NLRC5	EXON	+	chr16:57037203-57037223	CAACGGGCUUUCUGUGGCCG	9224
84166_14_15	NLRC5	EXON	+	chr16:57037220-57037240	CCGGGGUGCAUUGUGUGCUG	9225
84166_14_16	NLRC5	EXON	+	chr16:57037221-57037241	CGGGGUGCAUUGUGUGCUGA	9226
84166_14_20	NLRC5	EXON	+	chr16:57037238-57037258	UGAGGGCCGUGAGUGCGUGC	9227
84166_14_21	NLRC5	EXON	+	chr16:57037245-57037265	CGUGAGUGCGUGCUGGACCC	9228
84166_14_23	NLRC5	EXON	+	chr16:57037262-57037282	CCCUGGCAGAGCUGCACAUC	9229
84166_14_26	NLRC5	EXON	+	chr16:57037265-57037285	UGGCAGAGCUGCACAUCAGG	9230
84166_14_28	NLRC5	EXON	+	chr16:57037266-57037286	GGCAGAGCUGCACAUCAGGU	9231
84166_14_29	NLRC5	EXON	-	chr16:57037177-57037197	AGGCUGUGGAGAGCAGGAGA	9232
84166_14_34	NLRC5	EXON	-	chr16:57037183-57037203	UUACUGAGGCUGUGGAGAGC	9233
84166_14_39	NLRC5	EXON	-	chr16:57037191-57037211	GCCCGUUGUUACUGAGGCUG	9234
84166_14_41	NLRC5	EXON	-	chr16:57037197-57037217	CAGAAAGCCCGUUGUUACUG	9235
84166_14_44	NLRC5	EXON	-	chr16:57037223-57037243	CCUCAGCACACAAUGCACCC	9236
84166_14_45	NLRC5	EXON	-	chr16:57037247-57037267	CAGGGUCCAGCACGCACUCA	9237
84166_14_46	NLRC5	EXON	-	chr16:57037265-57037285	CCUGAUGUGCAGCUCUGCCA	9238
84166_14_47	NLRC5	EXON	-	chr16:57037266-57037286	ACCUGAUGUGCAGCUCUGCC	9239
84166_15_7	NLRC5	EXON	+	chr16:57039795-57039815	UGUGAUCUUCAUGUUUGCCC	9240
84166_15_11	NLRC5	EXON	+	chr16:57039804-57039824	CAUGUUUGCCCAGGAGCCAG	9241

84166_15_17	NLRC5	EXON	+	chr16:57039813-57039833	CCAGGAGCCAGAGGAGCAGA	9242
84166_15_19	NLRC5	EXON	+	chr16:57039814-57039834	CAGGAGCCAGAGGAGCAGAA	9243
84166_15_20	NLRC5	EXON	+	chr16:57039815-57039835	AGGAGCCAGAGGAGCAGAAG	9244
84166_15_23	NLRC5	EXON	+	chr16:57039822-57039842	AGAGGAGCAGAAGGGGCCCC	9245
84166_15_25	NLRC5	EXON	+	chr16:57039827-57039847	AGCAGAAGGGGCCCCAGGAG	9246
84166_15_27	NLRC5	EXON	+	chr16:57039831-57039851	GAAGGGGCCCCAGGAGAGGU	9247
84166_15_28	NLRC5	EXON	+	chr16:57039832-57039852	AAGGGGCCCCAGGAGAGGUA	9248
84166_15_29	NLRC5	EXON	-	chr16:57039763-57039783	AGGCUGUGAAGACAAAAGAG	9249
84166_15_30	NLRC5	EXON	-	chr16:57039764-57039784	CAGGCUGUGAAGACAAAAGA	9250
84166_15_32	NLRC5	EXON	-	chr16:57039765-57039785	GCAGGCUGUGAAGACAAAAG	9251
84166_15_39	NLRC5	EXON	-	chr16:57039783-57039803	AGAUCACAGUUUUGUGCUGC	9252
84166_15_42	NLRC5	EXON	-	chr16:57039815-57039835	CUUCUGCUCCUCUGGCUCCU	9253
84166_15_43	NLRC5	EXON	-	chr16:57039816-57039836	CCUUCUGCUCCUCUGGCUCC	9254
84166_15_45	NLRC5	EXON	-	chr16:57039823-57039843	UGGGGCCCCUUCUGCUCCUC	9255
84166_15_46	NLRC5	EXON	-	chr16:57039841-57039861	AUCGGGCCCUACCUCUCCUG	9256
84166_15_47	NLRC5	EXON	-	chr16:57039842-57039862	AAUCGGGCCCUACCUCUCCU	9257
84166_15_49	NLRC5	EXON	-	chr16:57039843-57039863	AAAUCGGGCCCUACCUCUCC	9258
84166_16_9	NLRC5	EXON	+	chr16:57040690-57040710	AGCUGCCUCUGAGCUCCCGA	9259
84166_16_11	NLRC5	EXON	+	chr16:57040696-57040716	CUCUGAGCUCCCGAAGGAUG	9260
84166_16_12	NLRC5	EXON	+	chr16:57040707-57040727	CGAAGGAUGAGGUACAGUGA	9261
84166_16_13	NLRC5	EXON	-	chr16:57040632-57040652	GCCCUGGAGGGACAUCACCA	9262
84166_16_14	NLRC5	EXON	-	chr16:57040644-57040664	UCAAGAAAUGCAGCCCUGGA	9263
84166_16_16	NLRC5	EXON	-	chr16:57040645-57040665	GUCAAGAAAUGCAGCCCUGG	9264
84166_16_18	NLRC5	EXON	-	chr16:57040648-57040668	GCUGUCAAGAAAUGCAGCCC	9265
84166_16_22	NLRC5	EXON	-	chr16:57040670-57040690	CAGAGGGCAUCUGGAGCAUG	9266

84166_16_24	NLRC5	EXON	-	chr16:57040679-57040699	GAGGCAGCUCAGAGGGCAUC	9267
84166_16_28	NLRC5	EXON	-	chr16:57040686-57040706	GAGCUCAGAGGCAGCUCAGA	9268
84166_16_29	NLRC5	EXON	-	chr16:57040687-57040707	GGAGCUCAGAGGCAGCUCAG	9269
84166_16_32	NLRC5	EXON	-	chr16:57040698-57040718	CUCAUCCUUCGGGAGCUCAG	9270
84166_16_35	NLRC5	EXON	-	chr16:57040708-57040728	AUCACUGUACCUCAUCCUUC	9271
84166_16_36	NLRC5	EXON	-	chr16:57040709-57040729	CAUCACUGUACCUCAUCCUU	9272
84166_17_5	NLRC5	EXON	+	chr16:57041476-57041496	CUGGGCAGGCUGACACAUUG	9273
84166_17_10	NLRC5	EXON	+	chr16:57041511-57041531	GCACCUAGAGCAGCUCUGCA	9274
84166_17_13	NLRC5	EXON	+	chr16:57041517-57041537	AGAGCAGCUCUGCAAGGCUC	9275
84166_17_15	NLRC5	EXON	+	chr16:57041518-57041538	GAGCAGCUCUGCAAGGCUCU	9276
84166_17_18	NLRC5	EXON	+	chr16:57041521-57041541	CAGCUCUGCAAGGCUCUGGG	9277
84166_17_19	NLRC5	EXON	+	chr16:57041536-57041556	CUGGGAGGAAGCUGCCACCU	9278
84166_17_22	NLRC5	EXON	+	chr16:57041559-57041579	UCACCUCCACCUCGAGUGAG	9279
84166_17_23	NLRC5	EXON	+	chr16:57041571-57041591	CGAGUGAGUGGUUUGUGUGU	9280
84166_17_24	NLRC5	EXON	-	chr16:57041477-57041497	ACAAUGUGUCAGCCUGCCCA	9281
84166_17_25	NLRC5	EXON	-	chr16:57041478-57041498	CACAAUGUGUCAGCCUGCCC	9282
84166_17_32	NLRC5	EXON	-	chr16:57041502-57041522	GCUCUAGGUGCUUUUCUUGG	9283
84166_17_33	NLRC5	EXON	-	chr16:57041505-57041525	GCUGCUCUAGGUGCUUUUCU	9284
84166_17_37	NLRC5	EXON	-	chr16:57041517-57041537	GAGCCUUGCAGAGCUGCUCU	9285
84166_17_41	NLRC5	EXON	-	chr16:57041553-57041573	CGAGGUGGAGGUGACCGAGG	9286
84166_17_42	NLRC5	EXON	-	chr16:57041556-57041576	ACUCGAGGUGGAGGUGACCG	9287
84166_17_44	NLRC5	EXON	-	chr16:57041565-57041585	AAACCACUCACUCGAGGUGG	9288
84166_17_46	NLRC5	EXON	-	chr16:57041568-57041588	CACAAACCACUCACUCGAGG	9289
84166_17_48	NLRC5	EXON	-	chr16:57041571-57041591	ACACACAAACCACUCACUCG	9290
84166_18_1	NLRC5	EXON	+	chr16:57041967-57041987	CUCCCCACCCCCAGCUUCUC	9291

84166_18_5	NLRC5	EXON	+	chr16:57041978-57041998	CAGCUUCUCAGGCAAUGCUC	9292
84166_18_6	NLRC5	EXON	+	chr16:57041979-57041999	AGCUUCUCAGGCAAUGCUCU	9293
84166_18_8	NLRC5	EXON	+	chr16:57041980-57042000	GCUUCUCAGGCAAUGCUCUG	9294
84166_18_10	NLRC5	EXON	+	chr16:57041981-57042001	CUUCUCAGGCAAUGCUCUGG	9295
84166_18_13	NLRC5	EXON	+	chr16:57041988-57042008	GGCAAUGCUCUGGGGGAUGA	9296
84166_18_14	NLRC5	EXON	+	chr16:57041998-57042018	UGGGGGAUGAAGGUGCAGCC	9297
84166_18_15	NLRC5	EXON	+	chr16:57042002-57042022	GGAUGAAGGUGCAGCCCGGC	9298
84166_18_17	NLRC5	EXON	+	chr16:57042018-57042038	CGGCUGGCUCAGCUGCUCCC	9299
84166_18_18	NLRC5	EXON	+	chr16:57042019-57042039	GGCUGGCUCAGCUGCUCCCA	9300
84166_18_21	NLRC5	EXON	+	chr16:57042023-57042043	GGCUCAGCUGCUCCCAGGGC	9301
84166_18_22	NLRC5	EXON	+	chr16:57042024-57042044	GCUCAGCUGCUCCCAGGGCU	9302
84166_18_26	NLRC5	EXON	+	chr16:57042059-57042079	CUUGAAGUGAGUAGCCCGCU	9303
84166_18_27	NLRC5	EXON	-	chr16:57041965-57041985	GAAGCUGGGGGUGGGGAGAA	9304
84166_18_28	NLRC5	EXON	-	chr16:57041966-57041986	AGAAGCUGGGGGUGGGGAGA	9305
84166_18_34	NLRC5	EXON	-	chr16:57041972-57041992	UGCCUGAGAAGCUGGGGGUG	9306
84166_18_37	NLRC5	EXON	-	chr16:57041973-57041993	UUGCCUGAGAAGCUGGGGGU	9307
84166_18_39	NLRC5	EXON	-	chr16:57041974-57041994	AUUGCCUGAGAAGCUGGGGG	9308
84166_18_41	NLRC5	EXON	-	chr16:57041977-57041997	AGCAUUGCCUGAGAAGCUGG	9309
84166_18_42	NLRC5	EXON	-	chr16:57041978-57041998	GAGCAUUGCCUGAGAAGCUG	9310
84166_18_43	NLRC5	EXON	-	chr16:57041979-57041999	AGAGCAUUGCCUGAGAAGCU	9311
84166_18_46	NLRC5	EXON	-	chr16:57041980-57042000	CAGAGCAUUGCCUGAGAAGC	9312
84166_18_53	NLRC5	EXON	-	chr16:57042019-57042039	UGGGAGCAGCUGAGCCAGCC	9313
84166_18_54	NLRC5	EXON	-	chr16:57042020-57042040	CUGGGAGCAGCUGAGCCAGC	9314
84166_18_57	NLRC5	EXON	-	chr16:57042038-57042058	ACUGCAGAGCUCCCAGCCCU	9315
84166_18_59	NLRC5	EXON	-	chr16:57042039-57042059	GACUGCAGAGCUCCCAGCCC	9316

84166_18_64	NLRC5	EXON	-	chr16:57042061-57042081	CUAGCGGGCUACUCACUUCA	9317
84166_19_3	NLRC5	EXON	+	chr16:57043506-57043526	AUCUCCAGCCUCAGUGAGAA	9318
84166_19_5	NLRC5	EXON	+	chr16:57043517-57043537	CAGUGAGAACGGUUUGUCCC	9319
84166_19_7	NLRC5	EXON	+	chr16:57043529-57043549	UUUGUCCCUGGAUGCCGUGU	9320
84166_19_8	NLRC5	EXON	+	chr16:57043530-57043550	UUGUCCCUGGAUGCCGUGUU	9321
84166_19_11	NLRC5	EXON	+	chr16:57043535-57043555	CCUGGAUGCCGUGUUGGGUU	9322
84166_19_12	NLRC5	EXON	+	chr16:57043540-57043560	AUGCCGUGUUGGGUUUGGUU	9323
84166_19_16	NLRC5	EXON	+	chr16:57043561-57043581	GGUGCUUCUCCACUCUGCAG	9324
84166_19_20	NLRC5	EXON	+	chr16:57043574-57043594	UCUGCAGUGGCUCUUCCGCU	9325
84166_19_21	NLRC5	EXON	+	chr16:57043582-57043602	GGCUCUUCCGCUUGGACAUC	9326
84166_19_25	NLRC5	EXON	-	chr16:57043498-57043518	GAGGCUGGAGAUCACAGGGG	9327
84166_19_27	NLRC5	EXON	-	chr16:57043501-57043521	ACUGAGGCUGGAGAUCACAG	9328
84166_19_28	NLRC5	EXON	-	chr16:57043502-57043522	CACUGAGGCUGGAGAUCACA	9329
84166_19_30	NLRC5	EXON	-	chr16:57043503-57043523	UCACUGAGGCUGGAGAUCAC	9330
84166_19_33	NLRC5	EXON	-	chr16:57043513-57043533	CAAACCGUUCUCACUGAGGC	9331
84166_19_35	NLRC5	EXON	-	chr16:57043517-57043537	GGGACAAACCGUUCUCACUG	9332
84166_19_37	NLRC5	EXON	-	chr16:57043537-57043557	CAAACCCAACACGGCAUCCA	9333
84166_19_38	NLRC5	EXON	-	chr16:57043538-57043558	CCAAACCCAACACGGCAUCC	9334
84166_19_41	NLRC5	EXON	-	chr16:57043546-57043566	GCACCGAACCAAACCCAACA	9335
84166_19_46	NLRC5	EXON	-	chr16:57043573-57043593	GCGGAAGAGCCACUGCAGAG	9336
84166_19_50	NLRC5	EXON	-	chr16:57043592-57043612	ACGCUCACCUGAUGUCCAAG	9337
84166_20_10	NLRC5	EXON	+	chr16:57045454-57045474	AGCCAACACAUCCUCCUGAG	9338
84166_20_11	NLRC5	EXON	+	chr16:57045455-57045475	GCCAACACAUCCUCCUGAGA	9339
84166_20_13	NLRC5	EXON	+	chr16:57045456-57045476	CCAACACAUCCUCCUGAGAG	9340
84166_20_14	NLRC5	EXON	+	chr16:57045470-57045490	UGAGAGGGGACAAGACAAGC	9341

84166_20_18	NLRC5	EXON	+	chr16:57045475-57045495	GGGGACAAGACAAGCAGGUG	9342
84166_20_21	NLRC5	EXON	+	chr16:57045478-57045498	GACAAGACAAGCAGGUGAGG	9343
84166_20_23	NLRC5	EXON	+	chr16:57045479-57045499	ACAAGACAAGCAGGUGAGGA	9344
84166_20_25	NLRC5	EXON	+	chr16:57045488-57045508	GCAGGUGAGGAGGGAACGCU	9345
84166_20_26	NLRC5	EXON	+	chr16:57045489-57045509	CAGGUGAGGAGGGAACGCUC	9346
84166_20_30	NLRC5	EXON	-	chr16:57045435-57045455	UUUCAAAGCUGGAAGCAGAG	9347
84166_20_35	NLRC5	EXON	-	chr16:57045446-57045466	GAUGUGUUGGCUUUCAAAGC	9348
84166_20_39	NLRC5	EXON	-	chr16:57045459-57045479	CCCCUCUCAGGAGGAUGUGU	9349
84166_20_41	NLRC5	EXON	-	chr16:57045468-57045488	UUGUCUUGUCCCCUCUCAGG	9350
84166_20_44	NLRC5	EXON	-	chr16:57045471-57045491	UGCUUGUCUUGUCCCCUCUC	9351
84166_21_2	NLRC5	EXON	+	chr16:57046538-57046558	AUCCCCCUCCUAGGGAUAUG	9352
84166_21_3	NLRC5	EXON	+	chr16:57046539-57046559	UCCCCCUCCUAGGGAUAUGU	9353
84166_21_5	NLRC5	EXON	+	chr16:57046546-57046566	CCUAGGGAUAUGUGGGCCAC	9354
84166_21_9	NLRC5	EXON	+	chr16:57046585-57046605	CCAGCUGCAGCCAAGUUCUU	9355
84166_21_11	NLRC5	EXON	+	chr16:57046586-57046606	CAGCUGCAGCCAAGUUCUUA	9356
84166_21_15	NLRC5	EXON	+	chr16:57046610-57046630	UCCGUCAGCGCUGCAUCCCC	9357
84166_21_18	NLRC5	EXON	+	chr16:57046619-57046639	GCUGCAUCCCCAGGAGCCUC	9358
84166_21_19	NLRC5	EXON	-	chr16:57046543-57046563	GCCCACAUAUCCCUAGGAGG	9359
84166_21_21	NLRC5	EXON	-	chr16:57046544-57046564	GGCCCACAUAUCCCUAGGAG	9360
84166_21_22	NLRC5	EXON	-	chr16:57046545-57046565	UGGCCCACAUAUCCCUAGGA	9361
84166_21_24	NLRC5	EXON	-	chr16:57046546-57046566	GUGGCCCACAUAUCCCUAGG	9362
84166_21_28	NLRC5	EXON	-	chr16:57046549-57046569	CCAGUGGCCCACAUAUCCCU	9363
84166_21_30	NLRC5	EXON	-	chr16:57046565-57046585	GAAGUCUGGCAAAGAUCCAG	9364
84166_21_32	NLRC5	EXON	-	chr16:57046579-57046599	UUGGCUGCAGCUGGGAAGUC	9365
84166_21_34	NLRC5	EXON	-	chr16:57046587-57046607	CUAAGAACUUGGCUGCAGCU	9366

84166_21_36	NLRC5	EXON	-	chr16:57046588-57046608	CCUAAGAACUUGGCUGCAGC	9367
84166_21_38	NLRC5	EXON	-	chr16:57046598-57046618	CUGACGGAACCCUAAGAACU	9368
84166_21_41	NLRC5	EXON	-	chr16:57046614-57046634	UCCUGGGGAUGCAGCGCUGA	9369
84166_21_44	NLRC5	EXON	-	chr16:57046629-57046649	GACAGUACCAGAGGCUCCUG	9370
84166_21_46	NLRC5	EXON	-	chr16:57046630-57046650	GGACAGUACCAGAGGCUCCU	9371
84166_21_47	NLRC5	EXON	-	chr16:57046631-57046651	GGGACAGUACCAGAGGCUCC	9372
84166_21_50	NLRC5	EXON	-	chr16:57046638-57046658	AAGGGCUGGGACAGUACCAG	9373
84166_22_5	NLRC5	EXON	+	chr16:57047541-57047561	CAGCCUCAGUGAGUGUCCUC	9374
84166_22_10	NLRC5	EXON	+	chr16:57047580-57047600	CCGCCUCUGUGCCACUCUGA	9375
84166_22_12	NLRC5	EXON	+	chr16:57047589-57047609	UGCCACUCUGAAGGACUGCC	9376
84166_22_14	NLRC5	EXON	+	chr16:57047590-57047610	GCCACUCUGAAGGACUGCCC	9377
84166_22_16	NLRC5	EXON	+	chr16:57047598-57047618	GAAGGACUGCCCGGGACCCC	9378
84166_22_20	NLRC5	EXON	+	chr16:57047618-57047638	UGGAACUGCAGUAAGUAACG	9379
84166_22_21	NLRC5	EXON	-	chr16:57047529-57047549	UGAGGCUGCAAAGGGGCAAU	9380
84166_22_22	NLRC5	EXON	-	chr16:57047530-57047550	CUGAGGCUGCAAAGGGGCAA	9381
84166_22_24	NLRC5	EXON	-	chr16:57047536-57047556	CACUCACUGAGGCUGCAAAG	9382
84166_22_25	NLRC5	EXON	-	chr16:57047537-57047557	ACACUCACUGAGGCUGCAAA	9383
84166_22_26	NLRC5	EXON	-	chr16:57047538-57047558	GACACUCACUGAGGCUGCAA	9384
84166_22_30	NLRC5	EXON	-	chr16:57047547-57047567	GCUCCAGAGGACACUCACUG	9385
84166_22_32	NLRC5	EXON	-	chr16:57047560-57047580	GUGAGGCUUGGGGGCUCCAG	9386
84166_22_35	NLRC5	EXON	-	chr16:57047569-57047589	CAGAGGCGGGUGAGGCUUGG	9387
84166_22_36	NLRC5	EXON	-	chr16:57047570-57047590	ACAGAGGCGGGUGAGGCUUG	9388
84166_22_38	NLRC5	EXON	-	chr16:57047571-57047591	CACAGAGGCGGGUGAGGCUU	9389
84166_22_40	NLRC5	EXON	-	chr16:57047572-57047592	GCACAGAGGCGGGUGAGGCU	9390
84166_22_43	NLRC5	EXON	-	chr16:57047577-57047597	GAGUGGCACAGAGGCGGGUG	9391

84166_22_45	NLRC5	EXON	-	chr16:57047582-57047602	CUUCAGAGUGGCACAGAGGC	9392
84166_22_46	NLRC5	EXON	-	chr16:57047583-57047603	CCUUCAGAGUGGCACAGAGG	9393
84166_22_48	NLRC5	EXON	-	chr16:57047586-57047606	AGUCCUUCAGAGUGGCACAG	9394
84166_22_50	NLRC5	EXON	-	chr16:57047594-57047614	UCCCGGGCAGUCCUUCAGAG	9395
84166_22_54	NLRC5	EXON	-	chr16:57047610-57047630	ACUGCAGUUCCAGGGGUCCC	9396
84166_22_56	NLRC5	EXON	-	chr16:57047611-57047631	UACUGCAGUUCCAGGGGUCC	9397
84166_22_58	NLRC5	EXON	-	chr16:57047617-57047637	GUUACUUACUGCAGUUCCAG	9398
84166_22_59	NLRC5	EXON	-	chr16:57047618-57047638	CGUUACUUACUGCAGUUCCA	9399
84166_22_60	NLRC5	EXON	-	chr16:57047619-57047639	UCGUUACUUACUGCAGUUCC	9400
84166_23_11	NLRC5	EXON	+	chr16:57051549-57051569	GUUCCUGAGUGACCAGAGCC	9401
84166_23_14	NLRC5	EXON	+	chr16:57051561-57051581	CCAGAGCCUGGAGACUCUAC	9402
84166_23_19	NLRC5	EXON	-	chr16:57051520-57051540	AAUCUGUGAAACAAAGCAGG	9403
84166_23_20	NLRC5	EXON	-	chr16:57051523-57051543	GACAAUCUGUGAAACAAAGC	9404
84166_23_22	NLRC5	EXON	-	chr16:57051545-57051565	CUGGUCACUCAGGAACUCAC	9405
84166_23_25	NLRC5	EXON	-	chr16:57051555-57051575	UCUCCAGGCUCUGGUCACUC	9406
84166_23_27	NLRC5	EXON	-	chr16:57051564-57051584	CCAGUAGAGUCUCCAGGCUC	9407
84166_23_28	NLRC5	EXON	-	chr16:57051570-57051590	AGCAGUCCAGUAGAGUCUCC	9408
84166_23_31	NLRC5	EXON	-	chr16:57051595-57051615	AGGCUCAGCUGAGGGAGUUG	9409
84166_23_35	NLRC5	EXON	-	chr16:57051603-57051623	ACUGCAGCAGGCUCAGCUGA	9410
84166_23_36	NLRC5	EXON	-	chr16:57051604-57051624	UACUGCAGCAGGCUCAGCUG	9411
84166_23_40	NLRC5	EXON	-	chr16:57051615-57051635	AACUCUCGUCUUACUGCAGC	9412
84166_24_4	NLRC5	EXON	+	chr16:57054741-57054761	CCUUUUCAGGCUGAGCCAGA	9413
84166_24_6	NLRC5	EXON	+	chr16:57054742-57054762	CUUUUCAGGCUGAGCCAGAC	9414
84166_24_12	NLRC5	EXON	+	chr16:57054771-57054791	CCCGAAAAGCCCCUUCCUGC	9415
84166_24_15	NLRC5	EXON	+	chr16:57054797-57054817	ACACCUUAAGCCUGUGUCCA	9416

84166_24_16	NLRC5	EXON	+	chr16:57054798-57054818	CACCUUAAGCCUGUGUCCAC	9417
84166_24_18	NLRC5	EXON	+	chr16:57054807-57054827	CCUGUGUCCACGGGUUAAAA	9418
84166_24_20	NLRC5	EXON	+	chr16:57054810-57054830	GUGUCCACGGGUUAAAAAGG	9419
84166_24_21	NLRC5	EXON	+	chr16:57054818-57054838	GGGUUAAAAAGGUGGAUCUC	9420
84166_24_23	NLRC5	EXON	+	chr16:57054821-57054841	UUAAAAAGGUGGAUCUCAGG	9421
84166_24_24	NLRC5	EXON	+	chr16:57054822-57054842	UAAAAAGGUGGAUCUCAGGU	9422
84166_24_28	NLRC5	EXON	+	chr16:57054833-57054853	AUCUCAGGUGGGCAUUCCCC	9423
84166_24_29	NLRC5	EXON	+	chr16:57054834-57054854	UCUCAGGUGGGCAUUCCCCU	9424
84166_24_30	NLRC5	EXON	-	chr16:57054736-57054756	CUCAGCCUGAAAAGGAAAGG	9425
84166_24_31	NLRC5	EXON	-	chr16:57054737-57054757	GCUCAGCCUGAAAAGGAAAG	9426
84166_24_33	NLRC5	EXON	-	chr16:57054738-57054758	GGCUCAGCCUGAAAAGGAAA	9427
84166_24_34	NLRC5	EXON	-	chr16:57054739-57054759	UGGCUCAGCCUGAAAAGGAA	9428
84166_24_38	NLRC5	EXON	-	chr16:57054744-57054764	CCGUCUGGCUCAGCCUGAAA	9429
84166_24_44	NLRC5	EXON	-	chr16:57054759-57054779	UUUUCGGGGACAGUCCCGUC	9430
84166_24_46	NLRC5	EXON	-	chr16:57054773-57054793	CAGCAGGAAGGGGCUUUUCG	9431
84166_24_47	NLRC5	EXON	-	chr16:57054774-57054794	CCAGCAGGAAGGGGCUUUUC	9432
84166_24_49	NLRC5	EXON	-	chr16:57054775-57054795	GCCAGCAGGAAGGGGCUUUU	9433
84166_24_53	NLRC5	EXON	-	chr16:57054783-57054803	AGGUGUUGGCCAGCAGGAAG	9434
84166_24_54	NLRC5	EXON	-	chr16:57054784-57054804	AAGGUGUUGGCCAGCAGGAA	9435
84166_24_55	NLRC5	EXON	-	chr16:57054785-57054805	UAAGGUGUUGGCCAGCAGGA	9436
84166_24_58	NLRC5	EXON	-	chr16:57054789-57054809	GGCUUAAGGUGUUGGCCAGC	9437
84166_24_61	NLRC5	EXON	-	chr16:57054797-57054817	UGGACACAGGCUUAAGGUGU	9438
84166_24_66	NLRC5	EXON	-	chr16:57054803-57054823	AACCCGUGGACACAGGCUUA	9439
84166_24_67	NLRC5	EXON	-	chr16:57054810-57054830	CCUUUUUAACCCGUGGACAC	9440
84166_24_68	NLRC5	EXON	-	chr16:57054817-57054837	AGAUCCACCUUUUUAACCCG	9441

84166_25_3	NLRC5	EXON	+	chr16:57055049-57055069	UUUGCACUUCAGAUCCAACG	9442
84166_25_8	NLRC5	EXON	+	chr16:57055052-57055072	GCACUUCAGAUCCAACGAGG	9443
84166_25_12	NLRC5	EXON	+	chr16:57055055-57055075	CUUCAGAUCCAACGAGGAGG	9444
84166_25_14	NLRC5	EXON	+	chr16:57055059-57055079	AGAUCCAACGAGGAGGAGGA	9445
84166_25_16	NLRC5	EXON	+	chr16:57055071-57055091	GAGGAGGAAGGCGUGUGCUG	9446
84166_25_17	NLRC5	EXON	+	chr16:57055072-57055092	AGGAGGAAGGCGUGUGCUGU	9447
84166_25_19	NLRC5	EXON	-	chr16:57055014-57055034	GACCUGGAUCAGACAGGACC	9448
84166_25_20	NLRC5	EXON	-	chr16:57055020-57055040	UGCAGGGACCUGGAUCAGAC	9449
84166_25_23	NLRC5	EXON	-	chr16:57055030-57055050	AGUUGCAUGGUGCAGGGACC	9450
84166_25_25	NLRC5	EXON	-	chr16:57055036-57055056	GUGCAAAGUUGCAUGGUGCA	9451
84166_25_27	NLRC5	EXON	-	chr16:57055037-57055057	AGUGCAAAGUUGCAUGGUGC	9452
84166_25_30	NLRC5	EXON	-	chr16:57055043-57055063	AUCUGAAGUGCAAAGUUGCA	9453
84166_25_33	NLRC5	EXON	-	chr16:57055066-57055086	CACGCCUUCCUCCUCCUCGU	9454
84166_26_1	NLRC5	EXON	+	chr16:57055413-57055433	CCCCUUUACCUCCGUCCAGC	9455
84166_26_4	NLRC5	EXON	+	chr16:57055421-57055441	CCUCCGUCCAGCAGGUUCAC	9456
84166_26_7	NLRC5	EXON	+	chr16:57055438-57055458	CACAGGCUGCAGCCUCAGCC	9457
84166_26_10	NLRC5	EXON	+	chr16:57055461-57055481	AGCACGUAGAGUCACUCUGC	9458
84166_26_13	NLRC5	EXON	-	chr16:57055416-57055436	CCUGCUGGACGGAGGUAAAG	9459
84166_26_15	NLRC5	EXON	-	chr16:57055417-57055437	ACCUGCUGGACGGAGGUAAA	9460
84166_26_16	NLRC5	EXON	-	chr16:57055418-57055438	AACCUGCUGGACGGAGGUAA	9461
84166_26_19	NLRC5	EXON	-	chr16:57055424-57055444	CCUGUGAACCUGCUGGACGG	9462
84166_26_20	NLRC5	EXON	-	chr16:57055427-57055447	CAGCCUGUGAACCUGCUGGA	9463
84166_26_23	NLRC5	EXON	-	chr16:57055431-57055451	GCUGCAGCCUGUGAACCUGC	9464
84166_26_26	NLRC5	EXON	-	chr16:57055453-57055473	ACUCUACGUGCUCCUGGCUG	9465
84166_26_28	NLRC5	EXON	-	chr16:57055459-57055479	AGAGUGACUCUACGUGCUCC	9466

84166_26_33	NLRC5	EXON	-	chr16:57055507-57055527	GUUGAAUGAGGUGGAGGCUG	9467
84166_26_35	NLRC5	EXON	-	chr16:57055513-57055533	GAGGGAGUUGAAUGAGGUGG	9468
84166_27_3	NLRC5	EXON	+	chr16:57058061-57058081	CAGUCUCUCAGCAAACCUGC	9469
84166_27_4	NLRC5	EXON	+	chr16:57058062-57058082	AGUCUCUCAGCAAACCUGCU	9470
84166_27_6	NLRC5	EXON	+	chr16:57058071-57058091	GCAAACCUGCUGGGCGACAG	9471
84166_27_9	NLRC5	EXON	+	chr16:57058088-57058108	CAGCGGACUCAGAUGCCUUC	9472
84166_27_10	NLRC5	EXON	+	chr16:57058103-57058123	CCUUCUGGAAUGUCUGCCGC	9473
84166_27_12	NLRC5	EXON	+	chr16:57058116-57058136	CUGCCGCAGGUGCCCAUCUC	9474
84166_27_15	NLRC5	EXON	+	chr16:57058133-57058153	CUCCGGUUUGCUUGAGUAAG	9475
84166_27_22	NLRC5	EXON	-	chr16:57058052-57058072	CUGAGAGACUGUAGGGGGUA	9476
84166_27_24	NLRC5	EXON	-	chr16:57058057-57058077	GUUUGCUGAGAGACUGUAGG	9477
84166_27_25	NLRC5	EXON	-	chr16:57058058-57058078	GGUUUGCUGAGAGACUGUAG	9478
84166_27_26	NLRC5	EXON	-	chr16:57058059-57058079	AGGUUUGCUGAGAGACUGUA	9479
84166_27_28	NLRC5	EXON	-	chr16:57058060-57058080	CAGGUUUGCUGAGAGACUGU	9480
84166_27_33	NLRC5	EXON	-	chr16:57058079-57058099	UGAGUCCGCUGUCGCCCAGC	9481
84166_27_36	NLRC5	EXON	-	chr16:57058106-57058126	CCUGCGGCAGACAUUCCAGA	9482
84166_27_39	NLRC5	EXON	-	chr16:57058122-57058142	AAACCGGAGAUGGGCACCUG	9483
84166_27_41	NLRC5	EXON	-	chr16:57058131-57058151	UACUCAAGCAAACCGGAGAU	9484
84166_27_42	NLRC5	EXON	-	chr16:57058132-57058152	UUACUCAAGCAAACCGGAGA	9485
84166_27_47	NLRC5	EXON	-	chr16:57058138-57058158	UUCCACUUACUCAAGCAAAC	9486
84166_28_6	NLRC5	EXON	+	chr16:57058974-57058994	GAGUCACAACAGCAUUUCUC	9487
84166_28_12	NLRC5	EXON	+	chr16:57058995-57059015	GGAAAGUGCCCUGUACCUGC	9488
84166_28_14	NLRC5	EXON	+	chr16:57059024-57059044	UGCCCUCCUGCCCACGUGUC	9489
84166_28_17	NLRC5	EXON	+	chr16:57059025-57059045	GCCCUCCUGCCCACGUGUCC	9490
84166_28_18	NLRC5	EXON	+	chr16:57059028-57059048	CUCCUGCCCACGUGUCCGGG	9491

84166_28_21	NLRC5	EXON	+	chr16:57059044-57059064	CGGGAGGCCUCAGUGAAGUA	9492
84166_28_24	NLRC5	EXON	+	chr16:57059045-57059065	GGGAGGCCUCAGUGAAGUAA	9493
84166_28_25	NLRC5	EXON	+	chr16:57059046-57059066	GGAGGCCUCAGUGAAGUAAG	9494
84166_28_26	NLRC5	EXON	+	chr16:57059053-57059073	UCAGUGAAGUAAGGGGAUGU	9495
84166_28_29	NLRC5	EXON	-	chr16:57058959-57058979	GACUCAGACUAGAAGGGAAA	9496
84166_28_32	NLRC5	EXON	-	chr16:57058965-57058985	UGUUGUGACUCAGACUAGAA	9497
84166_28_33	NLRC5	EXON	-	chr16:57058966-57058986	CUGUUGUGACUCAGACUAGA	9498
84166_28_42	NLRC5	EXON	-	chr16:57059006-57059026	CAGUGUCUCCAGCAGGUACA	9499
84166_28_43	NLRC5	EXON	-	chr16:57059007-57059027	GCAGUGUCUCCAGCAGGUAC	9500
84166_28_45	NLRC5	EXON	-	chr16:57059013-57059033	AGGAGGGCAGUGUCUCCAGC	9501
84166_28_46	NLRC5	EXON	-	chr16:57059029-57059049	UCCCGGACACGUGGGCAGGA	9502
84166_28_47	NLRC5	EXON	-	chr16:57059030-57059050	CUCCCGGACACGUGGGCAGG	9503
84166_28_49	NLRC5	EXON	-	chr16:57059033-57059053	GGCCUCCCGGACACGUGGGC	9504
84166_28_53	NLRC5	EXON	-	chr16:57059037-57059057	CUGAGGCCUCCCGGACACGU	9505
84166_28_54	NLRC5	EXON	-	chr16:57059038-57059058	ACUGAGGCCUCCCGGACACG	9506
84166_28_57	NLRC5	EXON	-	chr16:57059046-57059066	CUUACUUCACUGAGGCCUCC	9507
84166_28_59	NLRC5	EXON	-	chr16:57059054-57059074	AACAUCCCCUUACUUCACUG	9508
84166_29_2	NLRC5	EXON	+	chr16:57059448-57059468	AGGCCCUUCUCUCUGCAGCC	9509
84166_29_3	NLRC5	EXON	+	chr16:57059449-57059469	GGCCCUUCUCUCUGCAGCCU	9510
84166_29_8	NLRC5	EXON	+	chr16:57059468-57059488	UGGGCUCUGAGCAGAGCUUC	9511
84166_29_12	NLRC5	EXON	+	chr16:57059487-57059507	CCGGAUUCACUUCUCCAGAG	9512
84166_29_14	NLRC5	EXON	+	chr16:57059493-57059513	UCACUUCUCCAGAGAGGACC	9513
84166_29_18	NLRC5	EXON	+	chr16:57059497-57059517	UUCUCCAGAGAGGACCAGGC	9514
84166_29_20	NLRC5	EXON	+	chr16:57059498-57059518	UCUCCAGAGAGGACCAGGCU	9515
84166_29_22	NLRC5	EXON	+	chr16:57059510-57059530	ACCAGGCUGGGAAGACACUC	9516

84166_29_24	NLRC5	EXON	+	chr16:57059523-57059543	GACACUCAGGUAAUCCCUGC	9517
84166_29_25	NLRC5	EXON	+	chr16:57059524-57059544	ACACUCAGGUAAUCCCUGCA	9518
84166_29_26	NLRC5	EXON	-	chr16:57059449-57059469	AGGCUGCAGAGAGAAGGGCC	9519
84166_29_27	NLRC5	EXON	-	chr16:57059454-57059474	AGCCCAGGCUGCAGAGAGAA	9520
84166_29_28	NLRC5	EXON	-	chr16:57059455-57059475	GAGCCCAGGCUGCAGAGAGA	9521
84166_29_34	NLRC5	EXON	-	chr16:57059469-57059489	GGAAGCUCUGCUCAGAGCCC	9522
84166_29_36	NLRC5	EXON	-	chr16:57059490-57059510	CCUCUCUGGAGAAGUGAAUC	9523
84166_29_44	NLRC5	EXON	-	chr16:57059504-57059524	CUUCCCAGCCUGGUCCUCUC	9524
84166_29_47	NLRC5	EXON	-	chr16:57059514-57059534	ACCUGAGUGUCUUCCCAGCC	9525
84166_30_4	NLRC5	EXON	+	chr16:57061446-57061466	GGCUAAGUGAGUGCAGCUUC	9526
84166_30_6	NLRC5	EXON	+	chr16:57061464-57061484	UCCGGCCAGAGCACGUGUCC	9527
84166_30_8	NLRC5	EXON	+	chr16:57061468-57061488	GCCAGAGCACGUGUCCAGGC	9528
84166_30_9	NLRC5	EXON	+	chr16:57061475-57061495	CACGUGUCCAGGCUGGCCAC	9529
84166_30_12	NLRC5	EXON	+	chr16:57061501-57061521	GAGCAAGUCCCUGCAGCUGA	9530
84166_30_16	NLRC5	EXON	-	chr16:57061430-57061450	AGCCUGAGGGCAGAAAGCCA	9531
84166_30_17	NLRC5	EXON	-	chr16:57061431-57061451	UAGCCUGAGGGCAGAAAGCC	9532
84166_30_20	NLRC5	EXON	-	chr16:57061443-57061463	GCUGCACUCACUUAGCCUGA	9533
84166_30_21	NLRC5	EXON	-	chr16:57061444-57061464	AGCUGCACUCACUUAGCCUG	9534
84166_30_24	NLRC5	EXON	-	chr16:57061468-57061488	GCCUGGACACGUGCUCUGGC	9535
84166_30_27	NLRC5	EXON	-	chr16:57061472-57061492	GCCAGCCUGGACACGUGCUC	9536
84166_30_29	NLRC5	EXON	-	chr16:57061485-57061505	GCUCAAGCCGGUGGCCAGCC	9537
84166_30_31	NLRC5	EXON	-	chr16:57061494-57061514	CAGGGACUUGCUCAAGCCGG	9538
84166_30_32	NLRC5	EXON	-	chr16:57061497-57061517	CUGCAGGGACUUGCUCAAGC	9539
84166_30_33	NLRC5	EXON	-	chr16:57061512-57061532	CGUGAGCUCCGUCAGCUGCA	9540
84166_30_34	NLRC5	EXON	-	chr16:57061513-57061533	ACGUGAGCUCCGUCAGCUGC	9541

84166_31_2	NLRC5	EXON	+	chr16:57061614-57061634	CAGGCUGACCCAGUGCUGCC	9542
84166_31_3	NLRC5	EXON	+	chr16:57061615-57061635	AGGCUGACCCAGUGCUGCCU	9543
84166_31_5	NLRC5	EXON	+	chr16:57061629-57061649	CUGCCUGGGCCAGAAGCAGC	9544
84166_31_7	NLRC5	EXON	+	chr16:57061647-57061667	GCUGGCCAUCCUCCUGAGCU	9545
84166_31_10	NLRC5	EXON	+	chr16:57061650-57061670	GGCCAUCCUCCUGAGCUUGG	9546
84166_31_11	NLRC5	EXON	+	chr16:57061651-57061671	GCCAUCCUCCUGAGCUUGGU	9547
84166_31_12	NLRC5	EXON	+	chr16:57061652-57061672	CCAUCCUCCUGAGCUUGGUG	9548
84166_31_14	NLRC5	EXON	+	chr16:57061663-57061683	AGCUUGGUGGGGCGACCCGC	9549
84166_31_15	NLRC5	EXON	+	chr16:57061664-57061684	GCUUGGUGGGGCGACCCGCA	9550
84166_31_17	NLRC5	EXON	+	chr16:57061679-57061699	CCGCAGGGCUGUUCAGCCUC	9551
84166_31_19	NLRC5	EXON	-	chr16:57061607-57061627	CUGGGUCAGCCUGGAGACAG	9552
84166_31_22	NLRC5	EXON	-	chr16:57061616-57061636	CAGGCAGCACUGGGUCAGCC	9553
84166_31_25	NLRC5	EXON	-	chr16:57061625-57061645	CUUCUGGCCCAGGCAGCACU	9554
84166_31_26	NLRC5	EXON	-	chr16:57061626-57061646	GCUUCUGGCCCAGGCAGCAC	9555
84166_31_28	NLRC5	EXON	-	chr16:57061635-57061655	UGGCCAGCUGCUUCUGGCCC	9556
84166_31_29	NLRC5	EXON	-	chr16:57061641-57061661	GGAGGAUGGCCAGCUGCUUC	9557
84166_31_30	NLRC5	EXON	-	chr16:57061655-57061675	CCCCACCAAGCUCAGGAGGA	9558
84166_31_31	NLRC5	EXON	-	chr16:57061659-57061679	GUCGCCCCACCAAGCUCAGG	9559
84166_31_33	NLRC5	EXON	-	chr16:57061662-57061682	CGGGUCGCCCCACCAAGCUC	9560
84166_31_36	NLRC5	EXON	-	chr16:57061681-57061701	CUGAGGCUGAACAGCCCUGC	9561
84166_31_37	NLRC5	EXON	-	chr16:57061682-57061702	CCUGAGGCUGAACAGCCCUG	9562
84166_31_40	NLRC5	EXON	-	chr16:57061698-57061718	AGCGGGGGAGGAGGUACCUG	9563
84166_32_2	NLRC5	EXON	+	chr16:57065196-57065216	CCCCUUCUGUGACAGGGUGC	9564
84166_32_6	NLRC5	EXON	+	chr16:57065204-57065224	GUGACAGGGUGCAGGAGCCG	9565
84166_32_7	NLRC5	EXON	+	chr16:57065205-57065225	UGACAGGGUGCAGGAGCCGU	9566

84166_32_9	NLRC5	EXON	+	chr16:57065208-57065228	CAGGGUGCAGGAGCCGUGGG	9567
84166_32_12	NLRC5	EXON	+	chr16:57065219-57065239	AGCCGUGGGCGGACAGAGCC	9568
84166_32_13	NLRC5	EXON	+	chr16:57065220-57065240	GCCGUGGGCGGACAGAGCCA	9569
84166_32_16	NLRC5	EXON	+	chr16:57065250-57065270	CCUGUUAGAAGUCUGCGCCC	9570
84166_32_18	NLRC5	EXON	+	chr16:57065257-57065277	GAAGUCUGCGCCCAGGCCUC	9571
84166_32_20	NLRC5	EXON	+	chr16:57065276-57065296	CAGGCAGUGUCACUGAAAUC	9572
84166_32_25	NLRC5	EXON	+	chr16:57065293-57065313	AUCAGGUGAGUCCAGAGAAG	9573
84166_32_26	NLRC5	EXON	-	chr16:57065199-57065219	CCUGCACCCUGUCACAGAAG	9574
84166_32_28	NLRC5	EXON	-	chr16:57065200-57065220	UCCUGCACCCUGUCACAGAA	9575
84166_32_30	NLRC5	EXON	-	chr16:57065201-57065221	CUCCUGCACCCUGUCACAGA	9576
84166_32_34	NLRC5	EXON	-	chr16:57065224-57065244	ACCCUGGCUCUGUCCGCCCA	9577
84166_32_36	NLRC5	EXON	-	chr16:57065240-57065260	UUCUAACAGGGAGAGAACCC	9578
84166_32_40	NLRC5	EXON	-	chr16:57065252-57065272	CUGGGCGCAGACUUCUAACA	9579
84166_32_43	NLRC5	EXON	-	chr16:57065253-57065273	CCUGGGCGCAGACUUCUAAC	9580
84166_32_47	NLRC5	EXON	-	chr16:57065270-57065290	AGUGACACUGCCUGAGGCCU	9581
84166_32_48	NLRC5	EXON	-	chr16:57065271-57065291	CAGUGACACUGCCUGAGGCC	9582
84166_32_50	NLRC5	EXON	-	chr16:57065276-57065296	GAUUUCAGUGACACUGCCUG	9583
84166_33_5	NLRC5	EXON	+	chr16:57066548-57066568	GCAGCAGCUCUGUGUCCAGC	9584
84166_33_8	NLRC5	EXON	+	chr16:57066563-57066583	CCAGCUGGAAUUUCCUCGCC	9585
84166_33_15	NLRC5	EXON	+	chr16:57066584-57066604	GGAAGAGAAUCCAGAAGCUG	9586
84166_33_16	NLRC5	EXON	+	chr16:57066592-57066612	AUCCAGAAGCUGUGGCACUC	9587
84166_33_19	NLRC5	EXON	+	chr16:57066595-57066615	CAGAAGCUGUGGCACUCAGG	9588
84166_33_20	NLRC5	EXON	+	chr16:57066596-57066616	AGAAGCUGUGGCACUCAGGU	9589
84166_33_22	NLRC5	EXON	+	chr16:57066609-57066629	CUCAGGUGGGACCCAGCACC	9590
84166_33_24	NLRC5	EXON	+	chr16:57066610-57066630	UCAGGUGGGACCCAGCACCA	9591

84166_33_27	NLRC5	EXON	-	chr16:57066530-57066550	GCUGGGUCUCGGAGAUGCUG	9592
84166_33_31	NLRC5	EXON	-	chr16:57066541-57066561	ACAGAGCUGCUGCUGGGUCU	9593
84166_33_33	NLRC5	EXON	-	chr16:57066547-57066567	CUGGACACAGAGCUGCUGCU	9594
84166_33_35	NLRC5	EXON	-	chr16:57066548-57066568	GCUGGACACAGAGCUGCUGC	9595
84166_33_39	NLRC5	EXON	-	chr16:57066566-57066586	CCUGGCGAGGAAAUUCCAGC	9596
84166_33_44	NLRC5	EXON	-	chr16:57066579-57066599	UCUGGAUUCUCUUCCUGGCG	9597
84166_33_47	NLRC5	EXON	-	chr16:57066584-57066604	CAGCUUCUGGAUUCUCUUCC	9598
84166_33_48	NLRC5	EXON	-	chr16:57066597-57066617	CACCUGAGUGCCACAGCUUC	9599
84166_34_1	NLRC5	EXON	+	chr16:57067368-57067388	CUCCCUGUCUGUGUCCAGGU	9600
84166_34_4	NLRC5	EXON	+	chr16:57067384-57067404	AGGUUGGCUCACUGUGACCU	9601
84166_34_8	NLRC5	EXON	+	chr16:57067408-57067428	GCCCACCACAGCCUUCUUGU	9602
84166_34_9	NLRC5	EXON	+	chr16:57067409-57067429	CCCACCACAGCCUUCUUGUC	9603
84166_34_11	NLRC5	EXON	+	chr16:57067419-57067439	CCUUCUUGUCGGGCAGCUGA	9604
84166_34_15	NLRC5	EXON	+	chr16:57067433-57067453	AGCUGAUGGAGACAUGUGCC	9605
84166_34_16	NLRC5	EXON	+	chr16:57067448-57067468	GUGCCAGGCUGCAGCAGCUC	9606
84166_34_19	NLRC5	EXON	+	chr16:57067459-57067479	CAGCAGCUCAGGUCAGCGCC	9607
84166_34_21	NLRC5	EXON	-	chr16:57067373-57067393	AGCCAACCUGGACACAGACA	9608
84166_34_22	NLRC5	EXON	-	chr16:57067374-57067394	GAGCCAACCUGGACACAGAC	9609
84166_34_25	NLRC5	EXON	-	chr16:57067385-57067405	AAGGUCACAGUGAGCCAACC	9610
84166_34_28	NLRC5	EXON	-	chr16:57067404-57067424	GAAGGCUGUGGUGGGCUCCA	9611
84166_34_29	NLRC5	EXON	-	chr16:57067412-57067432	CCCGACAAGAAGGCUGUGGU	9612
84166_34_30	NLRC5	EXON	-	chr16:57067413-57067433	GCCCGACAAGAAGGCUGUGG	9613
84166_34_32	NLRC5	EXON	-	chr16:57067416-57067436	GCUGCCCGACAAGAAGGCUG	9614
84166_34_33	NLRC5	EXON	-	chr16:57067422-57067442	CCAUCAGCUGCCCGACAAGA	9615
84166_34_36	NLRC5	EXON	-	chr16:57067454-57067474	UGACCUGAGCUGCUGCAGCC	9616

84166_35_1	NLRC5	EXON	+	chr16:57067723-57067743	GGACCUUUUCAGCUUGUCUC	9617
84166_35_8	NLRC5	EXON	+	chr16:57067738-57067758	GUCUCAGGUUAACCUCUGUG	9618
84166_35_15	NLRC5	EXON	+	chr16:57067806-57067826	UCUCUGAGCUGAAGACAUUU	9619
84166_35_16	NLRC5	EXON	-	chr16:57067722-57067742	AGACAAGCUGAAAAGGUCCA	9620
84166_35_19	NLRC5	EXON	-	chr16:57067729-57067749	UAACCUGAGACAAGCUGAAA	9621
84166_35_22	NLRC5	EXON	-	chr16:57067753-57067773	UGGCAUCAUCGUCCUCACAG	9622
84166_35_24	NLRC5	EXON	-	chr16:57067773-57067793	GCUCUGCAGCAGCAGGGAAC	9623
84166_35_25	NLRC5	EXON	-	chr16:57067779-57067799	CAGGAGGCUCUGCAGCAGCA	9624
84166_35_27	NLRC5	EXON	-	chr16:57067780-57067800	GCAGGAGGCUCUGCAGCAGC	9625
84166_35_31	NLRC5	EXON	-	chr16:57067795-57067815	GCUCAGAGAGGGACAGCAGG	9626
84166_35_33	NLRC5	EXON	-	chr16:57067798-57067818	UCAGCUCAGAGAGGGACAGC	9627
84166_35_35	NLRC5	EXON	-	chr16:57067806-57067826	AAAUGUCUUCAGCUCAGAGA	9628
84166_35_37	NLRC5	EXON	-	chr16:57067807-57067827	GAAAUGUCUUCAGCUCAGAG	9629
84166_36_6	NLRC5	EXON	+	chr16:57069841-57069861	CUCCAGCUGUGUGAGCACCG	9630
84166_36_7	NLRC5	EXON	+	chr16:57069842-57069862	UCCAGCUGUGUGAGCACCGA	9631
84166_36_8	NLRC5	EXON	+	chr16:57069856-57069876	CACCGAGGGCCUCGCCCACC	9632
84166_36_9	NLRC5	EXON	+	chr16:57069863-57069883	GGCCUCGCCCACCUGGCAUC	9633
84166_36_11	NLRC5	EXON	+	chr16:57069868-57069888	CGCCCACCUGGCAUCUGGUC	9634
84166_36_12	NLRC5	EXON	+	chr16:57069869-57069889	GCCCACCUGGCAUCUGGUCU	9635
84166_36_14	NLRC5	EXON	+	chr16:57069886-57069906	UCUGGGCCACUGCCACCACU	9636
84166_36_17	NLRC5	EXON	+	chr16:57069889-57069909	GGGCCACUGCCACCACUUGG	9637
84166_36_21	NLRC5	EXON	+	chr16:57069895-57069915	CUGCCACCACUUGGAGGAGC	9638
84166_36_27	NLRC5	EXON	+	chr16:57069912-57069932	AGCUGGAGUGAGUUGCAGAG	9639
84166_36_29	NLRC5	EXON	+	chr16:57069915-57069935	UGGAGUGAGUUGCAGAGUGG	9640
84166_36_30	NLRC5	EXON	+	chr16:57069916-57069936	GGAGUGAGUUGCAGAGUGGA	9641

84166_36_31	NLRC5	EXON	-	chr16:57069820-57069840	UCAGCCUGGUGGGGGUCAAA	9642
84166_36_32	NLRC5	EXON	-	chr16:57069821-57069841	GUCAGCCUGGUGGGGGUCAA	9643
84166_36_34	NLRC5	EXON	-	chr16:57069828-57069848	GCUGGAGGUCAGCCUGGUGG	9644
84166_36_35	NLRC5	EXON	-	chr16:57069829-57069849	AGCUGGAGGUCAGCCUGGUG	9645
84166_36_37	NLRC5	EXON	-	chr16:57069830-57069850	CAGCUGGAGGUCAGCCUGGU	9646
84166_36_39	NLRC5	EXON	-	chr16:57069831-57069851	ACAGCUGGAGGUCAGCCUGG	9647
84166_36_41	NLRC5	EXON	-	chr16:57069834-57069854	CACACAGCUGGAGGUCAGCC	9648
84166_36_42	NLRC5	EXON	-	chr16:57069843-57069863	CUCGGUGCUCACACAGCUGG	9649
84166_36_44	NLRC5	EXON	-	chr16:57069846-57069866	GCCCUCGGUGCUCACACAGC	9650
84166_36_46	NLRC5	EXON	-	chr16:57069861-57069881	UGCCAGGUGGGCGAGGCCCU	9651
84166_36_47	NLRC5	EXON	-	chr16:57069868-57069888	GACCAGAUGCCAGGUGGGCG	9652
84166_36_49	NLRC5	EXON	-	chr16:57069873-57069893	GCCCAGACCAGAUGCCAGGU	9653
84166_36_50	NLRC5	EXON	-	chr16:57069874-57069894	GGCCCAGACCAGAUGCCAGG	9654
84166_36_52	NLRC5	EXON	-	chr16:57069877-57069897	AGUGGCCCAGACCAGAUGCC	9655
84166_36_53	NLRC5	EXON	-	chr16:57069895-57069915	GCUCCUCCAAGUGGUGGCAG	9656
84166_36_54	NLRC5	EXON	-	chr16:57069901-57069921	ACUCCAGCUCCUCCAAGUGG	9657
84166_36_55	NLRC5	EXON	-	chr16:57069904-57069924	CUCACUCCAGCUCCUCCAAG	9658
84166_37_4	NLRC5	EXON	+	chr16:57070537-57070557	GUCUAACAAUCAAUUUGAUG	9659
84166_37_8	NLRC5	EXON	+	chr16:57070540-57070560	UAACAAUCAAUUUGAUGAGG	9660
84166_37_9	NLRC5	EXON	+	chr16:57070541-57070561	AACAAUCAAUUUGAUGAGGA	9661
84166_37_10	NLRC5	EXON	+	chr16:57070549-57070569	AUUUGAUGAGGAGGGCACCA	9662
84166_37_15	NLRC5	EXON	+	chr16:57070560-57070580	AGGGCACCAAGGCGCUGAUG	9663
84166_37_16	NLRC5	EXON	+	chr16:57070561-57070581	GGGCACCAAGGCGCUGAUGA	9664
84166_37_20	NLRC5	EXON	+	chr16:57070570-57070590	GGCGCUGAUGAGGGCCCUUG	9665
84166_37_21	NLRC5	EXON	+	chr16:57070571-57070591	GCGCUGAUGAGGGCCCUUGA	9666

84166_37_24	NLRC5	EXON	+	chr16:57070572-57070592	CGCUGAUGAGGGCCCUUGAG	9667
84166_37_26	NLRC5	EXON	+	chr16:57070578-57070598	UGAGGGCCCUUGAGGGGAAA	9668
84166_37_28	NLRC5	EXON	+	chr16:57070590-57070610	AGGGGAAAUGGAUGCUAAAG	9669
84166_37_31	NLRC5	EXON	+	chr16:57070594-57070614	GAAAUGGAUGCUAAAGAGGC	9670
84166_37_33	NLRC5	EXON	+	chr16:57070609-57070629	GAGGCUGGAGUAAGUAGUGA	9671
84166_37_34	NLRC5	EXON	+	chr16:57070612-57070632	GCUGGAGUAAGUAGUGAUGG	9672
84166_37_38	NLRC5	EXON	-	chr16:57070522-57070542	UAGACAAGCUGCAGAAGACC	9673
84166_37_43	NLRC5	EXON	-	chr16:57070569-57070589	AAGGGCCCUCAUCAGCGCCU	9674
84166_37_48	NLRC5	EXON	-	chr16:57070587-57070607	UAGCAUCCAUUUCCCCUCAA	9675
84166_37_49	NLRC5	EXON	-	chr16:57070588-57070608	UUAGCAUCCAUUUCCCCUCA	9676
84166_38_3	NLRC5	EXON	+	chr16:57074611-57074631	UCUGCUGAACAGCUCCACCU	9677
84166_38_9	NLRC5	EXON	+	chr16:57074661-57074681	UGACCUGCCUGCAGAGCCUC	9678
84166_38_12	NLRC5	EXON	+	chr16:57074676-57074696	GCCUCAGGUGAGUGACCGAG	9679
84166_38_13	NLRC5	EXON	-	chr16:57074582-57074602	AGGCUGGAGAAGAGGAGGCC	9680
84166_38_14	NLRC5	EXON	-	chr16:57074587-57074607	GACUGAGGCUGGAGAAGAGG	9681
84166_38_16	NLRC5	EXON	-	chr16:57074590-57074610	GGUGACUGAGGCUGGAGAAG	9682
84166_38_22	NLRC5	EXON	-	chr16:57074598-57074618	CAGCAGAAGGUGACUGAGGC	9683
84166_38_25	NLRC5	EXON	-	chr16:57074602-57074622	UGUUCAGCAGAAGGUGACUG	9684
84166_38_27	NLRC5	EXON	-	chr16:57074611-57074631	AGGUGGAGCUGUUCAGCAGA	9685
84166_38_30	NLRC5	EXON	-	chr16:57074628-57074648	GUGAGUAAGCAAGGCCAAGG	9686
84166_38_34	NLRC5	EXON	-	chr16:57074631-57074651	UCUGUGAGUAAGCAAGGCCA	9687
84166_38_35	NLRC5	EXON	-	chr16:57074637-57074657	GCUUAGUCUGUGAGUAAGCA	9688
84166_38_37	NLRC5	EXON	-	chr16:57074659-57074679	GGCUCUGCAGGCAGGUCAUC	9689
84166_38_38	NLRC5	EXON	-	chr16:57074667-57074687	UCACCUGAGGCUCUGCAGGC	9690
84166_38_39	NLRC5	EXON	-	chr16:57074671-57074691	UCACUCACCUGAGGCUCUGC	9691

84166_38_40	NLRC5	EXON	-	chr16:57074680-57074700	GCCGCUCGGUCACUCACCUG	9692
84166_39_3	NLRC5	EXON	+	chr16:57076805-57076825	CCUGCUUUUCCAGACUGAAC	9693
84166_39_9	NLRC5	EXON	+	chr16:57076816-57076836	AGACUGAACAGGAACAGUAU	9694
84166_39_10	NLRC5	EXON	+	chr16:57076825-57076845	AGGAACAGUAUCGGUGAUGU	9695
84166_39_12	NLRC5	EXON	+	chr16:57076845-57076865	CGGUUGCUGCCACCUUUCUG	9696
84166_39_15	NLRC5	EXON	+	chr16:57076853-57076873	GCCACCUUUCUGAGGCUCUC	9697
84166_39_16	NLRC5	EXON	+	chr16:57076854-57076874	CCACCUUUCUGAGGCUCUCA	9698
84166_39_22	NLRC5	EXON	+	chr16:57076872-57076892	CAGGGCUGCCACCAGCCUAG	9699
84166_39_24	NLRC5	EXON	+	chr16:57076878-57076898	UGCCACCAGCCUAGAGGAGC	9700
84166_39_30	NLRC5	EXON	-	chr16:57076807-57076827	CUGUUCAGUCUGGAAAAGCA	9701
84166_39_31	NLRC5	EXON	-	chr16:57076808-57076828	CCUGUUCAGUCUGGAAAAGC	9702
84166_39_35	NLRC5	EXON	-	chr16:57076817-57076837	GAUACUGUUCCUGUUCAGUC	9703
84166_39_37	NLRC5	EXON	-	chr16:57076857-57076877	CCCUGAGAGCCUCAGAAAGG	9704
84166_39_38	NLRC5	EXON	-	chr16:57076860-57076880	CAGCCCUGAGAGCCUCAGAA	9705
84166_39_42	NLRC5	EXON	-	chr16:57076883-57076903	CUCCAGCUCCUCUAGGCUGG	9706
84166_39_43	NLRC5	EXON	-	chr16:57076886-57076906	UCACUCCAGCUCCUCUAGGC	9707
84166_39_44	NLRC5	EXON	-	chr16:57076890-57076910	CAACUCACUCCAGCUCCUCU	9708
84166_40_7	NLRC5	EXON	+	chr16:57077293-57077313	AGCUUGAGCCACAACCAGAU	9709
84166_40_9	NLRC5	EXON	+	chr16:57077302-57077322	CACAACCAGAUUGGAGACGC	9710
84166_40_12	NLRC5	EXON	+	chr16:57077332-57077352	CACUUAGCUACCAUCCUGCC	9711
84166_40_13	NLRC5	EXON	+	chr16:57077333-57077353	ACUUAGCUACCAUCCUGCCU	9712
84166_40_18	NLRC5	EXON	+	chr16:57077348-57077368	UGCCUGGGCUGCCAGAGCUC	9713
84166_40_24	NLRC5	EXON	-	chr16:57077290-57077310	UGGUUGUGGCUCAAGCUUGG	9714
84166_40_25	NLRC5	EXON	-	chr16:57077291-57077311	CUGGUUGUGGCUCAAGCUUG	9715
84166_40_28	NLRC5	EXON	-	chr16:57077292-57077312	UCUGGUUGUGGCUCAAGCUU	9716

84166_40_30	NLRC5	EXON	-	chr16:57077293-57077313	AUCUGGUUGUGGCUCAAGCU	9717
84166_40_32	NLRC5	EXON	-	chr16:57077304-57077324	CAGCGUCUCCAAUCUGGUUG	9718
84166_40_33	NLRC5	EXON	-	chr16:57077310-57077330	GGACACCAGCGUCUCCAAUC	9719
84166_40_34	NLRC5	EXON	-	chr16:57077331-57077351	GCAGGAUGGUAGCUAAGUGC	9720
84166_40_36	NLRC5	EXON	-	chr16:57077345-57077365	CUCUGGCAGCCCAGGCAGGA	9721
84166_40_38	NLRC5	EXON	-	chr16:57077349-57077369	UGAGCUCUGGCAGCCCAGGC	9722
84166_40_40	NLRC5	EXON	-	chr16:57077353-57077373	UUCCUGAGCUCUGGCAGCCC	9723
84166_40_41	NLRC5	EXON	-	chr16:57077362-57077382	CACUCUAUCUUCCUGAGCUC	9724
84166_41_2	NLRC5	EXON	+	chr16:57077704-57077724	CCCCCCUCCCACAGCCUCUC	9725
84166_41_5	NLRC5	EXON	+	chr16:57077705-57077725	CCCCCUCCCACAGCCUCUCA	9726
84166_41_7	NLRC5	EXON	+	chr16:57077725-57077745	GGGAAUAGCAUCAGCUCAGC	9727
84166_41_10	NLRC5	EXON	+	chr16:57077726-57077746	GGAAUAGCAUCAGCUCAGCC	9728
84166_41_11	NLRC5	EXON	+	chr16:57077727-57077747	GAAUAGCAUCAGCUCAGCCG	9729
84166_41_13	NLRC5	EXON	+	chr16:57077728-57077748	AAUAGCAUCAGCUCAGCCGG	9730
84166_41_15	NLRC5	EXON	+	chr16:57077739-57077759	CUCAGCCGGGGGAGUGCAGU	9731
84166_41_18	NLRC5	EXON	+	chr16:57077762-57077782	CAGAGUCUCUCGUUCUUUGC	9732
84166_41_21	NLRC5	EXON	+	chr16:57077769-57077789	UCUCGUUCUUUGCAGGCGCC	9733
84166_41_23	NLRC5	EXON	+	chr16:57077772-57077792	CGUUCUUUGCAGGCGCCUGG	9734
84166_41_29	NLRC5	EXON	+	chr16:57077796-57077816	GUUGAUGUGAGUGUCUGCCC	9735
84166_41_30	NLRC5	EXON	+	chr16:57077799-57077819	GAUGUGAGUGUCUGCCCAGG	9736
84166_41_32	NLRC5	EXON	-	chr16:57077707-57077727	CCUGAGAGGCUGUGGGAGGG	9737
84166_41_33	NLRC5	EXON	-	chr16:57077708-57077728	CCCUGAGAGGCUGUGGGAGG	9738
84166_41_35	NLRC5	EXON	-	chr16:57077709-57077729	UCCCUGAGAGGCUGUGGGAG	9739
84166_41_36	NLRC5	EXON	-	chr16:57077710-57077730	UUCCCUGAGAGGCUGUGGGA	9740
84166_41_38	NLRC5	EXON	-	chr16:57077711-57077731	AUUCCCUGAGAGGCUGUGGG	9741

84166_41_41	NLRC5	EXON	-	chr16:57077714-57077734	GCUAUUCCCUGAGAGGCUGU	9742
84166_41_43	NLRC5	EXON	-	chr16:57077715-57077735	UGCUAUUCCCUGAGAGGCUG	9743
84166_41_46	NLRC5	EXON	-	chr16:57077721-57077741	AGCUGAUGCUAUUCCCUGAG	9744
84166_41_50	NLRC5	EXON	-	chr16:57077747-57077767	CUCUGCCAACUGCACUCCCC	9745
84166_41_55	NLRC5	EXON	-	chr16:57077790-57077810	ACACUCACAUCAACUCCUCC	9746
84166_42_1	NLRC5	EXON	+	chr16:57077925-57077945	UUCCUCUCCUCUUCCAGGCU	9747
84166_42_6	NLRC5	EXON	+	chr16:57077939-57077959	CAGGCUUGGCUGCAAUGCCC	9748
84166_42_7	NLRC5	EXON	+	chr16:57077940-57077960	AGGCUUGGCUGCAAUGCCCU	9749
84166_42_10	NLRC5	EXON	+	chr16:57077941-57077961	GGCUUGGCUGCAAUGCCCUG	9750
84166_42_11	NLRC5	EXON	+	chr16:57077942-57077962	GCUUGGCUGCAAUGCCCUGG	9751
84166_42_14	NLRC5	EXON	+	chr16:57077957-57077977	CCUGGGGGAUCCCACAGCCC	9752
84166_42_16	NLRC5	EXON	+	chr16:57077958-57077978	CUGGGGGAUCCCACAGCCCU	9753
84166_42_17	NLRC5	EXON	+	chr16:57077959-57077979	UGGGGGAUCCCACAGCCCUG	9754
84166_42_18	NLRC5	EXON	+	chr16:57077963-57077983	GGAUCCCACAGCCCUGGGGC	9755
84166_42_20	NLRC5	EXON	+	chr16:57077969-57077989	CACAGCCCUGGGGCUGGCUC	9756
84166_42_24	NLRC5	EXON	+	chr16:57077989-57078009	AGGAGCUGCCCCAGCACCUG	9757
84166_42_25	NLRC5	EXON	+	chr16:57077990-57078010	GGAGCUGCCCCAGCACCUGA	9758
84166_42_27	NLRC5	EXON	+	chr16:57078005-57078025	CCUGAGGGUCCUACAGUGAG	9759
84166_42_29	NLRC5	EXON	-	chr16:57077930-57077950	AGCCAAGCCUGGAAGAGGAG	9760
84166_42_34	NLRC5	EXON	-	chr16:57077935-57077955	AUUGCAGCCAAGCCUGGAAG	9761
84166_42_37	NLRC5	EXON	-	chr16:57077941-57077961	CAGGGCAUUGCAGCCAAGCC	9762
84166_42_40	NLRC5	EXON	-	chr16:57077959-57077979	CAGGGCUGUGGGAUCCCCCA	9763
84166_42_41	NLRC5	EXON	-	chr16:57077960-57077980	CCAGGGCUGUGGGAUCCCCC	9764
84166_42_43	NLRC5	EXON	-	chr16:57077970-57077990	UGAGCCAGCCCCAGGGCUGU	9765
84166_42_45	NLRC5	EXON	-	chr16:57077971-57077991	CUGAGCCAGCCCCAGGGCUG	9766

84166_42_47	NLRC5	EXON	-	chr16:57077977-57077997	CAGCUCCUGAGCCAGCCCCA	9767
84166_42_48	NLRC5	EXON	-	chr16:57077978-57077998	GCAGCUCCUGAGCCAGCCCC	9768
84166_42_51	NLRC5	EXON	-	chr16:57078000-57078020	UGUAGGACCCUCAGGUGCUG	9769
84166_42_52	NLRC5	EXON	-	chr16:57078001-57078021	CUGUAGGACCCUCAGGUGCU	9770
84166_42_54	NLRC5	EXON	-	chr16:57078002-57078022	ACUGUAGGACCCUCAGGUGC	9771
84166_42_56	NLRC5	EXON	-	chr16:57078008-57078028	CCACUCACUGUAGGACCCUC	9772
84166_42_57	NLRC5	EXON	-	chr16:57078017-57078037	GGCAGGGGGCCACUCACUGU	9773
84166_43_4	NLRC5	EXON	+	chr16:57079046-57079066	CAGCCUACCAUUCAGCCAUC	9774
84166_43_5	NLRC5	EXON	+	chr16:57079047-57079067	AGCCUACCAUUCAGCCAUCU	9775
84166_43_6	NLRC5	EXON	+	chr16:57079053-57079073	CCAUUCAGCCAUCUGGGCCC	9776
84166_43_9	NLRC5	EXON	+	chr16:57079056-57079076	UUCAGCCAUCUGGGCCCAGG	9777
84166_43_10	NLRC5	EXON	+	chr16:57079057-57079077	UCAGCCAUCUGGGCCCAGGU	9778
84166_43_11	NLRC5	EXON	+	chr16:57079058-57079078	CAGCCAUCUGGGCCCAGGUG	9779
84166_43_14	NLRC5	EXON	+	chr16:57079070-57079090	CCCAGGUGGGGCCCUGAGCC	9780
84166_43_15	NLRC5	EXON	+	chr16:57079076-57079096	UGGGGCCCUGAGCCUGGCCC	9781
84166_43_17	NLRC5	EXON	+	chr16:57079082-57079102	CCUGAGCCUGGCCCAGGCCC	9782
84166_43_19	NLRC5	EXON	+	chr16:57079086-57079106	AGCCUGGCCCAGGCCCUGGA	9783
84166_43_21	NLRC5	EXON	+	chr16:57079100-57079120	CCUGGAUGGAUCCCCCCAUU	9784
84166_43_24	NLRC5	EXON	+	chr16:57079111-57079131	CCCCCCAUUUGGAAGAGAUC	9785
84166_43_27	NLRC5	EXON	+	chr16:57079119-57079139	UUGGAAGAGAUCAGGUAAGU	9786
84166_43_28	NLRC5	EXON	+	chr16:57079120-57079140	UGGAAGAGAUCAGGUAAGUA	9787
84166_43_30	NLRC5	EXON	+	chr16:57079121-57079141	GGAAGAGAUCAGGUAAGUAG	9788
84166_43_32	NLRC5	EXON	-	chr16:57079033-57079053	UAGGCUGGGGAAAGAGGAGA	9789
84166_43_33	NLRC5	EXON	-	chr16:57079034-57079054	GUAGGCUGGGGAAAGAGGAG	9790
84166_43_37	NLRC5	EXON	-	chr16:57079039-57079059	GAAUGGUAGGCUGGGGAAAG	9791

84166_43_40	NLRC5	EXON	-	chr16:57079046-57079066	GAUGGCUGAAUGGUAGGCUG	9792
84166_43_43	NLRC5	EXON	-	chr16:57079047-57079067	AGAUGGCUGAAUGGUAGGCU	9793
84166_43_44	NLRC5	EXON	-	chr16:57079048-57079068	CAGAUGGCUGAAUGGUAGGC	9794
84166_43_47	NLRC5	EXON	-	chr16:57079052-57079072	GGCCCAGAUGGCUGAAUGGU	9795
84166_43_48	NLRC5	EXON	-	chr16:57079056-57079076	CCUGGGCCCAGAUGGCUGAA	9796
84166_43_50	NLRC5	EXON	-	chr16:57079064-57079084	GGGCCCCACCUGGGCCCAGA	9797
84166_43_51	NLRC5	EXON	-	chr16:57079073-57079093	CCAGGCUCAGGGCCCCACCU	9798
84166_43_52	NLRC5	EXON	-	chr16:57079074-57079094	GCCAGGCUCAGGGCCCCACC	9799
84166_43_54	NLRC5	EXON	-	chr16:57079084-57079104	CAGGGCCUGGGCCAGGCUCA	9800
84166_43_55	NLRC5	EXON	-	chr16:57079085-57079105	CCAGGGCCUGGGCCAGGCUC	9801
84166_43_57	NLRC5	EXON	-	chr16:57079091-57079111	AUCCAUCCAGGGCCUGGGCC	9802
84166_43_58	NLRC5	EXON	-	chr16:57079096-57079116	GGGGGAUCCAUCCAGGGCCU	9803
84166_43_59	NLRC5	EXON	-	chr16:57079097-57079117	GGGGGGAUCCAUCCAGGGCC	9804
84166_43_62	NLRC5	EXON	-	chr16:57079102-57079122	CAAAUGGGGGGAUCCAUCCA	9805
84166_43_63	NLRC5	EXON	-	chr16:57079103-57079123	CCAAAUGGGGGGAUCCAUCC	9806
84166_43_66	NLRC5	EXON	-	chr16:57079114-57079134	CCUGAUCUCUUCCAAAUGGG	9807
84166_43_67	NLRC5	EXON	-	chr16:57079115-57079135	ACCUGAUCUCUUCCAAAUGG	9808
84166_43_69	NLRC5	EXON	-	chr16:57079116-57079136	UACCUGAUCUCUUCCAAAUG	9809
84166_43_71	NLRC5	EXON	-	chr16:57079117-57079137	UUACCUGAUCUCUUCCAAAU	9810
84166_43_74	NLRC5	EXON	-	chr16:57079118-57079138	CUUACCUGAUCUCUUCCAAA	9811
84166_44_1	NLRC5	EXON	+	chr16:57079202-57079222	AUCUCCCCUACCCUGCAGCU	9812
84166_44_3	NLRC5	EXON	+	chr16:57079205-57079225	UCCCCUACCCUGCAGCUUGG	9813
84166_44_5	NLRC5	EXON	+	chr16:57079217-57079237	CAGCUUGGCGGAAAACAACC	9814
84166_44_7	NLRC5	EXON	+	chr16:57079221-57079241	UUGGCGGAAAACAACCUGGC	9815
84166_44_11	NLRC5	EXON	+	chr16:57079224-57079244	GCGGAAAACAACCUGGCUGG	9816

84166_44_13	NLRC5	EXON	+	chr16:57079225-57079245	CGGAAAACAACCUGGCUGGA	9817
84166_44_14	NLRC5	EXON	+	chr16:57079226-57079246	GGAAAACAACCUGGCUGGAG	9818
84166_44_16	NLRC5	EXON	+	chr16:57079244-57079264	AGGGGUCCUGCGUUUCUGUA	9819
84166_44_25	NLRC5	EXON	-	chr16:57079209-57079229	UCCGCCAAGCUGCAGGGUAG	9820
84166_44_27	NLRC5	EXON	-	chr16:57079210-57079230	UUCCGCCAAGCUGCAGGGUA	9821
84166_44_29	NLRC5	EXON	-	chr16:57079211-57079231	UUUCCGCCAAGCUGCAGGGU	9822
84166_44_32	NLRC5	EXON	-	chr16:57079215-57079235	UUGUUUUCCGCCAAGCUGCA	9823
84166_44_33	NLRC5	EXON	-	chr16:57079216-57079236	GUUGUUUUCCGCCAAGCUGC	9824
84166_44_35	NLRC5	EXON	-	chr16:57079238-57079258	AACGCAGGACCCCUCCAGCC	9825
84166_44_36	NLRC5	EXON	-	chr16:57079253-57079273	GGAGCUCCAUACAGAAACGC	9826
84166_44_41	NLRC5	EXON	-	chr16:57079274-57079294	ACUCUAUCUGUCUGAGCAGC	9827
84166_44_42	NLRC5	EXON	-	chr16:57079275-57079295	UACUCUAUCUGUCUGAGCAG	9828
84166_45_1	NLRC5	EXON	+	chr16:57079527-57079547	GCCCUUCUCCAUCCCCAGCC	9829
84166_45_9	NLRC5	EXON	-	chr16:57079548-57079568	UGUCAAUCUUACAGGAAACC	9830
84166_45_11	NLRC5	EXON	-	chr16:57079556-57079576	AGUCUGGUUGUCAAUCUUAC	9831
84166_45_14	NLRC5	EXON	-	chr16:57079572-57079592	AGGUGAGGAGCUUGGCAGUC	9832
84166_45_15	NLRC5	EXON	-	chr16:57079580-57079600	GAAGCUGGAGGUGAGGAGCU	9833
84166_45_16	NLRC5	EXON	-	chr16:57079587-57079607	AGCUCGUGAAGCUGGAGGUG	9834
84166_45_20	NLRC5	EXON	-	chr16:57079592-57079612	AGGGCAGCUCGUGAAGCUGG	9835
84166_45_21	NLRC5	EXON	-	chr16:57079595-57079615	GGCAGGGCAGCUCGUGAAGC	9836
84166_45_25	NLRC5	EXON	-	chr16:57079611-57079631	UGUUCUAAUGAAGCAGGGCA	9837
84166_45_26	NLRC5	EXON	-	chr16:57079612-57079632	GUGUUCUAAUGAAGCAGGGC	9838
84166_45_28	NLRC5	EXON	-	chr16:57079616-57079636	GUGAGUGUUCUAAUGAAGCA	9839
84166_45_29	NLRC5	EXON	-	chr16:57079617-57079637	AGUGAGUGUUCUAAUGAAGC	9840
84166_46_3	NLRC5	EXON	+	chr16:57081084-57081104	CCCUACCCUGCAGGCUGUCC	9841

84166_46_7	NLRC5	EXON	+	chr16:57081095-57081115	AGGCUGUCCUGGAAUCUCCU	9842
84166_46_9	NLRC5	EXON	+	chr16:57081096-57081116	GGCUGUCCUGGAAUCUCCUC	9843
84166_46_10	NLRC5	EXON	+	chr16:57081097-57081117	GCUGUCCUGGAAUCUCCUCG	9844
84166_46_12	NLRC5	EXON	+	chr16:57081103-57081123	CUGGAAUCUCCUCGGGGAUG	9845
84166_46_14	NLRC5	EXON	+	chr16:57081118-57081138	GGAUGAGGCAGCUGCCGAGC	9846
84166_46_15	NLRC5	EXON	+	chr16:57081124-57081144	GGCAGCUGCCGAGCUGGCCC	9847
84166_46_17	NLRC5	EXON	+	chr16:57081139-57081159	GGCCCAGGUGCUGCCGCAGA	9848
84166_46_18	NLRC5	EXON	+	chr16:57081140-57081160	GCCCAGGUGCUGCCGCAGAU	9849
84166_46_19	NLRC5	EXON	+	chr16:57081144-57081164	AGGUGCUGCCGCAGAUGGGC	9850
84166_46_24	NLRC5	EXON	+	chr16:57081157-57081177	GAUGGGCCGGCUGAAGAGAG	9851
84166_46_29	NLRC5	EXON	+	chr16:57081166-57081186	GCUGAAGAGAGUGGAGUAUG	9852
84166_46_30	NLRC5	EXON	+	chr16:57081167-57081187	CUGAAGAGAGUGGAGUAUGA	9853
84166_46_31	NLRC5	EXON	+	chr16:57081168-57081188	UGAAGAGAGUGGAGUAUGAG	9854
84166_46_33	NLRC5	EXON	+	chr16:57081172-57081192	GAGAGUGGAGUAUGAGGGGC	9855
84166_46_36	NLRC5	EXON	+	chr16:57081173-57081193	AGAGUGGAGUAUGAGGGGCC	9856
84166_46_38	NLRC5	EXON	+	chr16:57081174-57081194	GAGUGGAGUAUGAGGGGCCG	9857
84166_46_40	NLRC5	EXON	+	chr16:57081175-57081195	AGUGGAGUAUGAGGGGCCGG	9858
84166_46_41	NLRC5	EXON	+	chr16:57081178-57081198	GGAGUAUGAGGGGCCGGGGG	9859
84166_46_43	NLRC5	EXON	-	chr16:57081086-57081106	CAGGACAGCCUGCAGGGUAG	9860
84166_46_44	NLRC5	EXON	-	chr16:57081087-57081107	CCAGGACAGCCUGCAGGGUA	9861
84166_46_46	NLRC5	EXON	-	chr16:57081088-57081108	UCCAGGACAGCCUGCAGGGU	9862
84166_46_48	NLRC5	EXON	-	chr16:57081092-57081112	AGAUUCCAGGACAGCCUGCA	9863
84166_46_49	NLRC5	EXON	-	chr16:57081093-57081113	GAGAUUCCAGGACAGCCUGC	9864
84166_46_51	NLRC5	EXON	-	chr16:57081105-57081125	CUCAUCCCCGAGGAGAUUCC	9865
84166_46_53	NLRC5	EXON	-	chr16:57081115-57081135	CGGCAGCUGCCUCAUCCCCG	9866

84166_46_57	NLRC5	EXON	-	chr16:57081135-57081155	CGGCAGCACCUGGGCCAGCU	9867
84166_46_58	NLRC5	EXON	-	chr16:57081144-57081164	GCCCAUCUGCGGCAGCACCU	9868
84166_46_59	NLRC5	EXON	-	chr16:57081145-57081165	GGCCCAUCUGCGGCAGCACC	9869
84166_46_62	NLRC5	EXON	-	chr16:57081155-57081175	CUCUUCAGCCGGCCCAUCUG	9870
84166_46_63	NLRC5	EXON	-	chr16:57081166-57081186	CAUACUCCACUCUCUUCAGC	9871
84166_47_3	NLRC5	EXON	+	chr16:57081508-57081528	UCACUGUCCACUGAGAAGCC	9872
84166_47_8	NLRC5	EXON	+	chr16:57081532-57081552	GAAGAAUCAGAUCACAGCUU	9873
84166_47_11	NLRC5	EXON	+	chr16:57081533-57081553	AAGAAUCAGAUCACAGCUUU	9874
84166_47_12	NLRC5	EXON	+	chr16:57081534-57081554	AGAAUCAGAUCACAGCUUUG	9875
84166_47_13	NLRC5	EXON	+	chr16:57081535-57081555	GAAUCAGAUCACAGCUUUGG	9876
84166_47_14	NLRC5	EXON	+	chr16:57081540-57081560	AGAUCACAGCUUUGGGGGCC	9877
84166_47_15	NLRC5	EXON	+	chr16:57081547-57081567	AGCUUUGGGGGCCUGGCUCC	9878
84166_47_19	NLRC5	EXON	+	chr16:57081554-57081574	GGGGCCUGGCUCCUGGCUGA	9879
84166_47_21	NLRC5	EXON	+	chr16:57081559-57081579	CUGGCUCCUGGCUGAAGGAC	9880
84166_47_24	NLRC5	EXON	+	chr16:57081565-57081585	CCUGGCUGAAGGACUGGCCC	9881
84166_47_25	NLRC5	EXON	+	chr16:57081566-57081586	CUGGCUGAAGGACUGGCCCA	9882
84166_47_26	NLRC5	EXON	+	chr16:57081567-57081587	UGGCUGAAGGACUGGCCCAG	9883
84166_47_27	NLRC5	EXON	+	chr16:57081588-57081608	GGUCUAGCAUCCAAGUCAUC	9884
84166_47_29	NLRC5	EXON	+	chr16:57081597-57081617	UCCAAGUCAUCCGGUAACAG	9885
84166_47_31	NLRC5	EXON	+	chr16:57081605-57081625	AUCCGGUAACAGAGGCCUGC	9886
84166_47_33	NLRC5	EXON	+	chr16:57081606-57081626	UCCGGUAACAGAGGCCUGCA	9887
84166_47_34	NLRC5	EXON	+	chr16:57081607-57081627	CCGGUAACAGAGGCCUGCAG	9888
84166_47_36	NLRC5	EXON	-	chr16:57081509-57081529	AGGCUUCUCAGUGGACAGUG	9889
84166_47_39	NLRC5	EXON	-	chr16:57081518-57081538	UUCUUCUCCAGGCUUCUCAG	9890
84166_47_41	NLRC5	EXON	-	chr16:57081529-57081549	CUGUGAUCUGAUUCUUCUCC	9891

84166_47_43	NLRC5	EXON	-	chr16:57081561-57081581	CAGUCCUUCAGCCAGGAGCC	9892
84166_47_44	NLRC5	EXON	-	chr16:57081568-57081588	CCUGGGCCAGUCCUUCAGCC	9893
84166_47_48	NLRC5	EXON	-	chr16:57081585-57081605	GACUUGGAUGCUAGACCCCU	9894
84166_47_49	NLRC5	EXON	-	chr16:57081586-57081606	UGACUUGGAUGCUAGACCCC	9895
84166_47_52	NLRC5	EXON	-	chr16:57081601-57081621	GCCUCUGUUACCGGAUGACU	9896
84166_47_54	NLRC5	EXON	-	chr16:57081610-57081630	CCCCUGCAGGCCUCUGUUAC	9897
84166_48_2	NLRC5	EXON	+	chr16:57082400-57082420	UAUCUGUGCCCCACAGCCUC	9898
84166_48_4	NLRC5	EXON	+	chr16:57082425-57082445	UAACCCCAUUCCCUGCGACA	9899
84166_48_10	NLRC5	EXON	+	chr16:57082446-57082466	GGCCCAGCACCUGAAGAGCC	9900
84166_48_11	NLRC5	EXON	+	chr16:57082454-57082474	ACCUGAAGAGCCAGGAGCCC	9901
84166_48_13	NLRC5	EXON	+	chr16:57082458-57082478	GAAGAGCCAGGAGCCCAGGC	9902
84166_48_16	NLRC5	EXON	+	chr16:57082488-57082508	CUUCUUUGACAACCAGCCCC	9903
84166_48_21	NLRC5	EXON	+	chr16:57082496-57082516	ACAACCAGCCCCAGGCCCCU	9904
84166_48_23	NLRC5	EXON	+	chr16:57082497-57082517	CAACCAGCCCCAGGCCCCUU	9905
84166_48_24	NLRC5	EXON	+	chr16:57082498-57082518	AACCAGCCCCAGGCCCCUUG	9906
84166_48_25	NLRC5	EXON	+	chr16:57082508-57082528	AGGCCCCUUGGGGUACUUGA	9907
84166_48_29	NLRC5	EXON	+	chr16:57082526-57082546	GAUGGCCCCCUCAAGACCUU	9908
84166_48_35	NLRC5	EXON	+	chr16:57082573-57082593	AUGAUCCACCUUUCGCCCAC	9909
84166_48_36	NLRC5	EXON	+	chr16:57082574-57082594	UGAUCCACCUUUCGCCCACU	9910
84166_48_40	NLRC5	EXON	+	chr16:57082588-57082608	CCCACUGGGAUAAUUGACUC	9911
84166_48_44	NLRC5	EXON	+	chr16:57082603-57082623	GACUCAGGAAAGAAGAGCCU	9912
84166_48_47	NLRC5	EXON	+	chr16:57082607-57082627	CAGGAAAGAAGAGCCUCGGC	9913
84166_48_48	NLRC5	EXON	+	chr16:57082608-57082628	AGGAAAGAAGAGCCUCGGCA	9914
84166_48_50	NLRC5	EXON	+	chr16:57082628-57082648	GGGCGCUCUGCACUCCACCC	9915
84166_48_53	NLRC5	EXON	+	chr16:57082631-57082651	CGCUCUGCACUCCACCCAGG	9916

84166_48_56	NLRC5	EXON	+	chr16:57082635-57082655	CUGCACUCCACCCAGGAGGA	9917
84166_48_59	NLRC5	EXON	+	chr16:57082663-57082683	UGUGUCCUGCUGCAGUCCUC	9918
84166_48_61	NLRC5	EXON	+	chr16:57082664-57082684	GUGUCCUGCUGCAGUCCUCA	9919
84166_48_64	NLRC5	EXON	+	chr16:57082677-57082697	GUCCUCAGGGAGAACUUUUU	9920
84166_48_67	NLRC5	EXON	+	chr16:57082678-57082698	UCCUCAGGGAGAACUUUUUU	9921
84166_48_70	NLRC5	EXON	+	chr16:57082685-57082705	GGAGAACUUUUUUGGGAACC	9922
84166_48_72	NLRC5	EXON	+	chr16:57082691-57082711	CUUUUUUGGGAACCAGGAGC	9923
84166_48_73	NLRC5	EXON	+	chr16:57082692-57082712	UUUUUUGGGAACCAGGAGCU	9924
84166_48_77	NLRC5	EXON	+	chr16:57082697-57082717	UGGGAACCAGGAGCUGGGUC	9925
84166_48_83	NLRC5	EXON	+	chr16:57082704-57082724	CAGGAGCUGGGUCUGGACAA	9926
84166_48_86	NLRC5	EXON	+	chr16:57082723-57082743	AAGGAGUACCCUGCAUUACG	9927
84166_48_87	NLRC5	EXON	+	chr16:57082724-57082744	AGGAGUACCCUGCAUUACGU	9928
84166_48_90	NLRC5	EXON	+	chr16:57082742-57082762	GUGGGAUAUGUGUGAUCAAU	9929
84166_48_93	NLRC5	EXON	+	chr16:57082743-57082763	UGGGAUAUGUGUGAUCAAUU	9930
84166_48_94	NLRC5	EXON	+	chr16:57082744-57082764	GGGAUAUGUGUGAUCAAUUG	9931
84166_48_97	NLRC5	EXON	+	chr16:57082764-57082784	GGGACAUGCGACACACAAUG	9932
84166_48_99	NLRC5	EXON	+	chr16:57082765-57082785	GGACAUGCGACACACAAUGA	9933
84166_48_100	NLRC5	EXON	+	chr16:57082792-57082812	AUGACAAUGCAUGACACGUA	9934
84166_48_101	NLRC5	EXON	+	chr16:57082802-57082822	AUGACACGUACGGUUAUAUG	9935
84166_48_103	NLRC5	EXON	+	chr16:57082825-57082845	CAGUGUGACCCCUUGACAUG	9936
84166_48_106	NLRC5	EXON	+	chr16:57082847-57082867	GCGUUACAUGAAAGUCAGUG	9937
84166_48_108	NLRC5	EXON	+	chr16:57082861-57082881	UCAGUGUGGCACGUGUUCUG	9938
84166_48_110	NLRC5	EXON	+	chr16:57082866-57082886	GUGGCACGUGUUCUGUGGCA	9939
84166_48_111	NLRC5	EXON	+	chr16:57082867-57082887	UGGCACGUGUUCUGUGGCAU	9940
84166_48_112	NLRC5	EXON	+	chr16:57082873-57082893	GUGUUCUGUGGCAUGGGUGC	9941

84166_48_115	NLRC5	EXON	+	chr16:57082889-57082909	GUGCUGGCAUCCCAAGUAGC	9942
84166_48_116	NLRC5	EXON	+	chr16:57082904-57082924	GUAGCAGGAUACAUGAUUGU	9943
84166_48_120	NLRC5	EXON	+	chr16:57082941-57082961	AUGACAAAUGUCCAUGUCAC	9944
84166_48_121	NLRC5	EXON	+	chr16:57082949-57082969	UGUCCAUGUCACAGGACUCA	9945
84166_48_122	NLRC5	EXON	+	chr16:57082953-57082973	CAUGUCACAGGACUCAUGGC	9946
84166_48_123	NLRC5	EXON	+	chr16:57082968-57082988	AUGGCUGGCCAGAUGACCUC	9947
84166_48_124	NLRC5	EXON	+	chr16:57082972-57082992	CUGGCCAGAUGACCUCAGGC	9948
84166_48_134	NLRC5	EXON	+	chr16:57083031-57083051	AUAUUUAUAGAUUGUGUGUA	9949
84166_48_140	NLRC5	EXON	+	chr16:57083046-57083066	GUGUAUGGAGCAGCUAAGUC	9950
84166_48_144	NLRC5	EXON	+	chr16:57083068-57083088	GAAAAGUCUUCCGCCCGAGC	9951
84166_48_145	NLRC5	EXON	+	chr16:57083069-57083089	AAAAGUCUUCCGCCCGAGCU	9952
84166_48_148	NLRC5	EXON	+	chr16:57083072-57083092	AGUCUUCCGCCCGAGCUGGG	9953
84166_48_151	NLRC5	EXON	+	chr16:57083073-57083093	GUCUUCCGCCCGAGCUGGGA	9954
84166_48_152	NLRC5	EXON	+	chr16:57083074-57083094	UCUUCCGCCCGAGCUGGGAG	9955
84166_48_158	NLRC5	EXON	+	chr16:57083102-57083122	GUCCAUGCACUGACCAGUCC	9956
84166_48_159	NLRC5	EXON	+	chr16:57083103-57083123	UCCAUGCACUGACCAGUCCA	9957
84166_48_160	NLRC5	EXON	+	chr16:57083104-57083124	CCAUGCACUGACCAGUCCAG	9958
84166_48_162	NLRC5	EXON	+	chr16:57083111-57083131	CUGACCAGUCCAGGGGCUCA	9959
84166_48_163	NLRC5	EXON	+	chr16:57083112-57083132	UGACCAGUCCAGGGGCUCAA	9960
84166_48_165	NLRC5	EXON	+	chr16:57083117-57083137	AGUCCAGGGGCUCAAGGGCC	9961
84166_48_166	NLRC5	EXON	+	chr16:57083118-57083138	GUCCAGGGGCUCAAGGGCCA	9962
84166_48_168	NLRC5	EXON	+	chr16:57083124-57083144	GGGCUCAAGGGCCAGGGCUC	9963
84166_48_172	NLRC5	EXON	+	chr16:57083135-57083155	CCAGGGCUCUGGAACAAGCC	9964
84166_48_173	NLRC5	EXON	+	chr16:57083136-57083156	CAGGGCUCUGGAACAAGCCA	9965
84166_48_177	NLRC5	EXON	+	chr16:57083229-57083249	UACUUACAUACUAGCUUCCA	9966

84166_48_179	NLRC5	EXON	+	chr16:57083234-57083254	ACAUACUAGCUUCCAAGGAC	9967
84166_48_183	NLRC5	EXON	+	chr16:57083237-57083257	UACUAGCUUCCAAGGACAGG	9968
84166_48_184	NLRC5	EXON	+	chr16:57083240-57083260	UAGCUUCCAAGGACAGGUGG	9969
84166_48_186	NLRC5	EXON	+	chr16:57083244-57083264	UUCCAAGGACAGGUGGAGGU	9970
84166_48_187	NLRC5	EXON	+	chr16:57083245-57083265	UCCAAGGACAGGUGGAGGUA	9971
84166_48_189	NLRC5	EXON	+	chr16:57083254-57083274	AGGUGGAGGUAGGGCCAGCC	9972
84166_48_191	NLRC5	EXON	+	chr16:57083257-57083277	UGGAGGUAGGGCCAGCCUGG	9973
84166_48_194	NLRC5	EXON	+	chr16:57083258-57083278	GGAGGUAGGGCCAGCCUGGC	9974
84166_48_196	NLRC5	EXON	+	chr16:57083263-57083283	UAGGGCCAGCCUGGCGGGAG	9975
84166_48_201	NLRC5	EXON	+	chr16:57083289-57083309	AGCCCAGUCUGUCCUAUGUA	9976
84166_48_202	NLRC5	EXON	+	chr16:57083290-57083310	GCCCAGUCUGUCCUAUGUAA	9977
84166_48_203	NLRC5	EXON	+	chr16:57083301-57083321	CCUAUGUAAGGGACAAAGCC	9978
84166_48_204	NLRC5	EXON	+	chr16:57083309-57083329	AGGGACAAAGCCAGGUCUAA	9979
84166_48_206	NLRC5	EXON	+	chr16:57083315-57083335	AAAGCCAGGUCUAAUGGUAC	9980
84166_48_207	NLRC5	EXON	+	chr16:57083316-57083336	AAGCCAGGUCUAAUGGUACU	9981
84166_48_210	NLRC5	EXON	+	chr16:57083320-57083340	CAGGUCUAAUGGUACUGGGU	9982
84166_48_212	NLRC5	EXON	+	chr16:57083321-57083341	AGGUCUAAUGGUACUGGGUA	9983
84166_48_213	NLRC5	EXON	+	chr16:57083322-57083342	GGUCUAAUGGUACUGGGUAG	9984
84166_48_214	NLRC5	EXON	+	chr16:57083323-57083343	GUCUAAUGGUACUGGGUAGG	9985
84166_48_215	NLRC5	EXON	+	chr16:57083346-57083366	CACUGCCAAGACAAUAAGCU	9986
84166_48_217	NLRC5	EXON	+	chr16:57083353-57083373	AAGACAAUAAGCUAGGCUAC	9987
84166_48_218	NLRC5	EXON	+	chr16:57083354-57083374	AGACAAUAAGCUAGGCUACU	9988
84166_48_219	NLRC5	EXON	+	chr16:57083371-57083391	ACUGGGUCCAGCUACUACUU	9989
84166_48_222	NLRC5	EXON	+	chr16:57083374-57083394	GGGUCCAGCUACUACUUUGG	9990
84166_48_223	NLRC5	EXON	+	chr16:57083375-57083395	GGUCCAGCUACUACUUUGGU	9991

84166_48_224	NLRC5	EXON	+	chr16:57083382-57083402	CUACUACUUUGGUGGGAUUC	9992
84166_48_233	NLRC5	EXON	+	chr16:57083433-57083453	CAGUGUUCUUGUUACUUCCA	9993
84166_48_239	NLRC5	EXON	+	chr16:57083447-57083467	CUUCCAAGGAGAACCAAGAA	9994
84166_48_243	NLRC5	EXON	+	chr16:57083469-57083489	GCUCUGUCACACUCGAAGCC	9995
84166_48_244	NLRC5	EXON	+	chr16:57083490-57083510	GGCUUGAUCAAUAAACACAA	9996
84166_48_249	NLRC5	EXON	-	chr16:57082399-57082419	AGGCUGUGGGGCACAGAUAU	9997
84166_48_251	NLRC5	EXON	-	chr16:57082411-57082431	GGGUUAUUCCAGAGGCUGUG	9998
84166_48_252	NLRC5	EXON	-	chr16:57082412-57082432	GGGGUUAUUCCAGAGGCUGU	9999
84166_48_253	NLRC5	EXON	-	chr16:57082413-57082433	UGGGGUUAUUCCAGAGGCUG	10000
84166_48_256	NLRC5	EXON	-	chr16:57082419-57082439	AGGGAAUGGGGUUAUUCCAG	10001
84166_48_258	NLRC5	EXON	-	chr16:57082431-57082451	GGGCCAUGUCGCAGGGAAUG	10002
84166_48_259	NLRC5	EXON	-	chr16:57082432-57082452	UGGGCCAUGUCGCAGGGAAU	10003
84166_48_261	NLRC5	EXON	-	chr16:57082433-57082453	CUGGGCCAUGUCGCAGGGAA	10004
84166_48_264	NLRC5	EXON	-	chr16:57082438-57082458	AGGUGCUGGGCCAUGUCGCA	10005
84166_48_267	NLRC5	EXON	-	chr16:57082439-57082459	CAGGUGCUGGGCCAUGUCGC	10006
84166_48_269	NLRC5	EXON	-	chr16:57082451-57082471	CUCCUGGCUCUUCAGGUGCU	10007
84166_48_270	NLRC5	EXON	-	chr16:57082452-57082472	GCUCCUGGCUCUUCAGGUGC	10008
84166_48_272	NLRC5	EXON	-	chr16:57082458-57082478	GCCUGGGCUCCUGGCUCUUC	10009
84166_48_273	NLRC5	EXON	-	chr16:57082467-57082487	CAAAGUCCAGCCUGGGCUCC	10010
84166_48_274	NLRC5	EXON	-	chr16:57082474-57082494	AAGAAGGCAAAGUCCAGCCU	10011
84166_48_276	NLRC5	EXON	-	chr16:57082475-57082495	AAAGAAGGCAAAGUCCAGCC	10012
84166_48_278	NLRC5	EXON	-	chr16:57082490-57082510	CUGGGGCUGGUUGUCAAAGA	10013
84166_48_281	NLRC5	EXON	-	chr16:57082503-57082523	UACCCCAAGGGGCCUGGGGC	10014
84166_48_282	NLRC5	EXON	-	chr16:57082507-57082527	CAAGUACCCCAAGGGGCCUG	10015
84166_48_283	NLRC5	EXON	-	chr16:57082508-57082528	UCAAGUACCCCAAGGGGCCU	10016

84166_48_284	NLRC5	EXON	-	chr16:57082509-57082529	AUCAAGUACCCCAAGGGGCC	10017
84166_48_287	NLRC5	EXON	-	chr16:57082514-57082534	GGGCCAUCAAGUACCCCAAG	10018
84166_48_289	NLRC5	EXON	-	chr16:57082515-57082535	GGGGCCAUCAAGUACCCCAA	10019
84166_48_291	NLRC5	EXON	-	chr16:57082516-57082536	GGGGGCCAUCAAGUACCCCA	10020
84166_48_294	NLRC5	EXON	-	chr16:57082534-57082554	GGAUUCCAAAGGUCUUGAGG	10021
84166_48_296	NLRC5	EXON	-	chr16:57082535-57082555	UGGAUUCCAAAGGUCUUGAG	10022
84166_48_297	NLRC5	EXON	-	chr16:57082536-57082556	CUGGAUUCCAAAGGUCUUGA	10023
84166_48_300	NLRC5	EXON	-	chr16:57082537-57082557	GCUGGAUUCCAAAGGUCUUG	10024
84166_48_303	NLRC5	EXON	-	chr16:57082545-57082565	AUCACUUGGCUGGAUUCCAA	10025
84166_48_306	NLRC5	EXON	-	chr16:57082555-57082575	AUUUGGGUGCAUCACUUGGC	10026
84166_48_308	NLRC5	EXON	-	chr16:57082559-57082579	GAUCAUUUGGGUGCAUCACU	10027
84166_48_309	NLRC5	EXON	-	chr16:57082571-57082591	GGGCGAAAGGUGGAUCAUUU	10028
84166_48_310	NLRC5	EXON	-	chr16:57082572-57082592	UGGGCGAAAGGUGGAUCAUU	10029
84166_48_313	NLRC5	EXON	-	chr16:57082581-57082601	UUAUCCCAGUGGGCGAAAGG	10030
84166_48_315	NLRC5	EXON	-	chr16:57082584-57082604	CAAUUAUCCCAGUGGGCGAA	10031
84166_48_320	NLRC5	EXON	-	chr16:57082591-57082611	CCUGAGUCAAUUAUCCCAGU	10032
84166_48_321	NLRC5	EXON	-	chr16:57082592-57082612	UCCUGAGUCAAUUAUCCCAG	10033
84166_48_324	NLRC5	EXON	-	chr16:57082623-57082643	GAGUGCAGAGCGCCCUGCCG	10034
84166_48_328	NLRC5	EXON	-	chr16:57082645-57082665	CACGUAUCCUUCCUCCUGGG	10035
84166_48_331	NLRC5	EXON	-	chr16:57082648-57082668	ACACACGUAUCCUUCCUCCU	10036
84166_48_332	NLRC5	EXON	-	chr16:57082649-57082669	GACACACGUAUCCUUCCUCC	10037
84166_48_335	NLRC5	EXON	-	chr16:57082671-57082691	UUCUCCCUGAGGACUGCAGC	10038
84166_48_338	NLRC5	EXON	-	chr16:57082682-57082702	UCCCAAAAAAGUUCUCCCUG	10039
84166_48_343	NLRC5	EXON	-	chr16:57082706-57082726	CUUUGUCCAGACCCAGCUCC	10040
84166_48_344	NLRC5	EXON	-	chr16:57082734-57082754	CACAUAUCCCACGUAAUGCA	10041

84166_48_346	NLRC5	EXON	-	chr16:57082735-57082755	ACACAUAUCCCACGUAAUGC	10042
84166_48_352	NLRC5	EXON	-	chr16:57082836-57082856	AUGUAACGCCACAUGUCAAG	10043
84166_48_353	NLRC5	EXON	-	chr16:57082837-57082857	CAUGUAACGCCACAUGUCAA	10044
84166_48_354	NLRC5	EXON	-	chr16:57082838-57082858	UCAUGUAACGCCACAUGUCA	10045
84166_48_360	NLRC5	EXON	-	chr16:57082902-57082922	AAUCAUGUAUCCUGCUACUU	10046
84166_48_362	NLRC5	EXON	-	chr16:57082903-57082923	CAAUCAUGUAUCCUGCUACU	10047
84166_48_366	NLRC5	EXON	-	chr16:57082955-57082975	CAGCCAUGAGUCCUGUGACA	10048
84166_48_370	NLRC5	EXON	-	chr16:57082979-57082999	UGGGCCAGCCUGAGGUCAUC	10049
84166_48_372	NLRC5	EXON	-	chr16:57082987-57083007	UUAGAUCUUGGGCCAGCCUG	10050
84166_48_377	NLRC5	EXON	-	chr16:57082998-57083018	AAAUUAAUAAAUUAGAUCUU	10051
84166_48_378	NLRC5	EXON	-	chr16:57082999-57083019	AAAAUUAAUAAAUUAGAUCU	10052
84166_48_386	NLRC5	EXON	-	chr16:57083081-57083101	CUCUCCCCUCCCAGCUCGGG	10053
84166_48_389	NLRC5	EXON	-	chr16:57083084-57083104	ACACUCUCCCCUCCCAGCUC	10054
84166_48_390	NLRC5	EXON	-	chr16:57083085-57083105	GACACUCUCCCCUCCCAGCU	10055
84166_48_393	NLRC5	EXON	-	chr16:57083107-57083127	CCCCUGGACUGGUCAGUGCA	10056
84166_48_395	NLRC5	EXON	-	chr16:57083118-57083138	UGGCCCUUGAGCCCCUGGAC	10057
84166_48_397	NLRC5	EXON	-	chr16:57083123-57083143	AGCCCUGGCCCUUGAGCCCC	10058
84166_48_401	NLRC5	EXON	-	chr16:57083138-57083158	CCUGGCUUGUUCCAGAGCCC	10059
84166_48_404	NLRC5	EXON	-	chr16:57083156-57083176	GGACUUAAUGGCUGAGUCCC	10060
84166_48_407	NLRC5	EXON	-	chr16:57083168-57083188	UGAGGCAGGAGGGGACUUAA	10061
84166_48_408	NLRC5	EXON	-	chr16:57083177-57083197	GCUGAGGAUUGAGGCAGGAG	10062
84166_48_410	NLRC5	EXON	-	chr16:57083178-57083198	GGCUGAGGAUUGAGGCAGGA	10063
84166_48_412	NLRC5	EXON	-	chr16:57083179-57083199	AGGCUGAGGAUUGAGGCAGG	10064
84166_48_415	NLRC5	EXON	-	chr16:57083182-57083202	GGUAGGCUGAGGAUUGAGGC	10065
84166_48_419	NLRC5	EXON	-	chr16:57083186-57083206	GAUGGGUAGGCUGAGGAUUG	10066

84166_48_421	NLRC5	EXON	-	chr16:57083193-57083213	GUUUAUAGAUGGGUAGGCUG	10067
84166_48_424	NLRC5	EXON	-	chr16:57083199-57083219	CAUCAAGUUUAUAGAUGGGU	10068
84166_48_425	NLRC5	EXON	-	chr16:57083203-57083223	GAGUCAUCAAGUUUAUAGAU	10069
84166_48_426	NLRC5	EXON	-	chr16:57083204-57083224	GGAGUCAUCAAGUUUAUAGA	10070
84166_48_430	NLRC5	EXON	-	chr16:57083225-57083245	AGCUAGUAUGUAAGUAAGGG	10071
84166_48_432	NLRC5	EXON	-	chr16:57083228-57083248	GGAAGCUAGUAUGUAAGUAA	10072
84166_48_434	NLRC5	EXON	-	chr16:57083229-57083249	UGGAAGCUAGUAUGUAAGUA	10073
84166_48_437	NLRC5	EXON	-	chr16:57083249-57083269	GCCCUACCUCCACCUGUCCU	10074
84166_48_441	NLRC5	EXON	-	chr16:57083271-57083291	CUUCUCCACUCCCGCCAGGC	10075
84166_48_442	NLRC5	EXON	-	chr16:57083275-57083295	UGGGCUUCUCCACUCCCGCC	10076
84166_48_446	NLRC5	EXON	-	chr16:57083294-57083314	UCCCUUACAUAGGACAGACU	10077
84166_48_447	NLRC5	EXON	-	chr16:57083295-57083315	GUCCCUUACAUAGGACAGAC	10078
84166_48_450	NLRC5	EXON	-	chr16:57083304-57083324	CCUGGCUUUGUCCCUUACAU	10079
84166_48_452	NLRC5	EXON	-	chr16:57083322-57083342	CUACCCAGUACCAUUAGACC	10080
84166_48_456	NLRC5	EXON	-	chr16:57083354-57083374	AGUAGCCUAGCUUAUUGUCU	10081
84166_48_457	NLRC5	EXON	-	chr16:57083381-57083401	AAUCCCACCAAAGUAGUAGC	10082
84166_48_461	NLRC5	EXON	-	chr16:57083415-57083435	UGGGUAACAUGUGAAGUGCA	10083
84166_48_465	NLRC5	EXON	-	chr16:57083434-57083454	UUGGAAGUAACAAGAACACU	10084
84166_48_467	NLRC5	EXON	-	chr16:57083435-57083455	CUUGGAAGUAACAAGAACAC	10085
84166_48_474	NLRC5	EXON	-	chr16:57083453-57083473	GAGCCAUUCUUGGUUCUCCU	10086
84166_48_477	NLRC5	EXON	-	chr16:57083463-57083483	GAGUGUGACAGAGCCAUUCU	10087
84166_48_484	NLRC5	EXON	-	chr16:57083490-57083510	UUGUGUUUAUUGAUCAAGCC	10088
84166_48_487	NLRC5	EXON	-	chr16:57083520-57083540	CAUUGGAUUCACGCUAGACG	10089

Table 2: gRNA targeting domains for exemplary inhibitory molecules

Id.	Target	Target Region	Strand	Genomic Location (hg38)	Guide RNA Targeting Domain Sequence	SEQ ID NO:
29126_1_1	CD274	Exon 1	+	chr9:5450495-5450520	CGGGCCUGGCGCAACGCUGAGCAGC	2942
29126_1_2	CD274	Exon 1	+	chr9:5450509-5450534	CGCUGAGCAGCUGGCGCGUCCCGCG	2943
29126_1_3	CD274	Exon 1	+	chr9:5450535-5450560	GGCCCCAGUUCUGCGCAGCUUCCCG	2944
29126_1_4	CD274	Exon 1	+	chr9:5450569-5450594	ACCAGCCGCGCUUCUGUCCGCCUGC	2945
29126_1_5	CD274	Exon 1	+	chr9:5450573-5450598	GCCGCGCUUCUGUCCGCCUGCAGGU	2946
29126_1_6	CD274	Exon 1	+	chr9:5450574-5450599	CCGCGCUUCUGUCCGCCUGCAGGUA	2947
29126_1_7	CD274	Exon 1	+	chr9:5450592-5450617	GCAGGUAGGGAGCGUUGUUCCUCCG	2948
29126_1_8	CD274	Exon 1	+	chr9:5450593-5450618	CAGGUAGGGAGCGUUGUUCCUCCGC	2949
29126_1_9	CD274	Exon 1	-	chr9:5450489-5450514	CAGCGUUGCGCCAGGCCCGGAGGCG	2950
29126_1_10	CD274	Exon 1	-	chr9:5450490-5450515	UCAGCGUUGCGCCAGGCCCGGAGGC	2951
29126_1_11	CD274	Exon 1	-	chr9:5450491-5450516	CUCAGCGUUGCGCCAGGCCCGGAGG	2952
29126_1_12	CD274	Exon 1	-	chr9:5450494-5450519	CUGCUCAGCGUUGCGCCAGGCCCGG	2953
29126_1_13	CD274	Exon 1	-	chr9:5450497-5450522	CAGCUGCUCAGCGUUGCGCCAGGCC	2954
29126_1_14	CD274	Exon 1	-	chr9:5450502-5450527	CGCGCCAGCUGCUCAGCGUUGCGCC	2955
29126_1_15	CD274	Exon 1	-	chr9:5450531-5450556	AAGCUGCGCAGAACUGGGGCCGCGC	2956
29126_1_16	CD274	Exon 1	-	chr9:5450532-5450557	GAAGCUGCGCAGAACUGGGGCCGCG	2957
29126_1_17	CD274	Exon 1	-	chr9:5450540-5450565	AGCCUCGGGAAGCUGCGCAGAACUG	2958
29126_1_18	CD274	Exon 1	-	chr9:5450541-5450566	GAGCCUCGGGAAGCUGCGCAGAACU	2959
29126_1_19	CD274	Exon 1	-	chr9:5450542-5450567	GGAGCCUCGGGAAGCUGCGCAGAAC	2960
29126_1_20	CD274	Exon 1	-	chr9:5450559-5450584	AGAAGCGCGGCUGGUGCGGAGCCUC	2961
29126_1_21	CD274	Exon 1	-	chr9:5450560-5450585	CAGAAGCGCGGCUGGUGCGGAGCCU	2962
29126_1_22	CD274	Exon 1	-	chr9:5450568-5450593	CAGGCGGACAGAAGCGCGGCUGGUG	2963
29126_1_23	CD274	Exon 1	-	chr9:5450573-5450598	ACCUGCAGGCGGACAGAAGCGCGGC	2964

29126_1_24	CD274	Exon 1	-	chr9:5450577-5450602	CCCUACCUGCAGGCGGACAGAAGCG	2965
29126_1_25	CD274	Exon 1	-	chr9:5450589-5450614	AGGAACAACGCUCCCUACCUGCAGG	2966
29126_1_26	CD274	Exon 1	-	chr9:5450592-5450617	CGGAGGAACAACGCUCCCUACCUGC	2967
29126_2_1	CD274	Exon 2	+	chr9:5456091-5456116	AUAAUUAGGGCAUUCCAGAAAGAUG	2968
29126_2_2	CD274	Exon 2	+	chr9:5456124-5456149	UGCUGUCUUUAUAUUCAUGACCUAC	2969
29126_2_3	CD274	Exon 2	+	chr9:5456138-5456163	UCAUGACCUACUGGCAUUUGCUGAA	2970
29126_2_4	CD274	Exon 2	-	chr9:5456092-5456117	UCAUCUUUCUGGAAUGCCCUAAUUA	2971
29126_2_5	CD274	Exon 2	-	chr9:5456108-5456133	AAGACAGCAAAUAUCCUCAUCUUUC	2972
29126_2_6	CD274	Exon 2	-	chr9:5456147-5456172	GUCUUACCGUUCAGCAAAUGCCAGU	2973
29126_3_1	CD274	Exon 3	+	chr9:5457065-5457090	UCUUUCUUUUUAGCAUUUACUGUCA	2974
29126_3_2	CD274	Exon 3	+	chr9:5457074-5457099	UUAGCAUUUACUGUCACGGUUCCCA	2975
29126_3_3	CD274	Exon 3	+	chr9:5457086-5457111	GUCACGGUUCCCAAGGACCUAUAUG	2976
29126_3_4	CD274	Exon 3	+	chr9:5457096-5457121	CCAAGGACCUAUAUGUGGUAGAGUA	2977
29126_3_5	CD274	Exon 3	+	chr9:5457149-5457174	UUCCCAGUAGAAAAACAAUUAGACC	2978
29126_3_6	CD274	Exon 3	+	chr9:5457169-5457194	AGACCUGGCUGCACUAAUUGUCUAU	2979
29126_3_7	CD274	Exon 3	+	chr9:5457170-5457195	GACCUGGCUGCACUAAUUGUCUAUU	2980
29126_3_8	CD274	Exon 3	+	chr9:5457176-5457201	GCUGCACUAAUUGUCUAUUGGGAAA	2981
29126_3_9	CD274	Exon 3	+	chr9:5457179-5457204	GCACUAAUUGUCUAUUGGGAAAUGG	2982
29126_3_10	CD274	Exon 3	+	chr9:5457207-5457232	AUAAGAACAUUAUUCAAUUUGUGCA	2983
29126_3_11	CD274	Exon 3	+	chr9:5457212-5457237	AACAUUAUUCAAUUUGUGCAUGGAG	2984
29126_3_12	CD274	Exon 3	+	chr9:5457224-5457249	UUUGUGCAUGGAGAGGAAGACCUGA	2985
29126_3_13	CD274	Exon 3	+	chr9:5457250-5457275	GGUUCAGCAUAGUAGCUACAGACAG	2986
29126_3_14	CD274	Exon 3	+	chr9:5457251-5457276	GUUCAGCAUAGUAGCUACAGACAGA	2987
29126_3_15	CD274	Exon 3	+	chr9:5457256-5457281	GCAUAGUAGCUACAGACAGAGGGCC	2988
29126_3_16	CD274	Exon 3	+	chr9:5457266-5457291	UACAGACAGAGGGCCCGGCUGUUGA	2989

29126_3_17	CD274	Exon 3	+	chr9:5457281-5457306	CGGCUGUUGAAGGACCAGCUCUCCC	2990
29126_3_18	CD274	Exon 3	+	chr9:5457282-5457307	GGCUGUUGAAGGACCAGCUCUCCCU	2991
29126_3_19	CD274	Exon 3	+	chr9:5457320-5457345	CUUCAGAUCACAGAUGUGAAAUUGC	2992
29126_3_20	CD274	Exon 3	+	chr9:5457327-5457352	UCACAGAUGUGAAAUUGCAGGAUGC	2993
29126_3_21	CD274	Exon 3	+	chr9:5457328-5457353	CACAGAUGUGAAAUUGCAGGAUGCA	2994
29126_3_22	CD274	Exon 3	+	chr9:5457329-5457354	ACAGAUGUGAAAUUGCAGGAUGCAG	2995
29126_3_23	CD274	Exon 3	+	chr9:5457354-5457379	GGGUGUACCGCUGCAUGAUCAGCUA	2996
29126_3_24	CD274	Exon 3	+	chr9:5457357-5457382	UGUACCGCUGCAUGAUCAGCUAUGG	2997
29126_3_25	CD274	Exon 3	+	chr9:5457393-5457418	ACAAGCGAAUUACUGUGAAAGUCAA	2998
29126_3_26	CD274	Exon 3	+	chr9:5457416-5457441	AAUGGUAAGAAUUAUUAUAGAUGAG	2999
29126_3_27	CD274	Exon 3	-	chr9:5457065-5457090	UGACAGUAAAUGCUAAAAAGAAAGA	3000
29126_3_28	CD274	Exon 3	-	chr9:5457098-5457123	CAUACUCUACCACAUAUAGGUCCUU	3001
29126_3_29	CD274	Exon 3	-	chr9:5457099-5457124	CCAUACUCUACCACAUAUAGGUCCU	3002
29126_3_30	CD274	Exon 3	-	chr9:5457106-5457131	AUUGCUACCAUACUCUACCACAUAU	3003
29126_3_31	CD274	Exon 3	-	chr9:5457154-5457179	AGCCAGGUCUAAUUGUUUUUCUACU	3004
29126_3_32	CD274	Exon 3	-	chr9:5457155-5457180	CAGCCAGGUCUAAUUGUUUUUCUAC	3005
29126_3_33	CD274	Exon 3	-	chr9:5457175-5457200	UUCCCAAUAGACAAUUAGUGCAGCC	3006
29126_3_34	CD274	Exon 3	-	chr9:5457247-5457272	UCUGUAGCUACUAUGCUGAACCUUC	3007
29126_3_35	CD274	Exon 3	-	chr9:5457282-5457307	AGGGAGAGCUGGUCCUUCAACAGCC	3008
29126_3_36	CD274	Exon 3	-	chr9:5457283-5457308	CAGGGAGAGCUGGUCCUUCAACAGC	3009
29126_3_37	CD274	Exon 3	-	chr9:5457298-5457323	AAGUGCAGCAUUUCCCAGGGAGAGC	3010
29126_3_38	CD274	Exon 3	-	chr9:5457306-5457331	GUGAUCUGAAGUGCAGCAUUUCCCA	3011
29126_3_39	CD274	Exon 3	-	chr9:5457307-5457332	UGUGAUCUGAAGUGCAGCAUUUCCC	3012
29126_3_40	CD274	Exon 3	-	chr9:5457364-5457389	GGCACCACCAUAGCUGAUCAUGCAG	3013
29126_3_41	CD274	Exon 3	-	chr9:5457390-5457415	ACUUUCACAGUAAUUCGCUUGUAGU	3014

29126_4_1	CD274	Exon 4	+	chr9:5462838-5462863	UACAACAAAAUCAACCAAAGAAUUU	3015
29126_4_2	CD274	Exon 4	+	chr9:5462844-5462869	AAAAUCAACCAAAGAAUUUUGGUUG	3016
29126_4_3	CD274	Exon 4	+	chr9:5462880-5462905	ACCUCUGAACAUGAACUGACAUGUC	3017
29126_4_4	CD274	Exon 4	+	chr9:5462886-5462911	GAACAUGAACUGACAUGUCAGGCUG	3018
29126_4_5	CD274	Exon 4	+	chr9:5462887-5462912	AACAUGAACUGACAUGUCAGGCUGA	3019
29126_4_6	CD274	Exon 4	+	chr9:5462898-5462923	ACAUGUCAGGCUGAGGGCUACCCCA	3020
29126_4_7	CD274	Exon 4	+	chr9:5462912-5462937	GGGCUACCCCAAGGCCGAAGUCAUC	3021
29126_4_8	CD274	Exon 4	+	chr9:5462941-5462966	CAAGCAGUGACCAUCAAGUCCUGAG	3022
29126_4_9	CD274	Exon 4	+	chr9:5462973-5462998	ACCACCACCACCAAUUCCAAGAGAG	3023
29126_4_10	CD274	Exon 4	+	chr9:5463047-5463072	UAAUGAGAUUUUCUACUGCACUUUU	3024
29126_4_11	CD274	Exon 4	+	chr9:5463063-5463088	UGCACUUUUAGGAGAUUAGAUCCUG	3025
29126_4_12	CD274	Exon 4	+	chr9:5463084-5463109	CCUGAGGAAAACCAUACAGCUGAAU	3026
29126_4_13	CD274	Exon 4	+	chr9:5463094-5463119	ACCAUACAGCUGAAUUGGUCAUCCC	3027
29126_4_14	CD274	Exon 4	-	chr9:5462831-5462856	UUGGUUGAUUUUGUUGUAUGGGGCU	3028
29126_4_15	CD274	Exon 4	-	chr9:5462836-5462861	AUUCUUUGGUUGAUUUUGUUGUAUG	3029
29126_4_16	CD274	Exon 4	-	chr9:5462837-5462862	AAUUCUUUGGUUGAUUUUGUUGUAU	3030
29126_4_17	CD274	Exon 4	-	chr9:5462838-5462863	AAAUUCUUUGGUUGAUUUUGUUGUA	3031
29126_4_18	CD274	Exon 4	-	chr9:5462855-5462880	GACUGGAUCCACAACCAAAAUUCUU	3032
29126_4_19	CD274	Exon 4	-	chr9:5462877-5462902	AUGUCAGUUCAUGUUCAGAGGUGAC	3033
29126_4_20	CD274	Exon 4	-	chr9:5462884-5462909	GCCUGACAUGUCAGUUCAUGUUCAG	3034
29126_4_21	CD274	Exon 4	-	chr9:5462921-5462946	GCUUGUCCAGAUGACUUCGGCCUUG	3035
29126_4_22	CD274	Exon 4	-	chr9:5462922-5462947	UGCUUGUCCAGAUGACUUCGGCCUU	3036
29126_4_23	CD274	Exon 4	-	chr9:5462923-5462948	CUGCUUGUCCAGAUGACUUCGGCCU	3037
29126_4_24	CD274	Exon 4	-	chr9:5462929-5462954	UGGUCACUGCUUGUCCAGAUGACUU	3038
29126_4_25	CD274	Exon 4	-	chr9:5462954-5462979	GGUGGUCUUACCACUCAGGACUUGA	3039

29126_4_26	CD274	Exon 4	-	chr9:5462963-5462988	AUUGGUGGUGGUGGUCUUACCACUC	3040
29126_4_27	CD274	Exon 4	-	chr9:5462977-5463002	UCCUCUCUCUUGGAAUUGGUGGUGG	3041
29126_4_28	CD274	Exon 4	-	chr9:5462980-5463005	UUCUCCUCUCUCUUGGAAUUGGUGG	3042
29126_4_29	CD274	Exon 4	-	chr9:5462983-5463008	AGCUUCUCCUCUCUCUUGGAAUUGG	3043
29126_4_30	CD274	Exon 4	-	chr9:5462986-5463011	AAAAGCUUCUCCUCUCUCUUGGAAU	3044
29126_4_31	CD274	Exon 4	-	chr9:5462992-5463017	ACAUUGAAAAGCUUCUCCUCUCUCU	3045
29126_4_32	CD274	Exon 4	-	chr9:5463022-5463047	GUUGUUGUGUUGAUUCUCAGUGUGC	3046
29126_4_33	CD274	Exon 4	-	chr9:5463087-5463112	CCAAUUCAGCUGUAUGGUUUUCCUC	3047
29126_4_34	CD274	Exon 4	-	chr9:5463098-5463123	ACCUGGGAUGACCAAUUCAGCUGUA	3048
29126_4_35	CD274	Exon 4	-	chr9:5463119-5463144	AAUGGACACAUUCAGAAUAUUACCU	3049
29126_4_36	CD274	Exon 4	-	chr9:5463120-5463145	UAAUGGACACAUUCAGAAUAUUACC	3050
29126_5_1	CD274	Exon 5	+	chr9:5465482-5465507	UUGUUUUGUUUUUCAGAACUACCUC	3051
29126_5_2	CD274	Exon 5	+	chr9:5465502-5465527	ACCUCUGGCACAUCCUCCAAAUGAA	3052
29126_5_3	CD274	Exon 5	+	chr9:5465512-5465537	CAUCCUCCAAAUGAAAGGACUCACU	3053
29126_5_4	CD274	Exon 5	+	chr9:5465521-5465546	AAUGAAAGGACUCACUUGGUAAUUC	3054
29126_5_5	CD274	Exon 5	+	chr9:5465522-5465547	AUGAAAGGACUCACUUGGUAAUUCU	3055
29126_5_6	CD274	Exon 5	+	chr9:5465543-5465568	UUCUGGGAGCCAUCUUAUUAUGCCU	3056
29126_5_7	CD274	Exon 5	+	chr9:5465579-5465604	UGACAUUCAUCUUCCGUUUAAGAAA	3057
29126_5_8	CD274	Exon 5	+	chr9:5465602-5465627	AAAGGUAGUAUUUCCUUAAUUGCAG	3058
29126_5_9	CD274	Exon 5	-	chr9:5465506-5465531	UCCUUUCAUUUGGAGGAUGUGCCAG	3059
29126_5_10	CD274	Exon 5	-	chr9:5465518-5465543	UUACCAAGUGAGUCCUUUCAUUUGG	3060
29126_5_11	CD274	Exon 5	-	chr9:5465521-5465546	GAAUUACCAAGUGAGUCCUUUCAUU	3061
29126_5_12	CD274	Exon 5	-	chr9:5465555-5465580	AGUGCUACACCAAGGCAUAAUAAGA	3062
29126_5_13	CD274	Exon 5	-	chr9:5465568-5465593	GAAGAUGAAUGUCAGUGCUACACCA	3063
29126_5_14	CD274	Exon 5	-	chr9:5465595-5465620	UAAGGAAAUACUACCUUUUCUUAAA	3064

29126_6_1	CD274	Exon 6	+	chr9:5466753-5466778	AUUUCUUUUUCUCAAGGGAGAAUGA	3065
29126_6_2	CD274	Exon 6	+	chr9:5466769-5466794	GGAGAAUGAUGGAUGUGAAAAAAUG	3066
29126_6_3	CD274	Exon 6	+	chr9:5466802-5466827	AAGAUACAAACUCAAAGAAGCAAAG	3067
29126_6_4	CD274	Exon 6	+	chr9:5466818-5466843	GAAGCAAAGUGGUAAGAAUAUCAGA	3068
29126_6_5	CD274	Exon 6	+	chr9:5466824-5466849	AAGUGGUAAGAAUAUCAGAAGGAAU	3069
29126_6_6	CD274	Exon 6	+	chr9:5466825-5466850	AGUGGUAAGAAUAUCAGAAGGAAUU	3070
29126_6_7	CD274	Exon 6	-	chr9:5466803-5466828	ACUUUGCUUCUUUGAGUUUGUAUCU	3071
29126_7_1	CD274	Exon 7	+	chr9:5467823-5467848	UAUUAUCACUCUCCAGAUACACAUU	3072
29126_7_2	CD274	Exon 7	+	chr9:5467826-5467851	UAUCACUCUCCAGAUACACAUUUGG	3073
29126_7_3	CD274	Exon 7	+	chr9:5467845-5467870	AUUUGGAGGAGACGUAAUCCAGCAU	3074
29126_7_4	CD274	Exon 7	+	chr9:5467866-5467891	GCAUUGGAACUUCUGAUCUUCAAGC	3075
29126_7_5	CD274	Exon 7	+	chr9:5467867-5467892	CAUUGGAACUUCUGAUCUUCAAGCA	3076
29126_7_6	CD274	Exon 7	+	chr9:5467882-5467907	UCUUCAAGCAGGGAUUCUCAACCUG	3077
29126_7_7	CD274	Exon 7	+	chr9:5467888-5467913	AGCAGGGAUUCUCAACCUGUGGUUU	3078
29126_7_8	CD274	Exon 7	+	chr9:5467889-5467914	GCAGGGAUUCUCAACCUGUGGUUUA	3079
29126_7_9	CD274	Exon 7	+	chr9:5467890-5467915	CAGGGAUUCUCAACCUGUGGUUUAG	3080
29126_7_10	CD274	Exon 7	+	chr9:5467898-5467923	CUCAACCUGUGGUUUAGGGGUUCAU	3081
29126_7_11	CD274	Exon 7	+	chr9:5467899-5467924	UCAACCUGUGGUUUAGGGGUUCAUC	3082
29126_7_12	CD274	Exon 7	+	chr9:5467900-5467925	CAACCUGUGGUUUAGGGGUUCAUCG	3083
29126_7_13	CD274	Exon 7	+	chr9:5467917-5467942	GUUCAUCGGGGCUGAGCGUGACAAG	3084
29126_7_14	CD274	Exon 7	+	chr9:5467921-5467946	AUCGGGGCUGAGCGUGACAAGAGGA	3085
29126_7_15	CD274	Exon 7	+	chr9:5467926-5467951	GGCUGAGCGUGACAAGAGGAAGGAA	3086
29126_7_16	CD274	Exon 7	+	chr9:5467927-5467952	GCUGAGCGUGACAAGAGGAAGGAAU	3087
29126_7_17	CD274	Exon 7	+	chr9:5467934-5467959	GUGACAAGAGGAAGGAAUGGGCCCG	3088
29126_7_18	CD274	Exon 7	+	chr9:5467935-5467960	UGACAAGAGGAAGGAAUGGGCCCGU	3089

29126_7_19	CD274	Exon 7	+	chr9:5467942-5467967	AGGAAGGAAUGGGCCCGUGGGAUGC	3090
29126_7_20	CD274	Exon 7	+	chr9:5467950-5467975	AUGGGCCCGUGGGAUGCAGGCAAUG	3091
29126_7_21	CD274	Exon 7	+	chr9:5467951-5467976	UGGGCCCGUGGGAUGCAGGCAAUGU	3092
29126_7_22	CD274	Exon 7	+	chr9:5467961-5467986	GGAUGCAGGCAAUGUGGGACUUAAA	3093
29126_7_23	CD274	Exon 7	+	chr9:5467979-5468004	ACUUAAAAGGCCCAAGCACUGAAAA	3094
29126_7_24	CD274	Exon 7	+	chr9:5467986-5468011	AGGCCCAAGCACUGAAAAUGGAACC	3095
29126_7_25	CD274	Exon 7	+	chr9:5467998-5468023	UGAAAAUGGAACCUGGCGAAAGCAG	3096
29126_7_26	CD274	Exon 7	+	chr9:5468001-5468026	AAAUGGAACCUGGCGAAAGCAGAGG	3097
29126_7_27	CD274	Exon 7	+	chr9:5468018-5468043	AGCAGAGGAGGAGAAUGAAGAAAGA	3098
29126_7_28	CD274	Exon 7	+	chr9:5468029-5468054	AGAAUGAAGAAAGAUGGAGUCAAAC	3099
29126_7_29	CD274	Exon 7	+	chr9:5468030-5468055	GAAUGAAGAAAGAUGGAGUCAAACA	3100
29126_7_30	CD274	Exon 7	+	chr9:5468037-5468062	GAAAGAUGGAGUCAAACAGGGAGCC	3101
29126_7_31	CD274	Exon 7	+	chr9:5468040-5468065	AGAUGGAGUCAAACAGGGAGCCUGG	3102
29126_7_32	CD274	Exon 7	+	chr9:5468041-5468066	GAUGGAGUCAAACAGGGAGCCUGGA	3103
29126_7_33	CD274	Exon 7	+	chr9:5468069-5468094	AGACCUUGAUACUUUCAAAUGCCUG	3104
29126_7_34	CD274	Exon 7	+	chr9:5468070-5468095	GACCUUGAUACUUUCAAAUGCCUGA	3105
29126_7_35	CD274	Exon 7	+	chr9:5468071-5468096	ACCUUGAUACUUUCAAAUGCCUGAG	3106
29126_7_36	CD274	Exon 7	+	chr9:5468092-5468117	UGAGGGGCUCAUCGACGCCUGUGAC	3107
29126_7_37	CD274	Exon 7	+	chr9:5468093-5468118	GAGGGGCUCAUCGACGCCUGUGACA	3108
29126_7_38	CD274	Exon 7	+	chr9:5468100-5468125	UCAUCGACGCCUGUGACAGGGAGAA	3109
29126_7_39	CD274	Exon 7	+	chr9:5468116-5468141	CAGGGAGAAAGGAUACUUCUGAACA	3110
29126_7_40	CD274	Exon 7	+	chr9:5468151-5468176	AAGCAAAUCAUCCAUUGCUCAUCCU	3111
29126_7_41	CD274	Exon 7	+	chr9:5468158-5468183	UCAUCCAUUGCUCAUCCUAGGAAGA	3112
29126_7_42	CD274	Exon 7	+	chr9:5468159-5468184	CAUCCAUUGCUCAUCCUAGGAAGAC	3113
29126_7_43	CD274	Exon 7	+	chr9:5468180-5468205	AGACGGGUUGAGAAUCCCUAAUUUG	3114

29126_7_44	CD274	Exon 7	+	chr9:5468181-5468206	GACGGGUUGAGAAUCCCUAAUUUGA	3115
29126_7_45	CD274	Exon 7	+	chr9:5468260-5468285	UCUGCAUGACUGAGAGUCUCAGUGU	3116
29126_7_46	CD274	Exon 7	+	chr9:5468265-5468290	AUGACUGAGAGUCUCAGUGUUGGAA	3117
29126_7_47	CD274	Exon 7	+	chr9:5468266-5468291	UGACUGAGAGUCUCAGUGUUGGAAC	3118
29126_7_48	CD274	Exon 7	+	chr9:5468313-5468338	UUUUCCUAUUUAUUUUGAGUCUGUG	3119
29126_7_49	CD274	Exon 7	+	chr9:5468335-5468360	GUGAGGUCUUCUUGUCAUGUGAGUG	3120
29126_7_50	CD274	Exon 7	+	chr9:5468438-5468463	UGAUUUGCUCACAUCUAGUAAAACA	3121
29126_7_51	CD274	Exon 7	+	chr9:5468451-5468476	UCUAGUAAAACAUGGAGUAUUUGUA	3122
29126_7_52	CD274	Exon 7	+	chr9:5468458-5468483	AAACAUGGAGUAUUUGUAAGGUGCU	3123
29126_7_53	CD274	Exon 7	+	chr9:5468487-5468512	CUCCUCUAUAACUACAAGUAUACAU	3124
29126_7_54	CD274	Exon 7	+	chr9:5468510-5468535	AUUGGAAGCAUAAAGAUCAAACCGU	3125
29126_7_55	CD274	Exon 7	+	chr9:5468519-5468544	AUAAAGAUCAAACCGUUGGUUGCAU	3126
29126_7_56	CD274	Exon 7	+	chr9:5468552-5468577	ACCUUUAUUUAACCCAUUAAUACUC	3127
29126_7_57	CD274	Exon 7	+	chr9:5469037-5469062	GGAAAACCCGAGCAGUGUUGCCAAG	3128
29126_7_58	CD274	Exon 7	+	chr9:5469040-5469065	AAACCCGAGCAGUGUUGCCAAGAGG	3129
29126_7_59	CD274	Exon 7	+	chr9:5469047-5469072	AGCAGUGUUGCCAAGAGGAGGAAAU	3130
29126_7_60	CD274	Exon 7	+	chr9:5469056-5469081	GCCAAGAGGAGGAAAUAGGCCAAUG	3131
29126_7_61	CD274	Exon 7	+	chr9:5469061-5469086	GAGGAGGAAAUAGGCCAAUGUGGUC	3132
29126_7_62	CD274	Exon 7	+	chr9:5469062-5469087	AGGAGGAAAUAGGCCAAUGUGGUCU	3133
29126_7_63	CD274	Exon 7	+	chr9:5469066-5469091	GGAAAUAGGCCAAUGUGGUCUGGGA	3134
29126_7_64	CD274	Exon 7	+	chr9:5469070-5469095	AUAGGCCAAUGUGGUCUGGGACGGU	3135
29126_7_65	CD274	Exon 7	+	chr9:5469121-5469146	CAGAGUAAUUUUCAUUUACAAAGAG	3136
29126_7_66	CD274	Exon 7	+	chr9:5469125-5469150	GUAAUUUUCAUUUACAAAGAGAGGU	3137
29126_7_67	CD274	Exon 7	+	chr9:5469156-5469181	UUAAAAUAACCCUGAAAAAUAACAC	3138
29126_7_68	CD274	Exon 7	+	chr9:5469233-5469258	AUCUAAUGCUUGUUUAUAUAGUGUC	3139

29126_7_69	CD274	Exon 7	+	chr9:5469553-5469578	AUUUUAGUGUUUCUUAUAUAGCAGA	3140
29126_7_70	CD274	Exon 7	+	chr9:5469574-5469599	CAGAUGGAAUGAAUUUGAAGUUCCC	3141
29126_7_71	CD274	Exon 7	+	chr9:5469575-5469600	AGAUGGAAUGAAUUUGAAGUUCCCA	3142
29126_7_72	CD274	Exon 7	+	chr9:5469581-5469606	AAUGAAUUUGAAGUUCCCAGGGCUG	3143
29126_7_73	CD274	Exon 7	+	chr9:5469712-5469737	CCACCAUUUGUUAAGUAUUUGCUCU	3144
29126_7_74	CD274	Exon 7	+	chr9:5469723-5469748	UAAGUAUUUGCUCUAGGACAGAGUU	3145
29126_7_75	CD274	Exon 7	+	chr9:5469747-5469772	UUGGAUUUGUUUAUGUUUGCUCAAA	3146
29126_7_76	CD274	Exon 7	+	chr9:5469757-5469782	UUAUGUUUGCUCAAAAGGAGACCCA	3147
29126_7_77	CD274	Exon 7	+	chr9:5469758-5469783	UAUGUUUGCUCAAAAGGAGACCCAU	3148
29126_7_78	CD274	Exon 7	+	chr9:5469767-5469792	UCAAAAGGAGACCCAUGGGCUCUCC	3149
29126_7_79	CD274	Exon 7	+	chr9:5469768-5469793	CAAAAGGAGACCCAUGGGCUCUCCA	3150
29126_7_80	CD274	Exon 7	+	chr9:5469836-5469861	UAACUCUGUAUGACAGAAUCAUGUC	3151
29126_7_81	CD274	Exon 7	+	chr9:5469913-5469938	UACUUGCAAAAUCACAUUUUCUUUC	3152
29126_7_82	CD274	Exon 7	+	chr9:5469922-5469947	AAUCACAUUUUCUUUCUGGAAAUUC	3153
29126_7_83	CD274	Exon 7	+	chr9:5470028-5470053	GUCAUCACUACACAGCCCUCCUAAG	3154
29126_7_84	CD274	Exon 7	+	chr9:5470036-5470061	UACACAGCCCUCCUAAGAGGCUUCC	3155
29126_7_85	CD274	Exon 7	+	chr9:5470039-5470064	ACAGCCCUCCUAAGAGGCUUCCUGG	3156
29126_7_86	CD274	Exon 7	+	chr9:5470061-5470086	UGGAGGUUUCGAGAUUCAGAUGCCC	3157
29126_7_87	CD274	Exon 7	+	chr9:5470062-5470087	GGAGGUUUCGAGAUUCAGAUGCCCU	3158
29126_7_88	CD274	Exon 7	+	chr9:5470090-5470115	AGAUCCCAGAGUUUCCUUUCCCUCU	3159
29126_7_89	CD274	Exon 7	+	chr9:5470101-5470126	UUUCCUUUCCCUCUUGGCCAUAUUC	3160
29126_7_90	CD274	Exon 7	+	chr9:5470115-5470140	UGGCCAUAUUCUGGUGUCAAUGACA	3161
29126_7_91	CD274	Exon 7	+	chr9:5470125-5470150	CUGGUGUCAAUGACAAGGAGUACCU	3162
29126_7_92	CD274	Exon 7	+	chr9:5470143-5470168	AGUACCUUGGCUUUGCCACAUGUCA	3163
29126_7_93	CD274	Exon 7	+	chr9:5470215-5470240	UGUACAUGUGCAUUUGUACAGUAAU	3164

29126_7_94	CD274	Exon 7	+	chr9:5470245-5470270	UGACAGUGUUCUUUGUGUGAAUUAC	3165
29126_7_95	CD274	Exon 7	+	chr9:5470257-5470282	UUGUGUGAAUUACAGGCAAGAAUUG	3166
29126_7_96	CD274	Exon 7	+	chr9:5470267-5470292	UACAGGCAAGAAUUGUGGCUGAGCA	3167
29126_7_97	CD274	Exon 7	+	chr9:5470314-5470339	AUUCCUAAGUCCUAACUCCUCCUUG	3168
29126_7_98	CD274	Exon 7	+	chr9:5470320-5470345	AAGUCCUAACUCCUCCUUGUGGUGU	3169
29126_7_99	CD274	Exon 7	+	chr9:5470330-5470355	UCCUCCUUGUGGUGUUGGAUUUGUA	3170
29126_7_100	CD274	Exon 7	+	chr9:5470368-5470393	CUUUUGUCUCAUGUUUCAUCGUAAA	3171
29126_7_101	CD274	Exon 7	+	chr9:5470374-5470399	UCUCAUGUUUCAUCGUAAAUGGCAU	3172
29126_7_102	CD274	Exon 7	+	chr9:5470462-5470487	AAAUAUUCUUAUUUAUUUUGUUACU	3173
29126_7_103	CD274	Exon 7	+	chr9:5470530-5470555	UAAAAUGUUCAGUUUAACAUCCCAG	3174
29126_7_104	CD274	Exon 7	+	chr9:5470544-5470569	UAACAUCCCAGUGGAGAAAGUUACU	3175
29126_7_105	CD274	Exon 7	-	chr9:5467838-5467863	AUUACGUCUCCUCCAAAUGUGUAUC	3176
29126_7_106	CD274	Exon 7	-	chr9:5467866-5467891	GCUUGAAGAUCAGAAGUUCCAAUGC	3177
29126_7_107	CD274	Exon 7	-	chr9:5467906-5467931	CAGCCCCGAUGAACCCCUAAACCAC	3178
29126_7_108	CD274	Exon 7	-	chr9:5467958-5467983	AAGUCCCACAUUGCCUGCAUCCCAC	3179
29126_7_109	CD274	Exon 7	-	chr9:5467959-5467984	UAAGUCCCACAUUGCCUGCAUCCCA	3180
29126_7_110	CD274	Exon 7	-	chr9:5467992-5468017	UCGCCAGGUUCCAUUUUCAGUGCUU	3181
29126_7_111	CD274	Exon 7	-	chr9:5467993-5468018	UUCGCCAGGUUCCAUUUUCAGUGCU	3182
29126_7_112	CD274	Exon 7	-	chr9:5468012-5468037	UUCAUUCUCCUCCUCUGCUUUCGCC	3183
29126_7_113	CD274	Exon 7	-	chr9:5468063-5468088	UUUGAAAGUAUCAAGGUCUCCCUCC	3184
29126_7_114	CD274	Exon 7	-	chr9:5468075-5468100	GCCCCUCAGGCAUUUGAAAGUAUCA	3185
29126_7_115	CD274	Exon 7	-	chr9:5468093-5468118	UGUCACAGGCGUCGAUGAGCCCCUC	3186
29126_7_116	CD274	Exon 7	-	chr9:5468112-5468137	CAGAAGUAUCCUUUCUCCCUGUCAC	3187
29126_7_117	CD274	Exon 7	-	chr9:5468149-5468174	GAUGAGCAAUGGAUGAUUUGCUUGG	3188
29126_7_118	CD274	Exon 7	-	chr9:5468152-5468177	UAGGAUGAGCAAUGGAUGAUUUGCU	3189

29126_7_119	CD274	Exon 7	-	chr9:5468165-5468190	CAACCCGUCUUCCUAGGAUGAGCAA	3190
29126_7_120	CD274	Exon 7	-	chr9:5468176-5468201	UUAGGGAUUCUCAACCCGUCUUCCU	3191
29126_7_121	CD274	Exon 7	-	chr9:5468198-5468223	UCUGCAGGAACUGACCCUCAAAUUA	3192
29126_7_122	CD274	Exon 7	-	chr9:5468199-5468224	UUCUGCAGGAACUGACCCUCAAAUU	3193
29126_7_123	CD274	Exon 7	-	chr9:5468218-5468243	GAGUGGAGGCAAAGGGCACUUCUGC	3194
29126_7_124	CD274	Exon 7	-	chr9:5468230-5468255	AAUUGAGGCAUUGAGUGGAGGCAAA	3195
29126_7_125	CD274	Exon 7	-	chr9:5468231-5468256	AAAUUGAGGCAUUGAGUGGAGGCAA	3196
29126_7_126	CD274	Exon 7	-	chr9:5468237-5468262	GAAAACAAAUUGAGGCAUUGAGUGG	3197
29126_7_127	CD274	Exon 7	-	chr9:5468240-5468265	GCAGAAAACAAAUUGAGGCAUUGAG	3198
29126_7_128	CD274	Exon 7	-	chr9:5468250-5468275	UCUCAGUCAUGCAGAAAACAAAUUG	3199
29126_7_129	CD274	Exon 7	-	chr9:5468320-5468345	AAGACCUCACAGACUCAAAAUAAAU	3200
29126_7_130	CD274	Exon 7	-	chr9:5468419-5468444	AAAUCAUUAAGCAGCAAGUUUAGUU	3201
29126_7_131	CD274	Exon 7	-	chr9:5468492-5468517	UUCCAAUGUAUACUUGUAGUUAUAG	3202
29126_7_132	CD274	Exon 7	-	chr9:5468534-5468559	UAAAGGUGACAUCCUAUGCAACCAA	3203
29126_7_133	CD274	Exon 7	-	chr9:5468556-5468581	ACCAGAGUAUUAAUGGGUUAAAUAA	3204
29126_7_134	CD274	Exon 7	-	chr9:5468567-5468592	AGAUUAGGUCAACCAGAGUAUUAAU	3205
29126_7_135	CD274	Exon 7	-	chr9:5468568-5468593	AAGAUUAGGUCAACCAGAGUAUUAA	3206
29126_7_136	CD274	Exon 7	-	chr9:5468587-5468612	ACACUUGAGGUCUGAGAAUAAGAUU	3207
29126_7_137	CD274	Exon 7	-	chr9:5468605-5468630	CCUUGUCUAACUGCACAGACACUUG	3208
29126_7_138	CD274	Exon 7	-	chr9:5468811-5468836	AUAUAGCUGUAAAUUGUAUUAUAAA	3209
29126_7_139	CD274	Exon 7	-	chr9:5469060-5469085	ACCACAUUGGCCUAUUUCCUCCUCU	3210
29126_7_140	CD274	Exon 7	-	chr9:5469078-5469103	UAUAUCCAACCGUCCCAGACCACAU	3211
29126_7_141	CD274	Exon 7	-	chr9:5469168-5469193	AAAGGAAUUCCAGUGUUAUUUUUCA	3212
29126_7_142	CD274	Exon 7	-	chr9:5469169-5469194	AAAAGGAAUUCCAGUGUUAUUUUUC	3213
29126_7_143	CD274	Exon 7	-	chr9:5469191-5469216	UCAGGAAUAAAUAUAAUGCUAGAAA	3214

29126_7_144	CD274	Exon 7	-	chr9:5469214-5469239	UUAGAUUAUAUGGCAAAGGCAAAUC	3215
29126_7_145	CD274	Exon 7	-	chr9:5469223-5469248	AAACAAGCAUUAGAUUAUAUGGCAA	3216
29126_7_146	CD274	Exon 7	-	chr9:5469229-5469254	CUAUAUAAACAAGCAUUAGAUUAUA	3217
29126_7_147	CD274	Exon 7	-	chr9:5469299-5469324	CCUUUCCAUACUUAAAUUUUUUUAG	3218
29126_7_148	CD274	Exon 7	-	chr9:5469599-5469624	AAAGAAGGCAUGGAUCCUCAGCCCU	3219
29126_7_149	CD274	Exon 7	-	chr9:5469600-5469625	CAAAGAAGGCAUGGAUCCUCAGCCC	3220
29126_7_150	CD274	Exon 7	-	chr9:5469614-5469639	AGAUAACUUAGAAACAAAGAAGGCA	3221
29126_7_151	CD274	Exon 7	-	chr9:5469619-5469644	GGGAAAGAUAACUUAGAAACAAAGA	3222
29126_7_152	CD274	Exon 7	-	chr9:5469644-5469669	CAUAUGAAAGAUAAUGAAAAGCUAU	3223
29126_7_153	CD274	Exon 7	-	chr9:5469645-5469670	UCAUAUGAAAGAUAAUGAAAAGCUA	3224
29126_7_154	CD274	Exon 7	-	chr9:5469674-5469699	UAUGUAGGACAUAUUUAACAUAUAC	3225
29126_7_155	CD274	Exon 7	-	chr9:5469694-5469719	AUGGUGGUUGUCUAAAUGUAUAUGU	3226
29126_7_156	CD274	Exon 7	-	chr9:5469715-5469740	CCUAGAGCAAAUACUUAACAAAUGG	3227
29126_7_157	CD274	Exon 7	-	chr9:5469718-5469743	UGUCCUAGAGCAAAUACUUAACAAA	3228
29126_7_158	CD274	Exon 7	-	chr9:5469781-5469806	ACUCAGUGCACCCUGGAGAGCCCAU	3229
29126_7_159	CD274	Exon 7	-	chr9:5469782-5469807	GACUCAGUGCACCCUGGAGAGCCCA	3230
29126_7_160	CD274	Exon 7	-	chr9:5469793-5469818	AGGACUAGAUUGACUCAGUGCACCC	3231
29126_7_161	CD274	Exon 7	-	chr9:5469818-5469843	AGAGUUAAUAAUAAGAUUGCUUUUU	3232
29126_7_162	CD274	Exon 7	-	chr9:5469949-5469974	GUAGCUAGCAGUCAAGGUACACUGC	3233
29126_7_163	CD274	Exon 7	-	chr9:5469960-5469985	UCUGGCACAGGGUAGCUAGCAGUCA	3234
29126_7_164	CD274	Exon 7	-	chr9:5469976-5470001	CAACGAAUGAGGCUUUUCUGGCACA	3235
29126_7_165	CD274	Exon 7	-	chr9:5469977-5470002	ACAACGAAUGAGGCUUUUCUGGCAC	3236
29126_7_166	CD274	Exon 7	-	chr9:5469983-5470008	UCAAGCACAACGAAUGAGGCUUUUC	3237
29126_7_167	CD274	Exon 7	-	chr9:5469992-5470017	UUCAAGGGUUCAAGCACAACGAAUG	3238
29126_7_168	CD274	Exon 7	-	chr9:5470012-5470037	AGUGAUGACAGCUGGUGGCAUUCAA	3239

29126_7_169	CD274	Exon 7	-	chr9:5470013-5470038	UAGUGAUGACAGCUGGUGGCAUUCA	3240
29126_7_170	CD274	Exon 7	-	chr9:5470022-5470047	AGGGCUGUGUAGUGAUGACAGCUGG	3241
29126_7_171	CD274	Exon 7	-	chr9:5470025-5470050	AGGAGGGCUGUGUAGUGAUGACAGC	3242
29126_7_172	CD274	Exon 7	-	chr9:5470046-5470071	GAAACCUCCAGGAAGCCUCUUAGGA	3243
29126_7_173	CD274	Exon 7	-	chr9:5470047-5470072	CGAAACCUCCAGGAAGCCUCUUAGG	3244
29126_7_174	CD274	Exon 7	-	chr9:5470050-5470075	UCUCGAAACCUCCAGGAAGCCUCUU	3245
29126_7_175	CD274	Exon 7	-	chr9:5470062-5470087	AGGGCAUCUGAAUCUCGAAACCUCC	3246
29126_7_176	CD274	Exon 7	-	chr9:5470086-5470111	GGAAAGGAAACUCUGGGAUCUCCCA	3247
29126_7_177	CD274	Exon 7	-	chr9:5470087-5470112	GGGAAAGGAAACUCUGGGAUCUCCC	3248
29126_7_178	CD274	Exon 7	-	chr9:5470097-5470122	AUGGCCAAGAGGGAAAGGAAACUCU	3249
29126_7_179	CD274	Exon 7	-	chr9:5470098-5470123	UAUGGCCAAGAGGGAAAGGAAACUC	3250
29126_7_180	CD274	Exon 7	-	chr9:5470107-5470132	ACACCAGAAUAUGGCCAAGAGGGAA	3251
29126_7_181	CD274	Exon 7	-	chr9:5470112-5470137	CAUUGACACCAGAAUAUGGCCAAGA	3252
29126_7_182	CD274	Exon 7	-	chr9:5470113-5470138	UCAUUGACACCAGAAUAUGGCCAAG	3253
29126_7_183	CD274	Exon 7	-	chr9:5470121-5470146	ACUCCUUGUCAUUGACACCAGAAUA	3254
29126_7_184	CD274	Exon 7	-	chr9:5470150-5470175	UCAGCCUUGACAUGUGGCAAAGCCA	3255
29126_7_185	CD274	Exon 7	-	chr9:5470161-5470186	ACACUGUUUCUUCAGCCUUGACAUG	3256
29126_7_186	CD274	Exon 7	-	chr9:5470191-5470216	AAACAGAUAACACAAGGAGCUCUGU	3257
29126_7_187	CD274	Exon 7	-	chr9:5470202-5470227	UGCACAUGUACAAACAGAUAACACA	3258
29126_7_188	CD274	Exon 7	-	chr9:5470320-5470345	ACACCACAAGGAGGAGUUAGGACUU	3259
29126_7_189	CD274	Exon 7	-	chr9:5470327-5470352	AAAUCCAACACCACAAGGAGGAGUU	3260
29126_7_190	CD274	Exon 7	-	chr9:5470334-5470359	GCCUUACAAAUCCAACACCACAAGG	3261
29126_7_191	CD274	Exon 7	-	chr9:5470337-5470362	AGUGCCUUACAAAUCCAACACCACA	3262
29126_7_192	CD274	Exon 7	-	chr9:5470369-5470394	AUUUACGAUGAAACAUGAGACAAAA	3263
29126_7_193	CD274	Exon 7	-	chr9:5470370-5470395	CAUUUACGAUGAAACAUGAGACAAA	3264

29126_7_194	CD274	Exon 7	-	chr9:5470416-5470441	AAAAGUGACAAUCAAAUGCAGAAUU	3265
29126_7_195	CD274	Exon 7	-	chr9:5470448-5470473	UAAGAAUAUUUUAUUAAAUUAAUGC	3266
29126_7_196	CD274	Exon 7	-	chr9:5470497-5470522	AAAAUAAACAAGAAAAUGGACAUGC	3267
29126_7_197	CD274	Exon 7	-	chr9:5470506-5470531	AUUAAACACAAAAUAAACAAGAAAA	3268
29126_7_198	CD274	Exon 7	-	chr9:5470553-5470578	AAUAUUCCAAGUAACUUUCUCCACU	3269
29126_7_199	CD274	Exon 7	-	chr9:5470554-5470579	AAAUAUUCCAAGUAACUUUCUCCAC	3270
84868_7_1	HAVCR2	Exon 7	+	chr5:157085921-157085946	UAUACCGUCUUGAAAUUUAAGUUUA	3271
84868_7_2	HAVCR2	Exon 7	+	chr5:157085939-157085964	AAGUUUAGGGACCACUCUCUGUCAA	3272
84868_7_3	HAVCR2	Exon 7	+	chr5:157085951-157085976	CACUCUCUGUCAAAGGAUCCAGCGC	3273
84868_7_4	HAVCR2	Exon 7	+	chr5:157085970-157085995	CAGCGCUGGUAAUAUAGAUUGCUGA	3274
84868_7_5	HAVCR2	Exon 7	+	chr5:157085992-157086017	UGAAGGCCUUUGCCUUCUUUCCACC	3275
84868_7_6	HAVCR2	Exon 7	+	chr5:157086053-157086078	UUCUGUGAAAAAUAUAGCUUCAGUU	3276
84868_7_7	HAVCR2	Exon 7	+	chr5:157086073-157086098	CAGUUUGGUCCACGAAUACAGAAGU	3277
84868_7_8	HAVCR2	Exon 7	+	chr5:157086115-157086140	UUUCAAGCACACAACAAGCAAAACU	3278
84868_7_9	HAVCR2	Exon 7	+	chr5:157086154-157086179	CAAUCAAAUGCACUUCGUUUUUCCC	3279
84868_7_10	HAVCR2	Exon 7	+	chr5:157086155-157086180	AAUCAAAUGCACUUCGUUUUUCCCU	3280
84868_7_11	HAVCR2	Exon 7	+	chr5:157086183-157086208	AGCUCCUGCCACAUCUCAGCCCUGC	3281
84868_7_12	HAVCR2	Exon 7	+	chr5:157086184-157086209	GCUCCUGCCACAUCUCAGCCCUGCA	3282
84868_7_13	HAVCR2	Exon 7	+	chr5:157086198-157086223	UCAGCCCUGCAGGGCAGUCUUCAUA	3283
84868_7_14	HAVCR2	Exon 7	+	chr5:157086199-157086224	CAGCCCUGCAGGGCAGUCUUCAUAA	3284
84868_7_15	HAVCR2	Exon 7	+	chr5:157086212-157086237	CAGUCUUCAUAAGGGAGACAAAAGA	3285
84868_7_16	HAVCR2	Exon 7	+	chr5:157086213-157086238	AGUCUUCAUAAGGGAGACAAAAGAA	3286
84868_7_17	HAVCR2	Exon 7	+	chr5:157086224-157086249	GGGAGACAAAAGAAGGGCUAUGCAC	3287

84868_7_18	HAVCR2	Exon 7	+	chr5:157086237-157086262	AGGGCUAUGCACUGGCACUGACAGU	3288
84868_7_19	HAVCR2	Exon 7	+	chr5:157086238-157086263	GGGCUAUGCACUGGCACUGACAGUU	3289
84868_7_20	HAVCR2	Exon 7	+	chr5:157086242-157086267	UAUGCACUGGCACUGACAGUUGGGC	3290
84868_7_21	HAVCR2	Exon 7	+	chr5:157086279-157086304	AAUAAGCCUAAAUCUCAACAUUCCA	3291
84868_7_22	HAVCR2	Exon 7	+	chr5:157086280-157086305	AUAAGCCUAAAUCUCAACAUUCCAA	3292
84868_7_23	HAVCR2	Exon 7	+	chr5:157086297-157086322	CAUUCCAAGGGAAUCUUCAAGAUCA	3293
84868_7_24	HAVCR2	Exon 7	+	chr5:157086306-157086331	GGAAUCUUCAAGAUCAAGGUAGACC	3294
84868_7_25	HAVCR2	Exon 7	+	chr5:157086332-157086357	GGUCCAGUCAUCUCUUAAUCUUUUA	3295
84868_7_26	HAVCR2	Exon 7	+	chr5:157086639-157086664	UCCAUCUCAAAAACAAAAAACAAAA	3296
84868_7_27	HAVCR2	Exon 7	+	chr5:157086640-157086665	CCAUCUCAAAAACAAAAAACAAAAA	3297
84868_7_28	HAVCR2	Exon 7	+	chr5:157086667-157086692	GAUCACAGAUCUCUUUGAAAAUCAG	3298
84868_7_29	HAVCR2	Exon 7	+	chr5:157086748-157086773	UUUCCCUAGUUUAUCUGAAGUUUCA	3299
84868_7_30	HAVCR2	Exon 7	+	chr5:157086774-157086799	GGACAUAUGAUGUGCCCGAAUUUCC	3300
84868_7_31	HAVCR2	Exon 7	+	chr5:157086857-157086882	UCUAACAUCCAUGAUUAACAGUCUC	3301
84868_7_32	HAVCR2	Exon 7	+	chr5:157086858-157086883	CUAACAUCCAUGAUUAACAGUCUCU	3302
84868_7_33	HAVCR2	Exon 7	+	chr5:157086862-157086887	CAUCCAUGAUUAACAGUCUCUGGGU	3303
84868_7_34	HAVCR2	Exon 7	+	chr5:157086863-157086888	AUCCAUGAUUAACAGUCUCUGGGUU	3304
84868_7_35	HAVCR2	Exon 7	+	chr5:157086875-157086900	CAGUCUCUGGGUUGGGUAACUCUGU	3305
84868_7_36	HAVCR2	Exon 7	+	chr5:157086889-157086914	GGUAACUCUGUUGGCUUAAAUACAG	3306
84868_7_37	HAVCR2	Exon 7	+	chr5:157086920-157086945	UGACAUGCCUGUUUAAGUUCAGUGC	3307
84868_7_38	HAVCR2	Exon 7	+	chr5:157086963-157086988	CAUGUGAGUCAUUAUCUUCUGAAAA	3308
84868_7_39	HAVCR2	Exon 7	+	chr5:157086964-157086989	AUGUGAGUCAUUAUCUUCUGAAAAU	3309

84868_7_40	HAVCR2	Exon 7	+	chr5:157086987-157087012	AUGGGAAAACUCUGCUCCAUAGCAG	3310
84868_7_41	HAVCR2	Exon 7	+	chr5:157087011-157087036	GUGGACAGAACCUCCAAAACCAGUC	3311
84868_7_42	HAVCR2	Exon 7	+	chr5:157087064-157087089	AGACAAAACACCAAGCUCAAAAAUA	3312
84868_7_43	HAVCR2	Exon 7	+	chr5:157087067-157087092	CAAAACACCAAGCUCAAAAAUAAGG	3313
84868_7_44	HAVCR2	Exon 7	+	chr5:157087071-157087096	ACACCAAGCUCAAAAAUAAGGUGGU	3314
84868_7_45	HAVCR2	Exon 7	+	chr5:157087079-157087104	CUCAAAAAUAAGGUGGUUGGAUCUA	3315
84868_7_46	HAVCR2	Exon 7	+	chr5:157087103-157087128	AUGGCAUUGCAAAGCGACAACCCAA	3316
84868_7_47	HAVCR2	Exon 7	+	chr5:157087111-157087136	GCAAAGCGACAACCCAAAGGUUGUG	3317
84868_7_48	HAVCR2	Exon 7	+	chr5:157087112-157087137	CAAAGCGACAACCCAAAGGUUGUGA	3318
84868_7_49	HAVCR2	Exon 7	+	chr5:157087150-157087175	CUGCUGACAUAGCAAUAAUACUCAU	3319
84868_7_50	HAVCR2	Exon 7	+	chr5:157087151-157087176	UGCUGACAUAGCAAUAAUACUCAUU	3320
84868_7_51	HAVCR2	Exon 7	+	chr5:157087183-157087208	UCCACUUCAUAUACGUUCUCUUCAA	3321
84868_7_52	HAVCR2	Exon 7	+	chr5:157087240-157087265	UCUGCUACUGCAUUUGCCAAUCCUG	3322
84868_7_53	HAVCR2	Exon 7	+	chr5:157087241-157087266	CUGCUACUGCAUUUGCCAAUCCUGA	3323
84868_7_54	HAVCR2	Exon 7	+	chr5:157087244-157087269	CUACUGCAUUUGCCAAUCCUGAGGG	3324
84868_7_55	HAVCR2	Exon 7	+	chr5:157087245-157087270	UACUGCAUUUGCCAAUCCUGAGGGA	3325
84868_7_56	HAVCR2	Exon 7	+	chr5:157087248-157087273	UGCAUUUGCCAAUCCUGAGGGAGGG	3326
84868_7_57	HAVCR2	Exon 7	+	chr5:157087252-157087277	UUUGCCAAUCCUGAGGGAGGGAGGU	3327
84868_7_58	HAVCR2	Exon 7	+	chr5:157087266-157087291	GGGAGGGAGGUUGGCCAAAGAGAUG	3328
84868_7_59	HAVCR2	Exon 7	+	chr5:157087272-157087297	GAGGUUGGCCAAAGAGAUGAGGCUG	3329
84868_7_60	HAVCR2	Exon 7	+	chr5:157087288-157087313	AUGAGGCUGUGGAAAUAAAGUGUUG	3330
84868_7_61	HAVCR2	Exon 7	-	chr5:157085953-157085978	CAGCGCUGGAUCCUUUGACAGAGAG	3331

84868_7_62	HAVCR2	Exon 7	-	chr5:157085972-157085997	CUUCAGCAAUCUAUAUUACCAGCGC	3332
84868_7_63	HAVCR2	Exon 7	-	chr5:157086001-157086026	CUGUUGCCUGGUGGAAAGAAGGCAA	3333
84868_7_64	HAVCR2	Exon 7	-	chr5:157086007-157086032	CAAAUUCUGUUGCCUGGUGGAAAGA	3334
84868_7_65	HAVCR2	Exon 7	-	chr5:157086015-157086040	CGGGGACACAAAUUCUGUUGCCUGG	3335
84868_7_66	HAVCR2	Exon 7	-	chr5:157086018-157086043	UGACGGGGACACAAAUUCUGUUGCC	3336
84868_7_67	HAVCR2	Exon 7	-	chr5:157086038-157086063	UUUCACAGAAGAAGAAGCAGUGACG	3337
84868_7_68	HAVCR2	Exon 7	-	chr5:157086039-157086064	UUUUCACAGAAGAAGAAGCAGUGAC	3338
84868_7_69	HAVCR2	Exon 7	-	chr5:157086040-157086065	UUUUUCACAGAAGAAGAAGCAGUGA	3339
84868_7_70	HAVCR2	Exon 7	-	chr5:157086085-157086110	UAUCUCUGACCAACUUCUGUAUUCG	3340
84868_7_71	HAVCR2	Exon 7	-	chr5:157086146-157086171	CGAAGUGCAUUUGAUUGGUGUGUAU	3341
84868_7_72	HAVCR2	Exon 7	-	chr5:157086156-157086181	CAGGGAAAAACGAAGUGCAUUUGAU	3342
84868_7_73	HAVCR2	Exon 7	-	chr5:157086179-157086204	GGCUGAGAUGUGGCAGGAGCUCCCA	3343
84868_7_74	HAVCR2	Exon 7	-	chr5:157086180-157086205	GGGCUGAGAUGUGGCAGGAGCUCCC	3344
84868_7_75	HAVCR2	Exon 7	-	chr5:157086190-157086215	CUGCCCUGCAGGGCUGAGAUGUGGC	3345
84868_7_76	HAVCR2	Exon 7	-	chr5:157086194-157086219	AAGACUGCCCUGCAGGGCUGAGAUG	3346
84868_7_77	HAVCR2	Exon 7	-	chr5:157086205-157086230	UCUCCCUUAUGAAGACUGCCCUGCA	3347
84868_7_78	HAVCR2	Exon 7	-	chr5:157086206-157086231	GUCUCCCUUAUGAAGACUGCCCUGC	3348
84868_7_79	HAVCR2	Exon 7	-	chr5:157086288-157086313	AGAUUCCCUUGGAAUGUUGAGAUUU	3349
84868_7_80	HAVCR2	Exon 7	-	chr5:157086304-157086329	UCUACCUUGAUCUUGAAGAUUCCCU	3350
84868_7_81	HAVCR2	Exon 7	-	chr5:157086332-157086357	UAAAAGAUUAAGAGAUGACUGGACC	3351
84868_7_82	HAVCR2	Exon 7	-	chr5:157086338-157086363	GAUCCUUAAAAGAUUAAGAGAUGAC	3352
84868_7_83	HAVCR2	Exon 7	-	chr5:157086698-157086723	CUUUUUUGGCACAGAAAGUCUAAAG	3353

84868_7_84	HAVCR2	Exon 7	-	chr5:157086699-157086724	ACUUUUUUGGCACAGAAAGUCUAAA	3354
84868_7_85	HAVCR2	Exon 7	-	chr5:157086700-157086725	AACUUUUUUGGCACAGAAAGUCUAA	3355
84868_7_86	HAVCR2	Exon 7	-	chr5:157086717-157086742	UGCUGAGGUGAAAGCAUAACUUUUU	3356
84868_7_87	HAVCR2	Exon 7	-	chr5:157086737-157086762	AUAAACUAGGGAAAACUGGGUGCUG	3357
84868_7_88	HAVCR2	Exon 7	-	chr5:157086745-157086770	AACUUCAGAUAAACUAGGGAAAACU	3358
84868_7_89	HAVCR2	Exon 7	-	chr5:157086746-157086771	AAACUUCAGAUAAACUAGGGAAAAC	3359
84868_7_90	HAVCR2	Exon 7	-	chr5:157086754-157086779	UGUCCAUGAAACUUCAGAUAAACUA	3360
84868_7_91	HAVCR2	Exon 7	-	chr5:157086755-157086780	AUGUCCAUGAAACUUCAGAUAAACU	3361
84868_7_92	HAVCR2	Exon 7	-	chr5:157086791-157086816	GGGUCUCUGGAGCUCCAGGAAAUUC	3362
84868_7_93	HAVCR2	Exon 7	-	chr5:157086792-157086817	GGGGUCUCUGGAGCUCCAGGAAAUU	3363
84868_7_94	HAVCR2	Exon 7	-	chr5:157086800-157086825	CUUGACGUGGGGUCUCUGGAGCUCC	3364
84868_7_95	HAVCR2	Exon 7	-	chr5:157086809-157086834	CUAGGAAUUCUUGACGUGGGGUCUC	3365
84868_7_96	HAVCR2	Exon 7	-	chr5:157086816-157086841	AUAUACACUAGGAAUUCUUGACGUG	3366
84868_7_97	HAVCR2	Exon 7	-	chr5:157086817-157086842	UAUAUACACUAGGAAUUCUUGACGU	3367
84868_7_98	HAVCR2	Exon 7	-	chr5:157086818-157086843	UUAUAUACACUAGGAAUUCUUGACG	3368
84868_7_99	HAVCR2	Exon 7	-	chr5:157086832-157086857	GCUCAAACGGGCUUUUAUAUACACU	3369
84868_7_100	HAVCR2	Exon 7	-	chr5:157086849-157086874	UAAUCAUGGAUGUUAGAGCUCAAAC	3370
84868_7_101	HAVCR2	Exon 7	-	chr5:157086850-157086875	UUAAUCAUGGAUGUUAGAGCUCAAA	3371
84868_7_102	HAVCR2	Exon 7	-	chr5:157086868-157086893	UACCCAACCCAGAGACUGUUAAUCA	3372
84868_7_103	HAVCR2	Exon 7	-	chr5:157086930-157086955	ACUGGGACCUGCACUGAACUUAAAC	3373
84868_7_104	HAVCR2	Exon 7	-	chr5:157086952-157086977	UAAUGACUCACAUGGGAAUUGAACU	3374
84868_7_105	HAVCR2	Exon 7	-	chr5:157086953-157086978	AUAAUGACUCACAUGGGAAUUGAAC	3375

84868_7_106	HAVCR2	Exon 7	-	chr5:157086964-157086989	AUUUUCAGAAGAUAAUGACUCACAU	3376
84868_7_107	HAVCR2	Exon 7	-	chr5:157086965-157086990	CAUUUUCAGAAGAUAAUGACUCACA	3377
84868_7_108	HAVCR2	Exon 7	-	chr5:157087006-157087031	GUUUUGGAGGUUCUGUCCACUGCUA	3378
84868_7_109	HAVCR2	Exon 7	-	chr5:157087024-157087049	AGCUGUGUCACCUGACUGGUUUUGG	3379
84868_7_110	HAVCR2	Exon 7	-	chr5:157087027-157087052	AUGAGCUGUGUCACCUGACUGGUUU	3380
84868_7_111	HAVCR2	Exon 7	-	chr5:157087033-157087058	GAAACUAUGAGCUGUGUCACCUGAC	3381
84868_7_112	HAVCR2	Exon 7	-	chr5:157087077-157087102	GAUCCAACCACCUUAUUUUUGAGCU	3382
84868_7_113	HAVCR2	Exon 7	-	chr5:157087126-157087151	GCAGGCAGCAACCCUCACAACCUUU	3383
84868_7_114	HAVCR2	Exon 7	-	chr5:157087127-157087152	AGCAGGCAGCAACCCUCACAACCUU	3384
84868_7_115	HAVCR2	Exon 7	-	chr5:157087149-157087174	UGAGUAUUAUUGCUAUGUCAGCAGC	3385
84868_7_116	HAVCR2	Exon 7	-	chr5:157087184-157087209	AUUGAAGAGAACGUAUAUGAAGUGG	3386
84868_7_117	HAVCR2	Exon 7	-	chr5:157087187-157087212	ACCAUUGAAGAGAACGUAUAUGAAG	3387
84868_7_118	HAVCR2	Exon 7	-	chr5:157087240-157087265	CAGGAUUGGCAAAUGCAGUAGCAGA	3388
84868_7_119	HAVCR2	Exon 7	-	chr5:157087241-157087266	UCAGGAUUGGCAAAUGCAGUAGCAG	3389
84868_7_120	HAVCR2	Exon 7	-	chr5:157087259-157087284	UUGGCCAACCUCCCUCCCUCAGGAU	3390
84868_7_121	HAVCR2	Exon 7	-	chr5:157087264-157087289	UCUCUUUGGCCAACCUCCCUCCCUC	3391
84868_7_122	HAVCR2	Exon 7	-	chr5:157087283-157087308	CUUUAUUUCCACAGCCUCAUCUCUU	3392
84868_6_1	HAVCR2	Exon 6	+	chr5:157088958-157088983	UCUUUGCUAUGAGAAUACCCUAGUA	3393
84868_6_2	HAVCR2	Exon 6	+	chr5:157088959-157088984	CUUUGCUAUGAGAAUACCCUAGUAA	3394
84868_6_3	HAVCR2	Exon 6	+	chr5:157088960-157088985	UUUGCUAUGAGAAUACCCUAGUAAG	3395
84868_6_4	HAVCR2	Exon 6	+	chr5:157088961-157088986	UUGCUAUGAGAAUACCCUAGUAAGG	3396
84868_6_5	HAVCR2	Exon 6	-	chr5:157088918-157088943	AAGGUAAGAAUAAUGGAAUGGGGUU	3397

84868_6_6	HAVCR2	Exon 6	-	chr5:157088919-157088944	UAAGGUAAGAAUAAUGGAAUGGGGU	3398
84868_6_7	HAVCR2	Exon 6	-	chr5:157088923-157088948	AAUUUAAGGUAAGAAUAAUGGAAUG	3399
84868_6_8	HAVCR2	Exon 6	-	chr5:157088924-157088949	GAAUUUAAGGUAAGAAUAAUGGAAU	3400
84868_6_9	HAVCR2	Exon 6	-	chr5:157088925-157088950	AGAAUUUAAGGUAAGAAUAAUGGAA	3401
84868_6_10	HAVCR2	Exon 6	-	chr5:157088930-157088955	GAUACAGAAUUUAAGGUAAGAAUAA	3402
84868_6_11	HAVCR2	Exon 6	-	chr5:157088942-157088967	UAGCAAAGAGAAGAUACAGAAUUUA	3403
84868_5_1	HAVCR2	Exon 5	+	chr5:157095361-157095386	GCUCCGAUGUAGAUGCCUAUUCUGA	3404
84868_5_2	HAVCR2	Exon 5	+	chr5:157095388-157095413	GUUGCUCCAGAGUCCCGUAAGUCAU	3405
84868_5_3	HAVCR2	Exon 5	+	chr5:157095415-157095440	GCCAAUCUAGAGUCCCGUAACUCAU	3406
84868_5_4	HAVCR2	Exon 5	+	chr5:157095424-157095449	GAGUCCCGUAACUCAUUGGCCAAUG	3407
84868_5_5	HAVCR2	Exon 5	+	chr5:157095437-157095462	CAUUGGCCAAUGUGGAUAUUUGCUA	3408
84868_5_6	HAVCR2	Exon 5	+	chr5:157095450-157095475	GGAUAUUUGCUAUGGAAACACAAAC	3409
84868_5_7	HAVCR2	Exon 5	-	chr5:157095325-157095350	CUGGGCUGGCUCUGGCUCUUAUCUU	3410
84868_5_8	HAVCR2	Exon 5	-	chr5:157095338-157095363	GCAGGGAUCUGUGCUGGGCUGGCUC	3411
84868_5_9	HAVCR2	Exon 5	-	chr5:157095344-157095369	AUCGGAGCAGGGAUCUGUGCUGGGC	3412
84868_5_10	HAVCR2	Exon 5	-	chr5:157095348-157095373	CUACAUCGGAGCAGGGAUCUGUGCU	3413
84868_5_11	HAVCR2	Exon 5	-	chr5:157095349-157095374	UCUACAUCGGAGCAGGGAUCUGUGC	3414
84868_5_12	HAVCR2	Exon 5	-	chr5:157095360-157095385	CAGAAUAGGCAUCUACAUCGGAGCA	3415
84868_5_13	HAVCR2	Exon 5	-	chr5:157095361-157095386	UCAGAAUAGGCAUCUACAUCGGAGC	3416
84868_5_14	HAVCR2	Exon 5	-	chr5:157095367-157095392	CAACCAUCAGAAUAGGCAUCUACAU	3417
84868_5_15	HAVCR2	Exon 5	-	chr5:157095379-157095404	GGGACUCUGGAGCAACCAUCAGAAU	3418
84868_5_16	HAVCR2	Exon 5	-	chr5:157095397-157095422	GAUUGGCCAAUGACUUACGGGACUC	3419

84868_5_17	HAVCR2	Exon 5	-	chr5:157095404-157095429	GACUCUAGAUUGGCCAAUGACUUAC	3420
84868_5_18	HAVCR2	Exon 5	-	chr5:157095405-157095430	GGACUCUAGAUUGGCCAAUGACUUA	3421
84868_5_19	HAVCR2	Exon 5	-	chr5:157095419-157095444	GCCAAUGAGUUACGGGACUCUAGAU	3422
84868_5_20	HAVCR2	Exon 5	-	chr5:157095431-157095456	AUAUCCACAUUGGCCAAUGAGUUAC	3423
84868_5_21	HAVCR2	Exon 5	-	chr5:157095432-157095457	AAUAUCCACAUUGGCCAAUGAGUUA	3424
84868_5_22	HAVCR2	Exon 5	-	chr5:157095446-157095471	GUGUUUCCAUAGCAAAUAUCCACAU	3425
84868_4_1	HAVCR2	Exon 4	+	chr5:157098847-157098872	AGUUACUUACUGUUAGAUUUAUAUC	3426
84868_4_2	HAVCR2	Exon 4	+	chr5:157098848-157098873	GUUACUUACUGUUAGAUUUAUAUCA	3427
84868_4_3	HAVCR2	Exon 4	+	chr5:157098851-157098876	ACUUACUGUUAGAUUUAUAUCAGGG	3428
84868_4_4	HAVCR2	Exon 4	-	chr5:157098884-157098909	UUUUAUAGCAGAGACACAGACACUG	3429
84868_4_5	HAVCR2	Exon 4	-	chr5:157098885-157098910	AUUUUAUAGCAGAGACACAGACACU	3430
84868_4_6	HAVCR2	Exon 4	-	chr5:157098886-157098911	GAUUUUAUAGCAGAGACACAGACAC	3431
84868_3_1	HAVCR2	Exon 3	+	chr5:157104641-157104666	CUCCUCUGCCCCAUGCAUAGUUACC	3432
84868_3_2	HAVCR2	Exon 3	+	chr5:157104642-157104667	UCCUCUGCCCCAUGCAUAGUUACCU	3433
84868_3_3	HAVCR2	Exon 3	+	chr5:157104655-157104680	GCAUAGUUACCUGGGCCAUGUCCCC	3434
84868_3_4	HAVCR2	Exon 3	+	chr5:157104658-157104683	UAGUUACCUGGGCCAUGUCCCCUGG	3435
84868_3_5	HAVCR2	Exon 3	+	chr5:157104671-157104696	CAUGUCCCCUGGUGGUAAGCAUCCU	3436
84868_3_6	HAVCR2	Exon 3	+	chr5:157104676-157104701	CCCCUGGUGGUAAGCAUCCUUGGAA	3437
84868_3_7	HAVCR2	Exon 3	+	chr5:157104704-157104729	CUGCAGUGAAGUCUCUCUGCCGAGU	3438
84868_3_8	HAVCR2	Exon 3	+	chr5:157104710-157104735	UGAAGUCUCUCUGCCGAGUCGGUGC	3439
84868_3_9	HAVCR2	Exon 3	+	chr5:157104711-157104736	GAAGUCUCUCUGCCGAGUCGGUGCA	3440
84868_3_10	HAVCR2	Exon 3	+	chr5:157104712-157104737	AAGUCUCUCUGCCGAGUCGGUGCAG	3441

84868_3_11	HAVCR2	Exon 3	+	chr5:157104721-157104746	UGCCGAGUCGGUGCAGGGGUGACCU	3442
84868_3_12	HAVCR2	Exon 3	+	chr5:157104744-157104769	CUUGGCUAAUGUCAGAAACAACAUA	3443
84868_3_13	HAVCR2	Exon 3	-	chr5:157104643-157104668	CAGGUAACUAUGCAUGGGGCAGAGG	3444
84868_3_14	HAVCR2	Exon 3	-	chr5:157104646-157104671	GCCCAGGUAACUAUGCAUGGGGCAG	3445
84868_3_15	HAVCR2	Exon 3	-	chr5:157104652-157104677	GACAUGGCCCAGGUAACUAUGCAUG	3446
84868_3_16	HAVCR2	Exon 3	-	chr5:157104653-157104678	GGACAUGGCCCAGGUAACUAUGCAU	3447
84868_3_17	HAVCR2	Exon 3	-	chr5:157104654-157104679	GGGACAUGGCCCAGGUAACUAUGCA	3448
84868_3_18	HAVCR2	Exon 3	-	chr5:157104667-157104692	UGCUUACCACCAGGGGACAUGGCCC	3449
84868_3_19	HAVCR2	Exon 3	-	chr5:157104673-157104698	CAAGGAUGCUUACCACCAGGGGACA	3450
84868_3_20	HAVCR2	Exon 3	-	chr5:157104679-157104704	CCUUUCCAAGGAUGCUUACCACCAG	3451
84868_3_21	HAVCR2	Exon 3	-	chr5:157104680-157104705	GCCUUUCCAAGGAUGCUUACCACCA	3452
84868_3_22	HAVCR2	Exon 3	-	chr5:157104681-157104706	AGCCUUUCCAAGGAUGCUUACCACC	3453
84868_3_23	HAVCR2	Exon 3	-	chr5:157104696-157104721	GAGAGACUUCACUGCAGCCUUUCCA	3454
84868_3_24	HAVCR2	Exon 3	-	chr5:157104726-157104751	AGCCAAGGUCACCCCUGCACCGACU	3455
84868_3_25	HAVCR2	Exon 3	-	chr5:157104746-157104771	CUUAUGUUGUUUCUGACAUUAGCCA	3456
84868_2_1	HAVCR2	Exon 2	+	chr5:157106602-157106627	GAUGGCAUGCAAAUGUCCACUCACC	3457
84868_2_2	HAVCR2	Exon 2	+	chr5:157106621-157106646	CUCACCUGGUUUGAUGACCAACUUC	3458
84868_2_3	HAVCR2	Exon 2	+	chr5:157106650-157106675	UAAAUUUUUCAUCAUUCAUUAUGCC	3459
84868_2_4	HAVCR2	Exon 2	+	chr5:157106651-157106676	AAAUUUUUCAUCAUUCAUUAUGCCU	3460
84868_2_5	HAVCR2	Exon 2	+	chr5:157106657-157106682	UUCAUCAUUCAUUAUGCCUGGGAUU	3461
84868_2_6	HAVCR2	Exon 2	+	chr5:157106663-157106688	AUUCAUUAUGCCUGGGAUUUGGAUC	3462
84868_2_7	HAVCR2	Exon 2	+	chr5:157106706-157106731	CUGUCUGCUAGAGUCACAUUCUCUA	3463

84868_2_8	HAVCR2	Exon 2	+	chr5:157106711-157106736	UGCUAGAGUCACAUUCUCUAUGGUC	3464
84868_2_9	HAVCR2	Exon 2	+	chr5:157106712-157106737	GCUAGAGUCACAUUCUCUAUGGUCA	3465
84868_2_10	HAVCR2	Exon 2	+	chr5:157106729-157106754	UAUGGUCAGGGACACAUCUCCUUUG	3466
84868_2_11	HAVCR2	Exon 2	+	chr5:157106754-157106779	CGGAAAUCCCCAUUUAGCCAGUAUC	3467
84868_2_12	HAVCR2	Exon 2	+	chr5:157106818-157106843	GCACCACGUUGCCACAUUCAAACAC	3468
84868_2_13	HAVCR2	Exon 2	+	chr5:157106823-157106848	ACGUUGCCACAUUCAAACACAGGAC	3469
84868_2_14	HAVCR2	Exon 2	+	chr5:157106844-157106869	GGACAGGCUCCUUUGCCCCAGCAGA	3470
84868_2_15	HAVCR2	Exon 2	+	chr5:157106845-157106870	GACAGGCUCCUUUGCCCCAGCAGAC	3471
84868_2_16	HAVCR2	Exon 2	+	chr5:157106852-157106877	UCCUUUGCCCCAGCAGACGGGCACG	3472
84868_2_17	HAVCR2	Exon 2	+	chr5:157106860-157106885	CCCAGCAGACGGGCACGAGGUUCCC	3473
84868_2_18	HAVCR2	Exon 2	+	chr5:157106861-157106886	CCAGCAGACGGGCACGAGGUUCCCU	3474
84868_2_19	HAVCR2	Exon 2	+	chr5:157106862-157106887	CAGCAGACGGGCACGAGGUUCCCUG	3475
84868_2_20	HAVCR2	Exon 2	+	chr5:157106865-157106890	CAGACGGGCACGAGGUUCCCUGGGG	3476
84868_2_21	HAVCR2	Exon 2	+	chr5:157106869-157106894	CGGGCACGAGGUUCCCUGGGGCGGC	3477
84868_2_22	HAVCR2	Exon 2	+	chr5:157106870-157106895	GGGCACGAGGUUCCCUGGGGCGGCU	3478
84868_2_23	HAVCR2	Exon 2	+	chr5:157106871-157106896	GGCACGAGGUUCCCUGGGGCGGCUG	3479
84868_2_24	HAVCR2	Exon 2	+	chr5:157106883-157106908	CCUGGGGCGGCUGGGGUGUAGAAGC	3480
84868_2_25	HAVCR2	Exon 2	+	chr5:157106884-157106909	CUGGGGCGGCUGGGGUGUAGAAGCA	3481
84868_2_26	HAVCR2	Exon 2	+	chr5:157106892-157106917	GCUGGGGUGUAGAAGCAGGGCAGAU	3482
84868_2_27	HAVCR2	Exon 2	+	chr5:157106931-157106956	ACCUCCGCUCUGUAUUCCACUUCUG	3483
84868_2_28	HAVCR2	Exon 2	+	chr5:157106952-157106977	UCUGAGGACCCUGCAUAGAGAGAGA	3484
84868_2_29	HAVCR2	Exon 2	-	chr5:157106621-157106646	GAAGUUGGUCAUCAAACCAGGUGAG	3485

84868_2_30	HAVCR2	Exon 2	-	chr5:157106628-157106653	UUAACCUGAAGUUGGUCAUCAAACC	3486
84868_2_31	HAVCR2	Exon 2	-	chr5:157106641-157106666	AAUGAUGAAAAAUUUAACCUGAAGU	3487
84868_2_32	HAVCR2	Exon 2	-	chr5:157106676-157106701	UCUACUGCUGCCGGAUCCAAAUCCC	3488
84868_2_33	HAVCR2	Exon 2	-	chr5:157106690-157106715	AGCAGACAGUGGGAUCUACUGCUGC	3489
84868_2_34	HAVCR2	Exon 2	-	chr5:157106705-157106730	AGAGAAUGUGACUCUAGCAGACAGU	3490
84868_2_35	HAVCR2	Exon 2	-	chr5:157106706-157106731	UAGAGAAUGUGACUCUAGCAGACAG	3491
84868_2_36	HAVCR2	Exon 2	-	chr5:157106751-157106776	ACUGGCUAAAUGGGGAUUUCCGCAA	3492
84868_2_37	HAVCR2	Exon 2	-	chr5:157106764-157106789	UGGACAUCCAGAUACUGGCUAAAUG	3493
84868_2_38	HAVCR2	Exon 2	-	chr5:157106765-157106790	UUGGACAUCCAGAUACUGGCUAAAU	3494
84868_2_39	HAVCR2	Exon 2	-	chr5:157106766-157106791	AUUGGACAUCCAGAUACUGGCUAAA	3495
84868_2_40	HAVCR2	Exon 2	-	chr5:157106774-157106799	UGUGAAUUAUUGGACAUCCAGAUAC	3496
84868_2_41	HAVCR2	Exon 2	-	chr5:157106789-157106814	GACUGAUGAAAGGGAUGUGAAUUAU	3497
84868_2_42	HAVCR2	Exon 2	-	chr5:157106803-157106828	AACGUGGUGCUCAGGACUGAUGAAA	3498
84868_2_43	HAVCR2	Exon 2	-	chr5:157106804-157106829	CAACGUGGUGCUCAGGACUGAUGAA	3499
84868_2_44	HAVCR2	Exon 2	-	chr5:157106816-157106841	GUUUGAAUGUGGCAACGUGGUGCUC	3500
84868_2_45	HAVCR2	Exon 2	-	chr5:157106824-157106849	UGUCCUGUGUUUGAAUGUGGCAACG	3501
84868_2_46	HAVCR2	Exon 2	-	chr5:157106832-157106857	AAGGAGCCUGUCCUGUGUUUGAAUG	3502
84868_2_47	HAVCR2	Exon 2	-	chr5:157106856-157106881	ACCUCGUGCCCGUCUGCUGGGGCAA	3503
84868_2_48	HAVCR2	Exon 2	-	chr5:157106862-157106887	CAGGGAACCUCGUGCCCGUCUGCUG	3504
84868_2_49	HAVCR2	Exon 2	-	chr5:157106863-157106888	CCAGGGAACCUCGUGCCCGUCUGCU	3505
84868_2_50	HAVCR2	Exon 2	-	chr5:157106864-157106889	CCCAGGGAACCUCGUGCCCGUCUGC	3506
84868_2_51	HAVCR2	Exon 2	-	chr5:157106885-157106910	CUGCUUCUACACCCCAGCCGCCCCA	3507

84868_2_52	HAVCR2	Exon 2	-	chr5:157106886-157106911	CCUGCUUCUACACCCCAGCCGCCCC	3508
84868_2_53	HAVCR2	Exon 2	-	chr5:157106931-157106956	CAGAAGUGGAAUACAGAGCGGAGGU	3509
84868_2_54	HAVCR2	Exon 2	-	chr5:157106935-157106960	UCCUCAGAAGUGGAAUACAGAGCGG	3510
84868_2_55	HAVCR2	Exon 2	-	chr5:157106938-157106963	GGGUCCUCAGAAGUGGAAUACAGAG	3511
84868_2_56	HAVCR2	Exon 2	-	chr5:157106950-157106975	UCUCUCUAUGCAGGGUCCUCAGAAG	3512
84868_1_1	HAVCR2	Exon 1	+	chr5:157108939-157108964	AGCAGCAGCAGCAGGACACAGUCAA	3513
84868_1_2	HAVCR2	Exon 1	+	chr5:157108940-157108965	GCAGCAGCAGCAGGACACAGUCAAA	3514
84868_1_3	HAVCR2	Exon 1	+	chr5:157108957-157108982	CAGUCAAAGGGAAGAUGUGAAAACA	3515
84868_1_4	HAVCR2	Exon 1	+	chr5:157108981-157109006	AUGGAGCUUGCAGAAGAAAAGUCAG	3516
84868_1_5	HAVCR2	Exon 1	+	chr5:157108995-157109020	AGAAAAGUCAGAGGACACCUCUGUU	3517
84868_1_6	HAVCR2	Exon 1	+	chr5:157109018-157109043	UUAGGCACAGUUUUAACUCUCCAAA	3518
84868_1_7	HAVCR2	Exon 1	+	chr5:157109023-157109048	CACAGUUUUAACUCUCCAAAUGGAC	3519
84868_1_8	HAVCR2	Exon 1	+	chr5:157109024-157109049	ACAGUUUUAACUCUCCAAAUGGACU	3520
84868_1_9	HAVCR2	Exon 1	+	chr5:157109100-157109125	CCACUGAGUGCUAGCUCAGCACACC	3521
84868_1_10	HAVCR2	Exon 1	+	chr5:157109101-157109126	CACUGAGUGCUAGCUCAGCACACCC	3522
84868_1_11	HAVCR2	Exon 1	+	chr5:157109140-157109165	CAGUGAUUCUUAUAGUAACACUGCC	3523
84868_1_12	HAVCR2	Exon 1	+	chr5:157109159-157109184	ACUGCCAGGUCUACAGUCACAUUAA	3524
84868_1_13	HAVCR2	Exon 1	-	chr5:157108917-157108942	CGACGAUGAUGAUACAAGUAAGUCU	3525
84868_1_14	HAVCR2	Exon 1	-	chr5:157109015-157109040	GGAGAGUUAAAACUGUGCCUAACAG	3526
84868_1_15	HAVCR2	Exon 1	-	chr5:157109041-157109066	AGUUGGAAGAAGUACCCAGUCCAUU	3527
84868_1_16	HAVCR2	Exon 1	-	chr5:157109063-157109088	CUCAUGUGAUUGUGGAGUAGACAGU	3528
84868_1_17	HAVCR2	Exon 1	-	chr5:157109076-157109101	GGGGCGGCUACUGCUCAUGUGAUUG	3529

84868_1_18	HAVCR2	Exon 1	-	chr5:157109097-157109122	GUGCUGAGCUAGCACUCAGUGGGGG	3530
84868_1_19	HAVCR2	Exon 1	-	chr5:157109100-157109125	GGUGUGCUGAGCUAGCACUCAGUGG	3531
84868_1_20	HAVCR2	Exon 1	-	chr5:157109101-157109126	GGGUGUGCUGAGCUAGCACUCAGUG	3532
84868_1_21	HAVCR2	Exon 1	-	chr5:157109102-157109127	CGGGUGUGCUGAGCUAGCACUCAGU	3533
84868_1_22	HAVCR2	Exon 1	-	chr5:157109103-157109128	CCGGGUGUGCUGAGCUAGCACUCAG	3534
84868_1_23	HAVCR2	Exon 1	-	chr5:157109126-157109151	AAGAAUCACUGGCAAUCAGACACCC	3535
84868_1_24	HAVCR2	Exon 1	-	chr5:157109127-157109152	UAAGAAUCACUGGCAAUCAGACACC	3536
84868_1_25	HAVCR2	Exon 1	-	chr5:157109142-157109167	CUGGCAGUGUUACUAUAAGAAUCAC	3537
84868_1_26	HAVCR2	Exon 1	-	chr5:157109166-157109191	GUUUCCUUUAAUGUGACUGUAGACC	3538
84868_1_27	HAVCR2	Exon 1	-	chr5:157109193-157109218	UGUAGUGUGGCAUGACAGAGAACUU	3539
84868_1_28	HAVCR2	Exon 1	-	chr5:157109211-157109236	GAACACUUACAGGAUGUGUGUAGUG	3540
84868_1_29	HAVCR2	Exon 1	-	chr5:157109226-157109251	ACAGGACAGACAUCAGAACACUUAC	3541
3902_1_1	LAG3	Exon 1	+	chr12:6772480-6772505	GGAAGGUGGAGGGAAGGCCGGGCAC	3542
3902_1_2	LAG3	Exon 1	+	chr12:6772481-6772506	GAAGGUGGAGGGAAGGCCGGGCACA	3543
3902_1_3	LAG3	Exon 1	+	chr12:6772482-6772507	AAGGUGGAGGGAAGGCCGGGCACAG	3544
3902_1_4	LAG3	Exon 1	+	chr12:6772488-6772513	GAGGGAAGGCCGGGCACAGGGGUGA	3545
3902_1_5	LAG3	Exon 1	+	chr12:6772508-6772533	GGUGAAGGCCCAGAGACCAGCAGAA	3546
3902_1_6	LAG3	Exon 1	+	chr12:6772525-6772550	CAGCAGAACGGCAUCCCAGCCACGA	3547
3902_1_7	LAG3	Exon 1	+	chr12:6772555-6772580	ACUUUGCUCUGUCUGCUCUCCGCCA	3548
3902_1_8	LAG3	Exon 1	+	chr12:6772573-6772598	UCCGCCACGGCCCUGCUCUGUUCCC	3549
3902_1_9	LAG3	Exon 1	+	chr12:6772574-6772599	CCGCCACGGCCCUGCUCUGUUCCCU	3550
3902_1_10	LAG3	Exon 1	+	chr12:6772599-6772624	GGGACACCCCCGCCCCCACCUCCUC	3551
3902_1_11	LAG3	Exon 1	+	chr12:6772635-6772660	UCUGCCCAGCUUUCCAGCUUUCCUC	3552
3902_1_12	LAG3	Exon	+	chr12:6772642	AGCUUUCCAGCUUUCCUCU	3553

		1		-6772667	GGAUUC	
3902_1_13	LAG3	Exon 1	+	chr12:6772649 -6772674	CAGCUUUCCUCUGGAUUCC GGCCUC	3554
3902_1_14	LAG3	Exon 1	+	chr12:6772676 -6772701	GUCAUCCCUCCCCACCCUCU CUCCA	3555
3902_1_15	LAG3	Exon 1	+	chr12:6772687 -6772712	CCACCCUCUCUCCAAGGCCC UCUCC	3556
3902_1_16	LAG3	Exon 1	+	chr12:6772793 -6772818	CCCCUUUCCUUUUCUGACCU CCUUU	3557
3902_1_17	LAG3	Exon 1	+	chr12:6772796 -6772821	CUUUCCUUUUCUGACCUCC UUUUGG	3558
3902_1_18	LAG3	Exon 1	+	chr12:6772797 -6772822	UUUCCUUUUCUGACCUCCU UUUGGA	3559
3902_1_19	LAG3	Exon 1	+	chr12:6772820 -6772845	GAGGGCUCAGCGCUGCCCA GACCAU	3560
3902_1_20	LAG3	Exon 1	+	chr12:6772830 -6772855	CGCUGCCCAGACCAUAGGA GAGAUG	3561
3902_1_21	LAG3	Exon 1	+	chr12:6772831 -6772856	GCUGCCCAGACCAUAGGAG AGAUGU	3562
3902_1_22	LAG3	Exon 1	+	chr12:6772834 -6772859	GCCCAGACCAUAGGAGAGA UGUGGG	3563
3902_1_23	LAG3	Exon 1	+	chr12:6772846 -6772871	GGAGAGAUGUGGGAGGCUC AGUUCC	3564
3902_1_24	LAG3	Exon 1	+	chr12:6772847 -6772872	GAGAGAUGUGGGAGGCUCA GUUCCU	3565
3902_1_25	LAG3	Exon 1	+	chr12:6772872 -6772897	GGGCUUGCUGUUUCUGCAG CCGCUU	3566
3902_1_26	LAG3	Exon 1	+	chr12:6772873 -6772898	GGCUUGCUGUUUCUGCAGC CGCUUU	3567
3902_1_27	LAG3	Exon 1	+	chr12:6772876 -6772901	UUGCUGUUUCUGCAGCCGC UUUGGG	3568
3902_1_28	LAG3	Exon 1	+	chr12:6772883 -6772908	UUCUGCAGCCGCUUUGGGU GGCUCC	3569
3902_1_29	LAG3	Exon 1	+	chr12:6772891 -6772916	CCGCUUUGGGUGGCUCCAG GUAAAA	3570
3902_1_30	LAG3	Exon 1	+	chr12:6772892 -6772917	CGCUUUGGGUGGCUCCAGG UAAAAC	3571
3902_1_31	LAG3	Exon 1	+	chr12:6772893 -6772918	GCUUUGGGUGGCUCCAGGU AAAACG	3572
3902_1_32	LAG3	Exon 1	+	chr12:6772897 -6772922	UGGGUGGCUCCAGGUAAAA CGGGGA	3573
3902_1_33	LAG3	Exon 1	+	chr12:6772900 -6772925	GUGGCUCCAGGUAAAACGG GGAUGG	3574
3902_1_34	LAG3	Exon 1	+	chr12:6772901 -6772926	UGGCUCCAGGUAAAACGGG GAUGGC	3575
3902_1_35	LAG3	Exon 1	+	chr12:6772904 -6772929	CUCCAGGUAAAACGGGGAU GGCGGG	3576
3902_1_36	LAG3	Exon 1	+	chr12:6772905 -6772930	UCCAGGUAAAACGGGGAUG GCGGGA	3577

3902_1_37	LAG3	Exon 1	-	chr12:6772500-6772525	GUCUCUGGGCCUUCACCCCUGUGCC	3578
3902_1_38	LAG3	Exon 1	-	chr12:6772519-6772544	CUGGGAUGCCGUUCUGCUGGUCUCU	3579
3902_1_39	LAG3	Exon 1	-	chr12:6772520-6772545	GCUGGGAUGCCGUUCUGCUGGUCUC	3580
3902_1_40	LAG3	Exon 1	-	chr12:6772527-6772552	CGUCGUGGCUGGGAUGCCGUUCUGC	3581
3902_1_41	LAG3	Exon 1	-	chr12:6772542-6772567	ACAGAGCAAAGUGGCCGUCGUGGCU	3582
3902_1_42	LAG3	Exon 1	-	chr12:6772543-6772568	GACAGAGCAAAGUGGCCGUCGUGGC	3583
3902_1_43	LAG3	Exon 1	-	chr12:6772547-6772572	AGCAGACAGAGCAAAGUGGCCGUCG	3584
3902_1_44	LAG3	Exon 1	-	chr12:6772556-6772581	GUGGCGGAGAGCAGACAGAGCAAAG	3585
3902_1_45	LAG3	Exon 1	-	chr12:6772577-6772602	CCCAGGGAACAGAGCAGGGCCGUGG	3586
3902_1_46	LAG3	Exon 1	-	chr12:6772580-6772605	UGUCCCAGGGAACAGAGCAGGGCCG	3587
3902_1_47	LAG3	Exon 1	-	chr12:6772586-6772611	CGGGGGUGUCCCAGGGAACAGAGCA	3588
3902_1_48	LAG3	Exon 1	-	chr12:6772587-6772612	GCGGGGGUGUCCCAGGGAACAGAGC	3589
3902_1_49	LAG3	Exon 1	-	chr12:6772598-6772623	AGGAGGUGGGGGCGGGGGUGUCCCA	3590
3902_1_50	LAG3	Exon 1	-	chr12:6772599-6772624	GAGGAGGUGGGGGCGGGGGUGUCCC	3591
3902_1_51	LAG3	Exon 1	-	chr12:6772608-6772633	AGGCAGCCUGAGGAGGUGGGGGCGG	3592
3902_1_52	LAG3	Exon 1	-	chr12:6772609-6772634	CAGGCAGCCUGAGGAGGUGGGGGCG	3593
3902_1_53	LAG3	Exon 1	-	chr12:6772610-6772635	UCAGGCAGCCUGAGGAGGUGGGGGC	3594
3902_1_54	LAG3	Exon 1	-	chr12:6772611-6772636	AUCAGGCAGCCUGAGGAGGUGGGGG	3595
3902_1_55	LAG3	Exon 1	-	chr12:6772614-6772639	CAGAUCAGGCAGCCUGAGGAGGUGG	3596
3902_1_56	LAG3	Exon 1	-	chr12:6772615-6772640	GCAGAUCAGGCAGCCUGAGGAGGUG	3597
3902_1_57	LAG3	Exon 1	-	chr12:6772616-6772641	GGCAGAUCAGGCAGCCUGAGGAGGU	3598
3902_1_58	LAG3	Exon 1	-	chr12:6772617-6772642	GGGCAGAUCAGGCAGCCUGAGGAGG	3599
3902_1_59	LAG3	Exon 1	-	chr12:6772620-6772645	GCUGGGCAGAUCAGGCAGCCUGAGG	3600
3902_1_60	LAG3	Exon 1	-	chr12:6772623-6772648	AAAGCUGGGCAGAUCAGGCAGCCUG	3601
3902_1_61	LAG3	Exon 1	-	chr12:6772633-6772658	GGAAAGCUGGAAAGCUGGGCAGAUC	3602

3902_1_62	LAG3	Exon 1	-	chr12:6772642 -6772667	GAAUCCAGAGGAAAGCUGG AAAGCU	3603
3902_1_63	LAG3	Exon 1	-	chr12:6772643 -6772668	GGAAUCCAGAGGAAAGCUG GAAAGC	3604
3902_1_64	LAG3	Exon 1	-	chr12:6772651 -6772676	CAGAGGCCGGAAUCCAGAG GAAAGC	3605
3902_1_65	LAG3	Exon 1	-	chr12:6772659 -6772684	GGGAUGACCAGAGGCCGGA AUCCAG	3606
3902_1_66	LAG3	Exon 1	-	chr12:6772669 -6772694	AGGGUGGGGAGGGAUGACC AGAGGC	3607
3902_1_67	LAG3	Exon 1	-	chr12:6772673 -6772698	AGAGAGGGUGGGGAGGGAU GACCAG	3608
3902_1_68	LAG3	Exon 1	-	chr12:6772684 -6772709	GAGGGCCUUGGAGAGAGGG UGGGGA	3609
3902_1_69	LAG3	Exon 1	-	chr12:6772685 -6772710	AGAGGGCCUUGGAGAGAGG GUGGGG	3610
3902_1_70	LAG3	Exon 1	-	chr12:6772688 -6772713	AGGAGAGGGCCUUGGAGAG AGGGUG	3611
3902_1_71	LAG3	Exon 1	-	chr12:6772689 -6772714	CAGGAGAGGGCCUUGGAGA GAGGGU	3612
3902_1_72	LAG3	Exon 1	-	chr12:6772690 -6772715	CCAGGAGAGGGCCUUGGAG AGAGGG	3613
3902_1_73	LAG3	Exon 1	-	chr12:6772693 -6772718	AGACCAGGAGAGGGCCUUG GAGAGA	3614
3902_1_74	LAG3	Exon 1	-	chr12:6772694 -6772719	GAGACCAGGAGAGGGCCUU GGAGAG	3615
3902_1_75	LAG3	Exon 1	-	chr12:6772701 -6772726	AAGAAGGGAGACCAGGAGA GGGCCU	3616
3902_1_76	LAG3	Exon 1	-	chr12:6772707 -6772732	UUCUAGAAGAAGGGAGACC AGGAGA	3617
3902_1_77	LAG3	Exon 1	-	chr12:6772708 -6772733	GUUCUAGAAGAAGGGAGAC CAGGAG	3618
3902_1_78	LAG3	Exon 1	-	chr12:6772713 -6772738	AAGGGGUUCUAGAAGAAGG GAGACC	3619
3902_1_79	LAG3	Exon 1	-	chr12:6772721 -6772746	GGUGGAGGAAGGGGUUCUA GAAGAA	3620
3902_1_80	LAG3	Exon 1	-	chr12:6772722 -6772747	AGGUGGAGGAAGGGGUUCU AGAAGA	3621
3902_1_81	LAG3	Exon 1	-	chr12:6772735 -6772760	UCUGCAGAGAGGGAGGUGG AGGAAG	3622
3902_1_82	LAG3	Exon 1	-	chr12:6772736 -6772761	UUCUGCAGAGAGGGAGGUG GAGGAA	3623
3902_1_83	LAG3	Exon 1	-	chr12:6772737 -6772762	GUUCUGCAGAGAGGGAGGU GGAGGA	3624
3902_1_84	LAG3	Exon 1	-	chr12:6772741 -6772766	AGAAGUUCUGCAGAGAGGG AGGUGG	3625
3902_1_85	LAG3	Exon 1	-	chr12:6772744 -6772769	AGGAGAAGUUCUGCAGAGA GGGAGG	3626
3902_1_86	LAG3	Exon 1	-	chr12:6772747 -6772772	UAAAGGAGAAGUUCUGCAG AGAGGG	3627

3902_1_87	LAG3	Exon 1	-	chr12:6772750-6772775	GGGUAAAGGAGAAGUUCUGCAGAGA	3628
3902_1_88	LAG3	Exon 1	-	chr12:6772751-6772776	GGGGUAAAGGAGAAGUUCUGCAGAG	3629
3902_1_89	LAG3	Exon 1	-	chr12:6772769-6772794	GGCAGUGGUGGGGGGUGGGGGGUAA	3630
3902_1_90	LAG3	Exon 1	-	chr12:6772775-6772800	AAAGGGGGCAGUGGUGGGGGGUGGG	3631
3902_1_91	LAG3	Exon 1	-	chr12:6772776-6772801	GAAAGGGGGCAGUGGUGGGGGGUGG	3632
3902_1_92	LAG3	Exon 1	-	chr12:6772777-6772802	GGAAAGGGGGCAGUGGUGGGGGGUG	3633
3902_1_93	LAG3	Exon 1	-	chr12:6772778-6772803	AGGAAAGGGGGCAGUGGUGGGGGGU	3634
3902_1_94	LAG3	Exon 1	-	chr12:6772779-6772804	AAGGAAAGGGGGCAGUGGUGGGGGG	3635
3902_1_95	LAG3	Exon 1	-	chr12:6772782-6772807	GAAAAGGAAAGGGGGCAGUGGUGGG	3636
3902_1_96	LAG3	Exon 1	-	chr12:6772783-6772808	AGAAAAGGAAAGGGGGCAGUGGUGG	3637
3902_1_97	LAG3	Exon 1	-	chr12:6772784-6772809	CAGAAAAGGAAAGGGGGCAGUGGUG	3638
3902_1_98	LAG3	Exon 1	-	chr12:6772785-6772810	UCAGAAAAGGAAAGGGGGCAGUGGU	3639
3902_1_99	LAG3	Exon 1	-	chr12:6772786-6772811	GUCAGAAAAGGAAAGGGGGCAGUGG	3640
3902_1_100	LAG3	Exon 1	-	chr12:6772789-6772814	GAGGUCAGAAAAGGAAAGGGGGCAG	3641
3902_1_101	LAG3	Exon 1	-	chr12:6772795-6772820	CAAAAGGAGGUCAGAAAAGGAAAGG	3642
3902_1_102	LAG3	Exon 1	-	chr12:6772796-6772821	CCAAAAGGAGGUCAGAAAAGGAAAG	3643
3902_1_103	LAG3	Exon 1	-	chr12:6772797-6772822	UCCAAAAGGAGGUCAGAAAAGGAAA	3644
3902_1_104	LAG3	Exon 1	-	chr12:6772798-6772823	CUCCAAAAGGAGGUCAGAAAAGGAA	3645
3902_1_105	LAG3	Exon 1	-	chr12:6772803-6772828	GAGCCCUCCAAAAGGAGGUCAGAAA	3646
3902_1_106	LAG3	Exon 1	-	chr12:6772813-6772838	GGGCAGCGCUGAGCCCUCCAAAAGG	3647
3902_1_107	LAG3	Exon 1	-	chr12:6772816-6772841	UCUGGGCAGCGCUGAGCCCUCCAAA	3648
3902_1_108	LAG3	Exon 1	-	chr12:6772838-6772863	GCCUCCCACAUCUCUCCUAUGGUCU	3649
3902_1_109	LAG3	Exon 1	-	chr12:6772839-6772864	AGCCUCCCACAUCUCUCCUAUGGUC	3650
3902_1_110	LAG3	Exon 1	-	chr12:6772844-6772869	AACUGAGCCUCCCACAUCUCUCCUA	3651
3902_1_111	LAG3	Exon 1	-	chr12:6772872-6772897	AAGCGGCUGCAGAAACAGCAAGCCC	3652

3902_1_112	LAG3	Exon 1	-	chr12:6772894-6772919	CCGUUUUACCUGGAGCCACCCAAAG	3653
3902_1_113	LAG3	Exon 1	-	chr12:6772909-6772934	ACCCUCCCGCCAUCCCCGUUUUACC	3654
3902_2_1	LAG3	Exon 2	+	chr12:6773182-6773207	CUCACCUAGUGAAGCCUCUCCAGCC	3655
3902_2_2	LAG3	Exon 2	+	chr12:6773183-6773208	UCACCUAGUGAAGCCUCUCCAGCCA	3656
3902_2_3	LAG3	Exon 2	+	chr12:6773184-6773209	CACCUAGUGAAGCCUCUCCAGCCAG	3657
3902_2_4	LAG3	Exon 2	+	chr12:6773190-6773215	GUGAAGCCUCUCCAGCCAGGGGCUG	3658
3902_2_5	LAG3	Exon 2	+	chr12:6773196-6773221	CCUCUCCAGCCAGGGGCUGAGGUCC	3659
3902_2_6	LAG3	Exon 2	+	chr12:6773199-6773224	CUCCAGCCAGGGGCUGAGGUCCCGG	3660
3902_2_7	LAG3	Exon 2	+	chr12:6773204-6773229	GCCAGGGGCUGAGGUCCCGGUGGUG	3661
3902_2_8	LAG3	Exon 2	+	chr12:6773205-6773230	CCAGGGGCUGAGGUCCCGGUGGUGU	3662
3902_2_9	LAG3	Exon 2	+	chr12:6773211-6773236	GCUGAGGUCCCGGUGGUGUGGGCCC	3663
3902_2_10	LAG3	Exon 2	+	chr12:6773214-6773239	GAGGUCCCGGUGGUGUGGGCCCAGG	3664
3902_2_11	LAG3	Exon 2	+	chr12:6773215-6773240	AGGUCCCGGUGGUGUGGGCCCAGGA	3665
3902_2_12	LAG3	Exon 2	+	chr12:6773216-6773241	GGUCCCGGUGGUGUGGGCCCAGGAG	3666
3902_2_13	LAG3	Exon 2	+	chr12:6773217-6773242	GUCCCGGUGGUGUGGGCCCAGGAGG	3667
3902_2_14	LAG3	Exon 2	+	chr12:6773259-6773284	CCCUGCAGCCCCACAAUCCCCCUCC	3668
3902_2_15	LAG3	Exon 2	+	chr12:6773284-6773309	AGGAUCUCAGCCUUCUGCGAAGAGC	3669
3902_2_16	LAG3	Exon 2	+	chr12:6773285-6773310	GGAUCUCAGCCUUCUGCGAAGAGCA	3670
3902_2_17	LAG3	Exon 2	+	chr12:6773286-6773311	GAUCUCAGCCUUCUGCGAAGAGCAG	3671
3902_2_18	LAG3	Exon 2	+	chr12:6773294-6773319	CCUUCUGCGAAGAGCAGGGGUCACU	3672
3902_2_19	LAG3	Exon 2	+	chr12:6773312-6773337	GGUCACUUGGCAGCAUCAGCCAGAC	3673
3902_2_20	LAG3	Exon 2	+	chr12:6773330-6773355	GCCAGACAGGUAUGCACCCCAAACU	3674
3902_2_21	LAG3	Exon 2	+	chr12:6773331-6773356	CCAGACAGGUAUGCACCCCAAACUU	3675
3902_2_22	LAG3	Exon 2	-	chr12:6773174-6773199	AGGCUUCACUAGGUGAGCAAAAGAG	3676
3902_2_23	LAG3	Exon 2	-	chr12:6773189-6773214	AGCCCCUGGCUGGAGAGGCUUCACU	3677

3902_2_24	LAG3	Exon 2	-	chr12:6773199-6773224	CCGGGACCUCAGCCCCUGGCUGGAG	3678
3902_2_25	LAG3	Exon 2	-	chr12:6773204-6773229	CACCACCGGGACCUCAGCCCCUGGC	3679
3902_2_26	LAG3	Exon 2	-	chr12:6773208-6773233	CCCACACCACCGGGACCUCAGCCCC	3680
3902_2_27	LAG3	Exon 2	-	chr12:6773222-6773247	AGCCCCCUCCUGGGCCCACACCACC	3681
3902_2_28	LAG3	Exon 2	-	chr12:6773223-6773248	GAGCCCCCUCCUGGGCCCACACCAC	3682
3902_2_29	LAG3	Exon 2	-	chr12:6773236-6773261	GGGAGCUGGGCAGGAGCCCCCUCCU	3683
3902_2_30	LAG3	Exon 2	-	chr12:6773237-6773262	GGGGAGCUGGGCAGGAGCCCCCUCC	3684
3902_2_31	LAG3	Exon 2	-	chr12:6773250-6773275	UUGUGGGGCUGCAGGGGAGCUGGGC	3685
3902_2_32	LAG3	Exon 2	-	chr12:6773254-6773279	GGGAUUGUGGGGCUGCAGGGGAGCU	3686
3902_2_33	LAG3	Exon 2	-	chr12:6773255-6773280	GGGGAUUGUGGGGCUGCAGGGGAGC	3687
3902_2_34	LAG3	Exon 2	-	chr12:6773261-6773286	CUGGAGGGGGAUUGUGGGGCUGCAG	3688
3902_2_35	LAG3	Exon 2	-	chr12:6773262-6773287	CCUGGAGGGGGAUUGUGGGGCUGCA	3689
3902_2_36	LAG3	Exon 2	-	chr12:6773263-6773288	UCCUGGAGGGGGAUUGUGGGGCUGC	3690
3902_2_37	LAG3	Exon 2	-	chr12:6773270-6773295	GCUGAGAUCCUGGAGGGGGAUUGUG	3691
3902_2_38	LAG3	Exon 2	-	chr12:6773271-6773296	GGCUGAGAUCCUGGAGGGGGAUUGU	3692
3902_2_39	LAG3	Exon 2	-	chr12:6773272-6773297	AGGCUGAGAUCCUGGAGGGGGAUUG	3693
3902_2_40	LAG3	Exon 2	-	chr12:6773279-6773304	UCGCAGAAGGCUGAGAUCCUGGAGG	3694
3902_2_41	LAG3	Exon 2	-	chr12:6773280-6773305	UUCGCAGAAGGCUGAGAUCCUGGAG	3695
3902_2_42	LAG3	Exon 2	-	chr12:6773281-6773306	CUUCGCAGAAGGCUGAGAUCCUGGA	3696
3902_2_43	LAG3	Exon 2	-	chr12:6773282-6773307	UCUUCGCAGAAGGCUGAGAUCCUGG	3697
3902_2_44	LAG3	Exon 2	-	chr12:6773285-6773310	UGCUCUUCGCAGAAGGCUGAGAUCC	3698
3902_2_45	LAG3	Exon 2	-	chr12:6773297-6773322	CCAAGUGACCCCUGCUCUUCGCAGA	3699
3902_2_46	LAG3	Exon 2	-	chr12:6773334-6773359	CCCAAGUUUGGGGUGCAUACCUGUC	3700
3902_3_1	LAG3	Exon 3	+	chr12:6773671-6773696	CAACUCCAUUCUCUUUCCCGCCCAG	3701
3902_3_2	LAG3	Exon 3	+	chr12:6773692-6773717	CCAGUGGCCCGCCCGCUGCCGCCCC	3702

3902_3_3	LAG3	Exon 3	+	chr12:6773703 -6773728	CCCGCUGCCGCCCCCGGCCA UCCCC	3703
3902_3_4	LAG3	Exon 3	+	chr12:6773710 -6773735	CCGCCCCCGGCCAUCCCCUG GCCCC	3704
3902_3_5	LAG3	Exon 3	+	chr12:6773721 -6773746	CAUCCCCUGGCCCCCGGCCC UCACC	3705
3902_3_6	LAG3	Exon 3	+	chr12:6773724 -6773749	CCCCUGGCCCCCGGCCCUCA CCCGG	3706
3902_3_7	LAG3	Exon 3	+	chr12:6773738 -6773763	CCCUCACCCGGCGGCGCCCU CCUCC	3707
3902_3_8	LAG3	Exon 3	+	chr12:6773739 -6773764	CCUCACCCGGCGGCGCCCUC CUCCU	3708
3902_3_9	LAG3	Exon 3	+	chr12:6773740 -6773765	CUCACCCGGCGGCGCCCUCC UCCUG	3709
3902_3_10	LAG3	Exon 3	+	chr12:6773741 -6773766	UCACCCGGCGGCGCCCUCCU CCUGG	3710
3902_3_11	LAG3	Exon 3	+	chr12:6773747 -6773772	GGCGGCGCCCUCCUCCUGGG GGCCC	3711
3902_3_12	LAG3	Exon 3	+	chr12:6773763 -6773788	UGGGGGCCCAGGCCCCGCCG CUACA	3712
3902_3_13	LAG3	Exon 3	+	chr12:6773775 -6773800	CCCCGCCGCUACACGGUGCU GAGCG	3713
3902_3_14	LAG3	Exon 3	+	chr12:6773776 -6773801	CCCGCCGCUACACGGUGCUG AGCGU	3714
3902_3_15	LAG3	Exon 3	+	chr12:6773782 -6773807	GCUACACGGUGCUGAGCGU GGGUCC	3715
3902_3_16	LAG3	Exon 3	+	chr12:6773785 -6773810	ACACGGUGCUGAGCGUGGG UCCCGG	3716
3902_3_17	LAG3	Exon 3	+	chr12:6773797 -6773822	GCGUGGGUCCCGGAGGCCU GCGCAG	3717
3902_3_18	LAG3	Exon 3	+	chr12:6773798 -6773823	CGUGGGUCCCGGAGGCCUG CGCAGC	3718
3902_3_19	LAG3	Exon 3	+	chr12:6773801 -6773826	GGGUCCCGGAGGCCUGCGC AGCGGG	3719
3902_3_20	LAG3	Exon 3	+	chr12:6773829 -6773854	CUGCCCCUGCAGCCCCGCGU CCAGC	3720
3902_3_21	LAG3	Exon 3	+	chr12:6773839 -6773864	AGCCCCGCGUCCAGCUGGA UGAGCG	3721
3902_3_22	LAG3	Exon 3	+	chr12:6773843 -6773868	CCGCGUCCAGCUGGAUGAG CGCGGC	3722
3902_3_23	LAG3	Exon 3	+	chr12:6773851 -6773876	AGCUGGAUGAGCGCGGCCG GCAGCG	3723
3902_3_24	LAG3	Exon 3	+	chr12:6773852 -6773877	GCUGGAUGAGCGCGGCCGG CAGCGC	3724
3902_3_25	LAG3	Exon 3	+	chr12:6773853 -6773878	CUGGAUGAGCGCGGCCGGC AGCGCG	3725
3902_3_26	LAG3	Exon 3	+	chr12:6773867 -6773892	CCGGCAGCGCGGGGACUUC UCGCUA	3726
3902_3_27	LAG3	Exon 3	+	chr12:6773882 -6773907	CUUCUCGCUAUGGCUGCGC CCAGCC	3727

3902_3_28	LAG3	Exon 3	+	chr12:6773889-6773914	CUAUGGCUGCGCCCAGCCCGGCGCG	3728
3902_3_29	LAG3	Exon 3	+	chr12:6773896-6773921	UGCGCCCAGCCCGGCGCGCGGACGC	3729
3902_3_30	LAG3	Exon 3	+	chr12:6773913-6773938	GCGGACGCCGGCGAGUACCGCGCCG	3730
3902_3_31	LAG3	Exon 3	+	chr12:6773924-6773949	CGAGUACCGCGCCGCGGUGCACCUC	3731
3902_3_32	LAG3	Exon 3	+	chr12:6773925-6773950	GAGUACCGCGCCGCGGUGCACCUCA	3732
3902_3_33	LAG3	Exon 3	+	chr12:6773981-6774006	GCGCCUGGGCCAGGCCUCGAGUAUG	3733
3902_3_34	LAG3	Exon 3	+	chr12:6773982-6774007	CGCCUGGGCCAGGCCUCGAGUAUGU	3734
3902_3_35	LAG3	Exon 3	+	chr12:6773983-6774008	GCCUGGGCCAGGCCUCGAGUAUGUG	3735
3902_3_36	LAG3	Exon 3	+	chr12:6773986-6774011	UGGGCCAGGCCUCGAGUAUGUGGGG	3736
3902_3_37	LAG3	Exon 3	+	chr12:6773987-6774012	GGGCCAGGCCUCGAGUAUGUGGGGC	3737
3902_3_38	LAG3	Exon 3	+	chr12:6773994-6774019	GCCUCGAGUAUGUGGGGCGGGACGA	3738
3902_3_39	LAG3	Exon 3	+	chr12:6773995-6774020	CCUCGAGUAUGUGGGGCGGGACGAU	3739
3902_3_40	LAG3	Exon 3	-	chr12:6773679-6773704	GCGGGCCACUGGGCGGGAAAGAGAA	3740
3902_3_41	LAG3	Exon 3	-	chr12:6773690-6773715	GGCGGCAGCGGGCGGGCCACUGGGC	3741
3902_3_42	LAG3	Exon 3	-	chr12:6773691-6773716	GGGCGGCAGCGGGCGGGCCACUGGG	3742
3902_3_43	LAG3	Exon 3	-	chr12:6773694-6773719	CGGGGGCGGCAGCGGGCGGGCCACU	3743
3902_3_44	LAG3	Exon 3	-	chr12:6773695-6773720	CCGGGGGCGGCAGCGGGCGGGCCAC	3744
3902_3_45	LAG3	Exon 3	-	chr12:6773702-6773727	GGGAUGGCCGGGGGCGGCAGCGGGC	3745
3902_3_46	LAG3	Exon 3	-	chr12:6773703-6773728	GGGGAUGGCCGGGGGCGGCAGCGGG	3746
3902_3_47	LAG3	Exon 3	-	chr12:6773706-6773731	CCAGGGGAUGGCCGGGGGCGGCAGC	3747
3902_3_48	LAG3	Exon 3	-	chr12:6773707-6773732	GCCAGGGGAUGGCCGGGGGCGGCAG	3748
3902_3_49	LAG3	Exon 3	-	chr12:6773713-6773738	CCGGGGGCCAGGGGAUGGCCGGGGG	3749
3902_3_50	LAG3	Exon 3	-	chr12:6773716-6773741	GGGCCGGGGGCCAGGGGAUGGCCGG	3750
3902_3_51	LAG3	Exon 3	-	chr12:6773717-6773742	AGGGCCGGGGGCCAGGGGAUGGCCG	3751
3902_3_52	LAG3	Exon 3	-	chr12:6773718-6773743	GAGGGCCGGGGGCCAGGGGAUGGCC	3752

3902_3_53	LAG3	Exon 3	-	chr12:6773719-6773744	UGAGGGCCGGGGGCCAGGGGAUGGC	3753
3902_3_54	LAG3	Exon 3	-	chr12:6773723-6773748	CGGGUGAGGGCCGGGGGCCAGGGGA	3754
3902_3_55	LAG3	Exon 3	-	chr12:6773727-6773752	CCGCCGGGUGAGGGCCGGGGGCCAG	3755
3902_3_56	LAG3	Exon 3	-	chr12:6773728-6773753	GCCGCCGGGUGAGGGCCGGGGGCCA	3756
3902_3_57	LAG3	Exon 3	-	chr12:6773729-6773754	CGCCGCCGGGUGAGGGCCGGGGGCC	3757
3902_3_58	LAG3	Exon 3	-	chr12:6773734-6773759	GAGGGCGCCGCCGGGUGAGGGCCGG	3758
3902_3_59	LAG3	Exon 3	-	chr12:6773735-6773760	GGAGGGCGCCGCCGGGUGAGGGCCG	3759
3902_3_60	LAG3	Exon 3	-	chr12:6773736-6773761	AGGAGGGCGCCGCCGGGUGAGGGCC	3760
3902_3_61	LAG3	Exon 3	-	chr12:6773737-6773762	GAGGAGGGCGCCGCCGGGUGAGGGC	3761
3902_3_62	LAG3	Exon 3	-	chr12:6773741-6773766	CCAGGAGGAGGGCGCCGCCGGGUGA	3762
3902_3_63	LAG3	Exon 3	-	chr12:6773742-6773767	CCCAGGAGGAGGGCGCCGCCGGGUG	3763
3902_3_64	LAG3	Exon 3	-	chr12:6773747-6773772	GGGCCCCCAGGAGGAGGGCGCCGCC	3764
3902_3_65	LAG3	Exon 3	-	chr12:6773748-6773773	UGGGCCCCCAGGAGGAGGGCGCCGC	3765
3902_3_66	LAG3	Exon 3	-	chr12:6773757-6773782	GGCGGGGCCUGGGCCCCCAGGAGGA	3766
3902_3_67	LAG3	Exon 3	-	chr12:6773758-6773783	CGGCGGGGCCUGGGCCCCCAGGAGG	3767
3902_3_68	LAG3	Exon 3	-	chr12:6773761-6773786	UAGCGGCGGGGCCUGGGCCCCCAGG	3768
3902_3_69	LAG3	Exon 3	-	chr12:6773764-6773789	GUGUAGCGGCGGGGCCUGGGCCCCC	3769
3902_3_70	LAG3	Exon 3	-	chr12:6773772-6773797	UCAGCACCGUGUAGCGGCGGGGCCU	3770
3902_3_71	LAG3	Exon 3	-	chr12:6773773-6773798	CUCAGCACCGUGUAGCGGCGGGGCC	3771
3902_3_72	LAG3	Exon 3	-	chr12:6773778-6773803	CCACGCUCAGCACCGUGUAGCGGCG	3772
3902_3_73	LAG3	Exon 3	-	chr12:6773779-6773804	CCCACGCUCAGCACCGUGUAGCGGC	3773
3902_3_74	LAG3	Exon 3	-	chr12:6773780-6773805	ACCCACGCUCAGCACCGUGUAGCGG	3774
3902_3_75	LAG3	Exon 3	-	chr12:6773783-6773808	GGGACCCACGCUCAGCACCGUGUAG	3775
3902_3_76	LAG3	Exon 3	-	chr12:6773808-6773833	GCAGCCUCCCGCUGCGCAGGCCUCC	3776
3902_3_77	LAG3	Exon 3	-	chr12:6773809-6773834	GGCAGCCUCCCGCUGCGCAGGCCUC	3777

3902_3_78	LAG3	Exon 3	-	chr12:6773816-6773841	CUGCAGGGGCAGCCUCCCGCUGCGC	3778
3902_3_79	LAG3	Exon 3	-	chr12:6773835-6773860	CAUCCAGCUGGACGCGGGGCUGCAG	3779
3902_3_80	LAG3	Exon 3	-	chr12:6773836-6773861	UCAUCCAGCUGGACGCGGGGCUGCA	3780
3902_3_81	LAG3	Exon 3	-	chr12:6773837-6773862	CUCAUCCAGCUGGACGCGGGGCUGC	3781
3902_3_82	LAG3	Exon 3	-	chr12:6773844-6773869	GGCCGCGCUCAUCCAGCUGGACGCG	3782
3902_3_83	LAG3	Exon 3	-	chr12:6773845-6773870	CGGCCGCGCUCAUCCAGCUGGACGC	3783
3902_3_84	LAG3	Exon 3	-	chr12:6773846-6773871	CCGGCCGCGCUCAUCCAGCUGGACG	3784
3902_3_85	LAG3	Exon 3	-	chr12:6773852-6773877	GCGCUGCCGGCCGCGCUCAUCCAGC	3785
3902_3_86	LAG3	Exon 3	-	chr12:6773870-6773895	CCAUAGCGAGAAGUCCCCGCGCUGC	3786
3902_3_87	LAG3	Exon 3	-	chr12:6773903-6773928	CUCGCCGGCGUCCGCGCGCCGGGCU	3787
3902_3_88	LAG3	Exon 3	-	chr12:6773904-6773929	ACUCGCCGGCGUCCGCGCGCCGGGC	3788
3902_3_89	LAG3	Exon 3	-	chr12:6773908-6773933	CGGUACUCGCCGGCGUCCGCGCGCC	3789
3902_3_90	LAG3	Exon 3	-	chr12:6773909-6773934	GCGGUACUCGCCGGCGUCCGCGCGC	3790
3902_3_91	LAG3	Exon 3	-	chr12:6773923-6773948	AGGUGCACCGCGGCGCGGUACUCGC	3791
3902_3_92	LAG3	Exon 3	-	chr12:6773933-6773958	CGGGUCCCUGAGGUGCACCGCGGCG	3792
3902_3_93	LAG3	Exon 3	-	chr12:6773938-6773963	UCCCGCGGGUCCCUGAGGUGCACCG	3793
3902_3_94	LAG3	Exon 3	-	chr12:6773948-6773973	CGCCGUCCUCUCCCGCGGGUCCCUG	3794
3902_3_95	LAG3	Exon 3	-	chr12:6773957-6773982	GUCUGCCUCCGCCGUCCUCUCCCGC	3795
3902_4_1	LAG3	Exon 4	+	chr12:6774585-6774610	CUUGCACAGUGACUGCCAGCCCCCC	3796
3902_4_2	LAG3	Exon 4	+	chr12:6774607-6774632	CCCAGGAUCUCUCAGAGCCUCCGAC	3797
3902_4_3	LAG3	Exon 4	+	chr12:6774608-6774633	CCAGGAUCUCUCAGAGCCUCCGACU	3798
3902_4_4	LAG3	Exon 4	+	chr12:6774661-6774686	CCCUGACCGCCCAGCCUCUGUGCAU	3799
3902_4_5	LAG3	Exon 4	+	chr12:6774667-6774692	CCGCCCAGCCUCUGUGCAUUGGUUC	3800
3902_4_6	LAG3	Exon 4	+	chr12:6774673-6774698	AGCCUCUGUGCAUUGGUUCCGGAAC	3801
3902_4_7	LAG3	Exon 4	+	chr12:6774674-6774699	GCCUCUGUGCAUUGGUUCCGGAACC	3802

3902_4_8	LAG3	Exon 4	+	chr12:6774675-6774700	CCUCUGUGCAUUGGUUCCGGAACCG	3803
3902_4_9	LAG3	Exon 4	+	chr12:6774680-6774705	GUGCAUUGGUUCCGGAACCGGGGCC	3804
3902_4_10	LAG3	Exon 4	+	chr12:6774681-6774706	UGCAUUGGUUCCGGAACCGGGGCCA	3805
3902_4_11	LAG3	Exon 4	+	chr12:6774697-6774722	CCGGGGCCAGGGCCGAGUCCCUGUC	3806
3902_4_12	LAG3	Exon 4	+	chr12:6774698-6774723	CGGGGCCAGGGCCGAGUCCCUGUCC	3807
3902_4_13	LAG3	Exon 4	+	chr12:6774722-6774747	CGGGAGUCCCCCCAUCACCACUUAG	3808
3902_4_14	LAG3	Exon 4	+	chr12:6774758-6774783	CUCUUCCUGCCCCAAGUCAGCCCCA	3809
3902_4_15	LAG3	Exon 4	+	chr12:6774765-6774790	UGCCCCAAGUCAGCCCCAUGGACUC	3810
3902_4_16	LAG3	Exon 4	+	chr12:6774766-6774791	GCCCCAAGUCAGCCCCAUGGACUCU	3811
3902_4_17	LAG3	Exon 4	+	chr12:6774772-6774797	AGUCAGCCCCAUGGACUCUGGGCCC	3812
3902_4_18	LAG3	Exon 4	+	chr12:6774773-6774798	GUCAGCCCCAUGGACUCUGGGCCCU	3813
3902_4_19	LAG3	Exon 4	+	chr12:6774774-6774799	UCAGCCCCAUGGACUCUGGGCCCUG	3814
3902_4_20	LAG3	Exon 4	+	chr12:6774798-6774823	GGGGCUGCAUCCUCACCUACAGAGA	3815
3902_4_21	LAG3	Exon 4	+	chr12:6774836-6774861	UCCAUCAUGUAUAACCUCACUGUUC	3816
3902_4_22	LAG3	Exon 4	+	chr12:6774837-6774862	CCAUCAUGUAUAACCUCACUGUUCU	3817
3902_4_23	LAG3	Exon 4	-	chr12:6774587-6774612	CUGGGGGGCUGGCAGUCACUGUGCA	3818
3902_4_24	LAG3	Exon 4	-	chr12:6774603-6774628	GAGGCUCUGAGAGAUCCUGGGGGGC	3819
3902_4_25	LAG3	Exon 4	-	chr12:6774607-6774632	GUCGGAGGCUCUGAGAGAUCCUGGG	3820
3902_4_26	LAG3	Exon 4	-	chr12:6774608-6774633	AGUCGGAGGCUCUGAGAGAUCCUGG	3821
3902_4_27	LAG3	Exon 4	-	chr12:6774609-6774634	CAGUCGGAGGCUCUGAGAGAUCCUG	3822
3902_4_28	LAG3	Exon 4	-	chr12:6774610-6774635	CCAGUCGGAGGCUCUGAGAGAUCCU	3823
3902_4_29	LAG3	Exon 4	-	chr12:6774611-6774636	CCCAGUCGGAGGCUCUGAGAGAUCC	3824
3902_4_30	LAG3	Exon 4	-	chr12:6774627-6774652	GAGCAGUUCAAAAUGACCCAGUCGG	3825
3902_4_31	LAG3	Exon 4	-	chr12:6774630-6774655	AAGGAGCAGUUCAAAAUGACCCAGU	3826
3902_4_32	LAG3	Exon 4	-	chr12:6774654-6774679	GAGGCUGGGCGGUCAGGGCGGCUGA	3827

3902_4_33	LAG3	Exon 4	-	chr12:6774661-6774686	AUGCACAGAGGCUGGGCGGUCAGGG	3828
3902_4_34	LAG3	Exon 4	-	chr12:6774664-6774689	CCAAUGCACAGAGGCUGGGCGGUCA	3829
3902_4_35	LAG3	Exon 4	-	chr12:6774665-6774690	ACCAAUGCACAGAGGCUGGGCGGUC	3830
3902_4_36	LAG3	Exon 4	-	chr12:6774670-6774695	CCGGAACCAAUGCACAGAGGCUGGG	3831
3902_4_37	LAG3	Exon 4	-	chr12:6774673-6774698	GUUCCGGAACCAAUGCACAGAGGCU	3832
3902_4_38	LAG3	Exon 4	-	chr12:6774674-6774699	GGUUCCGGAACCAAUGCACAGAGGC	3833
3902_4_39	LAG3	Exon 4	-	chr12:6774678-6774703	CCCCGGUUCCGGAACCAAUGCACAG	3834
3902_4_40	LAG3	Exon 4	-	chr12:6774694-6774719	AGGGACUCGGCCCUGGCCCCGGUUC	3835
3902_4_41	LAG3	Exon 4	-	chr12:6774700-6774725	CCGGACAGGGACUCGGCCCUGGCCC	3836
3902_4_42	LAG3	Exon 4	-	chr12:6774706-6774731	GGACUCCCGGACAGGGACUCGGCCC	3837
3902_4_43	LAG3	Exon 4	-	chr12:6774712-6774737	AUGGGGGGACUCCCGGACAGGGACU	3838
3902_4_44	LAG3	Exon 4	-	chr12:6774718-6774743	GUGGUGAUGGGGGGACUCCCGGACA	3839
3902_4_45	LAG3	Exon 4	-	chr12:6774719-6774744	AGUGGUGAUGGGGGGACUCCCGGAC	3840
3902_4_46	LAG3	Exon 4	-	chr12:6774724-6774749	CGCUAAGUGGUGAUGGGGGGACUCC	3841
3902_4_47	LAG3	Exon 4	-	chr12:6774732-6774757	AAGCUUUCCGCUAAGUGGUGAUGGG	3842
3902_4_48	LAG3	Exon 4	-	chr12:6774733-6774758	GAAGCUUUCCGCUAAGUGGUGAUGG	3843
3902_4_49	LAG3	Exon 4	-	chr12:6774734-6774759	GGAAGCUUUCCGCUAAGUGGUGAUG	3844
3902_4_50	LAG3	Exon 4	-	chr12:6774735-6774760	AGGAAGCUUUCCGCUAAGUGGUGAU	3845
3902_4_51	LAG3	Exon 4	-	chr12:6774736-6774761	GAGGAAGCUUUCCGCUAAGUGGUGA	3846
3902_4_52	LAG3	Exon 4	-	chr12:6774742-6774767	CAGGAAGAGGAAGCUUUCCGCUAAG	3847
3902_4_53	LAG3	Exon 4	-	chr12:6774760-6774785	CAUGGGGCUGACUUGGGGCAGGAAG	3848
3902_4_54	LAG3	Exon 4	-	chr12:6774766-6774791	AGAGUCCAUGGGGCUGACUUGGGGC	3849
3902_4_55	LAG3	Exon 4	-	chr12:6774770-6774795	GCCCAGAGUCCAUGGGGCUGACUUG	3850
3902_4_56	LAG3	Exon 4	-	chr12:6774771-6774796	GGCCCAGAGUCCAUGGGGCUGACUU	3851
3902_4_57	LAG3	Exon 4	-	chr12:6774772-6774797	GGGCCCAGAGUCCAUGGGGCUGACU	3852

3902_4_58	LAG3	Exon 4	-	chr12:6774781 -6774806	GCAGCCCCAGGGCCCAGAG UCCAUG	3853
3902_4_59	LAG3	Exon 4	-	chr12:6774782 -6774807	UGCAGCCCCAGGGCCCAGA GUCCAU	3854
3902_4_60	LAG3	Exon 4	-	chr12:6774783 -6774808	AUGCAGCCCCAGGGCCCAG AGUCCA	3855
3902_4_61	LAG3	Exon 4	-	chr12:6774797 -6774822	CUCUGUAGGUGAGGAUGCA GCCCCA	3856
3902_4_62	LAG3	Exon 4	-	chr12:6774798 -6774823	UCUCUGUAGGUGAGGAUGC AGCCCC	3857
3902_4_63	LAG3	Exon 4	-	chr12:6774811 -6774836	GACGUUGAAGCCAUCUCUG UAGGUG	3858
3902_4_64	LAG3	Exon 4	-	chr12:6774816 -6774841	AUGGAGACGUUGAAGCCAU CUCUGU	3859
3902_4_65	LAG3	Exon 4	-	chr12:6774840 -6774865	CCCAGAACAGUGAGGUUAU ACAUGA	3860
3902_4_66	LAG3	Exon 4	-	chr12:6774853 -6774878	AGUGGGGGAGUUACCCAGA ACAGUG	3861
3902_5_1	LAG3	Exon 5	+	chr12:6775250 -6775275	UUGGGUUUUCUUUUCUCUU CAGGUC	3862
3902_5_2	LAG3	Exon 5	+	chr12:6775281 -6775306	CCCCAACUCCCUUGACAGUG UACGC	3863
3902_5_3	LAG3	Exon 5	+	chr12:6775287 -6775312	CUCCCUUGACAGUGUACGC UGGAGC	3864
3902_5_4	LAG3	Exon 5	+	chr12:6775294 -6775319	GACAGUGUACGCUGGAGCA GGUUCC	3865
3902_5_5	LAG3	Exon 5	+	chr12:6775295 -6775320	ACAGUGUACGCUGGAGCAG GUUCCA	3866
3902_5_6	LAG3	Exon 5	+	chr12:6775298 -6775323	GUGUACGCUGGAGCAGGUU CCAGGG	3867
3902_5_7	LAG3	Exon 5	+	chr12:6775299 -6775324	UGUACGCUGGAGCAGGUUC CAGGGU	3868
3902_5_8	LAG3	Exon 5	+	chr12:6775300 -6775325	GUACGCUGGAGCAGGUUCC AGGGUG	3869
3902_5_9	LAG3	Exon 5	+	chr12:6775323 -6775348	UGGGGCUGCCCUGCCGCCU GCCUGC	3870
3902_5_10	LAG3	Exon 5	+	chr12:6775328 -6775353	CUGCCCUGCCGCCUGCCUGC UGGUG	3871
3902_5_11	LAG3	Exon 5	+	chr12:6775329 -6775354	UGCCCUGCCGCCUGCCUGCU GGUGU	3872
3902_5_12	LAG3	Exon 5	+	chr12:6775330 -6775355	GCCCUGCCGCCUGCCUGCUG GUGUG	3873
3902_5_13	LAG3	Exon 5	+	chr12:6775336 -6775361	CCGCCUGCCUGCUGGUGUG GGGACC	3874
3902_5_14	LAG3	Exon 5	+	chr12:6775357 -6775382	GACCCGGUCUUUCCUCACU GCCAAG	3875
3902_5_15	LAG3	Exon 5	+	chr12:6775368 -6775393	UCCUCACUGCCAAGUGGAC UCCUCC	3876
3902_5_16	LAG3	Exon 5	+	chr12:6775369 -6775394	CCUCACUGCCAAGUGGACU CCUCCU	3877

3902_5_17	LAG3	Exon 5	+	chr12:6775370-6775395	CUCACUGCCAAGUGGACUCCUCCUG	3878
3902_5_18	LAG3	Exon 5	+	chr12:6775371-6775396	UCACUGCCAAGUGGACUCCUCCUGG	3879
3902_5_19	LAG3	Exon 5	+	chr12:6775374-6775399	CUGCCAAGUGGACUCCUCCUGGGGG	3880
3902_5_20	LAG3	Exon 5	+	chr12:6775388-6775413	CCUCCUGGGGGAGGCCCUGACCUCC	3881
3902_5_21	LAG3	Exon 5	+	chr12:6775395-6775420	GGGGAGGCCCUGACCUCCUGGUGAC	3882
3902_5_22	LAG3	Exon 5	+	chr12:6775404-6775429	CUGACCUCCUGGUGACUGGAGACAA	3883
3902_5_23	LAG3	Exon 5	+	chr12:6775427-6775452	AAUGGCGACUUUACCCUUCGACUAG	3884
3902_5_24	LAG3	Exon 5	+	chr12:6775439-6775464	ACCCUUCGACUAGAGGAUGUGAGCC	3885
3902_5_25	LAG3	Exon 5	+	chr12:6775445-6775470	CGACUAGAGGAUGUGAGCCAGGCCC	3886
3902_5_26	LAG3	Exon 5	+	chr12:6775449-6775474	UAGAGGAUGUGAGCCAGGCCCAGGC	3887
3902_5_27	LAG3	Exon 5	+	chr12:6775450-6775475	AGAGGAUGUGAGCCAGGCCCAGGCU	3888
3902_5_28	LAG3	Exon 5	+	chr12:6775478-6775503	ACCUACACCUGCCAUAUCCAUCUGC	3889
3902_5_29	LAG3	Exon 5	+	chr12:6775508-6775533	CAGCAGCUCAAUGCCACUGUCACAU	3890
3902_5_30	LAG3	Exon 5	+	chr12:6775521-6775546	CCACUGUCACAUUGGCAAUCAUCAC	3891
3902_5_31	LAG3	Exon 5	+	chr12:6775532-6775557	UUGGCAAUCAUCACAGGUCAGCCUC	3892
3902_5_32	LAG3	Exon 5	+	chr12:6775535-6775560	GCAAUCAUCACAGGUCAGCCUCAGG	3893
3902_5_33	LAG3	Exon 5	+	chr12:6775536-6775561	CAAUCAUCACAGGUCAGCCUCAGGU	3894
3902_5_34	LAG3	Exon 5	+	chr12:6775541-6775566	AUCACAGGUCAGCCUCAGGUGGGAA	3895
3902_5_35	LAG3	Exon 5	-	chr12:6775283-6775308	CAGCGUACACUGUCAAGGGAGUUGG	3896
3902_5_36	LAG3	Exon 5	-	chr12:6775284-6775309	CCAGCGUACACUGUCAAGGGAGUUG	3897
3902_5_37	LAG3	Exon 5	-	chr12:6775285-6775310	UCCAGCGUACACUGUCAAGGGAGUU	3898
3902_5_38	LAG3	Exon 5	-	chr12:6775286-6775311	CUCCAGCGUACACUGUCAAGGGAGU	3899
3902_5_39	LAG3	Exon 5	-	chr12:6775292-6775317	AACCUGCUCCAGCGUACACUGUCAA	3900
3902_5_40	LAG3	Exon 5	-	chr12:6775293-6775318	GAACCUGCUCCAGCGUACACUGUCA	3901
3902_5_41	LAG3	Exon 5	-	chr12:6775320-6775345	GGCAGGCGGCAGGGCAGCCCCACCC	3902

3902_5_42	LAG3	Exon 5	-	chr12:6775334-6775359	UCCCCACACCAGCAGGCAGGCGGCA	3903
3902_5_43	LAG3	Exon 5	-	chr12:6775335-6775360	GUCCCCACACCAGCAGGCAGGCGGC	3904
3902_5_44	LAG3	Exon 5	-	chr12:6775339-6775364	CCGGGUCCCCACACCAGCAGGCAGG	3905
3902_5_45	LAG3	Exon 5	-	chr12:6775342-6775367	AGACCGGGUCCCCACACCAGCAGGC	3906
3902_5_46	LAG3	Exon 5	-	chr12:6775346-6775371	GGAAAGACCGGGUCCCCACACCAGC	3907
3902_5_47	LAG3	Exon 5	-	chr12:6775362-6775387	GUCCACUUGGCAGUGAGGAAAGACC	3908
3902_5_48	LAG3	Exon 5	-	chr12:6775363-6775388	AGUCCACUUGGCAGUGAGGAAAGAC	3909
3902_5_49	LAG3	Exon 5	-	chr12:6775372-6775397	CCCAGGAGGAGUCCACUUGGCAGUG	3910
3902_5_50	LAG3	Exon 5	-	chr12:6775380-6775405	GGGCCUCCCCCAGGAGGAGUCCACU	3911
3902_5_51	LAG3	Exon 5	-	chr12:6775391-6775416	CCAGGAGGUCAGGGCCUCCCCCAGG	3912
3902_5_52	LAG3	Exon 5	-	chr12:6775394-6775419	UCACCAGGAGGUCAGGGCCUCCCCC	3913
3902_5_53	LAG3	Exon 5	-	chr12:6775405-6775430	AUUGUCUCCAGUCACCAGGAGGUCA	3914
3902_5_54	LAG3	Exon 5	-	chr12:6775406-6775431	CAUUGUCUCCAGUCACCAGGAGGUC	3915
3902_5_55	LAG3	Exon 5	-	chr12:6775411-6775436	GUCGCCAUUGUCUCCAGUCACCAGG	3916
3902_5_56	LAG3	Exon 5	-	chr12:6775414-6775439	AAAGUCGCCAUUGUCUCCAGUCACC	3917
3902_5_57	LAG3	Exon 5	-	chr12:6775443-6775468	GCCUGGCUCACAUCCUCUAGUCGAA	3918
3902_5_58	LAG3	Exon 5	-	chr12:6775444-6775469	GGCCUGGCUCACAUCCUCUAGUCGA	3919
3902_5_59	LAG3	Exon 5	-	chr12:6775465-6775490	GCAGGUGUAGGUCCCAGCCUGGGCC	3920
3902_5_60	LAG3	Exon 5	-	chr12:6775470-6775495	AUAUGGCAGGUGUAGGUCCCAGCCU	3921
3902_5_61	LAG3	Exon 5	-	chr12:6775471-6775496	GAUAUGGCAGGUGUAGGUCCCAGCC	3922
3902_5_62	LAG3	Exon 5	-	chr12:6775482-6775507	UCCUGCAGAUGGAUAUGGCAGGUGU	3923
3902_5_63	LAG3	Exon 5	-	chr12:6775488-6775513	UGCUGUUCCUGCAGAUGGAUAUGGC	3924
3902_5_64	LAG3	Exon 5	-	chr12:6775492-6775517	GAGCUGCUGUUCCUGCAGAUGGAUA	3925
3902_5_65	LAG3	Exon 5	-	chr12:6775498-6775523	GGCAUUGAGCUGCUGUUCCUGCAGA	3926
3902_5_66	LAG3	Exon 5	-	chr12:6775524-6775549	CCUGUGAUGAUUGCCAAUGUGACAG	3927

3902_6_1	LAG3	Exon 6	+	chr12:6777254 -6777279	UCUUUUCAGUGACUCCCAA AUCCUU	3928
3902_6_2	LAG3	Exon 6	+	chr12:6777255 -6777280	CUUUUCAGUGACUCCCAAA UCCUUU	3929
3902_6_3	LAG3	Exon 6	+	chr12:6777263 -6777288	UGACUCCCAAAUCCUUUGG GUCACC	3930
3902_6_4	LAG3	Exon 6	+	chr12:6777271 -6777296	AAAUCCUUUGGGUCACCUG GAUCCC	3931
3902_6_5	LAG3	Exon 6	+	chr12:6777272 -6777297	AAUCCUUUGGGUCACCUGG AUCCCU	3932
3902_6_6	LAG3	Exon 6	+	chr12:6777273 -6777298	AUCCUUUGGGUCACCUGGA UCCCUG	3933
3902_6_7	LAG3	Exon 6	+	chr12:6777289 -6777314	GGAUCCCUGGGGAAGCUGC UUUGUG	3934
3902_6_8	LAG3	Exon 6	+	chr12:6777305 -6777330	UGCUUUGUGAGGUGACUCC AGUAUC	3935
3902_6_9	LAG3	Exon 6	+	chr12:6777324 -6777349	AGUAUCUGGACAAGAACGC UUUGUG	3936
3902_6_10	LAG3	Exon 6	+	chr12:6777334 -6777359	CAAGAACGCUUUGUGUGGA GCUCUC	3937
3902_6_11	LAG3	Exon 6	+	chr12:6777351 -6777376	GAGCUCUCUGGACACCCCA UCCCAG	3938
3902_6_12	LAG3	Exon 6	+	chr12:6777362 -6777387	ACACCCCAUCCCAGAGGAG UUUCUC	3939
3902_6_13	LAG3	Exon 6	+	chr12:6777369 -6777394	AUCCCAGAGGAGUUUCUCA GGACCU	3940
3902_6_14	LAG3	Exon 6	+	chr12:6777373 -6777398	CAGAGGAGUUUCUCAGGAC CUUGGC	3941
3902_6_15	LAG3	Exon 6	+	chr12:6777376 -6777401	AGGAGUUUCUCAGGACCUU GGCUGG	3942
3902_6_16	LAG3	Exon 6	+	chr12:6777382 -6777407	UUCUCAGGACCUUGGCUGG AGGCAC	3943
3902_6_17	LAG3	Exon 6	+	chr12:6777385 -6777410	UCAGGACCUUGGCUGGAGG CACAGG	3944
3902_6_18	LAG3	Exon 6	+	chr12:6777408 -6777433	GGAGGCCCAGCUCCUUUCCC AGCCU	3945
3902_6_19	LAG3	Exon 6	+	chr12:6777427 -6777452	CAGCCUUGGCAAUGCCAGC UGUACC	3946
3902_6_20	LAG3	Exon 6	+	chr12:6777428 -6777453	AGCCUUGGCAAUGCCAGCU GUACCA	3947
3902_6_21	LAG3	Exon 6	+	chr12:6777429 -6777454	GCCUUGGCAAUGCCAGCUG UACCAG	3948
3902_6_22	LAG3	Exon 6	+	chr12:6777430 -6777455	CCUUGGCAAUGCCAGCUGU ACCAGG	3949
3902_6_23	LAG3	Exon 6	+	chr12:6777435 -6777460	GCAAUGCCAGCUGUACCAG GGGGAG	3950
3902_6_24	LAG3	Exon 6	+	chr12:6777443 -6777468	AGCUGUACCAGGGGGAGAG GCUUCU	3951
3902_6_25	LAG3	Exon 6	+	chr12:6777479 -6777504	UGUACUUCACAGAGCUGUC UAGCCC	3952

3902_6_26	LAG3	Exon 6	+	chr12:6777486-6777511	CACAGAGCUGUCUAGCCCAGGUCCG	3953
3902_6_27	LAG3	Exon 6	+	chr12:6777501-6777526	CCCAGGUCCGAGGCCCCAGAAUGCC	3954
3902_6_28	LAG3	Exon 6	-	chr12:6777249-6777274	UUUGGGAGUCACUGAAAAGAGUAGA	3955
3902_6_29	LAG3	Exon 6	-	chr12:6777271-6777296	GGGAUCCAGGUGACCCAAAGGAUUU	3956
3902_6_30	LAG3	Exon 6	-	chr12:6777272-6777297	AGGGAUCCAGGUGACCCAAAGGAUU	3957
3902_6_31	LAG3	Exon 6	-	chr12:6777278-6777303	UUCCCCAGGGAUCCAGGUGACCCAA	3958
3902_6_32	LAG3	Exon 6	-	chr12:6777289-6777314	CACAAAGCAGCUUCCCCAGGGAUCC	3959
3902_6_33	LAG3	Exon 6	-	chr12:6777296-6777321	GUCACCUCACAAAGCAGCUUCCCCA	3960
3902_6_34	LAG3	Exon 6	-	chr12:6777297-6777322	AGUCACCUCACAAAGCAGCUUCCCC	3961
3902_6_35	LAG3	Exon 6	-	chr12:6777325-6777350	ACACAAAGCGUUCUUGUCCAGAUAC	3962
3902_6_36	LAG3	Exon 6	-	chr12:6777368-6777393	GGUCCUGAGAAACUCCUCUGGGAUG	3963
3902_6_37	LAG3	Exon 6	-	chr12:6777369-6777394	AGGUCCUGAGAAACUCCUCUGGGAU	3964
3902_6_38	LAG3	Exon 6	-	chr12:6777370-6777395	AAGGUCCUGAGAAACUCCUCUGGGA	3965
3902_6_39	LAG3	Exon 6	-	chr12:6777374-6777399	AGCCAAGGUCCUGAGAAACUCCUCU	3966
3902_6_40	LAG3	Exon 6	-	chr12:6777375-6777400	CAGCCAAGGUCCUGAGAAACUCCUC	3967
3902_6_41	LAG3	Exon 6	-	chr12:6777394-6777419	GCUGGGCCUCCUGUGCCUCCAGCCA	3968
3902_6_42	LAG3	Exon 6	-	chr12:6777416-6777441	CAUUGCCAAGGCUGGGAAAGGAGCU	3969
3902_6_43	LAG3	Exon 6	-	chr12:6777417-6777442	GCAUUGCCAAGGCUGGGAAAGGAGC	3970
3902_6_44	LAG3	Exon 6	-	chr12:6777423-6777448	CAGCUGGCAUUGCCAAGGCUGGGAA	3971
3902_6_45	LAG3	Exon 6	-	chr12:6777428-6777453	UGGUACAGCUGGCAUUGCCAAGGCU	3972
3902_6_46	LAG3	Exon 6	-	chr12:6777429-6777454	CUGGUACAGCUGGCAUUGCCAAGGC	3973
3902_6_47	LAG3	Exon 6	-	chr12:6777433-6777458	CCCCCUGGUACAGCUGGCAUUGCCA	3974
3902_6_48	LAG3	Exon 6	-	chr12:6777444-6777469	AAGAAGCCUCUCCCCCUGGUACAGC	3975
3902_6_49	LAG3	Exon 6	-	chr12:6777453-6777478	UGCUGCUCCAAGAAGCCUCUCCCCC	3976
3902_6_50	LAG3	Exon 6	-	chr12:6777504-6777529	CCUGGCAUUCUGGGGCCUCGGACCU	3977

3902_6_51	LAG3	Exon 6	-	chr12:6777505-6777530	UCCUGGCAUUCUGGGGCCUCGGACC	3978
3902_7_1	LAG3	Exon 7	+	chr12:6777778-6777803	CUUUCUCCAUAGGUGCCCAACGCUC	3979
3902_7_2	LAG3	Exon 7	+	chr12:6777779-6777804	UUUCUCCAUAGGUGCCCAACGCUCU	3980
3902_7_3	LAG3	Exon 7	+	chr12:6777790-6777815	GUGCCCAACGCUCUGGGAGAGCCCC	3981
3902_7_4	LAG3	Exon 7	+	chr12:6777805-6777830	GGAGAGCCCCAGGUGCCCUCCCAGC	3982
3902_7_5	LAG3	Exon 7	+	chr12:6777832-6777857	GCCACCUCCUGCUGUUUCUCAUCCU	3983
3902_7_6	LAG3	Exon 7	+	chr12:6777855-6777880	CUUGGUGUCCUUUCUCUGCUCCUUU	3984
3902_7_7	LAG3	Exon 7	+	chr12:6777862-6777887	UCCUUUCUCUGCUCCUUUUGGUGAC	3985
3902_7_8	LAG3	Exon 7	+	chr12:6777871-6777896	UGCUCCUUUUGGUGACUGGAGCCUU	3986
3902_7_9	LAG3	Exon 7	+	chr12:6777884-6777909	GACUGGAGCCUUUGGCUUUCACCUU	3987
3902_7_10	LAG3	Exon 7	+	chr12:6777894-6777919	UUUGGCUUUCACCUUUGGAGAAGAC	3988
3902_7_11	LAG3	Exon 7	+	chr12:6777903-6777928	CACCUUUGGAGAAGACAGGUGAGCC	3989
3902_7_12	LAG3	Exon 7	+	chr12:6777904-6777929	ACCUUUGGAGAAGACAGGUGAGCCA	3990
3902_7_13	LAG3	Exon 7	+	chr12:6777910-6777935	GGAGAAGACAGGUGAGCCAGGGACA	3991
3902_7_14	LAG3	Exon 7	-	chr12:6777775-6777800	CGUUGGGCACCUAUGGAGAAAGUAC	3992
3902_7_15	LAG3	Exon 7	-	chr12:6777787-6777812	GCUCUCCCAGAGCGUUGGGCACCUA	3993
3902_7_16	LAG3	Exon 7	-	chr12:6777796-6777821	GCACCUGGGGCUCUCCCAGAGCGUU	3994
3902_7_17	LAG3	Exon 7	-	chr12:6777797-6777822	GGCACCUGGGGCUCUCCCAGAGCGU	3995
3902_7_18	LAG3	Exon 7	-	chr12:6777814-6777839	AGGUGGCCUGCUGGGAGGGCACCUG	3996
3902_7_19	LAG3	Exon 7	-	chr12:6777815-6777840	GAGGUGGCCUGCUGGGAGGGCACCU	3997
3902_7_20	LAG3	Exon 7	-	chr12:6777816-6777841	GGAGGUGGCCUGCUGGGAGGGCACC	3998
3902_7_21	LAG3	Exon 7	-	chr12:6777823-6777848	AACAGCAGGAGGUGGCCUGCUGGGA	3999
3902_7_22	LAG3	Exon 7	-	chr12:6777824-6777849	AAACAGCAGGAGGUGGCCUGCUGGG	4000
3902_7_23	LAG3	Exon 7	-	chr12:6777827-6777852	GAGAAACAGCAGGAGGUGGCCUGCU	4001
3902_7_24	LAG3	Exon 7	-	chr12:6777828-6777853	UGAGAAACAGCAGGAGGUGGCCUGC	4002

3902_7_25	LAG3	Exon 7	-	chr12:6777836-6777861	ACCAAGGAUGAGAAACAGCAGGAGG	4003
3902_7_26	LAG3	Exon 7	-	chr12:6777839-6777864	GACACCAAGGAUGAGAAACAGCAGG	4004
3902_7_27	LAG3	Exon 7	-	chr12:6777842-6777867	AAGGACACCAAGGAUGAGAAACAGC	4005
3902_7_28	LAG3	Exon 7	-	chr12:6777857-6777882	CAAAAGGAGCAGAGAAAGGACACCA	4006
3902_7_29	LAG3	Exon 7	-	chr12:6777866-6777891	UCCAGUCACCAAAAGGAGCAGAGAA	4007
3902_7_30	LAG3	Exon 7	-	chr12:6777878-6777903	AAAGCCAAAGGCUCCAGUCACCAAA	4008
3902_7_31	LAG3	Exon 7	-	chr12:6777895-6777920	UGUCUUCUCCAAAGGUGAAAGCCAA	4009
3902_7_32	LAG3	Exon 7	-	chr12:6777908-6777933	UCCCUGGCUCACCUGUCUUCUCCAA	4010
3902_8_1	LAG3	Exon 8	+	chr12:6778218-6778243	UCUCUCUCUCCAUCUCUUCUCACAG	4011
3902_8_2	LAG3	Exon 8	+	chr12:6778250-6778275	CAAGACGAUUUUCUGCCUUAGAGCA	4012
3902_8_3	LAG3	Exon 8	+	chr12:6778251-6778276	AAGACGAUUUUCUGCCUUAGAGCAA	4013
3902_8_4	LAG3	Exon 8	+	chr12:6778267-6778292	UUAGAGCAAGGGAUUCACCCUCCGC	4014
3902_8_5	LAG3	Exon 8	+	chr12:6778285-6778310	CCUCCGCAGGCUCAGAGCAAGAUAG	4015
3902_8_6	LAG3	Exon 8	+	chr12:6778291-6778316	CAGGCUCAGAGCAAGAUAGAGGAGC	4016
3902_8_7	LAG3	Exon 8	+	chr12:6778367-6778392	AGCCCGAGCCGGAGCAGCUCUGACC	4017
3902_8_8	LAG3	Exon 8	+	chr12:6778375-6778400	CCGGAGCAGCUCUGACCUGGAGCUG	4018
3902_8_9	LAG3	Exon 8	+	chr12:6778439-6778464	UCCCUGUCAGCAGCAAGCCUGAGUC	4019
3902_8_10	LAG3	Exon 8	-	chr12:6778230-6778255	UCUUGGUCGCCACUGUGAGAAGAGA	4020
3902_8_11	LAG3	Exon 8	-	chr12:6778252-6778277	CUUGCUCUAAGGCAGAAAAUCGUCU	4021
3902_8_12	LAG3	Exon 8	-	chr12:6778268-6778293	UGCGGAGGGUGAAUCCCUUGCUCUA	4022
3902_8_13	LAG3	Exon 8	-	chr12:6778287-6778312	CUCUAUCUUGCUCUGAGCCUGCGGA	4023
3902_8_14	LAG3	Exon 8	-	chr12:6778288-6778313	CCUCUAUCUUGCUCUGAGCCUGCGG	4024
3902_8_15	LAG3	Exon 8	-	chr12:6778291-6778316	GCUCCUCUAUCUUGCUCUGAGCCUG	4025
3902_8_16	LAG3	Exon 8	-	chr12:6778393-6778418	GAGAUCUGCUGGCUGCCUCAGCUCC	4026
3902_8_17	LAG3	Exon 8	-	chr12:6778409-6778434	UUUGGACUGGGCUGCUGAGAUCUGC	4027

3902_8_18	LAG3	Exon 8	-	chr12:6778426-6778451	UGCUGACAGGGAGUUUAUUUGGACU	4028
3902_8_19	LAG3	Exon 8	-	chr12:6778427-6778452	CUGCUGACAGGGAGUUUAUUUGGAC	4029
3902_8_20	LAG3	Exon 8	-	chr12:6778432-6778457	GCUUGCUGCUGACAGGGAGUUUAUU	4030
3902_8_21	LAG3	Exon 8	-	chr12:6778443-6778468	GCCAGACUCAGGCUUGCUGCUGACA	4031
3902_8_22	LAG3	Exon 8	-	chr12:6778444-6778469	AGCCAGACUCAGGCUUGCUGCUGAC	4032
5133_5_1	PDCD1	Exon 5	+	chr2:241849905-241849930	UAUAAUUAUAAUAUAAUAGAACCAC	4033
5133_5_2	PDCD1	Exon 5	+	chr2:241849906-241849931	AUAAUUAUAAUAUAAUAGAACCACA	4034
5133_5_3	PDCD1	Exon 5	+	chr2:241849910-241849935	UUAUAAUAUAAUAGAACCACAGGGA	4035
5133_5_4	PDCD1	Exon 5	+	chr2:241849911-241849936	UAUAAUAUAAUAGAACCACAGGGAA	4036
5133_5_5	PDCD1	Exon 5	+	chr2:241849912-241849937	AUAAUAUAAUAGAACCACAGGGAAG	4037
5133_5_6	PDCD1	Exon 5	+	chr2:241849913-241849938	UAAUAUAAUAGAACCACAGGGAAGG	4038
5133_5_7	PDCD1	Exon 5	+	chr2:241849936-241849961	GGGGGAUCCCUUGUCCCAGCCACUC	4039
5133_5_8	PDCD1	Exon 5	+	chr2:241849946-241849971	UUGUCCCAGCCACUCAGGUGCCUGC	4040
5133_5_9	PDCD1	Exon 5	+	chr2:241849954-241849979	GCCACUCAGGUGCCUGCUGGCCGCC	4041
5133_5_10	PDCD1	Exon 5	+	chr2:241849961-241849986	AGGUGCCUGCUGGCCGCCUGGAUGC	4042
5133_5_11	PDCD1	Exon 5	+	chr2:241849964-241849989	UGCCUGCUGGCCGCCUGGAUGCUGG	4043
5133_5_12	PDCD1	Exon 5	+	chr2:241849976-241850001	GCCUGGAUGCUGGUGGCCCUGCCCC	4044
5133_5_13	PDCD1	Exon 5	+	chr2:241849981-241850006	GAUGCUGGUGGCCCUGCCCCAGGAG	4045
5133_5_14	PDCD1	Exon 5	+	chr2:241849982-241850007	AUGCUGGUGGCCCUGCCCCAGGAGU	4046
5133_5_15	PDCD1	Exon 5	+	chr2:241849983-241850008	UGCUGGUGGCCCUGCCCCAGGAGUG	4047
5133_5_16	PDCD1	Exon 5	+	chr2:241849984-241850009	GCUGGUGGCCCUGCCCCAGGAGUGG	4048
5133_5_17	PDCD1	Exon 5	+	chr2:241849996-241850021	GCCCCAGGAGUGGGGGUGCAGUGUG	4049
5133_5_18	PDCD1	Exon 5	+	chr2:241850004-241850029	AGUGGGGGUGCAGUGUGUGGAUGUG	4050
5133_5_19	PDCD1	Exon 5	+	chr2:241850009-241850034	GGGUGCAGUGUGUGGAUGUGAGGAG	4051
5133_5_20	PDCD1	Exon 5	+	chr2:241850014-241850039	CAGUGUGUGGAUGUGAGGAGUGGAU	4052

5133_5_21	PDCD1	Exon 5	+	chr2:241850020-241850045	GUGGAUGUGAGGAGUGGAUAGGCCA	4053
5133_5_22	PDCD1	Exon 5	+	chr2:241850023-241850048	GAUGUGAGGAGUGGAUAGGCCACGG	4054
5133_5_23	PDCD1	Exon 5	+	chr2:241850024-241850049	AUGUGAGGAGUGGAUAGGCCACGGC	4055
5133_5_24	PDCD1	Exon 5	+	chr2:241850025-241850050	UGUGAGGAGUGGAUAGGCCACGGCG	4056
5133_5_25	PDCD1	Exon 5	+	chr2:241850026-241850051	GUGAGGAGUGGAUAGGCCACGGCGG	4057
5133_5_26	PDCD1	Exon 5	+	chr2:241850033-241850058	GUGGAUAGGCCACGGCGGGGGUACU	4058
5133_5_27	PDCD1	Exon 5	+	chr2:241850039-241850064	AGGCCACGGCGGGGGUACUAGGCCC	4059
5133_5_28	PDCD1	Exon 5	+	chr2:241850040-241850065	GGCCACGGCGGGGGUACUAGGCCCC	4060
5133_5_29	PDCD1	Exon 5	+	chr2:241850041-241850066	GCCACGGCGGGGGUACUAGGCCCCG	4061
5133_5_30	PDCD1	Exon 5	+	chr2:241850042-241850067	CCACGGCGGGGGUACUAGGCCCCGG	4062
5133_5_31	PDCD1	Exon 5	+	chr2:241850066-241850091	GGGGAACGCCUGUACCUUCCCACCC	4063
5133_5_32	PDCD1	Exon 5	+	chr2:241850072-241850097	CGCCUGUACCUUCCCACCCAGGCCC	4064
5133_5_33	PDCD1	Exon 5	+	chr2:241850075-241850100	CUGUACCUUCCCACCCAGGCCCUGG	4065
5133_5_34	PDCD1	Exon 5	+	chr2:241850076-241850101	UGUACCUUCCCACCCAGGCCCUGGU	4066
5133_5_35	PDCD1	Exon 5	+	chr2:241850083-241850108	UCCCACCCAGGCCCUGGUGGGAGCC	4067
5133_5_36	PDCD1	Exon 5	+	chr2:241850107-241850132	CCGGCCAACCCCUUUAAAUAAUUUC	4068
5133_5_37	PDCD1	Exon 5	+	chr2:241850112-241850137	CAACCCCUUUAAAUAAUUUCAGGAA	4069
5133_5_38	PDCD1	Exon 5	+	chr2:241850113-241850138	AACCCCUUUAAAUAAUUUCAGGAAU	4070
5133_5_39	PDCD1	Exon 5	+	chr2:241850121-241850146	UAAAUAAUUUCAGGAAUGGGUUCCA	4071
5133_5_40	PDCD1	Exon 5	+	chr2:241850133-241850158	GGAAUGGGUUCCAAGGAGAGCUCCC	4072
5133_5_41	PDCD1	Exon 5	+	chr2:241850134-241850159	GAAUGGGUUCCAAGGAGAGCUCCCA	4073
5133_5_42	PDCD1	Exon 5	+	chr2:241850137-241850162	UGGGUUCCAAGGAGAGCUCCCAGGG	4074
5133_5_43	PDCD1	Exon 5	+	chr2:241850138-241850163	GGGUUCCAAGGAGAGCUCCCAGGGU	4075
5133_5_44	PDCD1	Exon 5	+	chr2:241850145-241850170	AAGGAGAGCUCCCAGGGUGGGCACA	4076
5133_5_45	PDCD1	Exon 5	+	chr2:241850146-241850171	AGGAGAGCUCCCAGGGUGGGCACAU	4077

5133_5_46	PDCD1	Exon 5	+	chr2:241850147-241850172	GGAGAGCUCCCAGGGUGGGCACAUG	4078
5133_5_47	PDCD1	Exon 5	+	chr2:241850148-241850173	GAGAGCUCCCAGGGUGGGCACAUGG	4079
5133_5_48	PDCD1	Exon 5	+	chr2:241850149-241850174	AGAGCUCCCAGGGUGGGCACAUGGG	4080
5133_5_49	PDCD1	Exon 5	+	chr2:241850156-241850181	CCAGGGUGGGCACAUGGGGGGCCCU	4081
5133_5_50	PDCD1	Exon 5	+	chr2:241850187-241850212	CUGCACUUCUGCCCUCCCAACACCC	4082
5133_5_51	PDCD1	Exon 5	+	chr2:241850190-241850215	CACUUCUGCCCUCCCAACACCCAGG	4083
5133_5_52	PDCD1	Exon 5	+	chr2:241850200-241850225	CUCCCAACACCCAGGUGGCCACAGC	4084
5133_5_53	PDCD1	Exon 5	+	chr2:241850201-241850226	UCCCAACACCCAGGUGGCCACAGCU	4085
5133_5_54	PDCD1	Exon 5	+	chr2:241850204-241850229	CAACACCCAGGUGGCCACAGCUGGG	4086
5133_5_55	PDCD1	Exon 5	+	chr2:241850205-241850230	AACACCCAGGUGGCCACAGCUGGGA	4087
5133_5_56	PDCD1	Exon 5	+	chr2:241850206-241850231	ACACCCAGGUGGCCACAGCUGGGAG	4088
5133_5_57	PDCD1	Exon 5	+	chr2:241850242-241850267	AACCCCAGCCCUGCCCUCCUGACCU	4089
5133_5_58	PDCD1	Exon 5	+	chr2:241850243-241850268	ACCCCAGCCCUGCCCUCCUGACCUU	4090
5133_5_59	PDCD1	Exon 5	+	chr2:241850251-241850276	CCUGCCCUCCUGACCUUGGGACCGU	4091
5133_5_60	PDCD1	Exon 5	+	chr2:241850270-241850295	GACCGUAGGAUGUCCCUCUCCCGAG	4092
5133_5_61	PDCD1	Exon 5	+	chr2:241850277-241850302	GGAUGUCCCUCUCCCGAGUGGUGUG	4093
5133_5_62	PDCD1	Exon 5	+	chr2:241850278-241850303	GAUGUCCCUCUCCCGAGUGGUGUGA	4094
5133_5_63	PDCD1	Exon 5	+	chr2:241850279-241850304	AUGUCCCUCUCCCGAGUGGUGUGAG	4095
5133_5_64	PDCD1	Exon 5	+	chr2:241850283-241850308	CCCUCUCCCGAGUGGUGUGAGGGGC	4096
5133_5_65	PDCD1	Exon 5	+	chr2:241850284-241850309	CCUCUCCCGAGUGGUGUGAGGGGCU	4097
5133_5_66	PDCD1	Exon 5	+	chr2:241850285-241850310	CUCUCCCGAGUGGUGUGAGGGGCUG	4098
5133_5_67	PDCD1	Exon 5	+	chr2:241850288-241850313	UCCCGAGUGGUGUGAGGGGCUGGGG	4099
5133_5_68	PDCD1	Exon 5	+	chr2:241850295-241850320	UGGUGUGAGGGGCUGGGGUGGAAUG	4100
5133_5_69	PDCD1	Exon 5	+	chr2:241850298-241850323	UGUGAGGGGCUGGGGUGGAAUGCGG	4101
5133_5_70	PDCD1	Exon 5	+	chr2:241850302-241850327	AGGGGCUGGGGUGGAAUGCGGCGGC	4102

5133_5_71	PDCD1	Exon 5	+	chr2:241850305-241850330	GGCUGGGGUGGAAUGCGGCGGCAGG	4103
5133_5_72	PDCD1	Exon 5	+	chr2:241850317-241850342	AUGCGGCGGCAGGAGGCCAGAGUGC	4104
5133_5_73	PDCD1	Exon 5	+	chr2:241850321-241850346	GGCGGCAGGAGGCCAGAGUGCUGGC	4105
5133_5_74	PDCD1	Exon 5	+	chr2:241850322-241850347	GCGGCAGGAGGCCAGAGUGCUGGCU	4106
5133_5_75	PDCD1	Exon 5	+	chr2:241850331-241850356	GGCCAGAGUGCUGGCUGGGCCUGAA	4107
5133_5_76	PDCD1	Exon 5	+	chr2:241850383-241850408	CUGCCUCAGCUUCCCUGCCCCACAA	4108
5133_5_77	PDCD1	Exon 5	+	chr2:241850384-241850409	UGCCUCAGCUUCCCUGCCCCACAAA	4109
5133_5_78	PDCD1	Exon 5	+	chr2:241850391-241850416	GCUUCCCUGCCCCACAAAGGGCCUG	4110
5133_5_79	PDCD1	Exon 5	+	chr2:241850401-241850426	CCCACAAAGGGCCUGAGGUGCUGCC	4111
5133_5_80	PDCD1	Exon 5	+	chr2:241850402-241850427	CCACAAAGGGCCUGAGGUGCUGCCU	4112
5133_5_81	PDCD1	Exon 5	+	chr2:241850414-241850439	UGAGGUGCUGCCUGGGCAUGUGUAA	4113
5133_5_82	PDCD1	Exon 5	+	chr2:241850417-241850442	GGUGCUGCCUGGGCAUGUGUAAAGG	4114
5133_5_83	PDCD1	Exon 5	+	chr2:241850420-241850445	GCUGCCUGGGCAUGUGUAAAGGUGG	4115
5133_5_84	PDCD1	Exon 5	+	chr2:241850421-241850446	CUGCCUGGGCAUGUGUAAAGGUGGA	4116
5133_5_85	PDCD1	Exon 5	+	chr2:241850422-241850447	UGCCUGGGCAUGUGUAAAGGUGGAG	4117
5133_5_86	PDCD1	Exon 5	+	chr2:241850449-241850474	GUUUCCUGCCCUGCCCACCACAGCC	4118
5133_5_87	PDCD1	Exon 5	+	chr2:241850482-241850507	UUCUGACCUUCCCUGAAACUUCUCU	4119
5133_5_88	PDCD1	Exon 5	+	chr2:241850490-241850515	UUCCCUGAAACUUCUCUAGGCCUGC	4120
5133_5_89	PDCD1	Exon 5	+	chr2:241850491-241850516	UCCCUGAAACUUCUCUAGGCCUGCA	4121
5133_5_90	PDCD1	Exon 5	+	chr2:241850507-241850532	AGGCCUGCAGGGAGCAGAUAACUCC	4122
5133_5_91	PDCD1	Exon 5	+	chr2:241850508-241850533	GGCCUGCAGGGAGCAGAUAACUCCU	4123
5133_5_92	PDCD1	Exon 5	+	chr2:241850509-241850534	GCCUGCAGGGAGCAGAUAACUCCUG	4124
5133_5_93	PDCD1	Exon 5	+	chr2:241850553-241850578	UACCUCCCACUCCUGUGCCCAGUCU	4125
5133_5_94	PDCD1	Exon 5	+	chr2:241850554-241850579	ACCUCCCACUCCUGUGCCCAGUCUU	4126
5133_5_95	PDCD1	Exon 5	+	chr2:241850567-241850592	GUGCCCAGUCUUGGGCCCUGCGUCC	4127

5133_5_96	PDCD1	Exon 5	+	chr2:241850568-241850593	UGCCCAGUCUUGGGCCCUGCGUCCA	4128
5133_5_97	PDCD1	Exon 5	+	chr2:241850576-241850601	CUUGGGCCCUGCGUCCAGGGCGUUU	4129
5133_5_98	PDCD1	Exon 5	+	chr2:241850577-241850602	UUGGGCCCUGCGUCCAGGGCGUUUC	4130
5133_5_99	PDCD1	Exon 5	+	chr2:241850591-241850616	CAGGGCGUUUCGGGAUGCCACUGCC	4131
5133_5_100	PDCD1	Exon 5	+	chr2:241850592-241850617	AGGGCGUUUCGGGAUGCCACUGCCA	4132
5133_5_101	PDCD1	Exon 5	+	chr2:241850593-241850618	GGGCGUUUCGGGAUGCCACUGCCAG	4133
5133_5_102	PDCD1	Exon 5	+	chr2:241850601-241850626	CGGGAUGCCACUGCCAGGGGCACCU	4134
5133_5_103	PDCD1	Exon 5	+	chr2:241850612-241850637	UGCCAGGGGCACCUUGGCUGCUCCA	4135
5133_5_104	PDCD1	Exon 5	+	chr2:241850640-241850665	CCAUCUCCAACCAGCCCCCAAGUUC	4136
5133_5_105	PDCD1	Exon 5	+	chr2:241850644-241850669	CUCCAACCAGCCCCCAAGUUCAGGC	4137
5133_5_106	PDCD1	Exon 5	+	chr2:241850647-241850672	CAACCAGCCCCCAAGUUCAGGCAGG	4138
5133_5_107	PDCD1	Exon 5	+	chr2:241850653-241850678	GCCCCCAAGUUCAGGCAGGAGGCUC	4139
5133_5_108	PDCD1	Exon 5	+	chr2:241850654-241850679	CCCCCAAGUUCAGGCAGGAGGCUCC	4140
5133_5_109	PDCD1	Exon 5	+	chr2:241850655-241850680	CCCCAAGUUCAGGCAGGAGGCUCCG	4141
5133_5_110	PDCD1	Exon 5	+	chr2:241850662-241850687	UUCAGGCAGGAGGCUCCGGGGCGUC	4142
5133_5_111	PDCD1	Exon 5	+	chr2:241850666-241850691	GGCAGGAGGCUCCGGGGCGUCAGGC	4143
5133_5_112	PDCD1	Exon 5	+	chr2:241850667-241850692	GCAGGAGGCUCCGGGGCGUCAGGCA	4144
5133_5_113	PDCD1	Exon 5	+	chr2:241850673-241850698	GGCUCCGGGGCGUCAGGCAGGGCCA	4145
5133_5_114	PDCD1	Exon 5	+	chr2:241850688-241850713	GGCAGGGCCACGGCGCCUUCAGCCC	4146
5133_5_115	PDCD1	Exon 5	+	chr2:241850689-241850714	GCAGGGCCACGGCGCCUUCAGCCCC	4147
5133_5_116	PDCD1	Exon 5	+	chr2:241850735-241850760	GCAGCAGCAGCAGCAGCAGAGAUUC	4148
5133_5_117	PDCD1	Exon 5	+	chr2:241850736-241850761	CAGCAGCAGCAGCAGCAGAGAUUCA	4149
5133_5_118	PDCD1	Exon 5	+	chr2:241850742-241850767	CAGCAGCAGCAGAGAUUCAGGGAGC	4150
5133_5_119	PDCD1	Exon 5	+	chr2:241850749-241850774	AGCAGAGAUUCAGGGAGCUGGACGC	4151
5133_5_120	PDCD1	Exon 5	+	chr2:241850763-241850788	GAGCUGGACGCAGGCAGCUCUGUGC	4152

5133_5_121	PDCD1	Exon 5	+	chr2:241850767-241850792	UGGACGCAGGCAGCUCUGUGCUGGC	4153
5133_5_122	PDCD1	Exon 5	+	chr2:241850791-241850816	CAGGACCUGAAGCAGUGACUGCAUC	4154
5133_5_123	PDCD1	Exon 5	+	chr2:241850804-241850829	AGUGACUGCAUCUGGCCCUCCCUGU	4155
5133_5_124	PDCD1	Exon 5	+	chr2:241850805-241850830	GUGACUGCAUCUGGCCCUCCCUGUA	4156
5133_5_125	PDCD1	Exon 5	+	chr2:241850806-241850831	UGACUGCAUCUGGCCCUCCCUGUAG	4157
5133_5_126	PDCD1	Exon 5	+	chr2:241850810-241850835	UGCAUCUGGCCCUCCCUGUAGGGGA	4158
5133_5_127	PDCD1	Exon 5	+	chr2:241850827-241850852	GUAGGGGACGGUGACACCUGCUGCC	4159
5133_5_128	PDCD1	Exon 5	+	chr2:241850828-241850853	UAGGGGACGGUGACACCUGCUGCCU	4160
5133_5_129	PDCD1	Exon 5	+	chr2:241850838-241850863	UGACACCUGCUGCCUGGGCUCACUG	4161
5133_5_130	PDCD1	Exon 5	+	chr2:241850839-241850864	GACACCUGCUGCCUGGGCUCACUGU	4162
5133_5_131	PDCD1	Exon 5	+	chr2:241850861-241850886	UGUGGGCAUUGAGACAUGAGUCCUG	4163
5133_5_132	PDCD1	Exon 5	+	chr2:241850864-241850889	GGGCAUUGAGACAUGAGUCCUGUGG	4164
5133_5_133	PDCD1	Exon 5	+	chr2:241850865-241850890	GGCAUUGAGACAUGAGUCCUGUGGU	4165
5133_5_134	PDCD1	Exon 5	+	chr2:241850866-241850891	GCAUUGAGACAUGAGUCCUGUGGUG	4166
5133_5_135	PDCD1	Exon 5	+	chr2:241850876-241850901	AUGAGUCCUGUGGUGGGGCUGUGCC	4167
5133_5_136	PDCD1	Exon 5	+	chr2:241850882-241850907	CCUGUGGUGGGGCUGUGCCUGGUGC	4168
5133_5_137	PDCD1	Exon 5	+	chr2:241850888-241850913	GUGGGGCUGUGCCUGGUGCAGGUGC	4169
5133_5_138	PDCD1	Exon 5	+	chr2:241850892-241850917	GGCUGUGCCUGGUGCAGGUGCAGGC	4170
5133_5_139	PDCD1	Exon 5	+	chr2:241850900-241850925	CUGGUGCAGGUGCAGGCUGGAGCCC	4171
5133_5_140	PDCD1	Exon 5	+	chr2:241850911-241850936	GCAGGCUGGAGCCCCGGUCGCCCCC	4172
5133_5_141	PDCD1	Exon 5	+	chr2:241850926-241850951	GGUCGCCCCCAGGCAGCUCAGCCCC	4173
5133_5_142	PDCD1	Exon 5	+	chr2:241850930-241850955	GCCCCCAGGCAGCUCAGCCCCUGGA	4174
5133_5_143	PDCD1	Exon 5	+	chr2:241850940-241850965	AGCUCAGCCCCUGGACGGCCUGCAA	4175
5133_5_144	PDCD1	Exon 5	+	chr2:241850967-241850992	GCCUGCACCCUGCCUGCUUCUCCUG	4176
5133_5_145	PDCD1	Exon 5	+	chr2:241850983-241851008	CUUCUCCUGAGGAAAUGCGCUGACC	4177

5133_5_146	PDCD1	Exon 5	+	chr2:241850984-241851009	UUCUCCUGAGGAAAUGCGCUGACCC	4178
5133_5_147	PDCD1	Exon 5	+	chr2:241850991-241851016	GAGGAAAUGCGCUGACCCGGGCUCA	4179
5133_5_148	PDCD1	Exon 5	+	chr2:241850994-241851019	GAAAUGCGCUGACCCGGGCUCAUGG	4180
5133_5_149	PDCD1	Exon 5	+	chr2:241850997-241851022	AUGCGCUGACCCGGGCUCAUGGUGG	4181
5133_5_150	PDCD1	Exon 5	+	chr2:241850998-241851023	UGCGCUGACCCGGGCUCAUGGUGGA	4182
5133_5_151	PDCD1	Exon 5	+	chr2:241851013-241851038	UCAUGGUGGAGGGUCUGCAGAACAC	4183
5133_5_152	PDCD1	Exon 5	+	chr2:241851016-241851041	UGGUGGAGGGUCUGCAGAACACUGG	4184
5133_5_153	PDCD1	Exon 5	+	chr2:241851022-241851047	AGGGUCUGCAGAACACUGGUGGCCA	4185
5133_5_154	PDCD1	Exon 5	+	chr2:241851029-241851054	GCAGAACACUGGUGGCCAAGGAAGC	4186
5133_5_155	PDCD1	Exon 5	+	chr2:241851036-241851061	ACUGGUGGCCAAGGAAGCCGGUCAG	4187
5133_5_156	PDCD1	Exon 5	+	chr2:241851037-241851062	CUGGUGGCCAAGGAAGCCGGUCAGA	4188
5133_5_157	PDCD1	Exon 5	+	chr2:241851038-241851063	UGGUGGCCAAGGAAGCCGGUCAGAG	4189
5133_5_158	PDCD1	Exon 5	+	chr2:241851062-241851087	GGGGCCAAGAGCAGUGUCCAUCCUC	4190
5133_5_159	PDCD1	Exon 5	+	chr2:241851071-241851096	AGCAGUGUCCAUCCUCAGGCCUCAG	4191
5133_5_160	PDCD1	Exon 5	+	chr2:241851075-241851100	GUGUCCAUCCUCAGGCCUCAGUGGC	4192
5133_5_161	PDCD1	Exon 5	+	chr2:241851076-241851101	UGUCCAUCCUCAGGCCUCAGUGGCU	4193
5133_5_162	PDCD1	Exon 5	+	chr2:241851086-241851111	CAGGCCUCAGUGGCUGGGCACUCCG	4194
5133_5_163	PDCD1	Exon 5	+	chr2:241851087-241851112	AGGCCUCAGUGGCUGGGCACUCCGA	4195
5133_5_164	PDCD1	Exon 5	+	chr2:241851108-241851133	CCGAGGGCCGUCAGCUGAGCCCCUG	4196
5133_5_165	PDCD1	Exon 5	+	chr2:241851109-241851134	CGAGGGCCGUCAGCUGAGCCCCUGC	4197
5133_5_166	PDCD1	Exon 5	+	chr2:241851112-241851137	GGGCCGUCAGCUGAGCCCCUGCGGG	4198
5133_5_167	PDCD1	Exon 5	+	chr2:241851113-241851138	GGCCGUCAGCUGAGCCCCUGCGGGC	4199
5133_5_168	PDCD1	Exon 5	+	chr2:241851114-241851139	GCCGUCAGCUGAGCCCCUGCGGGCG	4200
5133_5_169	PDCD1	Exon 5	+	chr2:241851115-241851140	CCGUCAGCUGAGCCCCUGCGGGCGG	4201
5133_5_170	PDCD1	Exon 5	+	chr2:241851121-241851146	GCUGAGCCCCUGCGGGCGGGGGAUG	4202

5133_5_171	PDCD1	Exon 5	+	chr2:241851137-241851162	CGGGGGAUGAGGUGCCCAUUCCGCU	4203
5133_5_172	PDCD1	Exon 5	+	chr2:241851148-241851173	GUGCCCAUUCCGCUAGGAAAGACAA	4204
5133_5_173	PDCD1	Exon 5	+	chr2:241851151-241851176	CCCAUUCCGCUAGGAAAGACAAUGG	4205
5133_5_174	PDCD1	Exon 5	+	chr2:241851170-241851195	CAAUGGUGGCAUACUCCGUCUGCUC	4206
5133_5_175	PDCD1	Exon 5	+	chr2:241851171-241851196	AAUGGUGGCAUACUCCGUCUGCUCA	4207
5133_5_176	PDCD1	Exon 5	+	chr2:241851178-241851203	GCAUACUCCGUCUGCUCAGGGACAC	4208
5133_5_177	PDCD1	Exon 5	+	chr2:241851179-241851204	CAUACUCCGUCUGCUCAGGGACACA	4209
5133_5_178	PDCD1	Exon 5	+	chr2:241851184-241851209	UCCGUCUGCUCAGGGACACAGGGCA	4210
5133_5_179	PDCD1	Exon 5	+	chr2:241851185-241851210	CCGUCUGCUCAGGGACACAGGGCAC	4211
5133_5_180	PDCD1	Exon 5	+	chr2:241851186-241851211	CGUCUGCUCAGGGACACAGGGCACG	4212
5133_5_181	PDCD1	Exon 5	+	chr2:241851187-241851212	GUCUGCUCAGGGACACAGGGCACGG	4213
5133_5_182	PDCD1	Exon 5	+	chr2:241851188-241851213	UCUGCUCAGGGACACAGGGCACGGG	4214
5133_5_183	PDCD1	Exon 5	+	chr2:241851194-241851219	CAGGGACACAGGGCACGGGGGGCUC	4215
5133_5_184	PDCD1	Exon 5	+	chr2:241851195-241851220	AGGGACACAGGGCACGGGGGGCUCC	4216
5133_5_185	PDCD1	Exon 5	+	chr2:241851196-241851221	GGGACACAGGGCACGGGGGGCUCCG	4217
5133_5_186	PDCD1	Exon 5	+	chr2:241851213-241851238	GGGCUCCGGGGUCUUCUCUCGCCAC	4218
5133_5_187	PDCD1	Exon 5	+	chr2:241851248-241851273	GCUCCCCAUAGUCCACAGAGAACAC	4219
5133_5_188	PDCD1	Exon 5	+	chr2:241851253-241851278	CCAUAGUCCACAGAGAACACAGGCA	4220
5133_5_189	PDCD1	Exon 5	+	chr2:241851259-241851284	UCCACAGAGAACACAGGCACGGCUG	4221
5133_5_190	PDCD1	Exon 5	+	chr2:241851260-241851285	CCACAGAGAACACAGGCACGGCUGA	4222
5133_5_191	PDCD1	Exon 5	+	chr2:241851261-241851286	CACAGAGAACACAGGCACGGCUGAG	4223
5133_5_192	PDCD1	Exon 5	+	chr2:241851277-241851302	ACGGCUGAGGGGUCCUCCUUCUUUG	4224
5133_5_193	PDCD1	Exon 5	+	chr2:241851284-241851309	AGGGGUCCUCCUUCUUUGAGGAGAA	4225
5133_5_194	PDCD1	Exon 5	+	chr2:241851285-241851310	GGGGUCCUCCUUCUUUGAGGAGAAA	4226
5133_5_195	PDCD1	Exon 5	+	chr2:241851290-241851315	CCUCCUUCUUUGAGGAGAAAGGGAG	4227

5133_5_196	PDCD1	Exon 5	+	chr2:241851291-241851316	CUCCUUCUUUGAGGAGAAAGGGAGA	4228
5133_5_197	PDCD1	Exon 5	-	chr2:241849858-241849883	GGAGUUCUGUCCUGUCUGGUGGCUG	4229
5133_5_198	PDCD1	Exon 5	-	chr2:241849864-241849889	UGCUAAGGAGUUCUGUCCUGUCUGG	4230
5133_5_199	PDCD1	Exon 5	-	chr2:241849867-241849892	GCAUGCUAAGGAGUUCUGUCCUGUC	4231
5133_5_200	PDCD1	Exon 5	-	chr2:241849884-241849909	UAUAAUUAAAUAUGAGAGCAUGCUA	4232
5133_5_201	PDCD1	Exon 5	-	chr2:241849929-241849954	UGGGACAAGGGAUCCCCCUUCCCUG	4233
5133_5_202	PDCD1	Exon 5	-	chr2:241849946-241849971	GCAGGCACCUGAGUGGCUGGGACAA	4234
5133_5_203	PDCD1	Exon 5	-	chr2:241849947-241849972	AGCAGGCACCUGAGUGGCUGGGACA	4235
5133_5_204	PDCD1	Exon 5	-	chr2:241849953-241849978	GCGGCCAGCAGGCACCUGAGUGGCU	4236
5133_5_205	PDCD1	Exon 5	-	chr2:241849954-241849979	GGCGGCCAGCAGGCACCUGAGUGGC	4237
5133_5_206	PDCD1	Exon 5	-	chr2:241849958-241849983	UCCAGGCGGCCAGCAGGCACCUGAG	4238
5133_5_207	PDCD1	Exon 5	-	chr2:241849969-241849994	GGCCACCAGCAUCCAGGCGGCCAGC	4239
5133_5_208	PDCD1	Exon 5	-	chr2:241849977-241850002	UGGGGCAGGGCCACCAGCAUCCAGG	4240
5133_5_209	PDCD1	Exon 5	-	chr2:241849980-241850005	UCCUGGGGCAGGGCCACCAGCAUCC	4241
5133_5_210	PDCD1	Exon 5	-	chr2:241849995-241850020	ACACUGCACCCCCACUCCUGGGGCA	4242
5133_5_211	PDCD1	Exon 5	-	chr2:241849996-241850021	CACACUGCACCCCCACUCCUGGGGC	4243
5133_5_212	PDCD1	Exon 5	-	chr2:241850000-241850025	UCCACACACUGCACCCCCACUCCUG	4244
5133_5_213	PDCD1	Exon 5	-	chr2:241850001-241850026	AUCCACACACUGCACCCCCACUCCU	4245
5133_5_214	PDCD1	Exon 5	-	chr2:241850002-241850027	CAUCCACACACUGCACCCCCACUCC	4246
5133_5_215	PDCD1	Exon 5	-	chr2:241850045-241850070	CCCCCGGGGCCUAGUACCCCCGCCG	4247
5133_5_216	PDCD1	Exon 5	-	chr2:241850064-241850089	GUGGGAAGGUACAGGCGUUCCCCCG	4248
5133_5_217	PDCD1	Exon 5	-	chr2:241850065-241850090	GGUGGGAAGGUACAGGCGUUCCCCC	4249
5133_5_218	PDCD1	Exon 5	-	chr2:241850066-241850091	GGGUGGGAAGGUACAGGCGUUCCCC	4250
5133_5_219	PDCD1	Exon 5	-	chr2:241850077-241850102	CACCAGGGCCUGGGUGGGAAGGUAC	4251
5133_5_220	PDCD1	Exon 5	-	chr2:241850083-241850108	GGCUCCCACCAGGGCCUGGGUGGGA	4252

5133_5_221	PDCD1	Exon 5	-	chr2:241850087-241850112	GCCGGGCUCCCACCAGGGCCUGGGU	4253
5133_5_222	PDCD1	Exon 5	-	chr2:241850088-241850113	GGCCGGGCUCCCACCAGGGCCUGGG	4254
5133_5_223	PDCD1	Exon 5	-	chr2:241850091-241850116	GUUGGCCGGGCUCCCACCAGGGCCU	4255
5133_5_224	PDCD1	Exon 5	-	chr2:241850092-241850117	GGUUGGCCGGGCUCCCACCAGGGCC	4256
5133_5_225	PDCD1	Exon 5	-	chr2:241850097-241850122	AAAGGGGUUGGCCGGGCUCCCACCA	4257
5133_5_226	PDCD1	Exon 5	-	chr2:241850098-241850123	UAAAGGGGUUGGCCGGGCUCCCACC	4258
5133_5_227	PDCD1	Exon 5	-	chr2:241850109-241850134	CUGAAAUUAUUUAAAGGGGUUGGCC	4259
5133_5_228	PDCD1	Exon 5	-	chr2:241850110-241850135	CCUGAAAUUAUUUAAAGGGGUUGGC	4260
5133_5_229	PDCD1	Exon 5	-	chr2:241850114-241850139	CAUUCCUGAAAUUAUUUAAAGGGGU	4261
5133_5_230	PDCD1	Exon 5	-	chr2:241850118-241850143	AACCCAUUCCUGAAAUUAUUUAAAG	4262
5133_5_231	PDCD1	Exon 5	-	chr2:241850119-241850144	GAACCCAUUCCUGAAAUUAUUUAAA	4263
5133_5_232	PDCD1	Exon 5	-	chr2:241850120-241850145	GGAACCCAUUCCUGAAAUUAUUUAA	4264
5133_5_233	PDCD1	Exon 5	-	chr2:241850146-241850171	AUGUGCCCACCCUGGGAGCUCUCCU	4265
5133_5_234	PDCD1	Exon 5	-	chr2:241850158-241850183	CUAGGGCCCCCCAUGUGCCCACCCU	4266
5133_5_235	PDCD1	Exon 5	-	chr2:241850159-241850184	CCUAGGGCCCCCCAUGUGCCCACCC	4267
5133_5_236	PDCD1	Exon 5	-	chr2:241850180-241850205	GGGAGGGCAGAAGUGCAGGCACCUA	4268
5133_5_237	PDCD1	Exon 5	-	chr2:241850181-241850206	UGGGAGGGCAGAAGUGCAGGCACCU	4269
5133_5_238	PDCD1	Exon 5	-	chr2:241850189-241850214	CUGGGUGUUGGGAGGGCAGAAGUGC	4270
5133_5_239	PDCD1	Exon 5	-	chr2:241850201-241850226	AGCUGUGGCCACCUGGGUGUUGGGA	4271
5133_5_240	PDCD1	Exon 5	-	chr2:241850202-241850227	CAGCUGUGGCCACCUGGGUGUUGGG	4272
5133_5_241	PDCD1	Exon 5	-	chr2:241850205-241850230	UCCCAGCUGUGGCCACCUGGGUGUU	4273
5133_5_242	PDCD1	Exon 5	-	chr2:241850206-241850231	CUCCCAGCUGUGGCCACCUGGGUGU	4274
5133_5_243	PDCD1	Exon 5	-	chr2:241850212-241850237	AGGCCCCUCCCAGCUGUGGCCACCU	4275
5133_5_244	PDCD1	Exon 5	-	chr2:241850213-241850238	CAGGCCCCUCCCAGCUGUGGCCACC	4276
5133_5_245	PDCD1	Exon 5	-	chr2:241850221-241850246	GGUUGACUCAGGCCCCUCCCAGCUG	4277

5133_5_246	PDCD1	Exon 5	-	chr2:241850237-241850262	AGGAGGGCAGGGCUGGGGUUGACUC	4278
5133_5_247	PDCD1	Exon 5	-	chr2:241850247-241850272	UCCCAAGGUCAGGAGGGCAGGGCUG	4279
5133_5_248	PDCD1	Exon 5	-	chr2:241850248-241850273	GUCCCAAGGUCAGGAGGGCAGGGCU	4280
5133_5_249	PDCD1	Exon 5	-	chr2:241850249-241850274	GGUCCCAAGGUCAGGAGGGCAGGGC	4281
5133_5_250	PDCD1	Exon 5	-	chr2:241850253-241850278	CUACGGUCCCAAGGUCAGGAGGGCA	4282
5133_5_251	PDCD1	Exon 5	-	chr2:241850254-241850279	CCUACGGUCCCAAGGUCAGGAGGGC	4283
5133_5_252	PDCD1	Exon 5	-	chr2:241850258-241850283	ACAUCCUACGGUCCCAAGGUCAGGA	4284
5133_5_253	PDCD1	Exon 5	-	chr2:241850259-241850284	GACAUCCUACGGUCCCAAGGUCAGG	4285
5133_5_254	PDCD1	Exon 5	-	chr2:241850262-241850287	AGGGACAUCCUACGGUCCCAAGGUC	4286
5133_5_255	PDCD1	Exon 5	-	chr2:241850267-241850292	GGGAGAGGGACAUCCUACGGUCCCA	4287
5133_5_256	PDCD1	Exon 5	-	chr2:241850275-241850300	CACCACUCGGGAGAGGGACAUCCUA	4288
5133_5_257	PDCD1	Exon 5	-	chr2:241850286-241850311	CCAGCCCCUCACACCACUCGGGAGA	4289
5133_5_258	PDCD1	Exon 5	-	chr2:241850287-241850312	CCCAGCCCCUCACACCACUCGGGAG	4290
5133_5_259	PDCD1	Exon 5	-	chr2:241850292-241850317	UCCACCCCAGCCCCUCACACCACUC	4291
5133_5_260	PDCD1	Exon 5	-	chr2:241850293-241850318	UUCCACCCCAGCCCCUCACACCACU	4292
5133_5_261	PDCD1	Exon 5	-	chr2:241850336-241850361	GGCCUUUCAGGCCCAGCCAGCACUC	4293
5133_5_262	PDCD1	Exon 5	-	chr2:241850353-241850378	GGGCAGGCAGAGCUGGAGGCCUUUC	4294
5133_5_263	PDCD1	Exon 5	-	chr2:241850362-241850387	GCAGUAAGCGGGCAGGCAGAGCUGG	4295
5133_5_264	PDCD1	Exon 5	-	chr2:241850365-241850390	GAGGCAGUAAGCGGGCAGGCAGAGC	4296
5133_5_265	PDCD1	Exon 5	-	chr2:241850374-241850399	AGGGAAGCUGAGGCAGUAAGCGGGC	4297
5133_5_266	PDCD1	Exon 5	-	chr2:241850378-241850403	GGGCAGGGAAGCUGAGGCAGUAAGC	4298
5133_5_267	PDCD1	Exon 5	-	chr2:241850379-241850404	GGGGCAGGGAAGCUGAGGCAGUAAG	4299
5133_5_268	PDCD1	Exon 5	-	chr2:241850389-241850414	GGCCCUUUGUGGGGCAGGGAAGCUG	4300
5133_5_269	PDCD1	Exon 5	-	chr2:241850398-241850423	AGCACCUCAGGCCCUUUGUGGGGCA	4301
5133_5_270	PDCD1	Exon 5	-	chr2:241850399-241850424	CAGCACCUCAGGCCCUUUGUGGGGC	4302

5133_5_271	PDCD1	Exon 5	-	chr2:241850403-241850428	CAGGCAGCACCUCAGGCCCUUUGUG	4303
5133_5_272	PDCD1	Exon 5	-	chr2:241850404-241850429	CCAGGCAGCACCUCAGGCCCUUUGU	4304
5133_5_273	PDCD1	Exon 5	-	chr2:241850405-241850430	CCCAGGCAGCACCUCAGGCCCUUUG	4305
5133_5_274	PDCD1	Exon 5	-	chr2:241850415-241850440	UUUACACAUGCCCAGGCAGCACCUC	4306
5133_5_275	PDCD1	Exon 5	-	chr2:241850427-241850452	AACCCCUCCACCUUUACACAUGCCC	4307
5133_5_276	PDCD1	Exon 5	-	chr2:241850456-241850481	AGCUCCUGGCUGUGGUGGGCAGGGC	4308
5133_5_277	PDCD1	Exon 5	-	chr2:241850460-241850485	GAAGAGCUCCUGGCUGUGGUGGGCA	4309
5133_5_278	PDCD1	Exon 5	-	chr2:241850461-241850486	AGAAGAGCUCCUGGCUGUGGUGGGC	4310
5133_5_279	PDCD1	Exon 5	-	chr2:241850465-241850490	GGUCAGAAGAGCUCCUGGCUGUGGU	4311
5133_5_280	PDCD1	Exon 5	-	chr2:241850466-241850491	AGGUCAGAAGAGCUCCUGGCUGUGG	4312
5133_5_281	PDCD1	Exon 5	-	chr2:241850469-241850494	GGAAGGUCAGAAGAGCUCCUGGCUG	4313
5133_5_282	PDCD1	Exon 5	-	chr2:241850475-241850500	UUUCAGGGAAGGUCAGAAGAGCUCC	4314
5133_5_283	PDCD1	Exon 5	-	chr2:241850491-241850516	UGCAGGCCUAGAGAAGUUUCAGGGA	4315
5133_5_284	PDCD1	Exon 5	-	chr2:241850495-241850520	UCCCUGCAGGCCUAGAGAAGUUUCA	4316
5133_5_285	PDCD1	Exon 5	-	chr2:241850496-241850521	CUCCCUGCAGGCCUAGAGAAGUUUC	4317
5133_5_286	PDCD1	Exon 5	-	chr2:241850513-241850538	UCCCCAGGAGUUAUCUGCUCCCUGC	4318
5133_5_287	PDCD1	Exon 5	-	chr2:241850533-241850558	AGGUACAUGGGGCUGGGGACUCCCC	4319
5133_5_288	PDCD1	Exon 5	-	chr2:241850543-241850568	CAGGAGUGGGAGGUACAUGGGGCUG	4320
5133_5_289	PDCD1	Exon 5	-	chr2:241850544-241850569	ACAGGAGUGGGAGGUACAUGGGGCU	4321
5133_5_290	PDCD1	Exon 5	-	chr2:241850545-241850570	CACAGGAGUGGGAGGUACAUGGGGC	4322
5133_5_291	PDCD1	Exon 5	-	chr2:241850549-241850574	UGGGCACAGGAGUGGGAGGUACAUG	4323
5133_5_292	PDCD1	Exon 5	-	chr2:241850550-241850575	CUGGGCACAGGAGUGGGAGGUACAU	4324
5133_5_293	PDCD1	Exon 5	-	chr2:241850551-241850576	ACUGGGCACAGGAGUGGGAGGUACA	4325
5133_5_294	PDCD1	Exon 5	-	chr2:241850558-241850583	GCCCAAGACUGGGCACAGGAGUGGG	4326
5133_5_295	PDCD1	Exon 5	-	chr2:241850561-241850586	AGGGCCCAAGACUGGGCACAGGAGU	4327

5133_5_296	PDCD1	Exon 5	-	chr2:241850562-241850587	CAGGGCCCAAGACUGGGCACAGGAG	4328
5133_5_297	PDCD1	Exon 5	-	chr2:241850567-241850592	GGACGCAGGGCCCAAGACUGGGCAC	4329
5133_5_298	PDCD1	Exon 5	-	chr2:241850573-241850598	CGCCCUGGACGCAGGGCCCAAGACU	4330
5133_5_299	PDCD1	Exon 5	-	chr2:241850574-241850599	ACGCCCUGGACGCAGGGCCCAAGAC	4331
5133_5_300	PDCD1	Exon 5	-	chr2:241850585-241850610	GGCAUCCCGAAACGCCCUGGACGCA	4332
5133_5_301	PDCD1	Exon 5	-	chr2:241850586-241850611	UGGCAUCCCGAAACGCCCUGGACGC	4333
5133_5_302	PDCD1	Exon 5	-	chr2:241850593-241850618	CUGGCAGUGGCAUCCCGAAACGCCC	4334
5133_5_303	PDCD1	Exon 5	-	chr2:241850611-241850636	GGAGCAGCCAAGGUGCCCCUGGCAG	4335
5133_5_304	PDCD1	Exon 5	-	chr2:241850617-241850642	GGCCUUGGAGCAGCCAAGGUGCCCC	4336
5133_5_305	PDCD1	Exon 5	-	chr2:241850626-241850651	GUUGGAGAUGGCCUUGGAGCAGCCA	4337
5133_5_306	PDCD1	Exon 5	-	chr2:241850637-241850662	CUUGGGGGCUGGUUGGAGAUGGCCU	4338
5133_5_307	PDCD1	Exon 5	-	chr2:241850643-241850668	CCUGAACUUGGGGGCUGGUUGGAGA	4339
5133_5_308	PDCD1	Exon 5	-	chr2:241850649-241850674	CUCCUGCCUGAACUUGGGGGCUGGU	4340
5133_5_309	PDCD1	Exon 5	-	chr2:241850653-241850678	GAGCCUCCUGCCUGAACUUGGGGGC	4341
5133_5_310	PDCD1	Exon 5	-	chr2:241850657-241850682	CCCGGAGCCUCCUGCCUGAACUUGG	4342
5133_5_311	PDCD1	Exon 5	-	chr2:241850658-241850683	CCCCGGAGCCUCCUGCCUGAACUUG	4343
5133_5_312	PDCD1	Exon 5	-	chr2:241850659-241850684	GCCCCGGAGCCUCCUGCCUGAACUU	4344
5133_5_313	PDCD1	Exon 5	-	chr2:241850660-241850685	CGCCCCGGAGCCUCCUGCCUGAACU	4345
5133_5_314	PDCD1	Exon 5	-	chr2:241850680-241850705	GGCGCCGUGGCCCUGCCUGACGCCC	4346
5133_5_315	PDCD1	Exon 5	-	chr2:241850698-241850723	CUGCGGCCCGGGGCUGAAGGCGCCG	4347
5133_5_316	PDCD1	Exon 5	-	chr2:241850706-241850731	CGACGACGCUGCGGCCCGGGGCUGA	4348
5133_5_317	PDCD1	Exon 5	-	chr2:241850713-241850738	ACGACGACGACGACGCUGCGGCCCG	4349
5133_5_318	PDCD1	Exon 5	-	chr2:241850714-241850739	GACGACGACGACGACGCUGCGGCCC	4350
5133_5_319	PDCD1	Exon 5	-	chr2:241850715-241850740	CGACGACGACGACGACGCUGCGGCC	4351
5133_5_320	PDCD1	Exon 5	-	chr2:241850720-241850745	GACGACGACGACGACGACGACGCUG	4352

5133_5_321	PDCD1	Exon 5	-	chr2:241850799-241850824	GAGGGCCAGAUGCAGUCACUGCUUC	4353
5133_5_322	PDCD1	Exon 5	-	chr2:241850822-241850847	CAGGUGUCACCGUCCCCUACAGGGA	4354
5133_5_323	PDCD1	Exon 5	-	chr2:241850823-241850848	GCAGGUGUCACCGUCCCCUACAGGG	4355
5133_5_324	PDCD1	Exon 5	-	chr2:241850826-241850851	GCAGCAGGUGUCACCGUCCCCUACA	4356
5133_5_325	PDCD1	Exon 5	-	chr2:241850827-241850852	GGCAGCAGGUGUCACCGUCCCCUAC	4357
5133_5_326	PDCD1	Exon 5	-	chr2:241850846-241850871	AAUGCCCACAGUGAGCCCAGGCAGC	4358
5133_5_327	PDCD1	Exon 5	-	chr2:241850853-241850878	AUGUCUCAAUGCCCACAGUGAGCCC	4359
5133_5_328	PDCD1	Exon 5	-	chr2:241850885-241850910	CCUGCACCAGGCACAGCCCCACCAC	4360
5133_5_329	PDCD1	Exon 5	-	chr2:241850902-241850927	CGGGGCUCCAGCCUGCACCUGCACC	4361
5133_5_330	PDCD1	Exon 5	-	chr2:241850925-241850950	GGGCUGAGCUGCCUGGGGGCGACCG	4362
5133_5_331	PDCD1	Exon 5	-	chr2:241850926-241850951	GGGGCUGAGCUGCCUGGGGGCGACC	4363
5133_5_332	PDCD1	Exon 5	-	chr2:241850927-241850952	AGGGGCUGAGCUGCCUGGGGGCGAC	4364
5133_5_333	PDCD1	Exon 5	-	chr2:241850934-241850959	GCCGUCCAGGGGCUGAGCUGCCUGG	4365
5133_5_334	PDCD1	Exon 5	-	chr2:241850935-241850960	GGCCGUCCAGGGGCUGAGCUGCCUG	4366
5133_5_335	PDCD1	Exon 5	-	chr2:241850936-241850961	AGGCCGUCCAGGGGCUGAGCUGCCU	4367
5133_5_336	PDCD1	Exon 5	-	chr2:241850937-241850962	CAGGCCGUCCAGGGGCUGAGCUGCC	4368
5133_5_337	PDCD1	Exon 5	-	chr2:241850950-241850975	GUGCAGGCCAUUGCAGGCCGUCCAG	4369
5133_5_338	PDCD1	Exon 5	-	chr2:241850951-241850976	GGUGCAGGCCAUUGCAGGCCGUCCA	4370
5133_5_339	PDCD1	Exon 5	-	chr2:241850952-241850977	GGGUGCAGGCCAUUGCAGGCCGUCC	4371
5133_5_340	PDCD1	Exon 5	-	chr2:241850961-241850986	AAGCAGGCAGGGUGCAGGCCAUUGC	4372
5133_5_341	PDCD1	Exon 5	-	chr2:241850971-241850996	UCCUCAGGAGAAGCAGGCAGGGUGC	4373
5133_5_342	PDCD1	Exon 5	-	chr2:241850977-241851002	CGCAUUUCCUCAGGAGAAGCAGGCA	4374
5133_5_343	PDCD1	Exon 5	-	chr2:241850978-241851003	GCGCAUUUCCUCAGGAGAAGCAGGC	4375
5133_5_344	PDCD1	Exon 5	-	chr2:241850982-241851007	GUCAGCGCAUUUCCUCAGGAGAAGC	4376
5133_5_345	PDCD1	Exon 5	-	chr2:241850991-241851016	UGAGCCCGGGUCAGCGCAUUUCCUC	4377

5133_5_346	PDCD1	Exon 5	-	chr2:241851009-241851034	UCUGCAGACCCUCCACCAUGAGCCC	4378
5133_5_347	PDCD1	Exon 5	-	chr2:241851010-241851035	UUCUGCAGACCCUCCACCAUGAGCC	4379
5133_5_348	PDCD1	Exon 5	-	chr2:241851047-241851072	UCUUGGCCCCUCUGACCGGCUUCCU	4380
5133_5_349	PDCD1	Exon 5	-	chr2:241851056-241851081	GGACACUGCUCUUGGCCCCUCUGAC	4381
5133_5_350	PDCD1	Exon 5	-	chr2:241851069-241851094	GAGGCCUGAGGAUGGACACUGCUCU	4382
5133_5_351	PDCD1	Exon 5	-	chr2:241851082-241851107	GUGCCCAGCCACUGAGGCCUGAGGA	4383
5133_5_352	PDCD1	Exon 5	-	chr2:241851086-241851111	CGGAGUGCCCAGCCACUGAGGCCUG	4384
5133_5_353	PDCD1	Exon 5	-	chr2:241851093-241851118	CGGCCCUCGGAGUGCCCAGCCACUG	4385
5133_5_354	PDCD1	Exon 5	-	chr2:241851111-241851136	CCGCAGGGGCUCAGCUGACGGCCCU	4386
5133_5_355	PDCD1	Exon 5	-	chr2:241851118-241851143	CCCCCGCCCGCAGGGGCUCAGCUGA	4387
5133_5_356	PDCD1	Exon 5	-	chr2:241851130-241851155	UGGGCACCUCAUCCCCCGCCCGCAG	4388
5133_5_357	PDCD1	Exon 5	-	chr2:241851131-241851156	AUGGGCACCUCAUCCCCCGCCCGCA	4389
5133_5_358	PDCD1	Exon 5	-	chr2:241851132-241851157	AAUGGGCACCUCAUCCCCCGCCCGC	4390
5133_5_359	PDCD1	Exon 5	-	chr2:241851154-241851179	CCACCAUUGUCUUUCCUAGCGGAAU	4391
5133_5_360	PDCD1	Exon 5	-	chr2:241851155-241851180	GCCACCAUUGUCUUUCCUAGCGGAA	4392
5133_5_361	PDCD1	Exon 5	-	chr2:241851160-241851185	AGUAUGCCACCAUUGUCUUUCCUAG	4393
5133_5_362	PDCD1	Exon 5	-	chr2:241851188-241851213	CCCGUGCCCUGUGUCCCUGAGCAGA	4394
5133_5_363	PDCD1	Exon 5	-	chr2:241851221-241851246	GAUUUCCAGUGGCGAGAGAAGACCC	4395
5133_5_364	PDCD1	Exon 5	-	chr2:241851237-241851262	GGACUAUGGGGAGCUGGAUUUCCAG	4396
5133_5_365	PDCD1	Exon 5	-	chr2:241851248-241851273	GUGUUCUCUGUGGACUAUGGGGAGC	4397
5133_5_366	PDCD1	Exon 5	-	chr2:241851254-241851279	GUGCCUGUGUUCUCUGUGGACUAUG	4398
5133_5_367	PDCD1	Exon 5	-	chr2:241851255-241851280	CGUGCCUGUGUUCUCUGUGGACUAU	4399
5133_5_368	PDCD1	Exon 5	-	chr2:241851256-241851281	CCGUGCCUGUGUUCUCUGUGGACUA	4400
5133_5_369	PDCD1	Exon 5	-	chr2:241851263-241851288	CCCUCAGCCGUGCCUGUGUUCUCUG	4401
5133_5_370	PDCD1	Exon 5	-	chr2:241851293-241851318	CCUCUCCCUUUCUCCUCAAAGAAGG	4402

5133_5_371	PDCD1	Exon 5	-	chr2:241851296-241851321	CUCCCUCUCCCUUUCUCCUCAAAGA	4403
5133_4_1	PDCD1	Exon 4	+	chr2:241851924-241851949	AUGCAGGAAAAGAGUGAGACUCACC	4404
5133_4_2	PDCD1	Exon 4	+	chr2:241851925-241851950	UGCAGGAAAAGAGUGAGACUCACCA	4405
5133_4_3	PDCD1	Exon 4	+	chr2:241851926-241851951	GCAGGAAAAGAGUGAGACUCACCAG	4406
5133_4_4	PDCD1	Exon 4	+	chr2:241851930-241851955	GAAAAGAGUGAGACUCACCAGGGGC	4407
5133_4_5	PDCD1	Exon 4	+	chr2:241851934-241851959	AGAGUGAGACUCACCAGGGGCUGGC	4408
5133_4_6	PDCD1	Exon 4	+	chr2:241851943-241851968	CUCACCAGGGGCUGGCCGGUGCGCC	4409
5133_4_7	PDCD1	Exon 4	+	chr2:241851975-241852000	UAUUGUCCCUGCAGAGAAACACACU	4410
5133_4_8	PDCD1	Exon 4	+	chr2:241851976-241852001	AUUGUCCCUGCAGAGAAACACACUU	4411
5133_4_9	PDCD1	Exon 4	+	chr2:241851977-241852002	UUGUCCCUGCAGAGAAACACACUUG	4412
5133_4_10	PDCD1	Exon 4	-	chr2:241851950-241851975	GGAGCCAGGCGCACCGGCCAGCCCC	4413
5133_4_11	PDCD1	Exon 4	-	chr2:241851961-241851986	CAGGGACAAUAGGAGCCAGGCGCAC	4414
5133_4_12	PDCD1	Exon 4	-	chr2:241851969-241851994	UUUCUCUGCAGGGACAAUAGGAGCC	4415
5133_4_13	PDCD1	Exon 4	-	chr2:241851976-241852001	AAGUGUGUUUCUCUGCAGGGACAAU	4416
5133_3_1	PDCD1	Exon 3	+	chr2:241852178-241852203	GGGGCUGGGAUGACGUUACCUCGUG	4417
5133_3_2	PDCD1	Exon 3	+	chr2:241852183-241852208	UGGGAUGACGUUACCUCGUGCGGCC	4418
5133_3_3	PDCD1	Exon 3	+	chr2:241852184-241852209	GGGAUGACGUUACCUCGUGCGGCCC	4419
5133_3_4	PDCD1	Exon 3	+	chr2:241852196-241852221	CCUCGUGCGGCCCGGGAGCAGAUGA	4420
5133_3_5	PDCD1	Exon 3	+	chr2:241852201-241852226	UGCGGCCCGGGAGCAGAUGACGGCC	4421
5133_3_6	PDCD1	Exon 3	+	chr2:241852222-241852247	GGCCAGGACCCAGACUAGCAGCACC	4422
5133_3_7	PDCD1	Exon 3	+	chr2:241852234-241852259	GACUAGCAGCACCAGGCUGCCCAGC	4423
5133_3_8	PDCD1	Exon 3	+	chr2:241852258-241852283	CAGGCCGCCCACGACACCAACCACC	4424
5133_3_9	PDCD1	Exon 3	+	chr2:241852259-241852284	AGGCCGCCCACGACACCAACCACCA	4425
5133_3_10	PDCD1	Exon 3	+	chr2:241852264-241852289	GCCCACGACACCAACCACCAGGGUU	4426
5133_3_11	PDCD1	Exon 3	+	chr2:241852270-241852295	GACACCAACCACCAGGGUUUGGAAC	4427

5133_3_12	PDCD1	Exon 3	+	chr2:241852307-241852332	CUGGGUGAGGGGCUGGGGUGGGCUG	4428
5133_3_13	PDCD1	Exon 3	+	chr2:241852308-241852333	UGGGUGAGGGGCUGGGGUGGGCUGU	4429
5133_3_14	PDCD1	Exon 3	+	chr2:241852329-241852354	CUGUGGGCACUUCUGCCCUUCUCUC	4430
5133_3_15	PDCD1	Exon 3	+	chr2:241852333-241852358	GGGCACUUCUGCCCUUCUCUCUGGA	4431
5133_3_16	PDCD1	Exon 3	+	chr2:241852334-241852359	GGCACUUCUGCCCUUCUCUCUGGAA	4432
5133_3_17	PDCD1	Exon 3	-	chr2:241852199-241852224	CCGUCAUCUGCUCCCGGGCCGCACG	4433
5133_3_18	PDCD1	Exon 3	-	chr2:241852209-241852234	UGGGUCCUGGCCGUCAUCUGCUCCC	4434
5133_3_19	PDCD1	Exon 3	-	chr2:241852210-241852235	CUGGGUCCUGGCCGUCAUCUGCUCC	4435
5133_3_20	PDCD1	Exon 3	-	chr2:241852227-241852252	AGCCUGGUGCUGCUAGUCUGGGUCC	4436
5133_3_21	PDCD1	Exon 3	-	chr2:241852233-241852258	CUGGGCAGCCUGGUGCUGCUAGUCU	4437
5133_3_22	PDCD1	Exon 3	-	chr2:241852234-241852259	GCUGGGCAGCCUGGUGCUGCUAGUC	4438
5133_3_23	PDCD1	Exon 3	-	chr2:241852248-241852273	GUCGUGGGCGGCCUGCUGGGCAGCC	4439
5133_3_24	PDCD1	Exon 3	-	chr2:241852256-241852281	UGGUUGGUGUCGUGGGCGGCCUGCU	4440
5133_3_25	PDCD1	Exon 3	-	chr2:241852257-241852282	GUGGUUGGUGUCGUGGGCGGCCUGC	4441
5133_3_26	PDCD1	Exon 3	-	chr2:241852265-241852290	AAACCCUGGUGGUUGGUGUCGUGGG	4442
5133_3_27	PDCD1	Exon 3	-	chr2:241852268-241852293	UCCAAACCCUGGUGGUUGGUGUCGU	4443
5133_3_28	PDCD1	Exon 3	-	chr2:241852269-241852294	UUCCAAACCCUGGUGGUUGGUGUCG	4444
5133_3_29	PDCD1	Exon 3	-	chr2:241852277-241852302	GGGGCCAGUUCCAAACCCUGGUGGU	4445
5133_3_30	PDCD1	Exon 3	-	chr2:241852281-241852306	GGUCGGGGCCAGUUCCAAACCCUGG	4446
5133_3_31	PDCD1	Exon 3	-	chr2:241852284-241852309	UCCGGUCGGGGCCAGUUCCAAACCC	4447
5133_3_32	PDCD1	Exon 3	-	chr2:241852301-241852326	UGGGGUCGGGGAGUGGGUCCGGUCG	4448
5133_3_33	PDCD1	Exon 3	-	chr2:241852347-241852372	CUGGUUUGUGCCCUUCCAGAGAGAA	4449
5133_3_34	PDCD1	Exon 3	-	chr2:241852348-241852373	ACUGGUUUGUGCCCUUCCAGAGAGA	4450
5133_2_1	PDCD1	Exon 2	+	chr2:241852618-241852643	ACCUGUCACCCUGAGCUCUGCCCGC	4451
5133_2_2	PDCD1	Exon 2	+	chr2:241852640-241852665	CGCAGGCUCUCUUUGAUCUGCGCCU	4452

5133_2_3	PDCD1	Exon 2	+	chr2:241852641-241852666	GCAGGCUCUCUUUGAUCUGCGCCUU	4453
5133_2_4	PDCD1	Exon 2	+	chr2:241852642-241852667	CAGGCUCUCUUUGAUCUGCGCCUUG	4454
5133_2_5	PDCD1	Exon 2	+	chr2:241852643-241852668	AGGCUCUCUUUGAUCUGCGCCUUGG	4455
5133_2_6	PDCD1	Exon 2	+	chr2:241852648-241852673	CUCUUUGAUCUGCGCCUUGGGGGCC	4456
5133_2_7	PDCD1	Exon 2	+	chr2:241852649-241852674	UCUUUGAUCUGCGCCUUGGGGGCCA	4457
5133_2_8	PDCD1	Exon 2	+	chr2:241852655-241852680	AUCUGCGCCUUGGGGGCCAGGGAGA	4458
5133_2_9	PDCD1	Exon 2	+	chr2:241852666-241852691	GGGGGCCAGGGAGAUGGCCCCACAG	4459
5133_2_10	PDCD1	Exon 2	+	chr2:241852670-241852695	GCCAGGGAGAUGGCCCCACAGAGGU	4460
5133_2_11	PDCD1	Exon 2	+	chr2:241852690-241852715	GAGGUAGGUGCCGCUGUCAUUGCGC	4461
5133_2_12	PDCD1	Exon 2	+	chr2:241852691-241852716	AGGUAGGUGCCGCUGUCAUUGCGCC	4462
5133_2_13	PDCD1	Exon 2	+	chr2:241852711-241852736	GCGCCGGGCCCUGACCACGCUCAUG	4463
5133_2_14	PDCD1	Exon 2	+	chr2:241852727-241852752	ACGCUCAUGUGGAAGUCACGCCCGU	4464
5133_2_15	PDCD1	Exon 2	+	chr2:241852728-241852753	CGCUCAUGUGGAAGUCACGCCCGUU	4465
5133_2_16	PDCD1	Exon 2	+	chr2:241852744-241852769	ACGCCCGUUGGGCAGUUGUGUGACA	4466
5133_2_17	PDCD1	Exon 2	+	chr2:241852750-241852775	GUUGGGCAGUUGUGUGACACGGAAG	4467
5133_2_18	PDCD1	Exon 2	+	chr2:241852759-241852784	UUGUGUGACACGGAAGCGGCAGUCC	4468
5133_2_19	PDCD1	Exon 2	+	chr2:241852763-241852788	GUGACACGGAAGCGGCAGUCCUGGC	4469
5133_2_20	PDCD1	Exon 2	+	chr2:241852764-241852789	UGACACGGAAGCGGCAGUCCUGGCC	4470
5133_2_21	PDCD1	Exon 2	+	chr2:241852768-241852793	ACGGAAGCGGCAGUCCUGGCCGGGC	4471
5133_2_22	PDCD1	Exon 2	+	chr2:241852774-241852799	GCGGCAGUCCUGGCCGGGCUGGCUG	4472
5133_2_23	PDCD1	Exon 2	+	chr2:241852781-241852806	UCCUGGCCGGGCUGGCUGCGGUCCU	4473
5133_2_24	PDCD1	Exon 2	+	chr2:241852782-241852807	CCUGGCCGGGCUGGCUGCGGUCCUC	4474
5133_2_25	PDCD1	Exon 2	+	chr2:241852783-241852808	CUGGCCGGGCUGGCUGCGGUCCUCG	4475
5133_2_26	PDCD1	Exon 2	+	chr2:241852787-241852812	CCGGGCUGGCUGCGGUCCUCGGGGA	4476
5133_2_27	PDCD1	Exon 2	+	chr2:241852790-241852815	GGCUGGCUGCGGUCCUCGGGGAAGG	4477

5133_2_28	PDCD1	Exon 2	+	chr2:241852807-241852832	GGGGAAGGCGGCCAGCUUGUCCGUC	4478
5133_2_29	PDCD1	Exon 2	+	chr2:241852814-241852839	GCGGCCAGCUUGUCCGUCUGGUUGC	4479
5133_2_30	PDCD1	Exon 2	+	chr2:241852815-241852840	CGGCCAGCUUGUCCGUCUGGUUGCU	4480
5133_2_31	PDCD1	Exon 2	+	chr2:241852816-241852841	GGCCAGCUUGUCCGUCUGGUUGCUG	4481
5133_2_32	PDCD1	Exon 2	+	chr2:241852825-241852850	GUCCGUCUGGUUGCUGGGGCUCAUG	4482
5133_2_33	PDCD1	Exon 2	+	chr2:241852859-241852884	UUUAGCACGAAGCUCUCCGAUGUGU	4483
5133_2_34	PDCD1	Exon 2	+	chr2:241852871-241852896	CUCUCCGAUGUGUUGGAGAAGCUGC	4484
5133_2_35	PDCD1	Exon 2	+	chr2:241852877-241852902	GAUGUGUUGGAGAAGCUGCAGGUGA	4485
5133_2_36	PDCD1	Exon 2	+	chr2:241852880-241852905	GUGUUGGAGAAGCUGCAGGUGAAGG	4486
5133_2_37	PDCD1	Exon 2	+	chr2:241852895-241852920	CAGGUGAAGGUGGCGUUGUCCCCUU	4487
5133_2_38	PDCD1	Exon 2	+	chr2:241852909-241852934	GUUGUCCCCUUCGGUCACCACGAGC	4488
5133_2_39	PDCD1	Exon 2	+	chr2:241852910-241852935	UUGUCCCCUUCGGUCACCACGAGCA	4489
5133_2_40	PDCD1	Exon 2	+	chr2:241852914-241852939	CCCCUUCGGUCACCACGAGCAGGGC	4490
5133_2_41	PDCD1	Exon 2	+	chr2:241852915-241852940	CCCUUCGGUCACCACGAGCAGGGCU	4491
5133_2_42	PDCD1	Exon 2	+	chr2:241852916-241852941	CCUUCGGUCACCACGAGCAGGGCUG	4492
5133_2_43	PDCD1	Exon 2	+	chr2:241852922-241852947	GUCACCACGAGCAGGGCUGGGGAGA	4493
5133_2_44	PDCD1	Exon 2	+	chr2:241852925-241852950	ACCACGAGCAGGGCUGGGGAGAAGG	4494
5133_2_45	PDCD1	Exon 2	+	chr2:241852926-241852951	CCACGAGCAGGGCUGGGGAGAAGGU	4495
5133_2_46	PDCD1	Exon 2	+	chr2:241852927-241852952	CACGAGCAGGGCUGGGGAGAAGGUG	4496
5133_2_47	PDCD1	Exon 2	+	chr2:241852928-241852953	ACGAGCAGGGCUGGGGAGAAGGUGG	4497
5133_2_48	PDCD1	Exon 2	+	chr2:241852929-241852954	CGAGCAGGGCUGGGGAGAAGGUGGG	4498
5133_2_49	PDCD1	Exon 2	+	chr2:241852930-241852955	GAGCAGGGCUGGGGAGAAGGUGGGG	4499
5133_2_50	PDCD1	Exon 2	+	chr2:241852937-241852962	GCUGGGGAGAAGGUGGGGGGGUUCC	4500
5133_2_51	PDCD1	Exon 2	+	chr2:241852938-241852963	CUGGGGAGAAGGUGGGGGGGUUCCA	4501
5133_2_52	PDCD1	Exon 2	+	chr2:241852947-241852972	AGGUGGGGGGGUUCCAGGGCCUGUC	4502

5133_2_53	PDCD1	Exon 2	+	chr2:241852948-241852973	GGUGGGGGGGUUCCAGGGCCUGUCU	4503
5133_2_54	PDCD1	Exon 2	+	chr2:241852949-241852974	GUGGGGGGGUUCCAGGGCCUGUCUG	4504
5133_2_55	PDCD1	Exon 2	+	chr2:241852963-241852988	GGGCCUGUCUGGGGAGUCUGAGAGA	4505
5133_2_56	PDCD1	Exon 2	+	chr2:241852970-241852995	UCUGGGGAGUCUGAGAGAUGGAGAG	4506
5133_2_57	PDCD1	Exon 2	+	chr2:241852975-241853000	GGAGUCUGAGAGAUGGAGAGAGGUG	4507
5133_2_58	PDCD1	Exon 2	-	chr2:241852600-241852625	GACAGGUGCGGCCUCGGAGGCCCCG	4508
5133_2_59	PDCD1	Exon 2	-	chr2:241852601-241852626	UGACAGGUGCGGCCUCGGAGGCCCC	4509
5133_2_60	PDCD1	Exon 2	-	chr2:241852602-241852627	GUGACAGGUGCGGCCUCGGAGGCCC	4510
5133_2_61	PDCD1	Exon 2	-	chr2:241852608-241852633	CUCAGGGUGACAGGUGCGGCCUCGG	4511
5133_2_62	PDCD1	Exon 2	-	chr2:241852611-241852636	GAGCUCAGGGUGACAGGUGCGGCCU	4512
5133_2_63	PDCD1	Exon 2	-	chr2:241852617-241852642	CGGGCAGAGCUCAGGGUGACAGGUG	4513
5133_2_64	PDCD1	Exon 2	-	chr2:241852622-241852647	GCCUGCGGGCAGAGCUCAGGGUGAC	4514
5133_2_65	PDCD1	Exon 2	-	chr2:241852629-241852654	AAAGAGAGCCUGCGGGCAGAGCUCA	4515
5133_2_66	PDCD1	Exon 2	-	chr2:241852630-241852655	CAAAGAGAGCCUGCGGGCAGAGCUC	4516
5133_2_67	PDCD1	Exon 2	-	chr2:241852641-241852666	AAGGCGCAGAUCAAAGAGAGCCUGC	4517
5133_2_68	PDCD1	Exon 2	-	chr2:241852642-241852667	CAAGGCGCAGAUCAAAGAGAGCCUG	4518
5133_2_69	PDCD1	Exon 2	-	chr2:241852665-241852690	UGUGGGGCCAUCUCCCUGGCCCCCA	4519
5133_2_70	PDCD1	Exon 2	-	chr2:241852674-241852699	ACCUACCUCUGUGGGGCCAUCUCCC	4520
5133_2_71	PDCD1	Exon 2	-	chr2:241852686-241852711	AAUGACAGCGGCACCUACCUCUGUG	4521
5133_2_72	PDCD1	Exon 2	-	chr2:241852687-241852712	CAAUGACAGCGGCACCUACCUCUGU	4522
5133_2_73	PDCD1	Exon 2	-	chr2:241852688-241852713	GCAAUGACAGCGGCACCUACCUCUG	4523
5133_2_74	PDCD1	Exon 2	-	chr2:241852703-241852728	UGGUCAGGGCCCGGCGCAAUGACAG	4524
5133_2_75	PDCD1	Exon 2	-	chr2:241852717-241852742	CUUCCACAUGAGCGUGGUCAGGGCC	4525
5133_2_76	PDCD1	Exon 2	-	chr2:241852722-241852747	CGUGACUUCCACAUGAGCGUGGUCA	4526
5133_2_77	PDCD1	Exon 2	-	chr2:241852723-241852748	GCGUGACUUCCACAUGAGCGUGGUC	4527

5133_2_78	PDCD1	Exon 2	-	chr2:241852728-241852753	AACGGGCGUGACUUCCACAUGAGCG	4528
5133_2_79	PDCD1	Exon 2	-	chr2:241852750-241852775	CUUCCGUGUCACACAACUGCCCAAC	4529
5133_2_80	PDCD1	Exon 2	-	chr2:241852751-241852776	GCUUCCGUGUCACACAACUGCCCAA	4530
5133_2_81	PDCD1	Exon 2	-	chr2:241852785-241852810	CCCGAGGACCGCAGCCAGCCCGGCC	4531
5133_2_82	PDCD1	Exon 2	-	chr2:241852790-241852815	CCUUCCCCGAGGACCGCAGCCAGCC	4532
5133_2_83	PDCD1	Exon 2	-	chr2:241852806-241852831	ACGGACAAGCUGGCCGCCUUCCCCG	4533
5133_2_84	PDCD1	Exon 2	-	chr2:241852821-241852846	AGCCCCAGCAACCAGACGGACAAGC	4534
5133_2_85	PDCD1	Exon 2	-	chr2:241852830-241852855	UACCGCAUGAGCCCCAGCAACCAGA	4535
5133_2_86	PDCD1	Exon 2	-	chr2:241852858-241852883	CACAUCGGAGAGCUUCGUGCUAAAC	4536
5133_2_87	PDCD1	Exon 2	-	chr2:241852878-241852903	UUCACCUGCAGCUUCUCCAACACAU	4537
5133_2_88	PDCD1	Exon 2	-	chr2:241852917-241852942	CCAGCCCUGCUCGUGGUGACCGAAG	4538
5133_2_89	PDCD1	Exon 2	-	chr2:241852918-241852943	CCCAGCCCUGCUCGUGGUGACCGAA	4539
5133_2_90	PDCD1	Exon 2	-	chr2:241852919-241852944	CCCCAGCCCUGCUCGUGGUGACCGA	4540
5133_2_91	PDCD1	Exon 2	-	chr2:241852929-241852954	CCCACCUUCUCCCCAGCCCUGCUCG	4541
5133_2_92	PDCD1	Exon 2	-	chr2:241852963-241852988	UCUCUCAGACUCCCCAGACAGGCCC	4542
5133_2_93	PDCD1	Exon 2	-	chr2:241852969-241852994	UCUCCAUCUCUCAGACUCCCCAGAC	4543
5133_1_1	PDCD1	Exon 1	+	chr2:241858750-241858775	GACCCCACCUACCUAAGAACCAUCC	4544
5133_1_2	PDCD1	Exon 1	+	chr2:241858786-241858811	CCAGUUGUAGCACCGCCCAGACGAC	4545
5133_1_3	PDCD1	Exon 1	+	chr2:241858791-241858816	UGUAGCACCGCCCAGACGACUGGCC	4546
5133_1_4	PDCD1	Exon 1	+	chr2:241858792-241858817	GUAGCACCGCCCAGACGACUGGCCA	4547
5133_1_5	PDCD1	Exon 1	+	chr2:241858801-241858826	CCCAGACGACUGGCCAGGGCGCCUG	4548
5133_1_6	PDCD1	Exon 1	+	chr2:241858802-241858827	CCAGACGACUGGCCAGGGCGCCUGU	4549
5133_1_7	PDCD1	Exon 1	+	chr2:241858816-241858841	AGGGCGCCUGUGGGAUCUGCAUGCC	4550
5133_1_8	PDCD1	Exon 1	+	chr2:241858855-241858880	CAGAGUGCCGCCUUCUCCACUGCUC	4551
5133_1_9	PDCD1	Exon 1	+	chr2:241858858-241858883	AGUGCCGCCUUCUCCACUGCUCAGG	4552

5133_1_10	PDCD1	Exon 1	+	chr2:241858861-241858886	GCCGCCUUCUCCACUGCUCAGGCGG	4553
5133_1_11	PDCD1	Exon 1	+	chr2:241858868-241858893	UCUCCACUGCUCAGGCGGAGGUGAG	4554
5133_1_12	PDCD1	Exon 1	+	chr2:241858872-241858897	CACUGCUCAGGCGGAGGUGAGCGGA	4555
5133_1_13	PDCD1	Exon 1	+	chr2:241858873-241858898	ACUGCUCAGGCGGAGGUGAGCGGAA	4556
5133_1_14	PDCD1	Exon 1	+	chr2:241858886-241858911	AGGUGAGCGGAAGGGAAACUGUCCC	4557
5133_1_15	PDCD1	Exon 1	+	chr2:241858891-241858916	AGCGGAAGGGAAACUGUCCCAGGUC	4558
5133_1_16	PDCD1	Exon 1	+	chr2:241858898-241858923	GGGAAACUGUCCCAGGUCAGGUUGA	4559
5133_1_17	PDCD1	Exon 1	+	chr2:241858899-241858924	GGAAACUGUCCCAGGUCAGGUUGAA	4560
5133_1_18	PDCD1	Exon 1	+	chr2:241858902-241858927	AACUGUCCCAGGUCAGGUUGAAGGG	4561
5133_1_19	PDCD1	Exon 1	+	chr2:241858903-241858928	ACUGUCCCAGGUCAGGUUGAAGGGA	4562
5133_1_20	PDCD1	Exon 1	-	chr2:241858743-241858768	UCUUAGGUAGGUGGGGUCGGCGGUC	4563
5133_1_21	PDCD1	Exon 1	-	chr2:241858748-241858773	AUGGUUCUUAGGUAGGUGGGGUCGG	4564
5133_1_22	PDCD1	Exon 1	-	chr2:241858751-241858776	AGGAUGGUUCUUAGGUAGGUGGGGU	4565
5133_1_23	PDCD1	Exon 1	-	chr2:241858755-241858780	GGCCAGGAUGGUUCUUAGGUAGGUG	4566
5133_1_24	PDCD1	Exon 1	-	chr2:241858756-241858781	CGGCCAGGAUGGUUCUUAGGUAGGU	4567
5133_1_25	PDCD1	Exon 1	-	chr2:241858757-241858782	GCGGCCAGGAUGGUUCUUAGGUAGG	4568
5133_1_26	PDCD1	Exon 1	-	chr2:241858760-241858785	CUGGCGGCCAGGAUGGUUCUUAGGU	4569
5133_1_27	PDCD1	Exon 1	-	chr2:241858764-241858789	UGGGCUGGCGGCCAGGAUGGUUCUU	4570
5133_1_28	PDCD1	Exon 1	-	chr2:241858772-241858797	GCUACAACUGGGCUGGCGGCCAGGA	4571
5133_1_29	PDCD1	Exon 1	-	chr2:241858776-241858801	CGGUGCUACAACUGGGCUGGCGGCC	4572
5133_1_30	PDCD1	Exon 1	-	chr2:241858781-241858806	CUGGGCGGUGCUACAACUGGGCUGG	4573
5133_1_31	PDCD1	Exon 1	-	chr2:241858784-241858809	CGUCUGGGCGGUGCUACAACUGGGC	4574
5133_1_32	PDCD1	Exon 1	-	chr2:241858788-241858813	CAGUCGUCUGGGCGGUGCUACAACU	4575
5133_1_33	PDCD1	Exon 1	-	chr2:241858789-241858814	CCAGUCGUCUGGGCGGUGCUACAAC	4576
5133_1_34	PDCD1	Exon 1	-	chr2:241858801-241858826	CAGGCGCCCUGGCCAGUCGUCUGGG	4577

5133_1_35	PDCD1	Exon 1	-	chr2:241858804-241858829	CCACAGGCGCCCUGGCCAGUCGUCU	4578
5133_1_36	PDCD1	Exon 1	-	chr2:241858805-241858830	CCCACAGGCGCCCUGGCCAGUCGUC	4579
5133_1_37	PDCD1	Exon 1	-	chr2:241858817-241858842	AGGCAUGCAGAUCCCACAGGCGCCC	4580
5133_1_38	PDCD1	Exon 1	-	chr2:241858825-241858850	GCUGCUCCAGGCAUGCAGAUCCCAC	4581
5133_1_39	PDCD1	Exon 1	-	chr2:241858842-241858867	GGCGGCACUCUGGUGGGGCUGCUCC	4582
5133_1_40	PDCD1	Exon 1	-	chr2:241858852-241858877	CAGUGGAGAAGGCGGCACUCUGGUG	4583
5133_1_41	PDCD1	Exon 1	-	chr2:241858853-241858878	GCAGUGGAGAAGGCGGCACUCUGGU	4584
5133_1_42	PDCD1	Exon 1	-	chr2:241858854-241858879	AGCAGUGGAGAAGGCGGCACUCUGG	4585
5133_1_43	PDCD1	Exon 1	-	chr2:241858857-241858882	CUGAGCAGUGGAGAAGGCGGCACUC	4586
5133_1_44	PDCD1	Exon 1	-	chr2:241858865-241858890	ACCUCCGCCUGAGCAGUGGAGAAGG	4587
5133_1_45	PDCD1	Exon 1	-	chr2:241858868-241858893	CUCACCUCCGCCUGAGCAGUGGAGA	4588
5133_1_46	PDCD1	Exon 1	-	chr2:241858874-241858899	CUUCCGCUCACCUCCGCCUGAGCAG	4589
5781_1_1	PTPN11	Exon 1	+	chr12:112418706-112418731	CGCGGAGCGCGCAGCUCACACCUGG	4590
5781_1_2	PTPN11	Exon 1	+	chr12:112418712-112418737	GCGCGCAGCUCACACCUGGCGGCCG	4591
5781_1_3	PTPN11	Exon 1	+	chr12:112418720-112418745	CUCACACCUGGCGGCCGCGGUUUCC	4592
5781_1_4	PTPN11	Exon 1	+	chr12:112418723-112418748	ACACCUGGCGGCCGCGGUUUCCAGG	4593
5781_1_5	PTPN11	Exon 1	+	chr12:112418731-112418756	CGGCCGCGGUUUCCAGGAGGAAGCA	4594
5781_1_6	PTPN11	Exon 1	+	chr12:112418740-112418765	UUUCCAGGAGGAAGCAAGGAUGCUU	4595
5781_1_7	PTPN11	Exon 1	+	chr12:112418753-112418778	GCAAGGAUGCUUUGGACACUGUGCG	4596
5781_1_8	PTPN11	Exon 1	+	chr12:112418764-112418789	UUGGACACUGUGCGUGGCGCCUCCG	4597
5781_1_9	PTPN11	Exon 1	+	chr12:112418787-112418812	CGCGGAGCCCCCGCGCUGCCAUUCC	4598
5781_1_10	PTPN11	Exon 1	+	chr12:112418798-112418823	CGCGCUGCCAUUCCCGGCCGUCGCU	4599
5781_1_11	PTPN11	Exon 1	+	chr12:112418812-112418837	CGGCCGUCGCUCGGUCCUCCGCUGA	4600

5781_1_12	PTPN11	Exon 1	+	chr12:112418813-112418838	GGCCGUCGCUCGGUCCUCCGCUGAC	4601
5781_1_13	PTPN11	Exon 1	+	chr12:112418820-112418845	GCUCGGUCCUCCGCUGACGGGAAGC	4602
5781_1_14	PTPN11	Exon 1	+	chr12:112418927-112418952	GGCCGGGGGGCAGCUGCACAGUCUC	4603
5781_1_15	PTPN11	Exon 1	+	chr12:112418928-112418953	GCCGGGGGGCAGCUGCACAGUCUCC	4604
5781_1_16	PTPN11	Exon 1	+	chr12:112418937-112418962	CAGCUGCACAGUCUCCGGGAUCCCC	4605
5781_1_17	PTPN11	Exon 1	+	chr12:112418942-112418967	GCACAGUCUCCGGGAUCCCCAGGCC	4606
5781_1_18	PTPN11	Exon 1	+	chr12:112418945-112418970	CAGUCUCCGGGAUCCCCAGGCCUGG	4607
5781_1_19	PTPN11	Exon 1	+	chr12:112418946-112418971	AGUCUCCGGGAUCCCCAGGCCUGGA	4608
5781_1_20	PTPN11	Exon 1	+	chr12:112418947-112418972	GUCUCCGGGAUCCCCAGGCCUGGAG	4609
5781_1_21	PTPN11	Exon 1	+	chr12:112418948-112418973	UCUCCGGGAUCCCCAGGCCUGGAGG	4610
5781_1_22	PTPN11	Exon 1	+	chr12:112418949-112418974	CUCCGGGAUCCCCAGGCCUGGAGGG	4611
5781_1_23	PTPN11	Exon 1	+	chr12:112418960-112418985	CCAGGCCUGGAGGGGGGUCUGUGCG	4612
5781_1_24	PTPN11	Exon 1	+	chr12:112418964-112418989	GCCUGGAGGGGGGUCUGUGCGCGGC	4613
5781_1_25	PTPN11	Exon 1	+	chr12:112418968-112418993	GGAGGGGGGUCUGUGCGCGGCCGGC	4614
5781_1_26	PTPN11	Exon 1	+	chr12:112418985-112419010	CGGCCGGCUGGCUCUGCCCCGCGUC	4615
5781_1_27	PTPN11	Exon 1	+	chr12:112418995-112419020	GCUCUGCCCCGCGUCCGGUCCCGAG	4616
5781_1_28	PTPN11	Exon 1	+	chr12:112418996-112419021	CUCUGCCCCGCGUCCGGUCCCGAGC	4617
5781_1_29	PTPN11	Exon 1	+	chr12:112419006-112419031	CGUCCGGUCCCGAGCGGGCCUCCCU	4618
5781_1_30	PTPN11	Exon 1	+	chr12:112419007-112419032	GUCCGGUCCCGAGCGGGCCUCCCUC	4619
5781_1_31	PTPN11	Exon 1	+	chr12:112419034-112419059	GCCAGCCCGAUGUGACCGAGCCCAG	4620
5781_1_32	PTPN11	Exon 1	+	chr12:112419047-112419072	GACCGAGCCCAGCGGAGCCUGAGCA	4621
5781_1_33	PTPN11	Exon 1	+	chr12:112419052-112419077	AGCCCAGCGGAGCCUGAGCAAGGAG	4622

5781_1_34	PTPN11	Exon 1	+	chr12:112419053-112419078	GCCCAGCGGAGCCUGAGCAAGGAGC	4623
5781_1_35	PTPN11	Exon 1	+	chr12:112419063-112419088	GCCUGAGCAAGGAGCGGGUCCGUCG	4624
5781_1_36	PTPN11	Exon 1	+	chr12:112419069-112419094	GCAAGGAGCGGGUCCGUCGCGGAGC	4625
5781_1_37	PTPN11	Exon 1	+	chr12:112419072-112419097	AGGAGCGGGUCCGUCGCGGAGCCGG	4626
5781_1_38	PTPN11	Exon 1	+	chr12:112419073-112419098	GGAGCGGGUCCGUCGCGGAGCCGGA	4627
5781_1_39	PTPN11	Exon 1	+	chr12:112419076-112419101	GCGGGUCCGUCGCGGAGCCGGAGGG	4628
5781_1_40	PTPN11	Exon 1	+	chr12:112419077-112419102	CGGGUCCGUCGCGGAGCCGGAGGGC	4629
5781_1_41	PTPN11	Exon 1	+	chr12:112419080-112419105	GUCCGUCGCGGAGCCGGAGGGCGGG	4630
5781_1_42	PTPN11	Exon 1	+	chr12:112419095-112419120	GGAGGGCGGGAGGAACAUGACAUCG	4631
5781_1_43	PTPN11	Exon 1	+	chr12:112419098-112419123	GGGCGGGAGGAACAUGACAUCGCGG	4632
5781_1_44	PTPN11	Exon 1	+	chr12:112419103-112419128	GGAGGAACAUGACAUCGCGGAGGUG	4633
5781_1_45	PTPN11	Exon 1	+	chr12:112419113-112419138	GACAUCGCGGAGGUGAGGAGCCCCG	4634
5781_1_46	PTPN11	Exon 1	+	chr12:112419114-112419139	ACAUCGCGGAGGUGAGGAGCCCCGA	4635
5781_1_47	PTPN11	Exon 1	+	chr12:112419115-112419140	CAUCGCGGAGGUGAGGAGCCCCGAG	4636
5781_1_48	PTPN11	Exon 1	+	chr12:112419120-112419145	CGGAGGUGAGGAGCCCCGAGGGGCC	4637
5781_1_49	PTPN11	Exon 1	-	chr12:112418729-112418754	CUUCCUCCUGGAAACCGCGGCCGCC	4638
5781_1_50	PTPN11	Exon 1	-	chr12:112418737-112418762	CAUCCUUGCUUCCUCCUGGAAACCG	4639
5781_1_51	PTPN11	Exon 1	-	chr12:112418746-112418771	UGUCCAAAGCAUCCUUGCUUCCUCC	4640
5781_1_52	PTPN11	Exon 1	-	chr12:112418786-112418811	GAAUGGCAGCGCGGGGGCUCCGCGG	4641
5781_1_53	PTPN11	Exon 1	-	chr12:112418789-112418814	CGGGAAUGGCAGCGCGGGGGCUCCG	4642
5781_1_54	PTPN11	Exon 1	-	chr12:112418797-112418822	GCGACGGCCGGGAAUGGCAGCGCGG	4643
5781_1_55	PTPN11	Exon 1	-	chr12:112418798-112418823	AGCGACGGCCGGGAAUGGCAGCGCG	4644

5781_1_56	PTPN11	Exon 1	-	chr12:112418799-112418824	GAGCGACGGCCGGGAAUGGCAGCGC	4645
5781_1_57	PTPN11	Exon 1	-	chr12:112418800-112418825	CGAGCGACGGCCGGGAAUGGCAGCG	4646
5781_1_58	PTPN11	Exon 1	-	chr12:112418808-112418833	CGGAGGACCGAGCGACGGCCGGGAA	4647
5781_1_59	PTPN11	Exon 1	-	chr12:112418813-112418838	GUCAGCGGAGGACCGAGCGACGGCC	4648
5781_1_60	PTPN11	Exon 1	-	chr12:112418814-112418839	CGUCAGCGGAGGACCGAGCGACGGC	4649
5781_1_61	PTPN11	Exon 1	-	chr12:112418818-112418843	UUCCCGUCAGCGGAGGACCGAGCGA	4650
5781_1_62	PTPN11	Exon 1	-	chr12:112418830-112418855	CGGACUUCCUGCUUCCCGUCAGCGG	4651
5781_1_63	PTPN11	Exon 1	-	chr12:112418833-112418858	CGGCGGACUUCCUGCUUCCCGUCAG	4652
5781_1_64	PTPN11	Exon 1	-	chr12:112418954-112418979	GACCCCCCUCCAGGCCUGGGGAUCC	4653
5781_1_65	PTPN11	Exon 1	-	chr12:112418961-112418986	GCGCACAGACCCCCCUCCAGGCCUG	4654
5781_1_66	PTPN11	Exon 1	-	chr12:112418962-112418987	CGCGCACAGACCCCCCUCCAGGCCU	4655
5781_1_67	PTPN11	Exon 1	-	chr12:112418963-112418988	CCGCGCACAGACCCCCCUCCAGGCC	4656
5781_1_68	PTPN11	Exon 1	-	chr12:112418968-112418993	GCCGGCCGCGCACAGACCCCCCUCC	4657
5781_1_69	PTPN11	Exon 1	-	chr12:112418991-112419016	GGACCGGACGCGGGGCAGAGCCAGC	4658
5781_1_70	PTPN11	Exon 1	-	chr12:112419004-112419029	GGAGGCCCGCUCGGGACCGGACGCG	4659
5781_1_71	PTPN11	Exon 1	-	chr12:112419005-112419030	GGGAGGCCCGCUCGGGACCGGACGC	4660
5781_1_72	PTPN11	Exon 1	-	chr12:112419006-112419031	AGGGAGGCCCGCUCGGGACCGGACG	4661
5781_1_73	PTPN11	Exon 1	-	chr12:112419012-112419037	GGCCCGAGGGAGGCCCGCUCGGGAC	4662
5781_1_74	PTPN11	Exon 1	-	chr12:112419017-112419042	GGGCUGGCCCGAGGGAGGCCCGCUC	4663
5781_1_75	PTPN11	Exon 1	-	chr12:112419018-112419043	CGGGCUGGCCCGAGGGAGGCCCGCU	4664
5781_1_76	PTPN11	Exon 1	-	chr12:112419027-112419052	CGGUCACAUCGGGCUGGCCCGAGGG	4665
5781_1_77	PTPN11	Exon 1	-	chr12:112419030-112419055	GCUCGGUCACAUCGGGCUGGCCCGA	4666

5781_1_78	PTPN11	Exon 1	-	chr12:112419031-112419056	GGCUCGGUCACAUCGGGCUGGCCCG	4667
5781_1_79	PTPN11	Exon 1	-	chr12:112419038-112419063	UCCGCUGGGCUCGGUCACAUCGGGC	4668
5781_1_80	PTPN11	Exon 1	-	chr12:112419042-112419067	AGGCUCCGCUGGGCUCGGUCACAUC	4669
5781_1_81	PTPN11	Exon 1	-	chr12:112419043-112419068	CAGGCUCCGCUGGGCUCGGUCACAU	4670
5781_1_82	PTPN11	Exon 1	-	chr12:112419052-112419077	CUCCUUGCUCAGGCUCCGCUGGGCU	4671
5781_1_83	PTPN11	Exon 1	-	chr12:112419057-112419082	ACCCGCUCCUUGCUCAGGCUCCGCU	4672
5781_1_84	PTPN11	Exon 1	-	chr12:112419058-112419083	GACCCGCUCCUUGCUCAGGCUCCGC	4673
5781_1_85	PTPN11	Exon 1	-	chr12:112419067-112419092	UCCGCGACGGACCCGCUCCUUGCUC	4674
5781_1_86	PTPN11	Exon 1	-	chr12:112419085-112419110	UUCCUCCCGCCCUCCGGCUCCGCGA	4675
5781_1_87	PTPN11	Exon 1	-	chr12:112419096-112419121	GCGAUGUCAUGUUCCUCCCGCCCUC	4676
5781_2_1	PTPN11	Exon 2	+	chr12:112446251-112446276	ACUUACUUUGUCUUUCUUUUUAAGA	4677
5781_2_2	PTPN11	Exon 2	+	chr12:112446271-112446296	UAAGAUGGUUUCACCCAAAUAUCAC	4678
5781_2_3	PTPN11	Exon 2	+	chr12:112446276-112446301	UGGUUUCACCCAAAUAUCACUGGUG	4679
5781_2_4	PTPN11	Exon 2	+	chr12:112446279-112446304	UUUCACCCAAAUAUCACUGGUGUGG	4680
5781_2_5	PTPN11	Exon 2	+	chr12:112446304-112446329	AGGCAGAAAACCUACUGUUGACAAG	4681
5781_2_6	PTPN11	Exon 2	+	chr12:112446313-112446338	ACCUACUGUUGACAAGAGGAGUUGA	4682
5781_2_7	PTPN11	Exon 2	+	chr12:112446324-112446349	ACAAGAGGAGUUGAUGGCAGUUUUU	4683
5781_2_8	PTPN11	Exon 2	+	chr12:112446329-112446354	AGGAGUUGAUGGCAGUUUUUUGGCA	4684
5781_2_9	PTPN11	Exon 2	+	chr12:112446349-112446374	UGGCAAGGCCUAGUAAAAGUAACCC	4685
5781_2_10	PTPN11	Exon 2	+	chr12:112446371-112446396	CCCUGGAGACUUCACACUUUCCGUU	4686
5781_2_11	PTPN11	Exon 2	+	chr12:112446379-112446404	ACUUCACACUUUCCGUUAGGUAAGU	4687
5781_2_12	PTPN11	Exon 2	+	chr12:112446393-112446418	GUUAGGUAAGUUGGAAUGAAAAGAG	4688

5781_2_13	PTPN11	Exon 2	-	chr12:112446287-112446312	UUCUGCCUCCACACCAGUGAUAUUU	4689
5781_2_14	PTPN11	Exon 2	-	chr12:112446288-112446313	UUUCUGCCUCCACACCAGUGAUAUU	4690
5781_2_15	PTPN11	Exon 2	-	chr12:112446317-112446342	GCCAUCAACUCCUCUUGUCAACAGU	4691
5781_2_16	PTPN11	Exon 2	-	chr12:112446360-112446385	UGAAGUCUCCAGGGUUACUUUUACU	4692
5781_2_17	PTPN11	Exon 2	-	chr12:112446374-112446399	CCUAACGGAAAGUGUGAAGUCUCCA	4693
5781_2_18	PTPN11	Exon 2	-	chr12:112446375-112446400	ACCUAACGGAAAGUGUGAAGUCUCC	4694
5781_2_19	PTPN11	Exon 2	-	chr12:112446394-112446419	UCUCUUUUCAUUCCAACUUACCUAA	4695
5781_3_1	PTPN11	Exon 3	+	chr12:112450298-112450323	UUCCAAUGGACUAUUUUAGAAGAAA	4696
5781_3_2	PTPN11	Exon 3	+	chr12:112450331-112450356	UCACCCACAUCAAGAUUCAGAACAC	4697
5781_3_3	PTPN11	Exon 3	+	chr12:112450352-112450377	ACACUGGUGAUUACUAUGACCUGUA	4698
5781_3_4	PTPN11	Exon 3	+	chr12:112450355-112450380	CUGGUGAUUACUAUGACCUGUAUGG	4699
5781_3_5	PTPN11	Exon 3	+	chr12:112450356-112450381	UGGUGAUUACUAUGACCUGUAUGGA	4700
5781_3_6	PTPN11	Exon 3	+	chr12:112450357-112450382	GGUGAUUACUAUGACCUGUAUGGAG	4701
5781_3_7	PTPN11	Exon 3	+	chr12:112450375-112450400	UAUGGAGGGGAGAAAUUUGCCACUU	4702
5781_3_8	PTPN11	Exon 3	+	chr12:112450384-112450409	GAGAAAUUUGCCACUUUGGCUGAGU	4703
5781_3_9	PTPN11	Exon 3	+	chr12:112450399-112450424	UUGGCUGAGUUGGUCCAGUAUUACA	4704
5781_3_10	PTPN11	Exon 3	+	chr12:112450409-112450434	UGGUCCAGUAUUACAUGGAACAUCA	4705
5781_3_11	PTPN11	Exon 3	+	chr12:112450410-112450435	GGUCCAGUAUUACAUGGAACAUCAC	4706
5781_3_12	PTPN11	Exon 3	+	chr12:112450430-112450455	AUCACGGGCAAUUAAAAGAGAAGAA	4707
5781_3_13	PTPN11	Exon 3	+	chr12:112450485-112450510	GAACUGUGCAGAUCCUACCUCUGAA	4708
5781_3_14	PTPN11	Exon 3	-	chr12:112450297-112450322	UUCUUCUAAAAUAGUCCAUUGGAAA	4709
5781_3_15	PTPN11	Exon 3	-	chr12:112450298-112450323	UUUCUUCUAAAAUAGUCCAUUGGAA	4710

5781_3_16	PTPN11	Exon 3	-	chr12:112450303-112450328	CUCCAUUUCUUCUAAAAUAGUCCAU	4711
5781_3_17	PTPN11	Exon 3	-	chr12:112450337-112450362	UCACCAGUGUUCUGAAUCUUGAUGU	4712
5781_3_18	PTPN11	Exon 3	-	chr12:112450338-112450363	AUCACCAGUGUUCUGAAUCUUGAUG	4713
5781_3_19	PTPN11	Exon 3	-	chr12:112450374-112450399	AGUGGCAAAUUUCUCCCCUCCAUAC	4714
5781_3_20	PTPN11	Exon 3	-	chr12:112450397-112450422	UAAUACUGGACCAACUCAGCCAAAG	4715
5781_3_21	PTPN11	Exon 3	-	chr12:112450416-112450441	UUGCCCGUGAUGUUCCAUGUAAUAC	4716
5781_3_22	PTPN11	Exon 3	-	chr12:112450483-112450508	CAGAGGUAGGAUCUGCACAGUUCAG	4717
5781_3_23	PTPN11	Exon 3	-	chr12:112450501-112450526	AAAAUGUUACUGACCUUUCAGAGGU	4718
5781_3_24	PTPN11	Exon 3	-	chr12:112450505-112450530	CACUAAAAUGUUACUGACCUUUCAG	4719
5781_4_1	PTPN11	Exon 4	+	chr12:112453170-112453195	UUUUUUAUUUUUUAAAAACUUUAGG	4720
5781_4_2	PTPN11	Exon 4	+	chr12:112453178-112453203	UUUUUAAAAACUUUAGGUGGUUUCA	4721
5781_4_3	PTPN11	Exon 4	+	chr12:112453190-112453215	UUAGGUGGUUUCAUGGACAUCUCUC	4722
5781_4_4	PTPN11	Exon 4	+	chr12:112453191-112453216	UAGGUGGUUUCAUGGACAUCUCUCU	4723
5781_4_5	PTPN11	Exon 4	+	chr12:112453223-112453248	AAGCAGAGAAAUUAUUAACUGAAAA	4724
5781_4_6	PTPN11	Exon 4	+	chr12:112453232-112453257	AAUUAUUAACUGAAAAAGGAAAACA	4725
5781_4_7	PTPN11	Exon 4	+	chr12:112453268-112453293	UUGUACGAGAGAGCCAGAGCCACCC	4726
5781_4_8	PTPN11	Exon 4	+	chr12:112453295-112453320	GAGAUUUUGUUCUUUCUGUGCGCAC	4727
5781_4_9	PTPN11	Exon 4	+	chr12:112453307-112453332	UUUCUGUGCGCACUGGUGAUGACAA	4728
5781_4_10	PTPN11	Exon 4	+	chr12:112453308-112453333	UUCUGUGCGCACUGGUGAUGACAAA	4729
5781_4_11	PTPN11	Exon 4	+	chr12:112453309-112453334	UCUGUGCGCACUGGUGAUGACAAAG	4730
5781_4_12	PTPN11	Exon 4	+	chr12:112453322-112453347	GUGAUGACAAAGGGGAGAGCAAUGA	4731
5781_4_13	PTPN11	Exon 4	+	chr12:112453360-112453385	GUGACCCAUGUUAUGAUUCGCUGUC	4732

5781_4_14	PTPN11	Exon 4	+	chr12:112453382-112453407	GUCAGGUAAAUCUCCAGUUGAAAAA	4733
5781_4_15	PTPN11	Exon 4	+	chr12:112453383-112453408	UCAGGUAAAUCUCCAGUUGAAAAAU	4734
5781_4_16	PTPN11	Exon 4	-	chr12:112453284-112453309	AAGAACAAAAUCUCCAGGGUGGCUC	4735
5781_4_17	PTPN11	Exon 4	-	chr12:112453290-112453315	CACAGAAAGAACAAAAUCUCCAGGG	4736
5781_4_18	PTPN11	Exon 4	-	chr12:112453293-112453318	GCGCACAGAAAGAACAAAAUCUCCA	4737
5781_4_19	PTPN11	Exon 4	-	chr12:112453294-112453319	UGCGCACAGAAAGAACAAAAUCUCC	4738
5781_4_20	PTPN11	Exon 4	-	chr12:112453367-112453392	UUUACCUGACAGCGAAUCAUAACAU	4739
5781_4_21	PTPN11	Exon 4	-	chr12:112453368-112453393	AUUUACCUGACAGCGAAUCAUAACA	4740
5781_5_1	PTPN11	Exon 5	+	chr12:112454555-112454580	CUUGAAAGGAACUGAAAUACGACGU	4741
5781_5_2	PTPN11	Exon 5	+	chr12:112454558-112454583	GAAAGGAACUGAAAUACGACGUUGG	4742
5781_5_3	PTPN11	Exon 5	+	chr12:112454561-112454586	AGGAACUGAAAUACGACGUUGGUGG	4743
5781_5_4	PTPN11	Exon 5	+	chr12:112454568-112454593	GAAAUACGACGUUGGUGGAGGAGAA	4744
5781_5_5	PTPN11	Exon 5	+	chr12:112454593-112454618	CGGUUUGAUUCUUUGACAGAUCUUG	4745
5781_5_6	PTPN11	Exon 5	+	chr12:112454617-112454642	GUGGAACAUUAUAAGAAGAAUCCUA	4746
5781_5_7	PTPN11	Exon 5	+	chr12:112454620-112454645	GAACAUUAUAAGAAGAAUCCUAUGG	4747
5781_5_8	PTPN11	Exon 5	+	chr12:112454629-112454654	AAGAAGAAUCCUAUGGUGGAAACAU	4748
5781_5_9	PTPN11	Exon 5	+	chr12:112454630-112454655	AGAAGAAUCCUAUGGUGGAAACAUU	4749
5781_5_10	PTPN11	Exon 5	+	chr12:112454653-112454678	UUGGGUACAGUACUACAACUCAAGC	4750
5781_5_11	PTPN11	Exon 5	+	chr12:112454665-112454690	CUACAACUCAAGCAGGUGAGCAGAU	4751
5781_5_12	PTPN11	Exon 5	-	chr12:112454641-112454666	GUACUGUACCCAAUGUUUCCACCAU	4752
5781_6_1	PTPN11	Exon 6	+	chr12:112456016-112456041	CUGAGACCACAGAUAAAGUCAAACA	4753
5781_6_2	PTPN11	Exon 6	+	chr12:112456023-112456048	CACAGAUAAAGUCAAACAAGGCUUU	4754

5781_6_3	PTPN11	Exon 6	+	chr12:112456024-112456049	ACAGAUAAAGUCAAACAAGGCUUUU	4755
5781_6_4	PTPN11	Exon 6	+	chr12:112456036-112456061	AAACAAGGCUUUUGGGAAGAAUUUG	4756
5781_6_5	PTPN11	Exon 6	-	chr12:112455952-112455977	CAGCAUUUAUACGAGUCGUGUUAAG	4757
5781_6_6	PTPN11	Exon 6	-	chr12:112455953-112455978	GCAGCAUUUAUACGAGUCGUGUUAA	4758
5781_6_7	PTPN11	Exon 6	-	chr12:112455954-112455979	AGCAGCAUUUAUACGAGUCGUGUUA	4759
5781_6_8	PTPN11	Exon 6	-	chr12:112456025-112456050	CAAAAGCCUUGUUUGACUUUAUCUG	4760
5781_7_1	PTPN11	Exon 7	+	chr12:112472931-112472956	CUUUCUUUCCAGACACUACAACAAC	4761
5781_7_2	PTPN11	Exon 7	+	chr12:112472961-112472986	UGCAAACUUCUCUACAGCCGAAAAG	4762
5781_7_3	PTPN11	Exon 7	+	chr12:112472962-112472987	GCAAACUUCUCUACAGCCGAAAAGA	4763
5781_7_4	PTPN11	Exon 7	+	chr12:112472969-112472994	UCUCUACAGCCGAAAAGAGGUCAA	4764
5781_7_5	PTPN11	Exon 7	-	chr12:112472942-112472967	UUUGCACUCCUGUUGUUGUAGUGUC	4765
5781_7_6	PTPN11	Exon 7	-	chr12:112472981-112473006	GUUUUCUUGCCUUUGACCCUCUUUU	4766
5781_7_7	PTPN11	Exon 7	-	chr12:112473035-112473060	AGCGGAAUAUUGAUACUUACAGGGC	4767
5781_7_8	PTPN11	Exon 7	-	chr12:112473039-112473064	ACUGAGCGGAAUAUUGAUACUUACA	4768
5781_7_9	PTPN11	Exon 7	-	chr12:112473040-112473065	UACUGAGCGGAAUAUUGAUACUUAC	4769
5781_8_1	PTPN11	Exon 8	+	chr12:112477636-112477661	UCUUUUUCUUCUAGUUGAUCAUACC	4770
5781_8_2	PTPN11	Exon 8	+	chr12:112477637-112477662	CUUUUUCUUCUAGUUGAUCAUACCA	4771
5781_8_3	PTPN11	Exon 8	+	chr12:112477653-112477678	AUCAUACCAGGGUUGUCCUACACGA	4772
5781_8_4	PTPN11	Exon 8	+	chr12:112477703-112477728	GAUUACAUCAAUGCAAAUAUCAUCA	4773
5781_8_5	PTPN11	Exon 8	-	chr12:112477631-112477656	GAUCAACUAGAAGAAAAAGAGACCA	4774
5781_8_6	PTPN11	Exon 8	-	chr12:112477662-112477687	GGAUCACCAUCGUGUAGGACAACCC	4775
5781_8_7	PTPN11	Exon 8	-	chr12:112477672-112477697	AGGCUCAUUGGGAUCACCAUCGUGU	4776

5781_8_8	PTPN11	Exon 8	-	chr12:112477688-112477713	UGAUGUAAUCUGAAACAGGCUCAUU	4777
5781_8_9	PTPN11	Exon 8	-	chr12:112477689-112477714	UUGAUGUAAUCUGAAACAGGCUCAU	4778
5781_8_10	PTPN11	Exon 8	-	chr12:112477697-112477722	UAUUUGCAUUGAUGUAAUCUGAAAC	4779
5781_9_1	PTPN11	Exon 9	+	chr12:112477890-112477915	CCAAAAAGAGUUACAUUGCCACACA	4780
5781_9_2	PTPN11	Exon 9	+	chr12:112477907-112477932	GCCACACAAGGCUGCCUGCAAAACA	4781
5781_9_3	PTPN11	Exon 9	+	chr12:112477921-112477946	CCUGCAAAACACGGUGAAUGACUUU	4782
5781_9_4	PTPN11	Exon 9	+	chr12:112477924-112477949	GCAAAACACGGUGAAUGACUUUUGG	4783
5781_9_5	PTPN11	Exon 9	+	chr12:112477928-112477953	AACACGGUGAAUGACUUUUGGCGGA	4784
5781_9_6	PTPN11	Exon 9	+	chr12:112477976-112478001	GUGAUUGUCAUGACAACGAAAGAAG	4785
5781_9_7	PTPN11	Exon 9	+	chr12:112477983-112478008	UCAUGACAACGAAAGAAGUGGAGAG	4786
5781_9_8	PTPN11	Exon 9	+	chr12:112477988-112478013	ACAACGAAAGAAGUGGAGAGAGGAA	4787
5781_9_9	PTPN11	Exon 9	-	chr12:112477846-112477871	GGUUUCAAAUUCAGGCUAGAAAUUU	4788
5781_9_10	PTPN11	Exon 9	-	chr12:112477859-112477884	AAUUGUUGCACUUGGUUUCAAAUUC	4789
5781_9_11	PTPN11	Exon 9	-	chr12:112477872-112477897	UUUUUGGGCUUUGAAUUGUUGCACU	4790
5781_9_12	PTPN11	Exon 9	-	chr12:112477892-112477917	CUUGUGUGGCAAUGUAACUCUUUUU	4791
5781_9_13	PTPN11	Exon 9	-	chr12:112477893-112477918	CCUUGUGUGGCAAUGUAACUCUUUU	4792
5781_9_14	PTPN11	Exon 9	-	chr12:112477911-112477936	ACCGUGUUUUGCAGGCAGCCUUGUG	4793
5781_9_15	PTPN11	Exon 9	-	chr12:112477924-112477949	CCAAAAGUCAUUCACCGUGUUUUGC	4794
5781_9_16	PTPN11	Exon 9	-	chr12:112477963-112477988	CAUGACAAUCACUCGGGAGUUUUCU	4795
5781_9_17	PTPN11	Exon 9	-	chr12:112477974-112477999	UCUUUCGUUGUCAUGACAAUCACUC	4796
5781_9_18	PTPN11	Exon 9	-	chr12:112477975-112478000	UUCUUUCGUUGUCAUGACAAUCACU	4797
5781_10_1	PTPN11	Exon 10	+	chr12:112482066-112482091	CUUCCAGAGUAAAUGUGUCAAAUAC	4798

5781_10_2	PTPN11	Exon 10	+	chr12:112482095-112482120	CUGAUGAGUAUGCUCUAAAAGAAUA	4799
5781_10_3	PTPN11	Exon 10	+	chr12:112482111-112482136	AAAAGAAUAUGGCGUCAUGCGUGUU	4800
5781_10_4	PTPN11	Exon 10	+	chr12:112482169-112482194	ACGCUAAGAGAACUUAAACUUUCAA	4801
5781_10_5	PTPN11	Exon 10	+	chr12:112482173-112482198	UAAGAGAACUUAAACUUUCAAAGGU	4802
5781_10_6	PTPN11	Exon 10	-	chr12:112482072-112482097	AGGCCAGUAUUUGACACAUUUACUC	4803
5781_10_7	PTPN11	Exon 10	-	chr12:112482097-112482122	CAUAUUCUUUUAGAGCAUACUCAUC	4804
5781_10_8	PTPN11	Exon 10	-	chr12:112482158-112482183	AGUUCUCUUAGCGUAUAGUCAUGAG	4805
5781_11_1	PTPN11	Exon 11	+	chr12:112486449-112486474	CUGGUUUUUCUUGGCUCUACUCCAG	4806
5781_11_2	PTPN11	Exon 11	+	chr12:112486456-112486481	UUCUUGGCUCUACUCCAGGGGAAUA	4807
5781_11_3	PTPN11	Exon 11	+	chr12:112486465-112486490	CUACUCCAGGGGAAUACGGAGAGAA	4808
5781_11_4	PTPN11	Exon 11	+	chr12:112486470-112486495	CCAGGGGAAUACGGAGAGAACGGUC	4809
5781_11_5	PTPN11	Exon 11	+	chr12:112486485-112486510	GAGAACGGUCUGGCAAUACCACUUU	4810
5781_11_6	PTPN11	Exon 11	+	chr12:112486491-112486516	GGUCUGGCAAUACCACUUUCGGACC	4811
5781_11_7	PTPN11	Exon 11	+	chr12:112486495-112486520	UGGCAAUACCACUUUCGGACCUGGC	4812
5781_11_8	PTPN11	Exon 11	+	chr12:112486502-112486527	ACCACUUUCGGACCUGGCCGGACCA	4813
5781_11_9	PTPN11	Exon 11	+	chr12:112486520-112486545	CGGACCACGGCGUGCCCAGCGACCC	4814
5781_11_10	PTPN11	Exon 11	+	chr12:112486521-112486546	GGACCACGGCGUGCCCAGCGACCCU	4815
5781_11_11	PTPN11	Exon 11	+	chr12:112486522-112486547	GACCACGGCGUGCCCAGCGACCCUG	4816
5781_11_12	PTPN11	Exon 11	+	chr12:112486523-112486548	ACCACGGCGUGCCCAGCGACCCUGG	4817
5781_11_13	PTPN11	Exon 11	+	chr12:112486531-112486556	GUGCCCAGCGACCCUGGGGGCGUGC	4818
5781_11_14	PTPN11	Exon 11	+	chr12:112486540-112486565	GACCCUGGGGGCGUGCUGGACUUCC	4819
5781_11_15	PTPN11	Exon 11	+	chr12:112486543-112486568	CCUGGGGGCGUGCUGGACUUCCUGG	4820

5781_11_16	PTPN11	Exon 11	+	chr12:112486546-112486571	GGGGGCGUGCUGGACUUCCUGGAGG	4821
5781_11_17	PTPN11	Exon 11	+	chr12:112486561-112486586	UUCCUGGAGGAGGUGCACCAUAAGC	4822
5781_11_18	PTPN11	Exon 11	+	chr12:112486573-112486598	GUGCACCAUAAGCAGGAGAGCAUCA	4823
5781_11_19	PTPN11	Exon 11	+	chr12:112486580-112486605	AUAAGCAGGAGAGCAUCAUGGAUGC	4824
5781_11_20	PTPN11	Exon 11	+	chr12:112486581-112486606	UAAGCAGGAGAGCAUCAUGGAUGCA	4825
5781_11_21	PTPN11	Exon 11	+	chr12:112486585-112486610	CAGGAGAGCAUCAUGGAUGCAGGGC	4826
5781_11_22	PTPN11	Exon 11	+	chr12:112486591-112486616	AGCAUCAUGGAUGCAGGGCCGGUCG	4827
5781_11_23	PTPN11	Exon 11	+	chr12:112486602-112486627	UGCAGGGCCGGUCGUGGUGCACUGC	4828
5781_11_24	PTPN11	Exon 11	+	chr12:112486627-112486652	AGGUGACAGCUCCUGCUGCCCCUCU	4829
5781_11_25	PTPN11	Exon 11	+	chr12:112486659-112486684	AGCCUGUCCCUGUCUCCUAGCGCCC	4830
5781_11_26	PTPN11	Exon 11	+	chr12:112486660-112486685	GCCUGUCCCUGUCUCCUAGCGCCCA	4831
5781_11_27	PTPN11	Exon 11	+	chr12:112486700-112486725	UACCCACUCCUAGCUCUUUAACUGU	4832
5781_11_28	PTPN11	Exon 11	+	chr12:112486723-112486748	GUAGGAAGAAUUUAAUAUCUGUUUG	4833
5781_11_29	PTPN11	Exon 11	+	chr12:112486744-112486769	UUUGAGGCAUAGAGCAACUGCAUUG	4834
5781_11_30	PTPN11	Exon 11	+	chr12:112486745-112486770	UUGAGGCAUAGAGCAACUGCAUUGA	4835
5781_11_31	PTPN11	Exon 11	+	chr12:112486762-112486787	UGCAUUGAGGGACAUUUUGAUCCCA	4836
5781_11_32	PTPN11	Exon 11	+	chr12:112486797-112486822	CUCCUAGACCCUACAGCACUGCCAU	4837
5781_11_33	PTPN11	Exon 11	+	chr12:112486803-112486828	GACCCUACAGCACUGCCAUUGGCCA	4838
5781_11_34	PTPN11	Exon 11	+	chr12:112486809-112486834	ACAGCACUGCCAUUGGCCAUGGCCA	4839
5781_11_35	PTPN11	Exon 11	+	chr12:112486895-112486920	AGUUGUGCAUUAAACAACUUCAUCC	4840
5781_11_36	PTPN11	Exon 11	-	chr12:112486473-112486498	CCAGACCGUUCUCUCCGUAUUCCCC	4841
5781_11_37	PTPN11	Exon 11	-	chr12:112486506-112486531	GCCGUGGUCCGGCCAGGUCCGAAAG	4842

5781_11_38	PTPN11	Exon 11	-	chr12:112486517-112486542	UCGCUGGGCACGCCGUGGUCCGGCC	4843
5781_11_39	PTPN11	Exon 11	-	chr12:112486522-112486547	CAGGGUCGCUGGGCACGCCGUGGUC	4844
5781_11_40	PTPN11	Exon 11	-	chr12:112486527-112486552	GCCCCCAGGGUCGCUGGGCACGCCG	4845
5781_11_41	PTPN11	Exon 11	-	chr12:112486537-112486562	AGUCCAGCACGCCCCCAGGGUCGCU	4846
5781_11_42	PTPN11	Exon 11	-	chr12:112486538-112486563	AAGUCCAGCACGCCCCCAGGGUCGC	4847
5781_11_43	PTPN11	Exon 11	-	chr12:112486545-112486570	CUCCAGGAAGUCCAGCACGCCCCCA	4848
5781_11_44	PTPN11	Exon 11	-	chr12:112486546-112486571	CCUCCAGGAAGUCCAGCACGCCCCC	4849
5781_11_45	PTPN11	Exon 11	-	chr12:112486566-112486591	CUCCUGCUUAUGGUGCACCUCCUCC	4850
5781_11_46	PTPN11	Exon 11	-	chr12:112486581-112486606	UGCAUCCAUGAUGCUCUCCUGCUUA	4851
5781_11_47	PTPN11	Exon 11	-	chr12:112486612-112486637	GCUGUCACCUGCAGUGCACCACGAC	4852
5781_11_48	PTPN11	Exon 11	-	chr12:112486641-112486666	ACAGGCUGUGGCCUAGAGGGGCAGC	4853
5781_11_49	PTPN11	Exon 11	-	chr12:112486648-112486673	GACAGGGACAGGCUGUGGCCUAGAG	4854
5781_11_50	PTPN11	Exon 11	-	chr12:112486649-112486674	AGACAGGGACAGGCUGUGGCCUAGA	4855
5781_11_51	PTPN11	Exon 11	-	chr12:112486650-112486675	GAGACAGGGACAGGCUGUGGCCUAG	4856
5781_11_52	PTPN11	Exon 11	-	chr12:112486658-112486683	GGCGCUAGGAGACAGGGACAGGCUG	4857
5781_11_53	PTPN11	Exon 11	-	chr12:112486664-112486689	GCCCUGGGCGCUAGGAGACAGGGAC	4858
5781_11_54	PTPN11	Exon 11	-	chr12:112486669-112486694	AGCAAGCCCUGGGCGCUAGGAGACA	4859
5781_11_55	PTPN11	Exon 11	-	chr12:112486670-112486695	AAGCAAGCCCUGGGCGCUAGGAGAC	4860
5781_11_56	PTPN11	Exon 11	-	chr12:112486677-112486702	UAGGUAAAAGCAAGCCCUGGGCGCU	4861
5781_11_57	PTPN11	Exon 11	-	chr12:112486684-112486709	GAGUGGGUAGGUAAAAGCAAGCCCU	4862
5781_11_58	PTPN11	Exon 11	-	chr12:112486685-112486710	GGAGUGGGUAGGUAAAAGCAAGCCC	4863
5781_11_59	PTPN11	Exon 11	-	chr12:112486701-112486726	UACAGUUAAAGAGCUAGGAGUGGGU	4864

5781_11_60	PTPN11	Exon 11	-	chr12:112486705-112486730	UUCCUACAGUUAAAGAGCUAGGAGU	4865
5781_11_61	PTPN11	Exon 11	-	chr12:112486706-112486731	CUUCCUACAGUUAAAGAGCUAGGAG	4866
5781_11_62	PTPN11	Exon 11	-	chr12:112486711-112486736	AAAUUCUUCCUACAGUUAAAGAGCU	4867
5781_11_63	PTPN11	Exon 11	-	chr12:112486786-112486811	GUAGGGUCUAGGAGAAAUAUGCCUU	4868
5781_11_64	PTPN11	Exon 11	-	chr12:112486787-112486812	UGUAGGGUCUAGGAGAAAUAUGCCU	4869
5781_11_65	PTPN11	Exon 11	-	chr12:112486802-112486827	GGCCAAUGGCAGUGCUGUAGGGUCU	4870
5781_11_66	PTPN11	Exon 11	-	chr12:112486808-112486833	GGCCAUGGCCAAUGGCAGUGCUGUA	4871
5781_11_67	PTPN11	Exon 11	-	chr12:112486809-112486834	UGGCCAUGGCCAAUGGCAGUGCUGU	4872
5781_11_68	PTPN11	Exon 11	-	chr12:112486821-112486846	AGCAUGUUGCCAUGGCCAUGGCCAA	4873
5781_11_69	PTPN11	Exon 11	-	chr12:112486828-112486853	UUAACUGAGCAUGUUGCCAUGGCCA	4874
5781_11_70	PTPN11	Exon 11	-	chr12:112486834-112486859	GCUGUUUUAACUGAGCAUGUUGCCA	4875
5781_11_71	PTPN11	Exon 11	-	chr12:112486890-112486915	AAGUUGUUUAAUGCACAACUUCUGG	4876
5781_11_72	PTPN11	Exon 11	-	chr12:112486893-112486918	AUGAAGUUGUUUAAUGCACAACUUC	4877
5781_11_73	PTPN11	Exon 11	-	chr12:112486921-112486946	AAGAAUAAGGAGAAACUGCAGAGCC	4878
5781_12_1	PTPN11	Exon 12	+	chr12:112488420-112488445	CUUUUUGUCCUUCUGCCCGCAGUGC	4879
5781_12_2	PTPN11	Exon 12	+	chr12:112488426-112488451	GUCCUUCUGCCCGCAGUGCUGGAAU	4880
5781_12_3	PTPN11	Exon 12	+	chr12:112488430-112488455	UUCUGCCCGCAGUGCUGGAAUUGGC	4881
5781_12_4	PTPN11	Exon 12	+	chr12:112488435-112488460	CCCGCAGUGCUGGAAUUGGCCGGAC	4882
5781_12_5	PTPN11	Exon 12	+	chr12:112488436-112488461	CCGCAGUGCUGGAAUUGGCCGGACA	4883
5781_12_6	PTPN11	Exon 12	+	chr12:112488483-112488508	UUCUUAUUGACAUCAUCAGAGAGAA	4884
5781_12_7	PTPN11	Exon 12	+	chr12:112488486-112488511	UUAUUGACAUCAUCAGAGAGAAAGG	4885
5781_12_8	PTPN11	Exon 12	+	chr12:112488487-112488512	UAUUGACAUCAUCAGAGAGAAAGGU	4886

5781_12_9	PTPN11	Exon 12	+	chr12:112488495-112488520	UCAUCAGAGAGAAAGGUGGGUCAUC	4887
5781_12_10	PTPN11	Exon 12	+	chr12:112488498-112488523	UCAGAGAGAAAGGUGGGUCAUCUGG	4888
5781_12_11	PTPN11	Exon 12	+	chr12:112488499-112488524	CAGAGAGAAAGGUGGGUCAUCUGGU	4889
5781_12_12	PTPN11	Exon 12	-	chr12:112488431-112488456	GGCCAAUUCCAGCACUGCGGGCAGA	4890
5781_12_13	PTPN11	Exon 12	-	chr12:112488438-112488463	CCUGUCCGGCCAAUUCCAGCACUGC	4891
5781_12_14	PTPN11	Exon 12	-	chr12:112488439-112488464	CCCUGUCCGGCCAAUUCCAGCACUG	4892
5781_12_15	PTPN11	Exon 12	-	chr12:112488457-112488482	AUCAAUCACAAUGAACGUCCCUGUC	4893
5781_13_1	PTPN11	Exon 13	+	chr12:112489037-112489062	AUUGACGUUCCCAAAACCAUCCAGA	4894
5781_13_2	PTPN11	Exon 13	+	chr12:112489042-112489067	CGUUCCCAAAACCAUCCAGAUGGUG	4895
5781_13_3	PTPN11	Exon 13	+	chr12:112489051-112489076	AACCAUCCAGAUGGUGCGGUCUCAG	4896
5781_13_4	PTPN11	Exon 13	+	chr12:112489056-112489081	UCCAGAUGGUGCGGUCUCAGAGGUC	4897
5781_13_5	PTPN11	Exon 13	+	chr12:112489057-112489082	CCAGAUGGUGCGGUCUCAGAGGUCA	4898
5781_13_6	PTPN11	Exon 13	+	chr12:112489061-112489086	AUGGUGCGGUCUCAGAGGUCAGGGA	4899
5781_13_7	PTPN11	Exon 13	+	chr12:112489097-112489122	GAAGCACAGUACCGAUUUAUCUAUA	4900
5781_13_8	PTPN11	Exon 13	+	chr12:112489100-112489125	GCACAGUACCGAUUUAUCUAUAUGG	4901
5781_13_9	PTPN11	Exon 13	+	chr12:112489132-112489157	GCAUUAUAUUGAAACACUACAGCGC	4902
5781_13_10	PTPN11	Exon 13	+	chr12:112489148-112489173	CUACAGCGCAGGAUUGAAGAAGAGC	4903
5781_13_11	PTPN11	Exon 13	+	chr12:112489161-112489186	UUGAAGAAGAGCAGGUACCAGCCUG	4904
5781_13_12	PTPN11	Exon 13	+	chr12:112489162-112489187	UGAAGAAGAGCAGGUACCAGCCUGA	4905
5781_13_13	PTPN11	Exon 13	+	chr12:112489166-112489191	GAAGAGCAGGUACCAGCCUGAGGGC	4906
5781_13_14	PTPN11	Exon 13	-	chr12:112489017-112489042	UCAAUAUCGCAGUCAACACCUACGA	4907
5781_13_15	PTPN11	Exon 13	-	chr12:112489049-112489074	GAGACCGCACCAUCUGGAUGGUUUU	4908

5781_13_16	PTPN11	Exon 13	-	chr12:112489050-112489075	UGAGACCGCACCAUCUGGAUGGUUU	4909
5781_13_17	PTPN11	Exon 13	-	chr12:112489056-112489081	GACCUCUGAGACCGCACCAUCUGGA	4910
5781_13_18	PTPN11	Exon 13	-	chr12:112489060-112489085	CCCUGACCUCUGAGACCGCACCAUC	4911
5781_13_19	PTPN11	Exon 13	-	chr12:112489093-112489118	GAUAAAUCGGUACUGUGCUUCUGUC	4912
5781_13_20	PTPN11	Exon 13	-	chr12:112489111-112489136	AUGCUGGACCGCCAUAUAGAUAAAU	4913
5781_13_21	PTPN11	Exon 13	-	chr12:112489132-112489157	GCGCUGUAGUGUUUCAAUAUAAUGC	4914
5781_14_1	PTPN11	Exon 14	+	chr12:112502127-112502152	CUCUUCCAAAUUUCAGAAAAGCAAG	4915
5781_14_2	PTPN11	Exon 14	+	chr12:112502132-112502157	CCAAAUUUCAGAAAAGCAAGAGGAA	4916
5781_14_3	PTPN11	Exon 14	+	chr12:112502133-112502158	CAAAUUUCAGAAAAGCAAGAGGAAA	4917
5781_14_4	PTPN11	Exon 14	+	chr12:112502167-112502192	UAUACAAAUAUUAAGUAUUCUCUAG	4918
5781_14_5	PTPN11	Exon 14	+	chr12:112502180-112502205	AGUAUUCUCUAGCGGACCAGACGAG	4919
5781_14_6	PTPN11	Exon 14	+	chr12:112502245-112502270	CCCUGUGCAGAGUAAGUAGUGCUGA	4920
5781_14_7	PTPN11	Exon 14	-	chr12:112502135-112502160	CCUUUCCUCUUGCUUUUCUGAAAUU	4921
5781_14_8	PTPN11	Exon 14	-	chr12:112502199-112502224	GAGAGGGCUCUGAUCUCCACUCGUC	4922
5781_14_9	PTPN11	Exon 14	-	chr12:112502220-112502245	UGGCGUUGGAGUACAAGGCGGGAGA	4923
5781_14_10	PTPN11	Exon 14	-	chr12:112502221-112502246	GUGGCGUUGGAGUACAAGGCGGGAG	4924
5781_14_11	PTPN11	Exon 14	-	chr12:112502226-112502251	ACAGGGUGGCGUUGGAGUACAAGGC	4925
5781_14_12	PTPN11	Exon 14	-	chr12:112502227-112502252	CACAGGGUGGCGUUGGAGUACAAGG	4926
5781_14_13	PTPN11	Exon 14	-	chr12:112502230-112502255	CUGCACAGGGUGGCGUUGGAGUACA	4927
5781_14_14	PTPN11	Exon 14	-	chr12:112502239-112502264	CUACUUACUCUGCACAGGGUGGCGU	4928
5781_14_15	PTPN11	Exon 14	-	chr12:112502245-112502270	UCAGCACUACUUACUCUGCACAGGG	4929
5781_14_16	PTPN11	Exon 14	-	chr12:112502248-112502273	CCUUCAGCACUACUUACUCUGCACA	4930

5781_14_17	PTPN11	Exon 14	-	chr12:112502249-112502274	UCCUUCAGCACUACUUACUCUGCAC	4931
5781_15_1	PTPN11	Exon 15	+	chr12:112504704-112504729	GACAGUGCUAGAGUCUAUGAAAACG	4932
5781_15_2	PTPN11	Exon 15	+	chr12:112504705-112504730	ACAGUGCUAGAGUCUAUGAAAACGU	4933
5781_15_3	PTPN11	Exon 15	+	chr12:112504769-112504794	CCUGCCAAAACUUCAGCACAGAAAU	4934
5781_15_4	PTPN11	Exon 15	-	chr12:112504693-112504718	ACUCUAGCACUGUCUUCUCUCAUUC	4935
5781_15_5	PTPN11	Exon 15	-	chr12:112504736-112504761	UCUGAAACUUUUCUGCUGUUGCAUC	4936
5781_15_6	PTPN11	Exon 15	-	chr12:112504772-112504797	CCUAUUUCUGUGCUGAAGUUUUGGC	4937
5781_15_7	PTPN11	Exon 15	-	chr12:112504776-112504801	AAUACCUAUUUCUGUGCUGAAGUUU	4938
5781_16_1	PTPN11	Exon 16	+	chr12:112505802-112505827	UCUUAACUUAUUUCUUCCCCAGAUG	4939
5781_16_2	PTPN11	Exon 16	+	chr12:112505869-112505894	AGAAAGUUUAUGUGAAGACAGAAUU	4940
5781_16_3	PTPN11	Exon 16	+	chr12:112505875-112505900	UUUAUGUGAAGACAGAAUUUGGAUU	4941
5781_16_4	PTPN11	Exon 16	+	chr12:112505879-112505904	UGUGAAGACAGAAUUUGGAUUUGGA	4942
5781_16_5	PTPN11	Exon 16	+	chr12:112505891-112505916	AUUUGGAUUUGGAAGGCUUGCAAUG	4943
5781_16_6	PTPN11	Exon 16	+	chr12:112506051-112506076	AUUUUAUAGAAUUUGUUUGAAAUUG	4944
5781_16_7	PTPN11	Exon 16	+	chr12:112506089-112506114	AUUGUGCGCUGUAUUUUGCAGAUUA	4945
5781_16_8	PTPN11	Exon 16	+	chr12:112506090-112506115	UUGUGCGCUGUAUUUUGCAGAUUAU	4946
5781_16_9	PTPN11	Exon 16	+	chr12:112506091-112506116	UGUGCGCUGUAUUUUGCAGAUUAUG	4947
5781_16_10	PTPN11	Exon 16	+	chr12:112506111-112506136	UUAUGGGGAUUCAAAUUCUAGUAAU	4948
5781_16_11	PTPN11	Exon 16	+	chr12:112506171-112506196	GUUUAAUUUUUUUUUUCCUCAUUGU	4949
5781_16_12	PTPN11	Exon 16	+	chr12:112506172-112506197	UUUAAUUUUUUUUUUCCUCAUUGUU	4950
5781_16_13	PTPN11	Exon 16	+	chr12:112506173-112506198	UUAAUUUUUUUUUUCCUCAUUGUUG	4951
5781_16_14	PTPN11	Exon 16	+	chr12:112506195-112506220	UUGGGGAUGAUGAGAAGAAAUGAUU	4952

5781_16_15	PTPN11	Exon 16	+	chr12:112506196-112506221	UGGGGAUGAUGAGAAGAAAUGAUUU	4953
5781_16_16	PTPN11	Exon 16	+	chr12:112506263-112506288	UCAUUUACCAUCAUGUAUCCAGUAG	4954
5781_16_17	PTPN11	Exon 16	+	chr12:112506280-112506305	UCCAGUAGUGGAUAAUUCAUUUUGA	4955
5781_16_18	PTPN11	Exon 16	+	chr12:112506293-112506318	AAUUCAUUUUGAUGGCUUCUAUUUU	4956
5781_16_19	PTPN11	Exon 16	+	chr12:112506348-112506373	GACUGUCAGAAGUUGACCUUUGCAC	4957
5781_16_20	PTPN11	Exon 16	+	chr12:112506378-112506403	UUAAAGAGUCAUAGAAAAAGAAUCA	4958
5781_16_21	PTPN11	Exon 16	+	chr12:112506395-112506420	AAGAAUCAUGGAUAUUUAUGAAUUA	4959
5781_16_22	PTPN11	Exon 16	+	chr12:112506402-112506427	AUGGAUAUUUAUGAAUUAAGGUAAG	4960
5781_16_23	PTPN11	Exon 16	+	chr12:112506407-112506432	UAUUUAUGAAUUAAGGUAAGAGGUG	4961
5781_16_24	PTPN11	Exon 16	+	chr12:112506453-112506478	UUCCAGCCGUUGACCAAUUAUAGUU	4962
5781_16_25	PTPN11	Exon 16	+	chr12:112506475-112506500	GUUCGGCUGUUGACUGAGAAGUUUG	4963
5781_16_26	PTPN11	Exon 16	+	chr12:112506478-112506503	CGGCUGUUGACUGAGAAGUUUGUGG	4964
5781_16_27	PTPN11	Exon 16	+	chr12:112506479-112506504	GGCUGUUGACUGAGAAGUUUGUGGU	4965
5781_16_28	PTPN11	Exon 16	+	chr12:112506537-112506562	AAUAAUUGUCUUGUACUUAGAAAAA	4966
5781_16_29	PTPN11	Exon 16	+	chr12:112506563-112506588	GGCGUCUAUGAAUGACCAGUGUUUU	4967
5781_16_30	PTPN11	Exon 16	+	chr12:112506991-112507016	UGGUUUUUUCUAAUCAGAAGAAAGC	4968
5781_16_31	PTPN11	Exon 16	+	chr12:112506992-112507017	GGUUUUUUCUAAUCAGAAGAAAGCU	4969
5781_16_32	PTPN11	Exon 16	+	chr12:112506993-112507018	GUUUUUUCUAAUCAGAAGAAAGCUG	4970
5781_16_33	PTPN11	Exon 16	+	chr12:112507061-112507086	GAUUCAAGAAAAGGGUGUGAAGUAG	4971
5781_16_34	PTPN11	Exon 16	+	chr12:112507074-112507099	GGUGUGAAGUAGAGGUGCAGUUAAG	4972
5781_16_35	PTPN11	Exon 16	+	chr12:112507075-112507100	GUGUGAAGUAGAGGUGCAGUUAAGU	4973
5781_16_36	PTPN11	Exon 16	+	chr12:112507076-112507101	UGUGAAGUAGAGGUGCAGUUAAGUG	4974

5781_16_37	PTPN11	Exon 16	+	chr12:112507077-112507102	GUGAAGUAGAGGUGCAGUUAAGUGG	4975
5781_16_38	PTPN11	Exon 16	+	chr12:112507078-112507103	UGAAGUAGAGGUGCAGUUAAGUGGG	4976
5781_16_39	PTPN11	Exon 16	+	chr12:112507097-112507122	AGUGGGGGGCCACUAGUCUAACAGA	4977
5781_16_40	PTPN11	Exon 16	+	chr12:112507115-112507140	UAACAGACGGUCACAACCAGUGCCA	4978
5781_16_41	PTPN11	Exon 16	+	chr12:112507125-112507150	UCACAACCAGUGCCAUGGAAAACCA	4979
5781_16_42	PTPN11	Exon 16	+	chr12:112507160-112507185	CAAAAGCAGAAGUUGCUAGUGACCU	4980
5781_16_43	PTPN11	Exon 16	+	chr12:112507161-112507186	AAAAGCAGAAGUUGCUAGUGACCUU	4981
5781_16_44	PTPN11	Exon 16	+	chr12:112507187-112507212	GGAAGCCGAAGCUGCUUACAGUAGC	4982
5781_16_45	PTPN11	Exon 16	+	chr12:112507188-112507213	GAAGCCGAAGCUGCUUACAGUAGCU	4983
5781_16_46	PTPN11	Exon 16	+	chr12:112507223-112507248	GAAAGUCAGACUAAGAAAUAAAGAG	4984
5781_16_47	PTPN11	Exon 16	+	chr12:112507224-112507249	AAAGUCAGACUAAGAAAUAAAGAGA	4985
5781_16_48	PTPN11	Exon 16	+	chr12:112507275-112507300	UUUCUGCUAGCCCUGAGCCUAUUUU	4986
5781_16_49	PTPN11	Exon 16	+	chr12:112507288-112507313	UGAGCCUAUUUUUGGAACCAGCACU	4987
5781_16_50	PTPN11	Exon 16	+	chr12:112507289-112507314	GAGCCUAUUUUUGGAACCAGCACUU	4988
5781_16_51	PTPN11	Exon 16	+	chr12:112507290-112507315	AGCCUAUUUUUGGAACCAGCACUUG	4989
5781_16_52	PTPN11	Exon 16	+	chr12:112507307-112507332	AGCACUUGGGGAAACUGAUCUUGUG	4990
5781_16_53	PTPN11	Exon 16	+	chr12:112507311-112507336	CUUGGGGAAACUGAUCUUGUGAGGA	4991
5781_16_54	PTPN11	Exon 16	+	chr12:112507322-112507347	UGAUCUUGUGAGGAUGGAUGUGUUU	4992
5781_16_55	PTPN11	Exon 16	+	chr12:112507323-112507348	GAUCUUGUGAGGAUGGAUGUGUUUA	4993
5781_16_56	PTPN11	Exon 16	+	chr12:112507330-112507355	UGAGGAUGGAUGUGUUUAGGGACAC	4994
5781_16_57	PTPN11	Exon 16	+	chr12:112507331-112507356	GAGGAUGGAUGUGUUUAGGGACACA	4995
5781_16_58	PTPN11	Exon 16	+	chr12:112507358-112507383	GCUUUUGAGAGCAGCACCACCCCAC	4996

5781_16_59	PTPN11	Exon 16	+	chr12:112507359-112507384	CUUUUGAGAGCAGCACCACCCCACU	4997
5781_16_60	PTPN11	Exon 16	+	chr12:112507360-112507385	UUUUGAGAGCAGCACCACCCCACUG	4998
5781_16_61	PTPN11	Exon 16	+	chr12:112507375-112507400	CACCCCACUGGGGCAUCCCCAGACU	4999
5781_16_62	PTPN11	Exon 16	+	chr12:112507376-112507401	ACCCCACUGGGGCAUCCCCAGACUU	5000
5781_16_63	PTPN11	Exon 16	+	chr12:112507404-112507429	AAACGUGACUCUUUCUUAAUGCCAC	5001
5781_16_64	PTPN11	Exon 16	+	chr12:112507405-112507430	AACGUGACUCUUUCUUAAUGCCACU	5002
5781_16_65	PTPN11	Exon 16	+	chr12:112507416-112507441	UUCUUAAUGCCACUGGGUUUUAGUC	5003
5781_16_66	PTPN11	Exon 16	+	chr12:112507430-112507455	GGGUUUUAGUCAGGCCACAGUGAGA	5004
5781_16_67	PTPN11	Exon 16	+	chr12:112507445-112507470	CACAGUGAGAAGGAACAGCCCUAAC	5005
5781_16_68	PTPN11	Exon 16	+	chr12:112507457-112507482	GAACAGCCCUAACAGGCCUCCAGCC	5006
5781_16_69	PTPN11	Exon 16	+	chr12:112507571-112507596	GCCUCAUAUGUUGAAUCAUCCAGUG	5007
5781_16_70	PTPN11	Exon 16	+	chr12:112507595-112507620	GCGGAUAUUUCAAUGAAAAUAUCAU	5008
5781_16_71	PTPN11	Exon 16	+	chr12:112507611-112507636	AAAUAUCAUUGGUUGACUUUUGUGA	5009
5781_16_72	PTPN11	Exon 16	+	chr12:112507625-112507650	GACUUUUGUGAUGGUAAUAAUGCUA	5010
5781_16_73	PTPN11	Exon 16	+	chr12:112507647-112507672	CUAUGGCAUCUUUGCCAUGAAGUUG	5011
5781_16_74	PTPN11	Exon 16	+	chr12:112507656-112507681	CUUUGCCAUGAAGUUGUGGCCUCCU	5012
5781_16_75	PTPN11	Exon 16	+	chr12:112507672-112507697	UGGCCUCCUUGGAUUCUUCUGACUU	5013
5781_16_76	PTPN11	Exon 16	+	chr12:112507683-112507708	GAUUCUUCUGACUUUGGCUUCUGAA	5014
5781_16_77	PTPN11	Exon 16	+	chr12:112507687-112507712	CUUCUGACUUUGGCUUCUGAAAGGA	5015
5781_16_78	PTPN11	Exon 16	+	chr12:112507704-112507729	UGAAAGGAAGGCCUAGAUCCAGCCC	5016
5781_16_79	PTPN11	Exon 16	+	chr12:112507707-112507732	AAGGAAGGCCUAGAUCCAGCCCUGG	5017
5781_16_80	PTPN11	Exon 16	+	chr12:112507723-112507748	CAGCCCUGGUGGUAGUUCCUUUCUG	5018

5781_16_81	PTPN11	Exon 16	+	chr12:112507747-112507772	GAGGUCUCUCAGUCCCUUGAGACUU	5019
5781_16_82	PTPN11	Exon 16	+	chr12:112507748-112507773	AGGUCUCUCAGUCCCUUGAGACUUU	5020
5781_16_83	PTPN11	Exon 16	+	chr12:112507749-112507774	GGUCUCUCAGUCCCUUGAGACUUUG	5021
5781_16_84	PTPN11	Exon 16	+	chr12:112507757-112507782	AGUCCCUUGAGACUUUGGGGUAGUU	5022
5781_16_85	PTPN11	Exon 16	+	chr12:112507843-112507868	UGAACUUUGAAUUGCUUCAGAACAC	5023
5781_16_86	PTPN11	Exon 16	+	chr12:112507848-112507873	UUUGAAUUGCUUCAGAACACAGGUG	5024
5781_16_87	PTPN11	Exon 16	+	chr12:112507856-112507881	GCUUCAGAACACAGGUGUGGCCUGA	5025
5781_16_88	PTPN11	Exon 16	+	chr12:112507871-112507896	UGUGGCCUGAAGGUAUUCCCUUAUU	5026
5781_16_89	PTPN11	Exon 16	+	chr12:112507872-112507897	GUGGCCUGAAGGUAUUCCCUUAUUA	5027
5781_16_90	PTPN11	Exon 16	+	chr12:112508001-112508026	CAUCGACUCAUUCUCCAUUUUGCUU	5028
5781_16_91	PTPN11	Exon 16	+	chr12:112508028-112508053	GUUUUGUCUUGACUUGACUUGACUU	5029
5781_16_92	PTPN11	Exon 16	+	chr12:112508029-112508054	UUUUGUCUUGACUUGACUUGACUUU	5030
5781_16_93	PTPN11	Exon 16	+	chr12:112508030-112508055	UUUGUCUUGACUUGACUUGACUUUG	5031
5781_16_94	PTPN11	Exon 16	+	chr12:112508031-112508056	UUGUCUUGACUUGACUUGACUUUGG	5032
5781_16_95	PTPN11	Exon 16	+	chr12:112508135-112508160	AGAUCAGUUGCUUUUAUACUCAGAA	5033
5781_16_96	PTPN11	Exon 16	+	chr12:112508151-112508176	UACUCAGAAUGGAAAUACCUGAUCU	5034
5781_16_97	PTPN11	Exon 16	+	chr12:112508200-112508225	GAUUUCAUUUAGAUUUCCCUCCACG	5035
5781_16_98	PTPN11	Exon 16	+	chr12:112508234-112508259	AACUAUCAUGUUCUUAUGUAAACUU	5036
5781_16_99	PTPN11	Exon 16	+	chr12:112508240-112508265	CAUGUUCUUAUGUAAACUUAGGCCA	5037
5781_16_100	PTPN11	Exon 16	+	chr12:112508263-112508288	CAAGGCCAGAGUUAUCAUAGUCCCU	5038
5781_16_101	PTPN11	Exon 16	+	chr12:112508272-112508297	AGUUAUCAUAGUCCCUAGGUUGCUA	5039
5781_16_102	PTPN11	Exon 16	+	chr12:112508288-112508313	AGGUUGCUACGGCUUAUCAUGUGCU	5040

5781_16_103	PTPN11	Exon 16	+	chr12:112508295-112508320	UACGGCUUAUCAUGUGCUUGGUAAA	5041
5781_16_104	PTPN11	Exon 16	+	chr12:112508305-112508330	CAUGUGCUUGGUAAAAGGUGAUCGC	5042
5781_16_105	PTPN11	Exon 16	+	chr12:112508336-112508361	UCAGACGAGUUUACUUUACAUGAGA	5043
5781_16_106	PTPN11	Exon 16	+	chr12:112508343-112508368	AGUUUACUUUACAUGAGAUGGAAUC	5044
5781_16_107	PTPN11	Exon 16	+	chr12:112508351-112508376	UUACAUGAGAUGGAAUCAGGCAGAG	5045
5781_16_108	PTPN11	Exon 16	+	chr12:112508355-112508380	AUGAGAUGGAAUCAGGCAGAGAGGC	5046
5781_16_109	PTPN11	Exon 16	+	chr12:112508356-112508381	UGAGAUGGAAUCAGGCAGAGAGGCU	5047
5781_16_110	PTPN11	Exon 16	+	chr12:112508363-112508388	GAAUCAGGCAGAGAGGCUGGGAUGA	5048
5781_16_111	PTPN11	Exon 16	+	chr12:112508376-112508401	AGGCUGGGAUGAUGGAGAAAGCUCG	5049
5781_16_112	PTPN11	Exon 16	+	chr12:112508401-112508426	AGGUGAAGUUUUAAAAAAAAAGUUG	5050
5781_16_113	PTPN11	Exon 16	+	chr12:112508406-112508431	AAGUUUUAAAAAAAAAGUUGUGGAA	5051
5781_16_114	PTPN11	Exon 16	+	chr12:112508421-112508446	AGUUGUGGAAAGGAAAGUUCCAAAG	5052
5781_16_115	PTPN11	Exon 16	+	chr12:112508424-112508449	UGUGGAAAGGAAAGUUCCAAAGAGG	5053
5781_16_116	PTPN11	Exon 16	+	chr12:112508433-112508458	GAAAGUUCCAAAGAGGUGGUUUCUG	5054
5781_16_117	PTPN11	Exon 16	+	chr12:112508450-112508475	GGUUUCUGAGGAAGUCAGAGCGCCC	5055
5781_16_118	PTPN11	Exon 16	+	chr12:112508451-112508476	GUUUCUGAGGAAGUCAGAGCGCCCA	5056
5781_16_119	PTPN11	Exon 16	+	chr12:112508470-112508495	CGCCCAGGGCCAGAGCAGUCAGUAA	5057
5781_16_120	PTPN11	Exon 16	+	chr12:112508471-112508496	GCCCAGGGCCAGAGCAGUCAGUAAU	5058
5781_16_121	PTPN11	Exon 16	+	chr12:112508480-112508505	CAGAGCAGUCAGUAAUGGGUGAAUG	5059
5781_16_122	PTPN11	Exon 16	+	chr12:112508488-112508513	UCAGUAAUGGGUGAAUGAGGUUGUU	5060
5781_16_123	PTPN11	Exon 16	+	chr12:112508496-112508521	GGGUGAAUGAGGUUGUUUGGAAAGU	5061
5781_16_124	PTPN11	Exon 16	+	chr12:112508512-112508537	UUGGAAAGUCGGUGUGACAGACACA	5062

5781_16_125	PTPN11	Exon 16	+	chr12:112508530-112508555	AGACACAUGGAUGCCAUCUACUUCU	5063
5781_16_126	PTPN11	Exon 16	+	chr12:112508537-112508562	UGGAUGCCAUCUACUUCUAGGUUGC	5064
5781_16_127	PTPN11	Exon 16	+	chr12:112508540-112508565	AUGCCAUCUACUUCUAGGUUGCUGG	5065
5781_16_128	PTPN11	Exon 16	+	chr12:112508541-112508566	UGCCAUCUACUUCUAGGUUGCUGGU	5066
5781_16_129	PTPN11	Exon 16	+	chr12:112508577-112508602	AUGCACAAUAUUCCAUAGCUCACUG	5067
5781_16_130	PTPN11	Exon 16	+	chr12:112508599-112508624	CUGAGGAUUUUAAAAUUAUAAGCAU	5068
5781_16_131	PTPN11	Exon 16	+	chr12:112508613-112508638	AUUAUAAGCAUAGGAUUUUAUAUUU	5069
5781_16_132	PTPN11	Exon 16	+	chr12:112508614-112508639	UUAUAAGCAUAGGAUUUUAUAUUUU	5070
5781_16_133	PTPN11	Exon 16	+	chr12:112508615-112508640	UAUAAGCAUAGGAUUUUAUAUUUUG	5071
5781_16_134	PTPN11	Exon 16	+	chr12:112508631-112508656	UAUAUUUUGGGGUGAAAGAAUUAUC	5072
5781_16_135	PTPN11	Exon 16	+	chr12:112508640-112508665	GGGUGAAAGAAUUAUCUGGCACAUU	5073
5781_16_136	PTPN11	Exon 16	+	chr12:112508646-112508671	AAGAAUUAUCUGGCACAUUAGGUAU	5074
5781_16_137	PTPN11	Exon 16	+	chr12:112508707-112508732	AUAACUUUUUUUAAAAAAAACUAAA	5075
5781_16_138	PTPN11	Exon 16	+	chr12:112508728-112508753	UAAAAGGCGCUUCAUGUCCAGUGUG	5076
5781_16_139	PTPN11	Exon 16	+	chr12:112508746-112508771	CAGUGUGUGGCCCUUCUGAAACUUA	5077
5781_16_140	PTPN11	Exon 16	+	chr12:112508770-112508795	AUGGUCAUCUCUCCCACUGAAACCA	5078
5781_16_141	PTPN11	Exon 16	+	chr12:112508785-112508810	ACUGAAACCAAGGUCUUUUCAAAUG	5079
5781_16_142	PTPN11	Exon 16	+	chr12:112508793-112508818	CAAGGUCUUUUCAAAUGUGGCUAAA	5080
5781_16_143	PTPN11	Exon 16	+	chr12:112508794-112508819	AAGGUCUUUUCAAAUGUGGCUAAAU	5081
5781_16_144	PTPN11	Exon 16	+	chr12:112508795-112508820	AGGUCUUUUCAAAUGUGGCUAAAUG	5082
5781_16_145	PTPN11	Exon 16	+	chr12:112508801-112508826	UUUCAAAUGUGGCUAAAUGGGGAUG	5083
5781_16_146	PTPN11	Exon 16	+	chr12:112508809-112508834	GUGGCUAAAUGGGGAUGAGGAGACA	5084

5781_16_147	PTPN11	Exon 16	+	chr12:112508810-112508835	UGGCUAAAUGGGGAUGAGGAGACAC	5085
5781_16_148	PTPN11	Exon 16	+	chr12:112508814-112508839	UAAAUGGGGAUGAGGAGACACGGGU	5086
5781_16_149	PTPN11	Exon 16	+	chr12:112508824-112508849	UGAGGAGACACGGGUAGGACUUUCU	5087
5781_16_150	PTPN11	Exon 16	+	chr12:112508860-112508885	CAUUCUUUAAAGAGCCAAGUUGCUU	5088
5781_16_151	PTPN11	Exon 16	+	chr12:112508861-112508886	AUUCUUUAAAGAGCCAAGUUGCUUC	5089
5781_16_152	PTPN11	Exon 16	+	chr12:112508862-112508887	UUCUUUAAAGAGCCAAGUUGCUUCG	5090
5781_16_153	PTPN11	Exon 16	+	chr12:112508873-112508898	GCCAAGUUGCUUCGGGGAAACAGCC	5091
5781_16_154	PTPN11	Exon 16	+	chr12:112508880-112508905	UGCUUCGGGGAAACAGCCAGGAAAA	5092
5781_16_155	PTPN11	Exon 16	+	chr12:112508899-112508924	GGAAAAUGGUCAAGAUUAUUUUUAG	5093
5781_16_156	PTPN11	Exon 16	+	chr12:112508911-112508936	AGAUUAUUUUUAGAGGUUAUUUUAU	5094
5781_16_157	PTPN11	Exon 16	+	chr12:112508912-112508937	GAUUAUUUUUAGAGGUUAUUUUAUU	5095
5781_16_158	PTPN11	Exon 16	+	chr12:112508913-112508938	AUUAUUUUUAGAGGUUAUUUUAUUG	5096
5781_16_159	PTPN11	Exon 16	+	chr12:112508955-112508980	UAACAUCUUGAGUUAUUUUUAAUUC	5097
5781_16_160	PTPN11	Exon 16	+	chr12:112508956-112508981	AACAUCUUGAGUUAUUUUUAAUUCA	5098
5781_16_161	PTPN11	Exon 16	+	chr12:112508957-112508982	ACAUCUUGAGUUAUUUUUAAUUCAG	5099
5781_16_162	PTPN11	Exon 16	+	chr12:112508958-112508983	CAUCUUGAGUUAUUUUUAAUUCAGG	5100
5781_16_163	PTPN11	Exon 16	+	chr12:112508964-112508989	GAGUUAUUUUUAAUUCAGGGGGAUG	5101
5781_16_164	PTPN11	Exon 16	+	chr12:112508969-112508994	AUUUUUAAUUCAGGGGGAUGUGGAA	5102
5781_16_165	PTPN11	Exon 16	+	chr12:112509013-112509038	GUUUUGUUGUAGCUUAGUAUCCAUA	5103
5781_16_166	PTPN11	Exon 16	+	chr12:112509014-112509039	UUUUGUUGUAGCUUAGUAUCCAUAA	5104
5781_16_167	PTPN11	Exon 16	+	chr12:112509076-112509101	GCAGCUUUUGUUUUCUGUAUGUUGU	5105
5781_16_168	PTPN11	Exon 16	+	chr12:112509077-112509102	CAGCUUUUGUUUUCUGUAUGUUGUU	5106

5781_16_169	PTPN11	Exon 16	+	chr12:112509078-112509103	AGCUUUUGUUUUCUGUAGUUGUUG	5107
5781_16_170	PTPN11	Exon 16	+	chr12:112509079-112509104	GCUUUUGUUUUCUGUAUGUUGUUGG	5108
5781_16_171	PTPN11	Exon 16	+	chr12:112509108-112509133	UCAACUUUCACACAUAGCAAGCACA	5109
5781_16_172	PTPN11	Exon 16	+	chr12:112509124-112509149	GCAAGCACAUGGCCUCCCUGAUGUC	5110
5781_16_173	PTPN11	Exon 16	+	chr12:112509138-112509163	UCCCUGAUGUCAGGAUGCCUUUGUU	5111
5781_16_174	PTPN11	Exon 16	+	chr12:112509254-112509279	CUAAAAAUUUGUUCCUUUUUCACUA	5112
5781_16_175	PTPN11	Exon 16	+	chr12:112509255-112509280	UAAAAAUUUGUUCCUUUUUCACUAU	5113
5781_16_176	PTPN11	Exon 16	+	chr12:112509269-112509294	UUUUUCACUAUGGGCAGUUCACACA	5114
5781_16_177	PTPN11	Exon 16	+	chr12:112509290-112509315	CACAAGGCAAAAACUAUUGAACAGU	5115
5781_16_178	PTPN11	Exon 16	+	chr12:112509429-112509454	UGAUUCUUUUAUUAAUAAAAGCUAA	5116
5781_16_179	PTPN11	Exon 16	+	chr12:112509430-112509455	GAUUCUUUUAUUAAUAAAAGCUAAU	5117
5781_16_180	PTPN11	Exon 16	+	chr12:112509436-112509461	UUUAUUAAUAAAAGCUAAUGGGAAA	5118
5781_16_181	PTPN11	Exon 16	+	chr12:112509553-112509578	UUUAUUGAUAAAUCUAUCCUUUAAA	5119
5781_16_182	PTPN11	Exon 16	+	chr12:112509566-112509591	CUAUCCUUUAAAAGGAAUACGUUUU	5120
5781_16_183	PTPN11	Exon 16	+	chr12:112509744-112509769	AAUAGUUUAUGUAGAGAAACAUUAG	5121
5781_16_184	PTPN11	Exon 16	+	chr12:112509775-112509800	UUAAUUGUCUCCCCACCUAUAUUUA	5122
5781_16_185	PTPN11	Exon 16	+	chr12:112509776-112509801	UAAUUGUCUCCCCACCUAUAUUUAU	5123
5781_16_186	PTPN11	Exon 16	+	chr12:112509847-112509872	AGUAAAAGUGUAUUUGUAAACUGUA	5124
5781_16_187	PTPN11	Exon 16	+	chr12:112509848-112509873	GUAAAAGUGUAUUUGUAAACUGUAU	5125
5781_16_188	PTPN11	Exon 16	+	chr12:112509862-112509887	GUAAACUGUAUGGGAACUAAAAAUU	5126
5781_16_189	PTPN11	Exon 16	+	chr12:112509888-112509913	GGAAUAAAACCAUUUUCUUAUAUGA	5127
5781_16_190	PTPN11	Exon 16	-	chr12:112505821-112505846	GGGAGAGGGUGAAAGUCCACAUCUG	5128

5781_16_191	PTPN11	Exon 16	-	chr12:112505822-112505847	AGGGAGAGGGUGAAAGUCCACAUCU	5129
5781_16_192	PTPN11	Exon 16	-	chr12:112505823-112505848	UAGGGAGAGGGUGAAAGUCCACAUC	5130
5781_16_193	PTPN11	Exon 16	-	chr12:112505840-112505865	UCUGUUCUUGAUCUUUUUAGGGAGA	5131
5781_16_194	PTPN11	Exon 16	-	chr12:112505841-112505866	GUCUGUUCUUGAUCUUUUUAGGGAG	5132
5781_16_195	PTPN11	Exon 16	-	chr12:112505846-112505871	CUUGCGUCUGUUCUUGAUCUUUUUA	5133
5781_16_196	PTPN11	Exon 16	-	chr12:112505847-112505872	UCUUGCGUCUGUUCUUGAUCUUUUU	5134
5781_16_197	PTPN11	Exon 16	-	chr12:112505929-112505954	AUGGUUUCAAAUUUUGCUUAUCAAA	5135
5781_16_198	PTPN11	Exon 16	-	chr12:112505953-112505978	GAGUUAAAAUACAGUGGUCUUUAAA	5136
5781_16_199	PTPN11	Exon 16	-	chr12:112505964-112505989	CAGGUAUUGUUGAGUUAAAAUACAG	5137
5781_16_200	PTPN11	Exon 16	-	chr12:112505988-112506013	CUGAGGAAAUGAGUAAUUGGGAAGC	5138
5781_16_201	PTPN11	Exon 16	-	chr12:112505995-112506020	UUCUUAUCUGAGGAAAUGAGUAAUU	5139
5781_16_202	PTPN11	Exon 16	-	chr12:112505996-112506021	CUUCUUAUCUGAGGAAAUGAGUAAU	5140
5781_16_203	PTPN11	Exon 16	-	chr12:112506010-112506035	UGUAGAGAUGAUUUCUUCUUAUCUG	5141
5781_16_204	PTPN11	Exon 16	-	chr12:112506164-112506189	GGAAAAAAAAAAUUAAACUGGUUAA	5142
5781_16_205	PTPN11	Exon 16	-	chr12:112506165-112506190	AGGAAAAAAAAAAUUAAACUGGUUA	5143
5781_16_206	PTPN11	Exon 16	-	chr12:112506171-112506196	ACAAUGAGGAAAAAAAAAAUUAAAC	5144
5781_16_207	PTPN11	Exon 16	-	chr12:112506190-112506215	UUUCUUCUCAUCAUCCCCAACAAUG	5145
5781_16_208	PTPN11	Exon 16	-	chr12:112506245-112506270	UAAAUGAGAUUGUUCUCACUUUUCU	5146
5781_16_209	PTPN11	Exon 16	-	chr12:112506273-112506298	GAAUUAUCCACUACUGGAUACAUGA	5147
5781_16_210	PTPN11	Exon 16	-	chr12:112506284-112506309	GCCAUCAAAAUGAAUUAUCCACUAC	5148
5781_16_211	PTPN11	Exon 16	-	chr12:112506324-112506349	CUCAGGCACUGGCUUAAUUCUCAUU	5149
5781_16_212	PTPN11	Exon 16	-	chr12:112506340-112506365	GUCAACUUCUGACAGUCUCAGGCAC	5150

5781_16_213	PTPN11	Exon 16	-	chr12:112506346-112506371	GCAAAGGUCAACUUCUGACAGUCUC	5151
5781_16_214	PTPN11	Exon 16	-	chr12:112506367-112506392	CUAUGACUCUUUAAUGCCAGUGCAA	5152
5781_16_215	PTPN11	Exon 16	-	chr12:112506458-112506483	AGCCGAACUAUAAUUGGUCAACGGC	5153
5781_16_216	PTPN11	Exon 16	-	chr12:112506462-112506487	CAACAGCCGAACUAUAAUUGGUCAA	5154
5781_16_217	PTPN11	Exon 16	-	chr12:112506469-112506494	UCUCAGUCAACAGCCGAACUAUAAU	5155
5781_16_218	PTPN11	Exon 16	-	chr12:112506520-112506545	CAAUUAUUCAAAUGCAAAGAAAAUA	5156
5781_16_219	PTPN11	Exon 16	-	chr12:112506581-112506606	UCGUUGUUUUGGCGACCAAAAACAC	5157
5781_16_220	PTPN11	Exon 16	-	chr12:112506597-112506622	AACCCUAUUCAAACAGUCGUUGUUU	5158
5781_16_221	PTPN11	Exon 16	-	chr12:112507028-112507053	CGAACACUGAACAAAUCAUUCAUCU	5159
5781_16_222	PTPN11	Exon 16	-	chr12:112507029-112507054	CCGAACACUGAACAAAUCAUUCAUC	5160
5781_16_223	PTPN11	Exon 16	-	chr12:112507109-112507134	UGGUUGUGACCGUCUGUUAGACUAG	5161
5781_16_224	PTPN11	Exon 16	-	chr12:112507134-112507159	UAAUAUCCUUGGUUUUCCAUGGCAC	5162
5781_16_225	PTPN11	Exon 16	-	chr12:112507140-112507165	UUUUGCUAAUAUCCUUGGUUUUCCA	5163
5781_16_226	PTPN11	Exon 16	-	chr12:112507150-112507175	CAACUUCUGCUUUUGCUAAUAUCCU	5164
5781_16_227	PTPN11	Exon 16	-	chr12:112507185-112507210	UACUGUAAGCAGCUUCGGCUUCCCA	5165
5781_16_228	PTPN11	Exon 16	-	chr12:112507195-112507220	UUGUCCCAGCUACUGUAAGCAGCUU	5166
5781_16_229	PTPN11	Exon 16	-	chr12:112507255-112507280	AGAAAUCAUUCAGGAAGCUUCUUGA	5167
5781_16_230	PTPN11	Exon 16	-	chr12:112507269-112507294	GGCUCAGGGCUAGCAGAAAUCAUUC	5168
5781_16_231	PTPN11	Exon 16	-	chr12:112507288-112507313	AGUGCUGGUUCCAAAAAUAGGCUCA	5169
5781_16_232	PTPN11	Exon 16	-	chr12:112507289-112507314	AAGUGCUGGUUCCAAAAAUAGGCUC	5170
5781_16_233	PTPN11	Exon 16	-	chr12:112507295-112507320	UUCCCCAAGUGCUGGUUCCAAAAAU	5171
5781_16_234	PTPN11	Exon 16	-	chr12:112507308-112507333	UCACAAGAUCAGUUUCCCCAAGUGC	5172

5781_16_235	PTPN11	Exon 16	-	chr12:112507377-112507402	CAAGUCUGGGGAUGCCCCAGUGGGG	5173
5781_16_236	PTPN11	Exon 16	-	chr12:112507380-112507405	UCCCAAGUCUGGGGAUGCCCCAGUG	5174
5781_16_237	PTPN11	Exon 16	-	chr12:112507381-112507406	UUCCCAAGUCUGGGGAUGCCCCAGU	5175
5781_16_238	PTPN11	Exon 16	-	chr12:112507382-112507407	UUUCCCAAGUCUGGGGAUGCCCCAG	5176
5781_16_239	PTPN11	Exon 16	-	chr12:112507394-112507419	GAAAGAGUCACGUUUCCCAAGUCUG	5177
5781_16_240	PTPN11	Exon 16	-	chr12:112507395-112507420	AGAAAGAGUCACGUUUCCCAAGUCU	5178
5781_16_241	PTPN11	Exon 16	-	chr12:112507396-112507421	AAGAAAGAGUCACGUUUCCCAAGUC	5179
5781_16_242	PTPN11	Exon 16	-	chr12:112507428-112507453	UCACUGUGGCCUGACUAAAACCCAG	5180
5781_16_243	PTPN11	Exon 16	-	chr12:112507447-112507472	CUGUUAGGGCUGUUCCUUCUCACUG	5181
5781_16_244	PTPN11	Exon 16	-	chr12:112507466-112507491	AUUCAACCUGGCUGGAGGCCUGUUA	5182
5781_16_245	PTPN11	Exon 16	-	chr12:112507467-112507492	CAUUCAACCUGGCUGGAGGCCUGUU	5183
5781_16_246	PTPN11	Exon 16	-	chr12:112507476-112507501	AAAUGAGCUCAUUCAACCUGGCUGG	5184
5781_16_247	PTPN11	Exon 16	-	chr12:112507479-112507504	CAAAAAUGAGCUCAUUCAACCUGGC	5185
5781_16_248	PTPN11	Exon 16	-	chr12:112507483-112507508	ACAACAAAAAUGAGCUCAUUCAACC	5186
5781_16_249	PTPN11	Exon 16	-	chr12:112507513-112507538	UAGAACAUUAGCAAAUCUUACUGGU	5187
5781_16_250	PTPN11	Exon 16	-	chr12:112507517-112507542	AAUGUAGAACAUUAGCAAAUCUUAC	5188
5781_16_251	PTPN11	Exon 16	-	chr12:112507550-112507575	AGGCAAAGAGGGAUGUCUUUGGAGA	5189
5781_16_252	PTPN11	Exon 16	-	chr12:112507556-112507581	CAUAUGAGGCAAAGAGGGAUGUCUU	5190
5781_16_253	PTPN11	Exon 16	-	chr12:112507566-112507591	GAUGAUUCAACAUAUGAGGCAAAGA	5191
5781_16_254	PTPN11	Exon 16	-	chr12:112507567-112507592	GGAUGAUUCAACAUAUGAGGCAAAG	5192
5781_16_255	PTPN11	Exon 16	-	chr12:112507575-112507600	UCCGCACUGGAUGAUUCAACAUAUG	5193
5781_16_256	PTPN11	Exon 16	-	chr12:112507593-112507618	GAUAUUUUCAUUGAAAUAUCCGCAC	5194

5781_16_257	PTPN11	Exon 16	-	chr12:112507664-112507689	AGAAUCCAAGGAGGCCACAACUUCA	5195
5781_16_258	PTPN11	Exon 16	-	chr12:112507678-112507703	AAGCCAAAGUCAGAAGAAUCCAAGG	5196
5781_16_259	PTPN11	Exon 16	-	chr12:112507681-112507706	CAGAAGCCAAAGUCAGAAGAAUCCA	5197
5781_16_260	PTPN11	Exon 16	-	chr12:112507718-112507743	AGGAACUACCACCAGGGCUGGAUCU	5198
5781_16_261	PTPN11	Exon 16	-	chr12:112507725-112507750	CUCAGAAAGGAACUACCACCAGGGC	5199
5781_16_262	PTPN11	Exon 16	-	chr12:112507729-112507754	AGACCUCAGAAAGGAACUACCACCA	5200
5781_16_263	PTPN11	Exon 16	-	chr12:112507730-112507755	GAGACCUCAGAAAGGAACUACCACC	5201
5781_16_264	PTPN11	Exon 16	-	chr12:112507743-112507768	CUCAAGGGACUGAGAGACCUCAGAA	5202
5781_16_265	PTPN11	Exon 16	-	chr12:112507763-112507788	CAGCCAAACUACCCCAAAGUCUCAA	5203
5781_16_266	PTPN11	Exon 16	-	chr12:112507764-112507789	GCAGCCAAACUACCCCAAAGUCUCA	5204
5781_16_267	PTPN11	Exon 16	-	chr12:112507791-112507816	CUGAUAUACAUUUUGUCAGUGAGAA	5205
5781_16_268	PTPN11	Exon 16	-	chr12:112507819-112507844	AAGGAAUAUUGGGGGGUGGAGGUGG	5206
5781_16_269	PTPN11	Exon 16	-	chr12:112507820-112507845	CAAGGAAUAUUGGGGGGUGGAGGUG	5207
5781_16_270	PTPN11	Exon 16	-	chr12:112507821-112507846	UCAAGGAAUAUUGGGGGGUGGAGGU	5208
5781_16_271	PTPN11	Exon 16	-	chr12:112507822-112507847	UUCAAGGAAUAUUGGGGGGUGGAGG	5209
5781_16_272	PTPN11	Exon 16	-	chr12:112507825-112507850	AAGUUCAAGGAAUAUUGGGGGGUGG	5210
5781_16_273	PTPN11	Exon 16	-	chr12:112507828-112507853	UCAAAGUUCAAGGAAUAUUGGGGGG	5211
5781_16_274	PTPN11	Exon 16	-	chr12:112507831-112507856	AAUUCAAAGUUCAAGGAAUAUUGGG	5212
5781_16_275	PTPN11	Exon 16	-	chr12:112507832-112507857	CAAUUCAAAGUUCAAGGAAUAUUGG	5213
5781_16_276	PTPN11	Exon 16	-	chr12:112507833-112507858	GCAAUUCAAAGUUCAAGGAAUAUUG	5214
5781_16_277	PTPN11	Exon 16	-	chr12:112507834-112507859	AGCAAUUCAAAGUUCAAGGAAUAUU	5215
5781_16_278	PTPN11	Exon 16	-	chr12:112507835-112507860	AAGCAAUUCAAAGUUCAAGGAAUAU	5216

5781_16_279	PTPN11	Exon 16	-	chr12:112507843-112507868	GUGUUCUGAAGCAAUUCAAAGUUCA	5217
5781_16_280	PTPN11	Exon 16	-	chr12:112507879-112507904	ACUUCCCUAAUAAGGGAAUACCUUC	5218
5781_16_281	PTPN11	Exon 16	-	chr12:112507891-112507916	GACAGCAGUGACACUUCCCUAAUAA	5219
5781_16_282	PTPN11	Exon 16	-	chr12:112507892-112507917	AGACAGCAGUGACACUUCCCUAAUA	5220
5781_16_283	PTPN11	Exon 16	-	chr12:112507948-112507973	AAGCUUCUUGCUGCAAAUACUGAAC	5221
5781_16_284	PTPN11	Exon 16	-	chr12:112508018-112508043	AAGUCAAGACAAAACCAAAGCAAAA	5222
5781_16_285	PTPN11	Exon 16	-	chr12:112508074-112508099	UUUGUACAAUCAAACUCUUGUGUGC	5223
5781_16_286	PTPN11	Exon 16	-	chr12:112508127-112508152	AUAAAAGCAACUGAUCUUAAGCAAC	5224
5781_16_287	PTPN11	Exon 16	-	chr12:112508171-112508196	UCUUAUAACAAAACUAGCCAAGAUC	5225
5781_16_288	PTPN11	Exon 16	-	chr12:112508219-112508244	CAUGAUAGUUUGCUGACCUCGUGGA	5226
5781_16_289	PTPN11	Exon 16	-	chr12:112508220-112508245	ACAUGAUAGUUUGCUGACCUCGUGG	5227
5781_16_290	PTPN11	Exon 16	-	chr12:112508223-112508248	AGAACAUGAUAGUUUGCUGACCUCG	5228
5781_16_291	PTPN11	Exon 16	-	chr12:112508265-112508290	CUAGGGACUAUGAUAACUCUGGCCU	5229
5781_16_292	PTPN11	Exon 16	-	chr12:112508271-112508296	AGCAACCUAGGGACUAUGAUAACUC	5230
5781_16_293	PTPN11	Exon 16	-	chr12:112508287-112508312	GCACAUGAUAAGCCGUAGCAACCUA	5231
5781_16_294	PTPN11	Exon 16	-	chr12:112508288-112508313	AGCACAUGAUAAGCCGUAGCAACCU	5232
5781_16_295	PTPN11	Exon 16	-	chr12:112508443-112508468	CUGACUUCCUCAGAAACCACCUCUU	5233
5781_16_296	PTPN11	Exon 16	-	chr12:112508475-112508500	ACCCAUUACUGACUGCUCUGGCCCU	5234
5781_16_297	PTPN11	Exon 16	-	chr12:112508476-112508501	CACCCAUUACUGACUGCUCUGGCCC	5235
5781_16_298	PTPN11	Exon 16	-	chr12:112508482-112508507	CUCAUUCACCCAUUACUGACUGCUC	5236
5781_16_299	PTPN11	Exon 16	-	chr12:112508546-112508571	UACCCACCAGCAACCUAGAAGUAGA	5237
5781_16_300	PTPN11	Exon 16	-	chr12:112508592-112508617	UAAUUUUAAAAUCCUCAGUGAGCUA	5238

5781_16_301	PTPN11	Exon 16	-	chr12:112508692-112508717	AAAAAGUUAUUAAGACUGUGAAAUU	5239
5781_16_302	PTPN11	Exon 16	-	chr12:112508748-112508773	CAUAAGUUUCAGAAGGGCCACACAC	5240
5781_16_303	PTPN11	Exon 16	-	chr12:112508759-112508784	GGAGAGAUGACCAUAAGUUUCAGAA	5241
5781_16_304	PTPN11	Exon 16	-	chr12:112508760-112508785	GGGAGAGAUGACCAUAAGUUUCAGA	5242
5781_16_305	PTPN11	Exon 16	-	chr12:112508785-112508810	CAUUUGAAAAGACCUUGGUUUCAGU	5243
5781_16_306	PTPN11	Exon 16	-	chr12:112508786-112508811	ACAUUUGAAAAGACCUUGGUUUCAG	5244
5781_16_307	PTPN11	Exon 16	-	chr12:112508795-112508820	CAUUUAGCCACAUUUGAAAAGACCU	5245
5781_16_308	PTPN11	Exon 16	-	chr12:112508877-112508902	UCCUGGCUGUUUCCCCGAAGCAACU	5246
5781_16_309	PTPN11	Exon 16	-	chr12:112508899-112508924	CUAAAAAUAAUCUUGACCAUUUUCC	5247
5781_16_310	PTPN11	Exon 16	-	chr12:112509036-112509061	AUGUCUAUAGUCUAAGUUUCCCUUA	5248
5781_16_311	PTPN11	Exon 16	-	chr12:112509074-112509099	AACAUACAGAAAACAAAAGCUGCAC	5249
5781_16_312	PTPN11	Exon 16	-	chr12:112509139-112509164	UAACAAAGGCAUCCUGACAUCAGGG	5250
5781_16_313	PTPN11	Exon 16	-	chr12:112509142-112509167	UCCUAACAAAGGCAUCCUGACAUCA	5251
5781_16_314	PTPN11	Exon 16	-	chr12:112509143-112509168	AUCCUAACAAAGGCAUCCUGACAUC	5252
5781_16_315	PTPN11	Exon 16	-	chr12:112509158-112509183	UAAGGGCAAAUACAGAUCCUAACAA	5253
5781_16_316	PTPN11	Exon 16	-	chr12:112509180-112509205	GGAAAAAAGAUUUCAACAAAAUUAA	5254
5781_16_317	PTPN11	Exon 16	-	chr12:112509181-112509206	AGGAAAAAAGAUUUCAACAAAAUUA	5255
5781_16_318	PTPN11	Exon 16	-	chr12:112509206-112509231	AUUUUGGAACUUUUCAAGAGGAAGA	5256
5781_16_319	PTPN11	Exon 16	-	chr12:112509213-112509238	AAACUAUAUUUUGGAACUUUUCAAG	5257
5781_16_320	PTPN11	Exon 16	-	chr12:112509227-112509252	AUGAAAGAUACAAUAAACUAUAUUU	5258
5781_16_321	PTPN11	Exon 16	-	chr12:112509270-112509295	UUGUGUGAACUGCCCAUAGUGAAAA	5259
5781_16_322	PTPN11	Exon 16	-	chr12:112509377-112509402	UUAUUAAUUACAUGAUUUGAGGCUU	5260

5781_16_323	PTPN11	Exon 16	-	chr12:112509383-112509408	GGCAAAUUAUUAAUUACAUGAUUUG	5261
5781_16_324	PTPN11	Exon 16	-	chr12:112509409-112509434	AAUCACAAUUAGGUCAUAAAUAAAC	5262
5781_16_325	PTPN11	Exon 16	-	chr12:112509424-112509449	UUUUAUUAAUAAAAGAAUCACAAUU	5263
5781_16_326	PTPN11	Exon 16	-	chr12:112509469-112509494	GUAGGUCUAGUCAUCAGCUUAAUCA	5264
5781_16_327	PTPN11	Exon 16	-	chr12:112509470-112509495	UGUAGGUCUAGUCAUCAGCUUAAUC	5265
5781_16_328	PTPN11	Exon 16	-	chr12:112509492-112509517	CAUAUACUGCAGGAAAAUUAAUUGU	5266
5781_16_329	PTPN11	Exon 16	-	chr12:112509507-112509532	UCUGGUACAAUACUUCAUAUACUGC	5267
5781_16_330	PTPN11	Exon 16	-	chr12:112509530-112509555	AAAUAUUACAUAUCUUUUAAUACUC	5268
5781_16_331	PTPN11	Exon 16	-	chr12:112509573-112509598	ACAUCCUAAAACGUAUUCCUUUUAA	5269
5781_16_332	PTPN11	Exon 16	-	chr12:112509683-112509708	GACUACAUAAUAUACGUGGGCAAAA	5270
5781_16_333	PTPN11	Exon 16	-	chr12:112509691-112509716	UGCAAAUAGACUACAUAAUAUACGU	5271
5781_16_334	PTPN11	Exon 16	-	chr12:112509692-112509717	UUGCAAAUAGACUACAUAAUAUACG	5272
5781_16_335	PTPN11	Exon 16	-	chr12:112509788-112509813	GCGCUAACACCCAUAAAUAUAGGUG	5273
5781_16_336	PTPN11	Exon 16	-	chr12:112509789-112509814	UGCGCUAACACCCAUAAAUAUAGGU	5274
5781_16_337	PTPN11	Exon 16	-	chr12:112509790-112509815	UUGCGCUAACACCCAUAAAUAUAGG	5275
5781_16_338	PTPN11	Exon 16	-	chr12:112509793-112509818	CAGUUGCGCUAACACCCAUAAAUAU	5276
5781_16_339	PTPN11	Exon 16	-	chr12:112509900-112509925	CGACAAAUGCCAUCAUAUAAGAAAA	5277

Exemplary preferred gRNA tareting domains useful in the compositions and methods of the invention are described in the tables below.

Table 3: gRNA Targeting Domains for human B2M

Id.	Locations	Target	Strand	gRNA Targeting Domain Sequence	SEQ ID NO:
CR0043	Chr15:44711472-	B2M	+	CACGCGUUUAAUAUAAGUGG	5492

8	44711494				
CR00439	Chr15:44711483-44711505	B2M	+	UAUAAGUGGAGGCGUCGCGC	5493
CR00440	Chr15:44711486-44711508	B2M	+	AAGUGGAGGCGUCGCGCUGG	5494
CR00441	Chr15:44711534-44711556	B2M	+	GGCCGAGAUGUCUCGCUCCG	5495
CR00442	Chr15:44711536-44711558	B2M	-	GGCCACGGAGCGAGACAUCU	5496
CR00443	Chr15:44711551-44711573	B2M	-	CGCGAGCACAGCUAAGGCCA	5497
CR00444	Chr15:44711557-44711579	B2M	-	GAGUAGCGCGAGCACAGCUA	5498
CR00445	Chr15:44711591-44711613	B2M	-	ACUCACGCUGGAUAGCCUCC	5499
CR00446	Chr15:44711603-44711625	B2M	-	AGGGUAGGAGAGACUCACGC	5500
CR00447	Chr15:44715412-44715434	B2M	+	CUCAGGUACUCCAAAGAUUC	5501
CR00448	Chr15:44715422-44715444	B2M	-	CGUGAGUAAACCUGAAUCUU	5502
CR00449	Chr15:44715507-44715529	B2M	-	CAGUAAGUCAACUUCAAUGU	5503
CR00450	Chr15:44715567-44715589	B2M	+	ACUUGUCUUUCAGCAAGGAC	5504
CR00451	Chr15:44715645-44715667	B2M	-	AGUCACAUGGUUCACACGGC	5505
CR00452	Chr15:44715649-44715671	B2M	-	ACAAAGUCACAUGGUUCACA	5506
CR00453	Chr15:44715672-44715694	B2M	+	CACAGCCCAAGAUAGUUAAG	5507
CR00454	Chr15:44715673-44715695	B2M	+	ACAGCCCAAGAUAGUUAAGU	5508
CR00455	Chr15:44715677-44715699	B2M	-	UUACCCCACUUAACUAUCUU	5509
CR00456	Chr15:44715678-44715700	B2M	-	CUUACCCCACUUAACUAUCU	5510
CR00457	Chr15:44717599-44717621	B2M	+	AGGUUUGAAGAUGCCGCAUU	5511
CR00458	Chr15:44717604-44717626	B2M	+	UGAAGAUGCCGCAUUUGGAU	5512
CR00459	Chr15:44717612-44717634	B2M	-	GAAUUCAUCCAAUCCAAAUG	5513
CR00460	Chr15:44717681-44717703	B2M	+	ACACUUUAUGCACAAAAUGU	5514
CR00461	Chr15:44717763-44717785	B2M	-	CUGCUCAGAUACAUCAAACA	5515
CR00462	Chr15:44717764-44717786	B2M	+	CAUGUUUGAUGUAUCUGAGC	5516

CR00463	Chr15:44717776-44717798	B2M	+	AUCUGAGCAGGUUGCUCCAC	5517
CR00464	Chr15:44717789-44717811	B2M	+	GCUCCACAGGUAGCUCUAGG	5518
CR00465	Chr15:44717805-44717827	B2M	+	UAGGAGGGCUGGCAACUUAG	5519
CR00466	Chr15:44717808-44717830	B2M	+	GAGGGCUGGCAACUUAGAGG	5520
CR00467	Chr15:44717809-44717831	B2M	+	AGGGCUGGCAACUUAGAGGU	5521
CR00468	Chr15:44717810-44717832	B2M	+	GGGCUGGCAACUUAGAGGUG	5522
CR00469	Chr15:44717851-44717873	B2M	-	UCUGACCAAGAUGUUGAUGU	5523
CR00470	Chr15:44717939-44717961	B2M	-	UCUAAGCAGAGUAUGUAAAU	5524
CR00471	Chr15:44717981-44718003	B2M	+	AAUAUAAUUGACAGGAUUAU	5525
CR00472	Chr15:44718056-44718078	B2M	+	CUUAUACAUUUGAUAAAGUA	5526
CR00473	Chr15:44718076-44718098	B2M	+	AGGCAUGGUUGUGGUUAAUC	5527

In the various aspects of the invention, the gRNA molecule may include a targeting domain listed above. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00465. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00443. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00445. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00444. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00449. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00442. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00453. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00461. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00439. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00452. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00455. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00463. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00467. In an embodiment, the

targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00466. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00446. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00440. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00454. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00460. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00438. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR00439. Such gRNA molecules, and combinations thereof, are suitable for use in, for example, the CRISPR systems, methods and cells and other aspects of the invention described herein.

Table 4: gRNA targeting domain sequences for human T-Cell Receptor Alpha (TRAC)

Id.	Target Name	Strand	Genomic Information	gRNA Targeting Domain Sequence	SEQ ID NO:
CR000920	TRAC	+	Chr14:22281089-22281111	CUCAAGGUUCAGAUCAGAAG	5528
CR000921	TRAC	+	Chr14:22281092-22281114	AAGGUUCAGAUCAGAAGAGG	5529
CR000922	TRAC	+	Chr14:22281111-22281133	GAGGCUUCUCACCCUGCAGC	5530
CR000923	TRAC	+	Chr14:22281112-22281134	AGGCUUCUCACCCUGCAGCA	5531
CR000924	TRAC	-	Chr14:22281122-22281144	GCUCACAGGUCCCUGCUGCA	5532
CR000925	TRAC	-	Chr14:22281123-22281145	UGCUCACAGGUCCCUGCUGC	5533
CR000926	TRAC	+	Chr14:22281126-22281148	GCAGCAGGGACCUGUGAGCA	5534
CR000927	TRAC	+	Chr14:22281136-22281158	CCUGUGAGCAUGGCAUGCCC	5535
CR000928	TRAC	-	Chr14:22281136-22281158	CCAGGGCAUGCCAUGCUCAC	5536
CR000929	TRAC	-	Chr14:22281153-22281175	CAAGUGCCCACAGGAAGCCA	5537
CR000930	TRAC	-	Chr14:22281154-22281176	ACAAGUGCCCACAGGAAGCC	5538
CR000931	TRAC	-	Chr14:22281162-22281184	UGGAGAUCACAAGUGCCCAC	5539
CR000932	TRAC	-	Chr14:22281182-22281204	GCCUUCCUUACCAAGACAGG	5540
CR000933	TRAC	-	Chr14:22281185-22281207	UGCGCCUUCCUUACCAAGAC	5541
CR000934	TRAC	+	Chr14:22281432-	CUUUCCCACAGAAUUUA	5542

			22281454	GCA	
CR000935	TRAC	+	Chr14:22281477-22281499	ACCAGAGAUGUCUGUGCAGG	5543
CR000936	TRAC	-	Chr14:22281478-22281500	GCCUCCUGCACAGACAUCUC	5544
CR000937	TRAC	-	Chr14:22281506-22281528	AUAUGUGCAGCUCAGGGUCA	5545
CR000938	TRAC	-	Chr14:22281512-22281534	GGUGUCAUAUGUGCAGCUCA	5546
CR000939	TRAC	-	Chr14:22281513-22281535	UGGUGUCAUAUGUGCAGCUC	5547
CR000940	TRAC	-	Chr14:22281533-22281555	UAAAUAAUAAUCACUCUCAC	5548
CR000941	TRAC	+	Chr14:22281539-22281561	AGAGUGAUUAUUAUUUAUUC	5549
CR000942	TRAC	+	Chr14:22281560-22281582	GGUACAAGCAGCCUCCCAGC	5550
CR000943	TRAC	-	Chr14:22281571-22281593	AGAAUCAUCUGCCUGCUGGG	5551
CR000944	TRAC	-	Chr14:22281574-22281596	ACGAGAAUCAUCUGCCUGCU	5552
CR000945	TRAC	-	Chr14:22281575-22281597	AACGAGAAUCAUCUGCCUGC	5553
CR000946	TRAC	-	Chr14:22281603-22281625	UCUGUUGCUUAUAAGCUUCU	5554
CR000947	TRAC	-	Chr14:22338946-22338968	GUUGGUGAGGUUGAUAAAUU	5555
CR000948	TRAC	-	Chr14:22338959-22338981	GCUGUAUGUGUGAGUUGGUG	5556
CR000949	TRAC	+	Chr14:22338963-22338985	ACCAACUCACACAUACAGCC	5557
CR000950	TRAC	+	Chr14:22338964-22338986	CCAACUCACACAUACAGCCA	5558
CR000951	TRAC	-	Chr14:22338981-22339003	AGCACAAGAAUAUAGAUCCC	5559
CR000952	TRAC	+	Chr14:22338992-22339014	UAUUCUUGUGCUCUCAGAGA	5560
CR000953	TRAC	+	Chr14:22513941-22513963	GGAAACACACCUCUUGUCUU	5561
CR000954	TRAC	+	Chr14:22513946-22513968	CACACCUCUUGUCUUUGGAA	5562
CR000955	TRAC	+	Chr14:22513947-22513969	ACACCUCUUGUCUUUGGAAA	5563
CR000956	TRAC	-	Chr14:22513950-22513972	GUGCCCUUUCCAAAGACAAG	5564
CR000957	TRAC	-	Chr14:22547504-22547526	ACACGGCAGGGUCAGGGUUC	5565
CR000958	TRAC	-	Chr14:22547511-22547533	AGCUGGUACACGGCAGGGUC	5566

CR000959	TRAC	-	Chr14:22547516-22547538	CUCUCAGCUGGUACACGGCA	5567
CR000960	TRAC	-	Chr14:22547517-22547539	UCUCUCAGCUGGUACACGGC	5568
CR000961	TRAC	-	Chr14:22547521-22547543	AGAGUCUCUCAGCUGGUACA	5569
CR000962	TRAC	-	Chr14:22547528-22547550	UGGAUUUAGAGUCUCUCAGC	5570
CR000963	TRAC	-	Chr14:22547548-22547570	UAGGCAGACAGACUUGUCAC	5571
CR000964	TRAC	-	Chr14:22547567-22547589	GAGAAUCAAAAUCGGUGAAU	5572
CR000965	TRAC	-	Chr14:22547575-22547597	AUUUGUUUGAGAAUCAAAAU	5573
CR000966	TRAC	+	Chr14:22547591-22547613	AACAAAUGUGUCACAAAGUA	5574
CR000967	TRAC	+	Chr14:22547635-22547657	ACAAAACUGUGCUAGACAUG	5575
CR000968	TRAC	+	Chr14:22547642-22547664	UGUGCUAGACAUGAGGUCUA	5576
CR000969	TRAC	+	Chr14:22547666-22547688	CUUCAAGAGCAACAGUGCUG	5577
CR000970	TRAC	+	Chr14:22547671-22547693	AGAGCAACAGUGCUGUGGCC	5578
CR000971	TRAC	-	Chr14:22547689-22547711	AAAGUCAGAUUUGUUGCUCC	5579
CR000972	TRAC	-	Chr14:22547725-22547747	UGGAAUAAUGCUGUUGUUGA	5580
CR000973	TRAC	-	Chr14:22547745-22547767	CUGGGGAAGAAGGUGUCUUC	5581
CR000974	TRAC	-	Chr14:22547762-22547784	AGCUGCCCUUACCUGGGCUG	5582
CR000975	TRAC	-	Chr14:22547763-22547785	AAGCUGCCCUUACCUGGGCU	5583
CR000976	TRAC	-	Chr14:22547764-22547786	AAAGCUGCCCUUACCUGGGC	5584
CR000977	TRAC	-	Chr14:22547768-22547790	CACCAAAGCUGCCCUUACCU	5585
CR000978	TRAC	-	Chr14:22547769-22547791	GCACCAAAGCUGCCCUUACC	5586
CR000979	TRAC	+	Chr14:22549633-22549655	AAGUUCCUGUGAUGUCAAGC	5587
CR000980	TRAC	-	Chr14:22549638-22549660	CUCGACCAGCUUGACAUCAC	5588
CR000981	TRAC	-	Chr14:22550558-22550580	CUGACAGGUUUUGAAAGUUU	5589
CR000982	TRAC	+	Chr14:22550565-22550587	UUUCAAAACCUGUCAGUGAU	5590
CR000983	TRAC	+	Chr14:22550566-22550588	UUCAAAACCUGUCAGUGAUU	5591

CR000984	TRAC	-	Chr14:22550573-22550595	UUCGGAACCCAAUCACUGAC	5592
CR000985	TRAC	+	Chr14:22550591-22550613	CCGAAUCCUCCUCCUGAAAG	5593
CR000986	TRAC	-	Chr14:22550591-22550613	CCACUUUCAGGAGGAGGAUU	5594
CR000987	TRAC	+	Chr14:22550595-22550617	AUCCUCCUCCUGAAAGUGGC	5595
CR000988	TRAC	+	Chr14:22550596-22550618	UCCUCCUCCUGAAAGUGGCC	5596
CR000989	TRAC	-	Chr14:22550597-22550619	ACCCGGCCACUUUCAGGAGG	5597
CR000990	TRAC	-	Chr14:22550600-22550622	UAAACCCGGCCACUUUCAGG	5598
CR000991	TRAC	-	Chr14:22550603-22550625	GAUUAAACCCGGCCACUUUC	5599
CR000992	TRAC	-	Chr14:22550614-22550636	CGUCAUGAGCAGAUUAAACC	5600
CR000993	TRAC	+	Chr14:22550620-22550642	UUAAUCUGCUCAUGACGCUG	5601
CR000994	TRAC	+	Chr14:22550626-22550648	UGCUCAUGACGCUGCGGCUG	5602
CR000995	TRAC	-	Chr14:22550650-22550672	UCAAGGCCCCUCACCUCAGC	5603
CR000996	TRAC	-	Chr14:22551620-22551642	AGGAAGGAGCGAGGGAGCAC	5604
CR000997	TRAC	-	Chr14:22551628-22551650	CAAUGCAGAGGAAGGAGCGA	5605
CR000998	TRAC	-	Chr14:22551629-22551651	GCAAUGCAGAGGAAGGAGCG	5606
CR000999	TRAC	-	Chr14:22551636-22551658	AAGAGGGGCAAUGCAGAGGA	5607
CR001000	TRAC	-	Chr14:22551640-22551662	GGAGAAGAGGGGCAAUGCAG	5608
CR001001	TRAC	-	Chr14:22551653-22551675	UCUGUUUGGAGAGGGAGAAG	5609
CR001002	TRAC	+	Chr14:22551655-22551677	UCUUCUCCCUCUCCAAACAG	5610
CR001003	TRAC	+	Chr14:22551656-22551678	CUUCUCCCUCUCCAAACAGA	5611
CR001004	TRAC	-	Chr14:22551661-22551683	GAGUUCCCUCUGUUUGGAGA	5612
CR001005	TRAC	-	Chr14:22551662-22551684	AGAGUUCCCUCUGUUUGGAG	5613
CR001006	TRAC	-	Chr14:22551667-22551689	GUAGGAGAGUUCCCUCUGUU	5614
CR001007	TRAC	+	Chr14:22551678-22551700	GAACUCUCCUACCCCCAAGG	5615
CR001008	TRAC	-	Chr14:22551685-22551707	GCUUUCACCUCCUUGGGGGU	5616

CR001009	TRAC	-	Chr14:22551689-22551711	AGCAGCUUUCACCUCCUUGG	5617
CR001010	TRAC	-	Chr14:22551690-22551712	UAGCAGCUUUCACCUCCUUG	5618
CR001011	TRAC	-	Chr14:22551691-22551713	GUAGCAGCUUUCACCUCCUU	5619
CR001012	TRAC	+	Chr14:22551710-22551732	CUACCACCUCUGUGCCCCCC	5620
CR001013	TRAC	-	Chr14:22551713-22551735	UUGCCGGGGGGGCACAGAGG	5621
CR001014	TRAC	-	Chr14:22551716-22551738	GCAUUGCCGGGGGGGCACAG	5622
CR001015	TRAC	-	Chr14:22551724-22551746	AGUUGGUGGCAUUGCCGGGG	5623

In the various aspects of the invention, the gRNA molecule may include a targeting domain listed above. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000961. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000977. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000984. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000993. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000981. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000992. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000986. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000963. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000985. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000966. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000990. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000978. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000991. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000983. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000960. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR001002. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g.

consists of, the targeting domain of CR001000. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR001009. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR001011. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR001012. Such gRNA molecules, and combinations thereof, are suitable for use in, for example, the CRISPR systems, methods and cells and other aspects of the invention described herein.

Table 5: gRNA targeting domains for human T-Cell Receptor Beta (Constant Domain 1 and Constant Domain 2)

Id.	Target Name	gRNA Targeting Domain Sequence	Genomic Information	SEQ ID NO:
CR000728	TRBC1	CAGGGAAGAAGCCUGUGGCC	Chr7:142791779-142791801	5624
CR000729	TRBC1	GUGGUCAGGGAAGAAGCCUG	Chr7:142791784-142791806	5625
CR000730	TRBC1	CUGACCACGUGGAGCUGAGC	Chr7:142791799-142791821	5626
CR000731	TRBC1	CACGGACCCGCAGCCCCUCA	Chr7:142791857-142791879	5627
CR000732	TRBC1	GGUGCACAGUGGGGUCAGCA	Chr7:142791839-142791861	5628
CR000733	TRBC1	GACGGGUUUGGCCCUAUCCU	Chr7:142792015-142792037	5629
CR000734	TRBC1	UGGCUCAAACACAGCGACCU	Chr7:142791712-142791734	5630
CR000735	TRBC1	AGGCUUCUUCCCUGACCACG	Chr7:142791788-142791810	5631
CR000736	TRBC1	CAGCUCAGCUCCACGUGGUC	Chr7:142791798-142791820	5632
CR000737	TRBC1	GCGCUGACGAUCUGGGUGAC	Chr7:142792032-142792054	5633
CR000738	TRBC1	CUUUCCAGAGGACCUGAACA	Chr7:142791680-142791702	5634
CR000739	TRBC1	UCAAACACAGCGACCUCGGG	Chr7:142791708-142791730	5635
CR000740	TRBC1	UGACGGGUUUGGCCCUAUCC	Chr7:142792016-142792038	5636
CR000741	TRBC1	GGCGCUGACGAUCUGGGUGA	Chr7:142792033-142792055	5637
CR000742	TRBC1	CGGGUGGGAACACCUUGUUC	Chr7:142791692-142791714	5638
CR000743	TRBC1	GAACAAGGUGUUCCCACCCG	Chr7:142791695-142791717	5639
CR000744	TRBC1	CAAACACAGCGACCUCGGGU	Chr7:142791707-142791729	5640

CR000745	TRBC1	GGCUCAAACACAGCGACCUC	Chr7:142791711-142791733	5641
CR000746	TRBC1	AGCUCAGCUCCACGUGGUCA	Chr7:142791797-142791819	5642
CR000747	TRBC1	GACGAUCUGGGUGACGGGUU	Chr7:142792027-142792049	5643
CR000748	TRBC2	UAUCAGGCUCCUCUGCUACG	Chr7:142670776-142670798	5644
CR000749	TRBC2	AUCAGGCUCCUCUGCUACGU	Chr7:142670777-142670799	5645
CR000750	TRBC2	CUACGUGGGCUUUUAUUUUC	Chr7:142670791-142670813	5646
CR000751	TRBC2	ACGUGGGCUUUUAUUUUCUG	Chr7:142670793-142670815	5647
CR000752	TRBC2	CGUGGGCUUUUAUUUUCUGG	Chr7:142670794-142670816	5648
CR000753	TRBC2	AAUAAAAGCCCACGUAGCAG	Chr7:142670785-142670807	5649
CR000754	TRBC2	ACCCCAAGAUACCUUGUUAU	Chr7:142670970-142670992	5650
CR000755	TRBC2	AGAUACCUUGUUAUAGGGAC	Chr7:142670976-142670998	5651
CR000756	TRBC2	GACAGGAAAGAAGAUCACUC	Chr7:142670993-142671015	5652
CR000757	TRBC2	UCUGGAAUGUUCUCAAACCA	Chr7:142671011-142671033	5653
CR000758	TRBC2	CUGGAAUGUUCUCAAACCAU	Chr7:142671012-142671034	5654
CR000759	TRBC2	UACUGGUAUCAACAAGAUCC	Chr7:142671048-142671070	5655
CR000760	TRBC2	GUAUCAACAAGAUCCAGGAA	Chr7:142671053-142671075	5656
CR000761	TRBC2	CACCUCAUCCACUAUUCCUA	Chr7:142671081-142671103	5657
CR000762	TRBC2	GGAGUUAAUUCCACAGAGAA	Chr7:142671102-142671124	5658
CR000763	TRBC2	AGUCAACAGUCUCCAGAAUA	Chr7:142671139-142671161	5659
CR000764	TRBC2	AACAGUCUCCAGAAUAAGGA	Chr7:142671143-142671165	5660
CR000765	TRBC2	CCCUGACCCUGGAGUCUGCC	Chr7:142671175-142671197	5661
CR000766	TRBC2	UAACAAGGUAUCUUGGGGUC	Chr7:142670966-142670988	5662
CR000767	TRBC2	CCCUAUAACAAGGUAUCUUG	Chr7:142670971-142670993	5663
CR000768	TRBC2	UCCCUAUAACAAGGUAUCUU	Chr7:142670972-142670994	5664
CR000769	TRBC2	GUCCCUAUAACAAGGUAUCU	Chr7:142670973-142670995	5665

CR000770	TRBC2	UCUUUCCUGUCCCUAUAACA	Chr7:142670981-142671003	5666
CR000771	TRBC2	GAUACCAGUACAUUUUGUCA	Chr7:142671035-142671057	5667
CR000772	TRBC2	AUGAGGUGUAGUUCCAUUCC	Chr7:142671066-142671088	5668
CR000773	TRBC2	CUCCAUAGGAAUAGUGGAUG	Chr7:142671083-142671105	5669
CR000774	TRBC2	AAUUAACUCCAUAGGAAUAG	Chr7:142671089-142671111	5670
CR000775	TRBC2	CUCUGUGGAAUUAACUCCAU	Chr7:142671097-142671119	5671
CR000776	TRBC2	UCUGGAGACUGUUGACUCAG	Chr7:142671133-142671155	5672
CR000777	TRBC2	AAAAUGCUCCGUCCUUAUUC	Chr7:142671151-142671173	5673
CR000778	TRBC2	CCUGGCAGACUCCAGGGUCA	Chr7:142671175-142671197	5674
CR000779	TRBC2	GCCUGGCAGACUCCAGGGUC	Chr7:142671176-142671198	5675
CR000780	TRBC2	UGAGGGCCUGGCAGACUCCA	Chr7:142671181-142671203	5676
CR000781	TRBC2	GUGAGGGCCUGGCAGACUCC	Chr7:142671182-142671204	5677
CR000782	TRBC2	GAGGUACUGAGAGGUAUGUG	Chr7:142671199-142671221	5678
CR000783	TRBC2	GCUGGCACAGAGGUACUGAG	Chr7:142671208-142671230	5679
CR000784	TRBC2	UGUAUUCACUGCUGGCACAG	Chr7:142671218-142671240	5680
CR000785	TRBC2	GAGCUGUCUGGUUCUGGUAG	Chr7:142791626-142791648	5681
CR000786	TRBC2	AGAGCUGUCUGGUUCUGGUA	Chr7:142791627-142791649	5682
CR000787	TRBC2	GAGAGCUGUCUGGUUCUGGU	Chr7:142791628-142791650	5683
CR000788	TRBC2	CUCUGAGAGCUGUCUGGUUC	Chr7:142791632-142791654	5684
CR000789	TRBC2	GGGUUGCUCUGAGAGCUGUC	Chr7:142791638-142791660	5685
CR000790	TRBC2	GAAAAACGUGUUCCCACCCA	Chr7:142801042-142801064	5686
CR000791	TRBC2	AGGCUUCUACCCCGACCACG	Chr7:142801135-142801157	5687
CR000792	TRBC2	CCGACCACGUGGAGCUGAGC	Chr7:142801146-142801168	5688
CR000793	TRBC2	CACAGACCCGCAGCCCCUCA	Chr7:142801204-142801226	5689
CR000794	TRBC2	UGGGUGGGAACACGUUUUUC	Chr7:142801039-142801061	5690

CR000795	TRBC2	CAAACACAGCGACCUUGGGU	Chr7:142801054-142801076	5691
CR000796	TRBC2	UCAAACACAGCGACCUUGGG	Chr7:142801055-142801077	5692
CR000797	TRBC2	GGCUCAAACACAGCGACCUU	Chr7:142801058-142801080	5693
CR000798	TRBC2	UGGCUCAAACACAGCGACCU	Chr7:142801059-142801081	5694
CR000799	TRBC2	CGGGGUAGAAGCCUGUGGCC	Chr7:142801126-142801148	5695
CR000800	TRBC2	GUGGUCGGGGUAGAAGCCUG	Chr7:142801131-142801153	5696
CR000801	TRBC2	AGCUCAGCUCCACGUGGUCG	Chr7:142801144-142801166	5697
CR000802	TRBC2	CAGCUCAGCUCCACGUGGUC	Chr7:142801145-142801167	5698
CR000803	TRBC2	CCAGCUCAGCUCCACGUGGU	Chr7:142801146-142801168	5699
CR000804	TRBC2	GACAGGUUUGGCCCUAUCCU	Chr7:142801362-142801384	5700
CR000805	TRBC2	UGACAGGUUUGGCCCUAUCC	Chr7:142801363-142801385	5701
CR000806	TRBC2	GACGAUCUGGGUGACAGGUU	Chr7:142801374-142801396	5702
CR000807	TRBC2	GCGCUGACGAUCUGGGUGAC	Chr7:142801379-142801401	5703
CR000808	TRBC2	CCCUGUUUUCUUUCAGACUG	Chr7:142801922-142801944	5704
CR000809	TRBC2	AGGAGAGACUCACUUACCGG	Chr7:142801950-142801972	5705
CR000810	TRBC2	AAAAGGAGAGACUCACUUAC	Chr7:142801953-142801975	5706
CR000811	TRBC2	UCAACAGAGUCUUACCAGCA	Chr7:142802092-142802114	5707
CR000812	TRBC2	CAACAGAGUCUUACCAGCAA	Chr7:142802093-142802115	5708
CR000813	TRBC2	AACAGAGUCUUACCAGCAAG	Chr7:142802094-142802116	5709
CR000814	TRBC2	AUCCUCUAUGAGAUCUUGCU	Chr7:142802131-142802153	5710
CR000815	TRBC2	UCCUCUAUGAGAUCUUGCUA	Chr7:142802132-142802154	5711
CR000816	TRBC2	CUAUGAGAUCUUGCUAGGGA	Chr7:142802136-142802158	5712
CR000817	TRBC2	GGCCACCUUGUAUGCCGUGC	Chr7:142802157-142802179	5713
CR000818	TRBC2	GGUCAGUGCCCUCGUGCUGA	Chr7:142802178-142802200	5714
CR000819	TRBC2	UGGCAGACAGGACCCCUUGC	Chr7:142802106-142802128	5715

CR000820	TRBC2	CAUAGAGGAUGGUGGCAGAC	Chr7:142802118-142802140	5716
CR000821	TRBC2	CAAGAUCUCAUAGAGGAUGG	Chr7:142802126-142802148	5717
CR000822	TRBC2	UAGCAAGAUCUCAUAGAGGA	Chr7:142802129-142802151	5718
CR000823	TRBC2	UCCCUAGCAAGAUCUCAUAG	Chr7:142802133-142802155	5719

In the various aspects of the invention, the gRNA molecule may include a targeting domain listed above. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000823. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000798. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000810. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000800. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000815. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000812. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000813. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000816. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000807. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000811. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000791. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000809. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000817. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000819. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000814. Such gRNA molecules, and combinations thereof, are suitable for use in, for example, the CRISPR systems, methods and cells and other aspects of the invention described herein.

Table 6: gRNA Targeting Domains for human PDCD1

Id.	Target Name	gRNA Targeting Domain Sequence	Genomic Information	SEQ ID NO:
CR000824	PDCD1	UCAGGCGGAGGUGAGCGGAA	Chr2:241858873-	5720

			241858895	
CR000825	PDCD1	CUCAGGCGGAGGUGAGCGGA	Chr2:241858872-241858894	5721
CR000826	PDCD1	ACUGCUCAGGCGGAGGUGAG	Chr2:241858868-241858890	5722
CR000827	PDCD1	GCUCACCUCCGCCUGAGCAG	Chr2:241858866-241858888	5723
CR000828	PDCD1	CUUCUCCACUGCUCAGGCGG	Chr2:241858861-241858883	5724
CR000829	PDCD1	CAGUGGAGAAGGCGGCACUC	Chr2:241858849-241858871	5725
CR000830	PDCD1	UGGAGAAGGCGGCACUCUGG	Chr2:241858846-241858868	5726
CR000831	PDCD1	GGAGAAGGCGGCACUCUGGU	Chr2:241858845-241858867	5727
CR000832	PDCD1	GAGAAGGCGGCACUCUGGUG	Chr2:241858844-241858866	5728
CR000833	PDCD1	AGGCGCCCUGGCCAGUCGUC	Chr2:241858797-241858819	5729
CR000834	PDCD1	GGCGCCCUGGCCAGUCGUCU	Chr2:241858796-241858818	5730
CR000835	PDCD1	GCCCUGGCCAGUCGUCUGGG	Chr2:241858793-241858815	5731
CR000836	PDCD1	CACCGCCCAGACGACUGGCC	Chr2:241858791-241858813	5732
CR000837	PDCD1	UGUAGCACCGCCCAGACGAC	Chr2:241858786-241858808	5733
CR000838	PDCD1	CGUCUGGGCGGUGCUACAAC	Chr2:241858781-241858803	5734
CR000839	PDCD1	GUCUGGGCGGUGCUACAACU	Chr2:241858780-241858802	5735
CR000840	PDCD1	GGGCGGUGCUACAACUGGGC	Chr2:241858776-241858798	5736
CR000841	PDCD1	CGGUGCUACAACUGGGCUGG	Chr2:241858773-241858795	5737
CR000842	PDCD1	CACCUACCUAAGAACCAUCC	Chr2:241858750-241858772	5738
CR000843	PDCD1	GAGAAGGUGGGGGGGUUCCA	Chr2:241852938-241852960	5739
CR000844	PDCD1	CGGUCACCACGAGCAGGGCU	Chr2:241852915-241852937	5740
CR000845	PDCD1	UCGGUCACCACGAGCAGGGC	Chr2:241852914-241852936	5741
CR000846	PDCD1	GCCCUGCUCGUGGUGACCGA	Chr2:241852911-241852933	5742
CR000847	PDCD1	CCCUUCGGUCACCACGAGCA	Chr2:241852910-241852932	5743
CR000848	PDCD1	CCCUGCUCGUGGUGACCGAA	Chr2:241852910-241852932	5744

CR000849	PDCD1	CCCCUUCGGUCACCACGAGC	Chr2:241852909-241852931	5745
CR000850	PDCD1	CCUGCUCGUGGUGACCGAAG	Chr2:241852909-241852931	5746
CR000851	PDCD1	GAAGGUGGCGUUGUCCCCUU	Chr2:241852895-241852917	5747
CR000852	PDCD1	GUUGGAGAAGCUGCAGGUGA	Chr2:241852877-241852899	5748
CR000853	PDCD1	CACGAAGCUCUCCGAUGUGU	Chr2:241852859-241852881	5749
CR000854	PDCD1	CGGAGAGCUUCGUGCUAAAC	Chr2:241852850-241852872	5750
CR000855	PDCD1	UCUGGUUGCUGGGGCUCAUG	Chr2:241852825-241852847	5751
CR000856	PDCD1	GCUUGUCCGUCUGGUUGCUG	Chr2:241852816-241852838	5752
CR000857	PDCD1	AGCUUGUCCGUCUGGUUGCU	Chr2:241852815-241852837	5753
CR000858	PDCD1	CAGCUUGUCCGUCUGGUUGC	Chr2:241852814-241852836	5754
CR000859	PDCD1	CAGCAACCAGACGGACAAGC	Chr2:241852813-241852835	5755
CR000860	PDCD1	AGGCGGCCAGCUUGUCCGUC	Chr2:241852807-241852829	5756
CR000861	PDCD1	CUGGCUGCGGUCCUCGGGGA	Chr2:241852787-241852809	5757
CR000862	PDCD1	CGGGCUGGCUGCGGUCCUCG	Chr2:241852783-241852805	5758
CR000863	PDCD1	CCGGGCUGGCUGCGGUCCUC	Chr2:241852782-241852804	5759
CR000864	PDCD1	CCCGAGGACCGCAGCCAGCC	Chr2:241852782-241852804	5760
CR000865	PDCD1	GCCGGGCUGGCUGCGGUCCU	Chr2:241852781-241852803	5761
CR000866	PDCD1	CGGAAGCGGCAGUCCUGGCC	Chr2:241852764-241852786	5762
CR000867	PDCD1	ACGGAAGCGGCAGUCCUGGC	Chr2:241852763-241852785	5763
CR000868	PDCD1	UGACACGGAAGCGGCAGUCC	Chr2:241852759-241852781	5764
CR000869	PDCD1	GCAGUUGUGUGACACGGAAG	Chr2:241852750-241852772	5765
CR000870	PDCD1	CGUGUCACACAACUGCCCAA	Chr2:241852743-241852765	5766
CR000871	PDCD1	GUGUCACACAACUGCCCAAC	Chr2:241852742-241852764	5767
CR000872	PDCD1	AUGUGGAAGUCACGCCCGUU	Chr2:241852728-241852750	5768
CR000873	PDCD1	CAUGUGGAAGUCACGCCCGU	Chr2:241852727-241852749	5769

CR000874	PDCD1	GCGUGACUUCCACAUGAGCG	Chr2:241852720-241852742	5770
CR000875	PDCD1	ACUUCCACAUGAGCGUGGUC	Chr2:241852715-241852737	5771
CR000876	PDCD1	CUUCCACAUGAGCGUGGUCA	Chr2:241852714-241852736	5772
CR000877	PDCD1	GGGCCCUGACCACGCUCAUG	Chr2:241852711-241852733	5773
CR000878	PDCD1	ACAUGAGCGUGGUCAGGGCC	Chr2:241852709-241852731	5774
CR000879	PDCD1	AGGGCCCGGCGCAAUGACAG	Chr2:241852695-241852717	5775
CR000880	PDCD1	GGUGCCGCUGUCAUUGCGCC	Chr2:241852691-241852713	5776
CR000881	PDCD1	AGGUGCCGCUGUCAUUGCGC	Chr2:241852690-241852712	5777
CR000882	PDCD1	GACAGCGGCACCUACCUCUG	Chr2:241852680-241852702	5778
CR000883	PDCD1	ACAGCGGCACCUACCUCUGU	Chr2:241852679-241852701	5779
CR000884	PDCD1	CCAGGGAGAUGGCCCCACAG	Chr2:241852666-241852688	5780
CR000885	PDCD1	GAUCUGCGCCUUGGGGGCCA	Chr2:241852649-241852671	5781
CR000886	PDCD1	UGAUCUGCGCCUUGGGGGCC	Chr2:241852648-241852670	5782
CR000887	PDCD1	CUCUUUGAUCUGCGCCUUGG	Chr2:241852643-241852665	5783
CR000888	PDCD1	UCUCUUUGAUCUGCGCCUUG	Chr2:241852642-241852664	5784
CR000889	PDCD1	CUCUCUUUGAUCUGCGCCUU	Chr2:241852641-241852663	5785
CR000890	PDCD1	GCUCUCUUUGAUCUGCGCCU	Chr2:241852640-241852662	5786
CR000891	PDCD1	CGCAGAUCAAAGAGAGCCUG	Chr2:241852634-241852656	5787
CR000892	PDCD1	GCAGAUCAAAGAGAGCCUGC	Chr2:241852633-241852655	5788
CR000893	PDCD1	AGAGCCUGCGGGCAGAGCUC	Chr2:241852622-241852644	5789
CR000894	PDCD1	AGGGUUUGGAACUGGCCGGC	Chr2:241852278-241852300	5790
CR000895	PDCD1	CACCAGGGUUUGGAACUGGC	Chr2:241852274-241852296	5791
CR000896	PDCD1	CGGCCAGUUCCAAACCCUGG	Chr2:241852273-241852295	5792
CR000897	PDCD1	CAACCACCAGGGUUUGGAAC	Chr2:241852270-241852292	5793
CR000898	PDCD1	CAGUUCCAAACCCUGGUGGU	Chr2:241852269-241852291	5794

CR000899	PDCD1	CGACACCAACCACCAGGGUU	Chr2:241852264-241852286	5795
CR000900	PDCD1	AACCCUGGUGGUUGGUGUCG	Chr2:241852261-241852283	5796
CR000901	PDCD1	ACCCUGGUGGUUGGUGUCGU	Chr2:241852260-241852282	5797
CR000902	PDCD1	GCCCACGACACCAACCACCA	Chr2:241852259-241852281	5798
CR000903	PDCD1	CGCCCACGACACCAACCACC	Chr2:241852258-241852280	5799
CR000904	PDCD1	CUGGUGGUUGGUGUCGUGGG	Chr2:241852257-241852279	5800
CR000905	PDCD1	UGGUGUCGUGGGCGGCCUGC	Chr2:241852249-241852271	5801
CR000906	PDCD1	GGUGUCGUGGGCGGCCUGCU	Chr2:241852248-241852270	5802
CR000907	PDCD1	GGUGCUGCUAGUCUGGGUCC	Chr2:241852219-241852241	5803
CR000908	PDCD1	UCCUGGCCGUCAUCUGCUCC	Chr2:241852202-241852224	5804
CR000909	PDCD1	CCCGGGAGCAGAUGACGGCC	Chr2:241852201-241852223	5805
CR000910	PDCD1	CCUGGCCGUCAUCUGCUCCC	Chr2:241852201-241852223	5806
CR000911	PDCD1	GACGUUACCUCGUGCGGCCC	Chr2:241852184-241852206	5807
CR000912	PDCD1	UGACGUUACCUCGUGCGGCC	Chr2:241852183-241852205	5808
CR000913	PDCD1	UGGGAUGACGUUACCUCGUG	Chr2:241852178-241852200	5809
CR000914	PDCD1	CUGCAGGGACAAUAGGAGCC	Chr2:241851961-241851983	5810
CR000915	PDCD1	ACAAUAGGAGCCAGGCGCAC	Chr2:241851953-241851975	5811
CR000916	PDCD1	CAGGGGCUGGCCGGUGCGCC	Chr2:241851943-241851965	5812
CR000917	PDCD1	AAAAGAGUGAGACUCACCAG	Chr2:241851926-241851948	5813
CR000918	PDCD1	GAAAAGAGUGAGACUCACCA	Chr2:241851925-241851947	5814
CR000919	PDCD1	GGAAAAGAGUGAGACUCACC	Chr2:241851924-241851946	5815

In the various aspects of the invention, the gRNA molecule may include a targeting domain listed above. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000847. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000902. In an embodiment, the targeting domain

of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000852. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000826. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000904. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000839. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000828. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000835. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000829. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000879. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000870. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000831. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000848. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000855. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR000838. Such gRNA molecules, and combinations thereof, are suitable for use in, for example, the CRISPR systems, methods and cells, and other aspects of the invention described herein.

Table 6b. gRNA Targeting Domains for human FKBP1A

ID	Target	Strand	Target Sequence Location	gRNA Targeting Domain Sequence	SEQ ID NO:
CR002054	FKBP1A	-	Chr20:1393120-1393142	CGCACGCAGGGCUGGGCGUG	6662
CR002055	FKBP1A	-	Chr20:1393119-1393141	GCACGCAGGGCUGGGCGUGA	6663
CR002056	FKBP1A	-	Chr20:1393118-1393140	CACGCAGGGCUGGGCGUGAG	6664
CR002057	FKBP1A	-	Chr20:1393117-1393139	ACGCAGGGCUGGGCGUGAGG	6665
CR002058	FKBP1A	-	Chr20:1393101-1393123	GAGGGGGCGUGCGCGUGCGC	6666
CR002059	FKBP1A	-	Chr20:1393088-1393110	CGUGCGCAGGCGACGCGCCG	6667
CR002060	FKBP1A	-	Chr20:1393081-1393103	AGGCGACGCGCCGAGGUACU	6668
CR002061	FKBP1A	+	Chr20:1393071-1393093	CACGGCUCUGCCUAGUACCU	6669

CR002062	FKBP1A	-	Chr20:1393070-1393092	CGAGGUACUAGGCAGAGCCG	6670
CR002063	FKBP1A	-	Chr20:1393057-1393079	AGAGCCGUGGAACCGCCGCC	6671
CR002064	FKBP1A	+	Chr20:1393053-1393075	GCGACCUGGCGGCGGUUCCA	6672
CR002065	FKBP1A	-	Chr20:1393047-1393069	AACCGCCGCCAGGUCGCUGU	6673
CR002066	FKBP1A	+	Chr20:1393045-1393067	GACCAACAGCGACCUGGCGG	6674
CR002067	FKBP1A	+	Chr20:1393042-1393064	GUGGACCAACAGCGACCUGG	6675
CR002068	FKBP1A	+	Chr20:1393039-1393061	GGCGUGGACCAACAGCGACC	6676
CR002069	FKBP1A	+	Chr20:1393023-1393045	GGGCGGCGCGACGGGCGGCG	6677
CR002070	FKBP1A	+	Chr20:1393018-1393040	CGGGCGGGCGGCGCGACGGG	6678
CR002071	FKBP1A	+	Chr20:1393015-1393037	GAGCGGGCGGGCGGCGCGAC	6679
CR002072	FKBP1A	+	Chr20:1393014-1393036	UGAGCGGGCGGGCGGCGCGA	6680
CR002073	FKBP1A	+	Chr20:1393006-1393028	GCGGACGCUGAGCGGGCGGG	6681
CR002074	FKBP1A	+	Chr20:1393003-1393025	GCGGCGGACGCUGAGCGGGC	6682
CR002075	FKBP1A	+	Chr20:1393002-1393024	GGCGGCGGACGCUGAGCGGG	6683
CR002076	FKBP1A	+	Chr20:1392999-1393021	GGCGGCGGCGGACGCUGAGC	6684
CR002077	FKBP1A	+	Chr20:1392998-1393020	UGGCGGCGGCGGACGCUGAG	6685
CR002078	FKBP1A	-	Chr20:1392995-1393017	CUCAGCGUCCGCCGCCGCCA	6686
CR002079	FKBP1A	-	Chr20:1392994-1393016	UCAGCGUCCGCCGCCGCCAU	6687
CR002080	FKBP1A	+	Chr20:1392987-1393009	CUGCACUCCCAUGGCGGCGG	6688
CR002081	FKBP1A	-	Chr20:1392986-1393008	CGCCGCCGCCAUGGGAGUGC	6689
CR002082	FKBP1A	+	Chr20:1392984-1393006	CACCUGCACUCCCAUGGCGG	6690
CR002083	FKBP1A	-	Chr20:1392983-1393005	CGCCGCCAUGGGAGUGCAGG	6691
CR002084	FKBP1A	+	Chr20:1392981-1393003	UUCCACCUGCACUCCCAUGG	6692
CR002085	FKBP1A	+	Chr20:1392978-1393000	GGUUUCCACCUGCACUCCCA	6693
CR002086	FKBP1A	-	Chr20:1392967-1392989	CAGGUGGAAACCAUCUCCCC	6694

CR002087	FKBP1A	+	Chr20:1392957-1392979	CUCACCGUCUCCUGGGGAGA	6695
CR002088	FKBP1A	+	Chr20:1392951-1392973	CCACUACUCACCGUCUCCUG	6696
CR002089	FKBP1A	+	Chr20:1392950-1392972	GCCACUACUCACCGUCUCCU	6697
CR002090	FKBP1A	+	Chr20:1392949-1392971	CGCCACUACUCACCGUCUCC	6698
CR002091	FKBP1A	-	Chr20:1392880-1392902	UGCCCGUCUCUGUCUCCUCA	6699
CR002092	FKBP1A	-	Chr20:1392860-1392882	GGGCGCACCUUCCCCAAGCG	6700
CR002093	FKBP1A	+	Chr20:1392853-1392875	GGUCUGGCCGCGCUUGGGGA	6701
CR002094	FKBP1A	+	Chr20:1392849-1392871	CGCAGGUCUGGCCGCGCUUG	6702
CR002095	FKBP1A	+	Chr20:1392848-1392870	ACGCAGGUCUGGCCGCGCUU	6703
CR002096	FKBP1A	+	Chr20:1392847-1392869	CACGCAGGUCUGGCCGCGCU	6704
CR002097	FKBP1A	-	Chr20:1392846-1392868	CAAGCGCGGCCAGACCUGCG	6705
CR002098	FKBP1A	+	Chr20:1392837-1392859	UGUAGUGCACCACGCAGGUC	6706
CR002099	FKBP1A	+	Chr20:1392832-1392854	ACCGGUGUAGUGCACCACGC	6707
CR002100	FKBP1A	+	Chr20:1392814-1392836	CCGCUGGGCCCCCGACUCAC	6708
CR002101	FKBP1A	-	Chr20:1375602-1375624	UUACAGUCGUCUUUUUCACA	6709
CR002102	FKBP1A	-	Chr20:1375588-1375610	UUCACAGGGAUGCUUGAAGA	6710
CR002103	FKBP1A	-	Chr20:1375566-1375588	GAAAGAAAUUUGAUUCCUCC	6711
CR002104	FKBP1A	-	Chr20:1375565-1375587	AAAGAAAUUUGAUUCCUCCC	6712
CR002105	FKBP1A	+	Chr20:1375551-1375573	GGGCUUGUUUCUGUCCCGGG	6713
CR002106	FKBP1A	+	Chr20:1375548-1375570	AAAGGGCUUGUUUCUGUCCC	6714
CR002107	FKBP1A	+	Chr20:1375547-1375569	UAAAGGGCUUGUUUCUGUCC	6715
CR002108	FKBP1A	-	Chr20:1375534-1375556	AAGCCCUUUAAGUUUAUGCU	6716
CR002109	FKBP1A	+	Chr20:1375531-1375553	UUGCCUAGCAUAAACUUAAA	6717
CR002110	FKBP1A	+	Chr20:1375530-1375552	CUUGCCUAGCAUAAACUUAA	6718
CR002111	FKBP1A	-	Chr20:1375526-1375548	UAAGUUUAUGCUAGGCAAGC	6719

CR002112	FKBP1A	-	Chr20:1375523-1375545	GUUUAUGCUAGGCAAGCAGG	6720
CR002113	FKBP1A	-	Chr20:1375513-1375535	GGCAAGCAGGAGGUGAUCCG	6721
CR002114	FKBP1A	-	Chr20:1375509-1375531	AGCAGGAGGUGAUCCGAGGC	6722
CR002115	FKBP1A	-	Chr20:1375508-1375530	GCAGGAGGUGAUCCGAGGCU	6723
CR002116	FKBP1A	-	Chr20:1375501-1375523	GUGAUCCGAGGCUGGGAAGA	6724
CR002117	FKBP1A	-	Chr20:1375500-1375522	UGAUCCGAGGCUGGGAAGAA	6725
CR002118	FKBP1A	-	Chr20:1375499-1375521	GAUCCGAGGCUGGGAAGAAG	6726
CR002119	FKBP1A	+	Chr20:1375496-1375518	CAACCCCUUCUUCCCAGCCU	6727
CR002120	FKBP1A	+	Chr20:1375473-1375495	ACAAAUGAGAGAGCAUACCU	6728
CR002121	FKBP1A	+	Chr20:1375472-1375494	AACAAAUGAGAGAGCAUACC	6729
CR002122	FKBP1A	-	Chr20:1372231-1372253	GUUCUUUUCACAGAUGAGUG	6730
CR002123	FKBP1A	-	Chr20:1372230-1372252	UUCUUUUCACAGAUGAGUGU	6731
CR002124	FKBP1A	+	Chr20:1372199-1372221	AUCUGGAGAUAUAGUCAGUU	6732
CR002125	FKBP1A	-	Chr20:1372188-1372210	AUAUCUCCAGAUUAUGCCUA	6733
CR002126	FKBP1A	+	Chr20:1372182-1372204	GUGGCACCAUAGGCAUAAUC	6734
CR002127	FKBP1A	-	Chr20:1372179-1372201	GAUUAUGCCUAUGGUGCCAC	6735
CR002128	FKBP1A	-	Chr20:1372178-1372200	AUUAUGCCUAUGGUGCCACU	6736
CR002129	FKBP1A	+	Chr20:1372172-1372194	UGGGUGCCCAGUGGCACCAU	6737
CR002130	FKBP1A	-	Chr20:1372170-1372192	UAUGGUGCCACUGGGCACCC	6738
CR002131	FKBP1A	+	Chr20:1372163-1372185	GAUGAUGCCUGGGUGCCCAG	6739
CR002132	FKBP1A	+	Chr20:1372153-1372175	CAUGUGGUGGGAUGAUGCCU	6740
CR002133	FKBP1A	+	Chr20:1372152-1372174	GCAUGUGGUGGGAUGAUGCC	6741
CR002134	FKBP1A	+	Chr20:1372141-1372163	AGACGAGAGUGGCAUGUGGU	6742
CR002135	FKBP1A	+	Chr20:1372140-1372162	AAGACGAGAGUGGCAUGUGG	6743
CR002136	FKBP1A	+	Chr20:1372137-1372159	UCGAAGACGAGAGUGGCAUG	6744

CR002137	FKBP1A	-	Chr20:1372132-1372154	UGCCACUCUCGUCUUCGAUG	6745
CR002138	FKBP1A	+	Chr20:1372130-1372152	CUCCACAUCGAAGACGAGAG	6746
CR002139	FKBP1A	-	Chr20:1372117-1372139	CGAUGUGGAGCUUCUAAAAC	6747
CR002140	FKBP1A	-	Chr20:1372108-1372130	GCUUCUAAAACUGGAAUGAC	6748
CR002141	FKBP1A	-	Chr20:1372103-1372125	UAAAACUGGAAUGACAGGAA	6749

In the various aspects of the invention, the gRNA molecule may include a targeting domain listed above. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002100. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002097. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002091. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002085. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002086. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002089. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002088. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002095. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002096. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002080. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002109. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002112. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002110. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002108. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002104. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002115. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002116. In an

embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002087. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002107. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002113. Such gRNA molecules, including combinations thereof, are suitable for use in, for example, the CRISPR systems, methods and cells and other aspects of the invention described herein.

Table 6c. gRNA Targeting Domains for human CIITA

Id.	Target	Strand	Chromosomal location	gRNA targeting domain sequence	SEQ ID NO:
CR002939	CIITA	+	Chr16:10877252-10877274	GGCAUCCUUGGGGAAGCUGA	7717
CR002940	CIITA	-	Chr16:10877257-10877279	UCGUGCCCUCAGCUUCCCCA	7718
CR002941	CIITA	+	Chr16:10877259-10877281	UUGGGGAAGCUGAGGGCACG	7719
CR002942	CIITA	+	Chr16:10877262-10877284	GGGAAGCUGAGGGCACGAGG	7720
CR002943	CIITA	+	Chr16:10877263-10877285	GGAAGCUGAGGGCACGAGGA	7721
CR002944	CIITA	+	Chr16:10877264-10877286	GAAGCUGAGGGCACGAGGAG	7722
CR002945	CIITA	+	Chr16:10877278-10877300	GAGGAGGGGCUGCCAGACUC	7723
CR002946	CIITA	+	Chr16:10877279-10877301	AGGAGGGGCUGCCAGACUCC	7724
CR002947	CIITA	-	Chr16:10877290-10877312	AGGCAGCAGCUCCCGGAGUC	7725
CR002948	CIITA	+	Chr16:10877292-10877314	AGACUCCGGGAGCUGCUGCC	7726
CR002949	CIITA	+	Chr16:10877296-10877318	UCCGGGAGCUGCUGCCUGGC	7727
CR002950	CIITA	+	Chr16:10877297-10877319	CCGGGAGCUGCUGCCUGGCU	7728
CR002951	CIITA	-	Chr16:10877297-10877319	CCCAGCCAGGCAGCAGCUCC	7729
CR002952	CIITA	-	Chr16:10877310-10877332	AUUGUGUAGGAAUCCCAGCC	7730
CR002953	CIITA	+	Chr16:10877321-10877343	UUCCUACACAAUGCGUUGCC	7731
CR002954	CIITA	-	Chr16:10877323-10877345	AGCCAGGCAACGCAUUGUGU	7732
CR002955	CIITA	+	Chr16:10877337-10877359	UGCCUGGCUCCACGCCCUGC	7733
CR002956	CIITA	+	Chr16:10877338-	GCCUGGCUCCACGCCC	7734

			10877360	UGCU	
CR002957	CIITA	-	Chr16:10877339-10877361	ACCCAGCAGGGCGUGGAGCC	7735
CR002958	CIITA	-	Chr16:10877346-10877368	AGGUAGGACCCAGCAGGGCG	7736
CR002959	CIITA	-	Chr16:10877351-10877373	CUGACAGGUAGGACCCAGCA	7737
CR002960	CIITA	-	Chr16:10877352-10877374	UCUGACAGGUAGGACCCAGC	7738
CR002961	CIITA	+	Chr16:10895283-10895305	CAGCUCACAGUGUGCCACCA	7739
CR002962	CIITA	+	Chr16:10895289-10895311	ACAGUGUGCCACCAUGGAGU	7740
CR002963	CIITA	+	Chr16:10895290-10895312	CAGUGUGCCACCAUGGAGUU	7741
CR002964	CIITA	+	Chr16:10895291-10895313	AGUGUGCCACCAUGGAGUUG	7742
CR002965	CIITA	-	Chr16:10895297-10895319	UAGGGGCCCCAACUCCAUGG	7743
CR002966	CIITA	-	Chr16:10895300-10895322	UUCUAGGGGCCCCAACUCCA	7744
CR002967	CIITA	+	Chr16:10895302-10895324	AUGGAGUUGGGGCCCCUAGA	7745
CR002968	CIITA	+	Chr16:10895305-10895327	GAGUUGGGGCCCCUAGAAGG	7746
CR002969	CIITA	+	Chr16:10895313-10895335	GCCCCUAGAAGGUGGCUACC	7747
CR002970	CIITA	-	Chr16:10895314-10895336	UCCAGGUAGCCACCUUCUAG	7748
CR002971	CIITA	-	Chr16:10895315-10895337	CUCCAGGUAGCCACCUUCUA	7749
CR002972	CIITA	-	Chr16:10895316-10895338	GCUCCAGGUAGCCACCUUCU	7750
CR002973	CIITA	-	Chr16:10895331-10895353	CAUCGCUGUUAAGAAGCUCC	7751
CR002974	CIITA	-	Chr16:10895358-10895380	AGAAGUGGUAGAGGCACAGG	7752
CR002975	CIITA	-	Chr16:10895359-10895381	UAGAAGUGGUAGAGGCACAG	7753
CR002976	CIITA	-	Chr16:10895360-10895382	AUAGAAGUGGUAGAGGCACA	7754
CR002977	CIITA	-	Chr16:10895361-10895383	CAUAGAAGUGGUAGAGGCAC	7755
CR002978	CIITA	-	Chr16:10895367-10895389	UCUGGUCAUAGAAGUGGUAG	7756
CR002979	CIITA	+	Chr16:10895370-10895392	CUACCACUUCUAUGACCAGA	7757
CR002980	CIITA	-	Chr16:10895373-10895395	GGUCCAUCUGGUCAUAGAAG	7758

CR002981	CIITA	+	Chr16:10895376-10895398	CUUCUAUGACCAGAUGGACC	7759
CR002982	CIITA	+	Chr16:10895380-10895402	UAUGACCAGAUGGACCUGGC	7760
CR002983	CIITA	-	Chr16:10895385-10895407	CUUCUCCAGCCAGGUCCAUC	7761
CR002984	CIITA	-	Chr16:10895394-10895416	CAAUCUCUUCUUCUCCAGCC	7762
CR002985	CIITA	-	Chr16:10895671-10895693	CAGUUGAUGGUGUCUGUGUC	7763
CR002986	CIITA	-	Chr16:10895672-10895694	GCAGUUGAUGGUGUCUGUGU	7764
CR002987	CIITA	-	Chr16:10895684-10895706	GCUGAACUGGUCGCAGUUGA	7765
CR002988	CIITA	+	Chr16:10895687-10895709	UCAACUGCGACCAGUUCAGC	7766
CR002989	CIITA	-	Chr16:10895697-10895719	CACACAACAGCCUGCUGAAC	7767
CR002990	CIITA	+	Chr16:10895703-10895725	CAGCAGGCUGUUGUGUGACA	7768
CR002991	CIITA	+	Chr16:10895707-10895729	AGGCUGUUGUGUGACAUGGA	7769
CR002992	CIITA	+	Chr16:10895723-10895745	UGGAAGGUGAUGAAGAGACC	7770
CR002993	CIITA	+	Chr16:10895724-10895746	GGAAGGUGAUGAAGAGACCA	7771
CR002994	CIITA	+	Chr16:10895727-10895749	AGGUGAUGAAGAGACCAGGG	7772
CR002995	CIITA	-	Chr16:10895741-10895763	GAUAUUGGCAUAAGCCUCCC	7773
CR002996	CIITA	-	Chr16:10895756-10895778	AGGUGCUUCCUCACCGAUAU	7774
CR002997	CIITA	+	Chr16:10898674-10898696	ACUGGACCAGUAUGUCUUCC	7775
CR002998	CIITA	-	Chr16:10898680-10898702	GGGAGUCCUGGAAGACAUAC	7776
CR002999	CIITA	+	Chr16:10898686-10898708	UGUCUUCCAGGACUCCCAGC	7777
CR003000	CIITA	+	Chr16:10898689-10898711	CUUCCAGGACUCCCAGCUGG	7778
CR003001	CIITA	+	Chr16:10898690-10898712	UUCCAGGACUCCCAGCUGGA	7779
CR003002	CIITA	-	Chr16:10898692-10898714	GGCCCUCCAGCUGGGAGUCC	7780
CR003003	CIITA	-	Chr16:10898700-10898722	CUUGCUCAGGCCCUCCAGCU	7781
CR003004	CIITA	-	Chr16:10898701-10898723	CCUUGCUCAGGCCCUCCAGC	7782
CR003005	CIITA	+	Chr16:10898701-10898723	CCAGCUGGAGGGCCUGAGCA	7783

CR003006	CIITA	-	Chr16:10898713-10898735	UACUGAAAAUGUCCUUGCUC	7784
CR003007	CIITA	+	Chr16:10898930-10898952	AUAGGACCAGAUGAAGUGAU	7785
CR003008	CIITA	-	Chr16:10898936-10898958	CUCUCACCGAUCACUUCAUC	7786
CR003009	CIITA	+	Chr16:10898941-10898963	UGAAGUGAUCGGUGAGAGUA	7787
CR003010	CIITA	+	Chr16:10898960-10898982	AUGGAGAUGCCAGCAGAAGU	7788
CR003011	CIITA	+	Chr16:10898961-10898983	UGGAGAUGCCAGCAGAAGUU	7789
CR003012	CIITA	-	Chr16:10898969-10898991	CUUUUCUGCCCAACUUCUGC	7790
CR003013	CIITA	-	Chr16:10901514-10901536	UGCCGGAAGCUCCUCUGGGA	7791
CR003014	CIITA	-	Chr16:10901518-10901540	GGUCUGCCGGAAGCUCCUCU	7792
CR003015	CIITA	-	Chr16:10901519-10901541	AGGUCUGCCGGAAGCUCCUC	7793
CR003016	CIITA	+	Chr16:10901529-10901551	UUCCGGCAGACCUGAAGCAC	7794
CR003017	CIITA	-	Chr16:10901531-10901553	UUCCAGUGCUUCAGGUCUGC	7795
CR003018	CIITA	+	Chr16:10902040-10902062	GAGCCCCCCACUGUGGUGAC	7796
CR003019	CIITA	-	Chr16:10902043-10902065	CUGCCAGUCACCACAGUGGG	7797
CR003020	CIITA	-	Chr16:10902044-10902066	ACUGCCAGUCACCACAGUGG	7798
CR003021	CIITA	-	Chr16:10902045-10902067	GACUGCCAGUCACCACAGUG	7799
CR003022	CIITA	-	Chr16:10902046-10902068	AGACUGCCAGUCACCACAGU	7800
CR003023	CIITA	-	Chr16:10902047-10902069	GAGACUGCCAGUCACCACAG	7801
CR003024	CIITA	+	Chr16:10902054-10902076	GGUGACUGGCAGUCUCCUAG	7802
CR003025	CIITA	+	Chr16:10902055-10902077	GUGACUGGCAGUCUCCUAGU	7803
CR003026	CIITA	-	Chr16:10902069-10902091	AGUCGCUCACUGGUCCCACU	7804

In the various aspects of the invention, the gRNA molecule may include a targeting domain listed above. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002939. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002940. In an embodiment, the targeting domain

of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002941. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002942. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002943. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002944. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002945. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002946. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002947. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002948. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002949. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002950. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002951. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002952. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002953. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002954. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002955. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002956. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002957. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002958. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002959. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002960. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002961. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002962. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002963. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002964. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002965. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting

domain of CR002966. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002967. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002968. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002969. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002970. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002971. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002972. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002973. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002974. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002975. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002976. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002977. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002978. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002979. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002980. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002981. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002982. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002983. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002984. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002985. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002986. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002987. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002988. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002989. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002990. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002991. In an embodiment, the targeting domain of the

gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002992. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002993. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002994. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002995. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002996. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002997. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002998. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR002999. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003000. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003001. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003002. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003003. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003004. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003005. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003006. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003007. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003008. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003009. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003010. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003011. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003012. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003013. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003014. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003015. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003016. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting

domain of CR003017. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003018. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003019. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003020. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003021. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003022. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003023. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003024. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003025. In an embodiment, the targeting domain of the gRNA of the invention comprises, e.g. consists of, the targeting domain of CR003026. Such gRNA molecules, and combinations thereof, are suitable for use in, for example, the CRISPR systems, methods and cells and other aspects of the invention described herein.

Table 6d. Targeting Domains for human LILRB1, an exemplary target of an NK inhibitory molecule.

Id.	Target	Region	Strand	Chromosomal location	gRNA targeting domain sequence	SEQ ID NO:
10859_2_1	LILRB1	EXON	+	chr19:54630390-54630410	UAAAAAGGGGAAGUUAAGAG	10090
10859_2_2	LILRB1	EXON	+	chr19:54630399-54630419	GAAGUUAAGAGGGGACUAUU	10091
10859_2_23	LILRB1	EXON	+	chr19:54630503-54630523	CUGCCACACGCAGCUCAGCC	10092
10859_2_24	LILRB1	EXON	+	chr19:54630504-54630524	UGCCACACGCAGCUCAGCCU	10093
10859_2_25	LILRB1	EXON	+	chr19:54630507-54630527	CACACGCAGCUCAGCCUGGG	10094
10859_2_29	LILRB1	EXON	+	chr19:54630560-54630580	AUCUGAGUCUGCCUGCAGCA	10095
10859_2_31	LILRB1	EXON	+	chr19:54630566-54630586	GUCUGCCUGCAGCAUGGACC	10096
10859_2_32	LILRB1	EXON	+	chr19:54630567-54630587	UCUGCCUGCAGCAUGGACCU	10097
10859_2_35	LILRB1	EXON	+	chr19:54630589-54630609	GUCUUCCCUGAAGCAUCUCC	10098
10859_2_36	LILRB1	EXON	+	chr19:54630590-54630610	UCUUCCCUGAAGCAUCUCCA	10099
10859_2_39	LILRB1	EXON	+	chr19:54630594-54630614	CCCUGAAGCAUCUCCAGGGC	10100
10859_	LILRB	EXON	+	chr19:5463059	UGAAGCAUCUCCAGGGC	10101

2_42	1			7-54630617	UGG	
10859_2_44	LILRB1	EXON	+	chr19:54630598-54630618	GAAGCAUCUCCAGGGCUGGA	10102
10859_2_45	LILRB1	EXON	+	chr19:54630611-54630631	GGCUGGAGGGACGACUGCCA	10103
10859_2_47	LILRB1	EXON	+	chr19:54630616-54630636	GAGGGACGACUGCCAUGGUA	10104
10859_2_58	LILRB1	EXON	-	chr19:54630436-54630456	CUUUCUUGACACUGGAUUGU	10105
10859_2_60	LILRB1	EXON	-	chr19:54630437-54630457	UCUUUCUUGACACUGGAUUG	10106
10859_2_62	LILRB1	EXON	-	chr19:54630444-54630464	GUUGACUUCUUUCUUGACAC	10107
10859_2_65	LILRB1	EXON	-	chr19:54630474-54630494	AAGAGAAAUGCAGGGAAAUA	10108
10859_2_67	LILRB1	EXON	-	chr19:54630475-54630495	GAAGAGAAAUGCAGGGAAAU	10109
10859_2_70	LILRB1	EXON	-	chr19:54630482-54630502	GAGCACAGAAGAGAAAUGCA	10110
10859_2_72	LILRB1	EXON	-	chr19:54630483-54630503	UGAGCACAGAAGAGAAAUGC	10111
10859_2_80	LILRB1	EXON	-	chr19:54630509-54630529	CGCCCAGGCUGAGCUGCGUG	10112
10859_2_82	LILRB1	EXON	-	chr19:54630524-54630544	CGCAUCUGGCUGUGCCGCCC	10113
10859_2_83	LILRB1	EXON	-	chr19:54630538-54630558	GCAGAGACGCAUCUCGCAUC	10114
10859_2_85	LILRB1	EXON	-	chr19:54630574-54630594	AAGACCCAGGUCCAUGCUGC	10115
10859_2_87	LILRB1	EXON	-	chr19:54630587-54630607	AGAUGCUUCAGGGAAGACCC	10116
10859_2_88	LILRB1	EXON	-	chr19:54630597-54630617	CCAGCCCUGGAGAUGCUUCA	10117
10859_2_90	LILRB1	EXON	-	chr19:54630598-54630618	UCCAGCCCUGGAGAUGCUUC	10118
10859_2_94	LILRB1	EXON	-	chr19:54630610-54630630	GGCAGUCGUCCCUCCAGCCC	10119
10859_2_98	LILRB1	EXON	-	chr19:54630631-54630651	GUGUUGUGGGGUCCUUACCA	10120
10859_3_3	LILRB1	EXON	+	chr19:54631010-54631030	UCUCUAUCCUGCCAGCACCG	10121
10859_3_4	LILRB1	EXON	+	chr19:54631011-54631031	CUCUAUCCUGCCAGCACCGA	10122
10859_3_7	LILRB1	EXON	+	chr19:54631032-54631052	GGCUCAUCCAUCCACAGAGC	10123
10859_3_8	LILRB1	EXON	+	chr19:54631033-54631053	GCUCAUCCAUCCACAGAGCA	10124
10859_3_10	LILRB1	EXON	+	chr19:54631039-54631059	CCAUCCACAGAGCAGGGCAG	10125

10859_3_12	LILRB1	EXON	+	chr19:54631040-54631060	CAUCCACAGAGCAGGGCAGU	10126
10859_3_15	LILRB1	EXON	+	chr19:54631043-54631063	CCACAGAGCAGGGCAGUGGG	10127
10859_3_17	LILRB1	EXON	+	chr19:54631069-54631089	CGCCAUGACCCCCAUCCUCA	10128
10859_3_18	LILRB1	EXON	+	chr19:54631085-54631105	CUCACGGUCCUGAUCUGUCU	10129
10859_3_24	LILRB1	EXON	+	chr19:54631101-54631121	GUCUCGGUGAGAUUUGAAGA	10130
10859_3_25	LILRB1	EXON	+	chr19:54631104-54631124	UCGGUGAGAUUUGAAGAAGG	10131
10859_3_28	LILRB1	EXON	-	chr19:54631020-54631040	GAUGAGCCCUCGGUGCUGGC	10132
10859_3_30	LILRB1	EXON	-	chr19:54631024-54631044	GAUGGAUGAGCCCUCGGUGC	10133
10859_3_31	LILRB1	EXON	-	chr19:54631030-54631050	UCUGUGGAUGGAUGAGCCCU	10134
10859_3_33	LILRB1	EXON	-	chr19:54631042-54631062	CCACUGCCCUGCUCUGUGGA	10135
10859_3_35	LILRB1	EXON	-	chr19:54631046-54631066	CCUCCCACUGCCCUGCUCUG	10136
10859_3_37	LILRB1	EXON	-	chr19:54631074-54631094	GACCGUGAGGAUGGGGGUCA	10137
10859_3_38	LILRB1	EXON	-	chr19:54631080-54631100	GAUCAGGACCGUGAGGAUGG	10138
10859_3_39	LILRB1	EXON	-	chr19:54631081-54631101	AGAUCAGGACCGUGAGGAUG	10139
10859_3_40	LILRB1	EXON	-	chr19:54631082-54631102	CAGAUCAGGACCGUGAGGAU	10140
10859_3_42	LILRB1	EXON	-	chr19:54631083-54631103	ACAGAUCAGGACCGUGAGGA	10141
10859_3_45	LILRB1	EXON	-	chr19:54631087-54631107	CGAGACAGAUCAGGACCGUG	10142
10859_3_50	LILRB1	EXON	-	chr19:54631096-54631116	AAAUCUCACCGAGACAGAUC	10143
10859_4_3	LILRB1	EXON	+	chr19:54631259-54631279	CUCUCUUCCAGGGCUGAGUC	10144
10859_4_4	LILRB1	EXON	+	chr19:54631260-54631280	UCUCUUCCAGGGCUGAGUCU	10145
10859_4_7	LILRB1	EXON	+	chr19:54631267-54631287	CAGGGCUGAGUCUGGGCCCC	10146
10859_4_8	LILRB1	EXON	+	chr19:54631280-54631300	GGGCCCCCGGACCCACGUGC	10147
10859_4_9	LILRB1	EXON	+	chr19:54631284-54631304	CCCCGGACCCACGUGCAGGC	10148
10859_4_11	LILRB1	EXON	-	chr19:54631255-54631275	CAGCCCUGGAAGAGAGUUCC	10149
10859_4_15	LILRB1	EXON	-	chr19:54631269-54631289	CGGGGGCCCAGACUCAGCCC	10150

10859_4_17	LILRB1	EXON	-	chr19:54631286-54631306	CUGCCUGCACGUGGGUCCGG	10151
10859_4_18	LILRB1	EXON	-	chr19:54631287-54631307	CCUGCCUGCACGUGGGUCCG	10152
10859_4_20	LILRB1	EXON	-	chr19:54631288-54631308	ACCUGCCUGCACGUGGGUCC	10153
10859_4_21	LILRB1	EXON	-	chr19:54631289-54631309	CACCUGCCUGCACGUGGGUC	10154
10859_4_24	LILRB1	EXON	-	chr19:54631294-54631314	AGACUCACCUGCCUGCACGU	10155
10859_4_25	LILRB1	EXON	-	chr19:54631295-54631315	CAGACUCACCUGCCUGCACG	10156
10859_5_5	LILRB1	EXON	+	chr19:54631502-54631522	ACCUCCCCAAGCCCACCCUC	10157
10859_5_6	LILRB1	EXON	+	chr19:54631503-54631523	CCUCCCCAAGCCCACCCUCU	10158
10859_5_8	LILRB1	EXON	+	chr19:54631513-54631533	CCCACCCUCUGGGCUGAACC	10159
10859_5_10	LILRB1	EXON	+	chr19:54631530-54631550	ACCAGGCUCUGUGAUCACCC	10160
10859_5_12	LILRB1	EXON	+	chr19:54631531-54631551	CCAGGCUCUGUGAUCACCCA	10161
10859_5_15	LILRB1	EXON	+	chr19:54631532-54631552	CAGGCUCUGUGAUCACCCAG	10162
10859_5_16	LILRB1	EXON	+	chr19:54631550-54631570	AGGGGAGUCCUGUGACCCUC	10163
10859_5_19	LILRB1	EXON	+	chr19:54631557-54631577	UCCUGUGACCCUCAGGUGUC	10164
10859_5_20	LILRB1	EXON	+	chr19:54631558-54631578	CCUGUGACCCUCAGGUGUCA	10165
10859_5_22	LILRB1	EXON	+	chr19:54631559-54631579	CUGUGACCCUCAGGUGUCAG	10166
10859_5_24	LILRB1	EXON	+	chr19:54631560-54631580	UGUGACCCUCAGGUGUCAGG	10167
10859_5_25	LILRB1	EXON	+	chr19:54631561-54631581	GUGACCCUCAGGUGUCAGGG	10168
10859_5_28	LILRB1	EXON	+	chr19:54631566-54631586	CCUCAGGUGUCAGGGGGGCC	10169
10859_5_30	LILRB1	EXON	+	chr19:54631575-54631595	UCAGGGGGGCCAGGAGACCC	10170
10859_5_38	LILRB1	EXON	+	chr19:54631613-54631633	GAGAAAAGAAAACAGCACCC	10171
10859_5_40	LILRB1	EXON	+	chr19:54631622-54631642	AAACAGCACCCUGGAUUACA	10172
10859_5_42	LILRB1	EXON	+	chr19:54631632-54631652	CUGGAUUACACGGAUCCCAC	10173
10859_5_48	LILRB1	EXON	+	chr19:54631647-54631667	CCCACAGGAGCUUGUGAAGA	10174
10859_5_49	LILRB1	EXON	+	chr19:54631648-54631668	CCACAGGAGCUUGUGAAGAA	10175

10859_5_53	LILRB1	EXON	+	chr19:54631676-54631696	UCCCCAUCCCAUCCAUCACC	10176
10859_5_54	LILRB1	EXON	+	chr19:54631677-54631697	CCCCAUCCCAUCCAUCACCU	10177
10859_5_58	LILRB1	EXON	+	chr19:54631687-54631707	UCCAUCACCUGGGAACACAC	10178
10859_5_59	LILRB1	EXON	+	chr19:54631688-54631708	CCAUCACCUGGGAACACACA	10179
10859_5_60	LILRB1	EXON	+	chr19:54631691-54631711	UCACCUGGGAACACACAGGG	10180
10859_5_61	LILRB1	EXON	+	chr19:54631708-54631728	GGGCGGUAUCGCUGUUACUA	10181
10859_5_62	LILRB1	EXON	+	chr19:54631723-54631743	UACUAUGGUAGCGACACUGC	10182
10859_5_68	LILRB1	EXON	+	chr19:54631749-54631769	CUCAGAGAGCAGUGACCCCC	10183
10859_5_69	LILRB1	EXON	+	chr19:54631755-54631775	GAGCAGUGACCCCCUGGAGC	10184
10859_5_70	LILRB1	EXON	+	chr19:54631758-54631778	CAGUGACCCCCUGGAGCUGG	10185
10859_5_71	LILRB1	EXON	+	chr19:54631765-54631785	CCCCUGGAGCUGGUGGUGAC	10186
10859_5_75	LILRB1	EXON	+	chr19:54631781-54631801	UGACAGGUGAGCUGACACUC	10187
10859_5_76	LILRB1	EXON	+	chr19:54631782-54631802	GACAGGUGAGCUGACACUCA	10188
10859_5_77	LILRB1	EXON	+	chr19:54631783-54631803	ACAGGUGAGCUGACACUCAG	10189
10859_5_79	LILRB1	EXON	-	chr19:54631486-54631506	AGGUGCCCUGGAAGGAAAUC	10190
10859_5_82	LILRB1	EXON	-	chr19:54631494-54631514	GCUUGGGGAGGUGCCCUGGA	10191
10859_5_85	LILRB1	EXON	-	chr19:54631498-54631518	GUGGGCUUGGGGAGGUGCCC	10192
10859_5_89	LILRB1	EXON	-	chr19:54631506-54631526	CCCAGAGGGUGGGCUUGGGG	10193
10859_5_90	LILRB1	EXON	-	chr19:54631509-54631529	CAGCCCAGAGGGUGGGCUUG	10194
10859_5_92	LILRB1	EXON	-	chr19:54631510-54631530	UCAGCCCAGAGGGUGGGCUU	10195
10859_5_95	LILRB1	EXON	-	chr19:54631511-54631531	UUCAGCCCAGAGGGUGGGCU	10196
10859_5_97	LILRB1	EXON	-	chr19:54631516-54631536	CCUGGUUCAGCCCAGAGGGU	10197
10859_5_98	LILRB1	EXON	-	chr19:54631517-54631537	GCCUGGUUCAGCCCAGAGGG	10198
10859_5_100	LILRB1	EXON	-	chr19:54631520-54631540	AGAGCCUGGUUCAGCCCAGA	10199
10859_5_101	LILRB1	EXON	-	chr19:54631521-54631541	CAGAGCCUGGUUCAGCCCAG	10200

10859_5_104	LILRB1	EXON	-	chr19:54631534-54631554	CCCUGGGUGAUCACAGAGCC	10201
10859_5_106	LILRB1	EXON	-	chr19:54631550-54631570	GAGGGUCACAGGACUCCCCU	10202
10859_5_107	LILRB1	EXON	-	chr19:54631551-54631571	UGAGGGUCACAGGACUCCCC	10203
10859_5_109	LILRB1	EXON	-	chr19:54631561-54631581	CCCUGACACCUGAGGGUCAC	10204
10859_5_111	LILRB1	EXON	-	chr19:54631568-54631588	CUGGCCCCCCUGACACCUGA	10205
10859_5_112	LILRB1	EXON	-	chr19:54631569-54631589	CCUGGCCCCCCUGACACCUG	10206
10859_5_115	LILRB1	EXON	-	chr19:54631587-54631607	GACGGUACUCCUGGGUCUCC	10207
10859_5_119	LILRB1	EXON	-	chr19:54631595-54631615	UCUAUAUAGACGGUACUCCU	10208
10859_5_120	LILRB1	EXON	-	chr19:54631596-54631616	CUCUAUAUAGACGGUACUCC	10209
10859_5_125	LILRB1	EXON	-	chr19:54631605-54631625	UUUUCUUUUCUCUAUAUAGA	10210
10859_5_126	LILRB1	EXON	-	chr19:54631633-54631653	UGUGGGAUCCGUGUAAUCCA	10211
10859_5_127	LILRB1	EXON	-	chr19:54631634-54631654	CUGUGGGAUCCGUGUAAUCC	10212
10859_5_131	LILRB1	EXON	-	chr19:54631650-54631670	CCUUCUUCACAAGCUCCUGU	10213
10859_5_132	LILRB1	EXON	-	chr19:54631651-54631671	CCCUUCUUCACAAGCUCCUG	10214
10859_5_135	LILRB1	EXON	-	chr19:54631674-54631694	UGAUGGAUGGGAUGGGGAAC	10215
10859_5_137	LILRB1	EXON	-	chr19:54631680-54631700	CCCAGGUGAUGGAUGGGAUG	10216
10859_5_140	LILRB1	EXON	-	chr19:54631681-54631701	UCCCAGGUGAUGGAUGGGAU	10217
10859_5_141	LILRB1	EXON	-	chr19:54631682-54631702	UUCCCAGGUGAUGGAUGGGA	10218
10859_5_144	LILRB1	EXON	-	chr19:54631686-54631706	UGUGUUCCCAGGUGAUGGAU	10219
10859_5_146	LILRB1	EXON	-	chr19:54631687-54631707	GUGUGUUCCCAGGUGAUGGA	10220
10859_5_148	LILRB1	EXON	-	chr19:54631691-54631711	CCCUGUGUGUUCCCAGGUGA	10221
10859_5_150	LILRB1	EXON	-	chr19:54631697-54631717	AUACCGCCCUGUGUGUUCCC	10222
10859_5_151	LILRB1	EXON	-	chr19:54631749-54631769	GGGGGUCACUGCUCUCUGAG	10223
10859_5_153	LILRB1	EXON	-	chr19:54631767-54631787	CUGUCACCACCAGCUCCAGG	10224
10859_5_154	LILRB1	EXON	-	chr19:54631768-54631788	CCUGUCACCACCAGCUCCAG	10225

10859_5_155	LILRB1	EXON	-	chr19:54631769-54631789	ACCUGUCACCACCAGCUCCA	10226
10859_5_157	LILRB1	EXON	-	chr19:54631770-54631790	CACCUGUCACCACCAGCUCC	10227
10859_6_2	LILRB1	EXON	+	chr19:54631956-54631976	CUCAGCCCAGCCCAGCCCCG	10228
10859_6_6	LILRB1	EXON	+	chr19:54631966-54631986	CCCAGCCCCGUGGUGAACUC	10229
10859_6_8	LILRB1	EXON	+	chr19:54631969-54631989	AGCCCCGUGGUGAACUCAGG	10230
10859_6_10	LILRB1	EXON	+	chr19:54631970-54631990	GCCCCGUGGUGAACUCAGGA	10231
10859_6_12	LILRB1	EXON	+	chr19:54631998-54632018	AACCCUCCAGUGUGACUCAC	10232
10859_6_13	LILRB1	EXON	+	chr19:54632001-54632021	CCUCCAGUGUGACUCACAGG	10233
10859_6_14	LILRB1	EXON	+	chr19:54632011-54632031	GACUCACAGGUGGCAUUUGA	10234
10859_6_17	LILRB1	EXON	+	chr19:54632028-54632048	UGAUGGCUUCAUUCUGUGUA	10235
10859_6_21	LILRB1	EXON	+	chr19:54632032-54632052	GGCUUCAUUCUGUGUAAGGA	10236
10859_6_29	LILRB1	EXON	+	chr19:54632080-54632100	AACUCCCAGCCCCAUGCCCG	10237
10859_6_30	LILRB1	EXON	+	chr19:54632081-54632101	ACUCCCAGCCCCAUGCCCGU	10238
10859_6_32	LILRB1	EXON	+	chr19:54632106-54632126	GUCCCGCGCCAUCUUCUCCG	10239
10859_6_33	LILRB1	EXON	+	chr19:54632107-54632127	UCCCGCGCCAUCUUCUCCGU	10240
10859_6_37	LILRB1	EXON	+	chr19:54632129-54632149	GCCCCGUGAGCCCGAGUCGC	10241
10859_6_38	LILRB1	EXON	+	chr19:54632132-54632152	CCGUGAGCCCGAGUCGCAGG	10242
10859_6_39	LILRB1	EXON	+	chr19:54632135-54632155	UGAGCCCGAGUCGCAGGUGG	10243
10859_6_40	LILRB1	EXON	+	chr19:54632141-54632161	CGAGUCGCAGGUGGUGGUAC	10244
10859_6_44	LILRB1	EXON	+	chr19:54632177-54632197	ACUCGAACUCUCCCUAUGAG	10245
10859_6_46	LILRB1	EXON	+	chr19:54632199-54632219	GUCUCUACCCAGUGAUCUCC	10246
10859_6_48	LILRB1	EXON	+	chr19:54632208-54632228	CAGUGAUCUCCUGGAGCUCC	10247
10859_6_49	LILRB1	EXON	+	chr19:54632215-54632235	CUCCUGGAGCUCCUGGUCCU	10248
10859_6_53	LILRB1	EXON	-	chr19:54631921-54631941	UAGGCUCCUAGGAGAGAAGG	10249
10859_6_57	LILRB1	EXON	-	chr19:54631924-54631944	AUGUAGGCUCCUAGGAGAGA	10250

10859_6_62	LILRB1	EXON	-	chr19:54631932-54631952	UGGGUUUGAUGUAGGCUCCU	10251
10859_6_65	LILRB1	EXON	-	chr19:54631940-54631960	UGAGAGGGUGGGUUUGAUGU	10252
10859_6_66	LILRB1	EXON	-	chr19:54631951-54631971	CUGGGCUGGGCUGAGAGGGU	10253
10859_6_67	LILRB1	EXON	-	chr19:54631952-54631972	GCUGGGCUGGGCUGAGAGGG	10254
10859_6_69	LILRB1	EXON	-	chr19:54631955-54631975	GGGGCUGGGCUGGGCUGAGA	10255
10859_6_70	LILRB1	EXON	-	chr19:54631956-54631976	CGGGGCUGGGCUGGGCUGAG	10256
10859_6_75	LILRB1	EXON	-	chr19:54631964-54631984	GUUCACCACGGGGCUGGGCU	10257
10859_6_76	LILRB1	EXON	-	chr19:54631965-54631985	AGUUCACCACGGGGCUGGGC	10258
10859_6_79	LILRB1	EXON	-	chr19:54631969-54631989	CCUGAGUUCACCACGGGGCU	10259
10859_6_80	LILRB1	EXON	-	chr19:54631970-54631990	UCCUGAGUUCACCACGGGGC	10260
10859_6_83	LILRB1	EXON	-	chr19:54631974-54631994	UCCCUCCUGAGUUCACCACG	10261
10859_6_84	LILRB1	EXON	-	chr19:54631975-54631995	UUCCCUCCUGAGUUCACCAC	10262
10859_6_85	LILRB1	EXON	-	chr19:54631976-54631996	AUUCCCUCCUGAGUUCACCA	10263
10859_6_89	LILRB1	EXON	-	chr19:54632003-54632023	CACCUGUGAGUCACACUGGA	10264
10859_6_90	LILRB1	EXON	-	chr19:54632004-54632024	CCACCUGUGAGUCACACUGG	10265
10859_6_92	LILRB1	EXON	-	chr19:54632007-54632027	AUGCCACCUGUGAGUCACAC	10266
10859_6_104	LILRB1	EXON	-	chr19:54632070-54632090	GCUGGGAGUUCAGGCAUUGU	10267
10859_6_105	LILRB1	EXON	-	chr19:54632071-54632091	GGCUGGGAGUUCAGGCAUUG	10268
10859_6_107	LILRB1	EXON	-	chr19:54632079-54632099	GGGCAUGGGGCUGGGAGUUC	10269
10859_6_108	LILRB1	EXON	-	chr19:54632087-54632107	CGACCCACGGGCAUGGGGCU	10270
10859_6_110	LILRB1	EXON	-	chr19:54632088-54632108	ACGACCCACGGGCAUGGGGC	10271
10859_6_113	LILRB1	EXON	-	chr19:54632092-54632112	CGGGACGACCCACGGGCAUG	10272
10859_6_114	LILRB1	EXON	-	chr19:54632093-54632113	GCGGGACGACCCACGGGCAU	10273
10859_6_116	LILRB1	EXON	-	chr19:54632094-54632114	CGCGGGACGACCCACGGGCA	10274
10859_6_118	LILRB1	EXON	-	chr19:54632099-54632119	GAUGGCGCGGGACGACCCAC	10275

10859_6_119	LILRB1	EXON	-	chr19:54632100-54632120	AGAUGGCGCGGGACGACCCA	10276
10859_6_121	LILRB1	EXON	-	chr19:54632111-54632131	GCCCACGGAGAAGAUGGCGC	10277
10859_6_123	LILRB1	EXON	-	chr19:54632112-54632132	GGCCCACGGAGAAGAUGGCG	10278
10859_6_125	LILRB1	EXON	-	chr19:54632117-54632137	CACGGGGCCCACGGAGAAGA	10279
10859_6_129	LILRB1	EXON	-	chr19:54632126-54632146	ACUCGGGCUCACGGGGCCCA	10280
10859_6_131	LILRB1	EXON	-	chr19:54632133-54632153	ACCUGCGACUCGGGCUCACG	10281
10859_6_132	LILRB1	EXON	-	chr19:54632134-54632154	CACCUGCGACUCGGGCUCAC	10282
10859_6_133	LILRB1	EXON	-	chr19:54632135-54632155	CCACCUGCGACUCGGGCUCA	10283
10859_6_136	LILRB1	EXON	-	chr19:54632142-54632162	UGUACCACCACCUGCGACUC	10284
10859_6_137	LILRB1	EXON	-	chr19:54632143-54632163	CUGUACCACCACCUGCGACU	10285
10859_6_143	LILRB1	EXON	-	chr19:54632191-54632211	CUGGGUAGAGACCACUCAUA	10286
10859_6_144	LILRB1	EXON	-	chr19:54632192-54632212	ACUGGGUAGAGACCACUCAU	10287
10859_6_148	LILRB1	EXON	-	chr19:54632209-54632229	AGGAGCUCCAGGAGAUCACU	10288
10859_6_149	LILRB1	EXON	-	chr19:54632210-54632230	CAGGAGCUCCAGGAGAUCAC	10289
10859_6_154	LILRB1	EXON	-	chr19:54632220-54632240	CACCUAGGACCAGGAGCUCC	10290
10859_6_156	LILRB1	EXON	-	chr19:54632229-54632249	UGAAUUUCUCACCUAGGACC	10291
10859_6_159	LILRB1	EXON	-	chr19:54632235-54632255	AUGCUGUGAAUUUCUCACCU	10292
10859_7_7	LILRB1	EXON	+	chr19:54632477-54632497	CCAUCACUCUCAGUGCAGCC	10293
10859_7_8	LILRB1	EXON	+	chr19:54632488-54632508	AGUGCAGCCAGGUCCUAUCG	10294
10859_7_12	LILRB1	EXON	+	chr19:54632497-54632517	AGGUCCUAUCGUGGCCCCUG	10295
10859_7_13	LILRB1	EXON	+	chr19:54632519-54632539	GAGACCCUGACUCUGCAGUG	10296
10859_7_14	LILRB1	EXON	+	chr19:54632531-54632551	CUGCAGUGUGGCUCUGAUGC	10297
10859_7_16	LILRB1	EXON	+	chr19:54632557-54632577	CAACAGAUUUGUUCUGUAUA	10298
10859_7_18	LILRB1	EXON	+	chr19:54632561-54632581	AGAUUUGUUCUGUAUAAGGA	10299
10859_7_21	LILRB1	EXON	+	chr19:54632562-54632582	GAUUUGUUCUGUAUAAGGAC	10300

10859_7_23	LILRB1	EXON	+	chr19:54632563-54632583	AUUUGUUCUGUAUAAGGACG	10301
10859_7_27	LILRB1	EXON	+	chr19:54632588-54632608	CGUGACUUCCUUCAGCUCGC	10302
10859_7_30	LILRB1	EXON	+	chr19:54632602-54632622	GCUCGCUGGCGCACAGCCCC	10303
10859_7_32	LILRB1	EXON	+	chr19:54632606-54632626	GCUGGCGCACAGCCCCAGGC	10304
10859_7_33	LILRB1	EXON	+	chr19:54632607-54632627	CUGGCGCACAGCCCCAGGCU	10305
10859_7_34	LILRB1	EXON	+	chr19:54632617-54632637	GCCCCAGGCUGGGCUCUCCC	10306
10859_7_36	LILRB1	EXON	+	chr19:54632632-54632652	CUCCCAGGCCAACUUCACCC	10307
10859_7_37	LILRB1	EXON	+	chr19:54632633-54632653	UCCCAGGCCAACUUCACCCU	10308
10859_7_42	LILRB1	EXON	+	chr19:54632654-54632674	GGCCCUGUGAGCCGCUCCUA	10309
10859_7_43	LILRB1	EXON	+	chr19:54632655-54632675	GCCCUGUGAGCCGCUCCUAC	10310
10859_7_45	LILRB1	EXON	+	chr19:54632656-54632676	CCCUGUGAGCCGCUCCUACG	10311
10859_7_46	LILRB1	EXON	+	chr19:54632657-54632677	CCUGUGAGCCGCUCCUACGG	10312
10859_7_47	LILRB1	EXON	+	chr19:54632675-54632695	GGGGGCCAGUACAGAUGCUA	10313
10859_7_49	LILRB1	EXON	+	chr19:54632700-54632720	CACACAACCUCUCCUCCGAG	10314
10859_7_50	LILRB1	EXON	+	chr19:54632704-54632724	CAACCUCUCCUCCGAGUGGU	10315
10859_7_52	LILRB1	EXON	+	chr19:54632722-54632742	GUCGGCCCCCAGCGACCCCC	10316
10859_7_53	LILRB1	EXON	+	chr19:54632738-54632758	CCCCUGGACAUCCUGAUCGC	10317
10859_7_56	LILRB1	EXON	+	chr19:54632743-54632763	GGACAUCCUGAUCGCAGGUG	10318
10859_7_59	LILRB1	EXON	+	chr19:54632753-54632773	AUCGCAGGUGAGGAGCCCAG	10319
10859_7_60	LILRB1	EXON	+	chr19:54632754-54632774	UCGCAGGUGAGGAGCCCAGC	10320
10859_7_61	LILRB1	EXON	-	chr19:54632446-54632466	CACCUGGGAAAAGGUGGUCA	10321
10859_7_64	LILRB1	EXON	-	chr19:54632452-54632472	UAGAAACACCUGGGAAAAGG	10322
10859_7_65	LILRB1	EXON	-	chr19:54632455-54632475	UCUUAGAAACACCUGGGAAA	10323
10859_7_66	LILRB1	EXON	-	chr19:54632461-54632481	AUGGCUUCUUAGAAACACCU	10324
10859_7_68	LILRB1	EXON	-	chr19:54632462-54632482	GAUGGCUUCUUAGAAACACC	10325

10859_7_72	LILRB1	EXON	-	chr19:54632480-54632500	CCUGGCUGCACUGAGAGUGA	10326
10859_7_75	LILRB1	EXON	-	chr19:54632498-54632518	UCAGGGGCCACGAUAGGACC	10327
10859_7_76	LILRB1	EXON	-	chr19:54632504-54632524	GUCUCCUCAGGGGCCACGAU	10328
10859_7_78	LILRB1	EXON	-	chr19:54632514-54632534	CAGAGUCAGGGUCUCCUCAG	10329
10859_7_79	LILRB1	EXON	-	chr19:54632515-54632535	GCAGAGUCAGGGUCUCCUCA	10330
10859_7_80	LILRB1	EXON	-	chr19:54632516-54632536	UGCAGAGUCAGGGUCUCCUC	10331
10859_7_83	LILRB1	EXON	-	chr19:54632526-54632546	AGAGCCACACUGCAGAGUCA	10332
10859_7_84	LILRB1	EXON	-	chr19:54632527-54632547	CAGAGCCACACUGCAGAGUC	10333
10859_7_93	LILRB1	EXON	-	chr19:54632599-54632619	GCUGUGCGCCAGCGAGCUGA	10334
10859_7_99	LILRB1	EXON	-	chr19:54632621-54632641	GCCUGGGAGAGCCCAGCCUG	10335
10859_7_100	LILRB1	EXON	-	chr19:54632622-54632642	GGCCUGGGAGAGCCCAGCCU	10336
10859_7_102	LILRB1	EXON	-	chr19:54632623-54632643	UGGCCUGGGAGAGCCCAGCC	10337
10859_7_106	LILRB1	EXON	-	chr19:54632637-54632657	GCCCAGGGUGAAGUUGGCCU	10338
10859_7_107	LILRB1	EXON	-	chr19:54632638-54632658	GGCCCAGGGUGAAGUUGGCC	10339
10859_7_110	LILRB1	EXON	-	chr19:54632643-54632663	CACAGGGCCCAGGGUGAAGU	10340
10859_7_112	LILRB1	EXON	-	chr19:54632652-54632672	GGAGCGGCUCACAGGGCCCA	10341
10859_7_113	LILRB1	EXON	-	chr19:54632653-54632673	AGGAGCGGCUCACAGGGCCC	10342
10859_7_115	LILRB1	EXON	-	chr19:54632659-54632679	CCCCGUAGGAGCGGCUCACA	10343
10859_7_116	LILRB1	EXON	-	chr19:54632660-54632680	CCCCCGUAGGAGCGGCUCAC	10344
10859_7_118	LILRB1	EXON	-	chr19:54632668-54632688	UGUACUGGCCCCCGUAGGAG	10345
10859_7_119	LILRB1	EXON	-	chr19:54632673-54632693	GCAUCUGUACUGGCCCCCGU	10346
10859_7_123	LILRB1	EXON	-	chr19:54632683-54632703	GUGCACCGUAGCAUCUGUAC	10347
10859_7_124	LILRB1	EXON	-	chr19:54632710-54632730	GGGCCGACCACUCGGAGGAG	10348
10859_7_126	LILRB1	EXON	-	chr19:54632715-54632735	GCUGGGGGCCGACCACUCGG	10349
10859_7_129	LILRB1	EXON	-	chr19:54632718-54632738	GUCGCUGGGGGCCGACCACU	10350

10859_7_132	LILRB1	EXON	-	chr19:54632730-54632750	GAUGUCCAGGGGGUCGCUGG	10351
10859_7_133	LILRB1	EXON	-	chr19:54632731-54632751	GGAUGUCCAGGGGGUCGCUG	10352
10859_7_135	LILRB1	EXON	-	chr19:54632732-54632752	AGGAUGUCCAGGGGGUCGCU	10353
10859_7_137	LILRB1	EXON	-	chr19:54632733-54632753	CAGGAUGUCCAGGGGGUCGC	10354
10859_7_139	LILRB1	EXON	-	chr19:54632740-54632760	CUGCGAUCAGGAUGUCCAGG	10355
10859_7_140	LILRB1	EXON	-	chr19:54632741-54632761	CCUGCGAUCAGGAUGUCCAG	10356
10859_7_141	LILRB1	EXON	-	chr19:54632742-54632762	ACCUGCGAUCAGGAUGUCCA	10357
10859_7_144	LILRB1	EXON	-	chr19:54632743-54632763	CACCUGCGAUCAGGAUGUCC	10358
10859_7_146	LILRB1	EXON	-	chr19:54632752-54632772	UGGGCUCCUCACCUGCGAUC	10359
10859_8_4	LILRB1	EXON	+	chr19:54633022-54633042	CUAUGACAGAGUCUCCCUCU	10360
10859_8_7	LILRB1	EXON	+	chr19:54633031-54633051	AGUCUCCCUCUCGGUGCAGC	10361
10859_8_8	LILRB1	EXON	+	chr19:54633032-54633052	GUCUCCCUCUCGGUGCAGCC	10362
10859_8_9	LILRB1	EXON	+	chr19:54633040-54633060	CUCGGUGCAGCCGGGCCCCA	10363
10859_8_10	LILRB1	EXON	+	chr19:54633043-54633063	GGUGCAGCCGGGCCCCACGG	10364
10859_8_13	LILRB1	EXON	+	chr19:54633050-54633070	CCGGGCCCCACGGUGGCCUC	10365
10859_8_17	LILRB1	EXON	+	chr19:54633082-54633102	GACCCUGCUGUGUCAGUCAC	10366
10859_8_19	LILRB1	EXON	+	chr19:54633083-54633103	ACCCUGCUGUGUCAGUCACA	10367
10859_8_21	LILRB1	EXON	+	chr19:54633087-54633107	UGCUGUGUCAGUCACAGGGA	10368
10859_8_23	LILRB1	EXON	+	chr19:54633112-54633132	GCAAACUUUCCUUCUGACCA	10369
10859_8_26	LILRB1	EXON	+	chr19:54633115-54633135	AACUUUCCUUCUGACCAAGG	10370
10859_8_28	LILRB1	EXON	+	chr19:54633116-54633136	ACUUUCCUUCUGACCAAGGA	10371
10859_8_30	LILRB1	EXON	+	chr19:54633117-54633137	CUUUCCUUCUGACCAAGGAG	10372
10859_8_31	LILRB1	EXON	+	chr19:54633118-54633138	UUUCCUUCUGACCAAGGAGG	10373
10859_8_35	LILRB1	EXON	+	chr19:54633135-54633155	AGGGGGCAGCUGAUGACCCA	10374
10859_8_36	LILRB1	EXON	+	chr19:54633172-54633192	GUACCAAUCUCAAAAAUACC	10375

10859_8_39	LILRB1	EXON	+	chr19:54633187-54633207	AUACCAGGCUGAAUUCCCCA	10376
10859_8_40	LILRB1	EXON	+	chr19:54633188-54633208	UACCAGGCUGAAUUCCCCAU	10377
10859_8_44	LILRB1	EXON	+	chr19:54633211-54633231	UCCUGUGACCUCAGCCCAUG	10378
10859_8_46	LILRB1	EXON	+	chr19:54633212-54633232	CCUGUGACCUCAGCCCAUGC	10379
10859_8_47	LILRB1	EXON	+	chr19:54633213-54633233	CUGUGACCUCAGCCCAUGCG	10380
10859_8_48	LILRB1	EXON	+	chr19:54633222-54633242	CAGCCCAUGCGGGGACCUAC	10381
10859_8_49	LILRB1	EXON	+	chr19:54633230-54633250	GCGGGGACCUACAGGUGCUA	10382
10859_8_52	LILRB1	EXON	+	chr19:54633280-54633300	GACUCACCCCAGUGACCCCC	10383
10859_8_54	LILRB1	EXON	+	chr19:54633289-54633309	CAGUGACCCCCUGGAGCUCG	10384
10859_8_55	LILRB1	EXON	+	chr19:54633296-54633316	CCCCUGGAGCUCGUGGUCUC	10385
10859_8_58	LILRB1	EXON	+	chr19:54633299-54633319	CUGGAGCUCGUGGUCUCAGG	10386
10859_8_59	LILRB1	EXON	+	chr19:54633300-54633320	UGGAGCUCGUGGUCUCAGGU	10387
10859_8_61	LILRB1	EXON	+	chr19:54633301-54633321	GGAGCUCGUGGUCUCAGGUG	10388
10859_8_62	LILRB1	EXON	+	chr19:54633302-54633322	GAGCUCGUGGUCUCAGGUGG	10389
10859_8_63	LILRB1	EXON	-	chr19:54632998-54633018	GUCCUGGAGAGAAGAAGGAU	10390
10859_8_64	LILRB1	EXON	-	chr19:54632999-54633019	UGUCCUGGAGAGAAGAAGGA	10391
10859_8_66	LILRB1	EXON	-	chr19:54633003-54633023	GAACUGUCCUGGAGAGAAGA	10392
10859_8_74	LILRB1	EXON	-	chr19:54633014-54633034	ACUCUGUCAUAGAACUGUCC	10393
10859_8_79	LILRB1	EXON	-	chr19:54633039-54633059	GGGGCCCGGCUGCACCGAGA	10394
10859_8_81	LILRB1	EXON	-	chr19:54633040-54633060	UGGGGCCCGGCUGCACCGAG	10395
10859_8_86	LILRB1	EXON	-	chr19:54633053-54633073	CCUGAGGCCACCGUGGGGCC	10396
10859_8_87	LILRB1	EXON	-	chr19:54633058-54633078	UCUCUCCUGAGGCCACCGUG	10397
10859_8_88	LILRB1	EXON	-	chr19:54633059-54633079	UUCUCUCCUGAGGCCACCGU	10398
10859_8_90	LILRB1	EXON	-	chr19:54633060-54633080	GUUCUCUCCUGAGGCCACCG	10399
10859_8_92	LILRB1	EXON	-	chr19:54633069-54633089	CAGGGUCACGUUCUCUCCUG	10400

10859_8_94	LILRB1	EXON	-	chr19:54633087-54633107	UCCCUGUGACUGACACAGCA	10401
10859_8_95	LILRB1	EXON	-	chr19:54633088-54633108	AUCCCUGUGACUGACACAGC	10402
10859_8_100	LILRB1	EXON	-	chr19:54633124-54633144	CUGCCCCCUCCUUGGUCAGA	10403
10859_8_105	LILRB1	EXON	-	chr19:54633132-54633152	GUCAUCAGCUGCCCCCUCCU	10404
10859_8_109	LILRB1	EXON	-	chr19:54633154-54633174	ACGUUGAUCUUAGACGCCAU	10405
10859_8_110	LILRB1	EXON	-	chr19:54633155-54633175	UACGUUGAUCUUAGACGCCA	10406
10859_8_117	LILRB1	EXON	-	chr19:54633178-54633198	CAGCCUGGUAUUUUUGAGAU	10407
10859_8_119	LILRB1	EXON	-	chr19:54633193-54633213	GACCCAUGGGGAAUUCAGCC	10408
10859_8_120	LILRB1	EXON	-	chr19:54633205-54633225	CUGAGGUCACAGGACCCAUG	10409
10859_8_123	LILRB1	EXON	-	chr19:54633206-54633226	GCUGAGGUCACAGGACCCAU	10410
10859_8_125	LILRB1	EXON	-	chr19:54633207-54633227	GGCUGAGGUCACAGGACCCA	10411
10859_8_127	LILRB1	EXON	-	chr19:54633215-54633235	CCCGCAUGGGCUGAGGUCAC	10412
10859_8_129	LILRB1	EXON	-	chr19:54633222-54633242	GUAGGUCCCCGCAUGGGCUG	10413
10859_8_131	LILRB1	EXON	-	chr19:54633228-54633248	GCACCUGUAGGUCCCCGCAU	10414
10859_8_132	LILRB1	EXON	-	chr19:54633229-54633249	AGCACCUGUAGGUCCCCGCA	10415
10859_8_134	LILRB1	EXON	-	chr19:54633240-54633260	CUGUGAGCCGUAGCACCUGU	10416
10859_8_139	LILRB1	EXON	-	chr19:54633267-54633287	GUGAGUCAGCAGGUAGGGUU	10417
10859_8_141	LILRB1	EXON	-	chr19:54633272-54633292	CUGGGGUGAGUCAGCAGGUA	10418
10859_8_142	LILRB1	EXON	-	chr19:54633273-54633293	ACUGGGGUGAGUCAGCAGGU	10419
10859_8_144	LILRB1	EXON	-	chr19:54633277-54633297	GGUCACUGGGGUGAGUCAGC	10420
10859_8_146	LILRB1	EXON	-	chr19:54633289-54633309	CGAGCUCCAGGGGGUCACUG	10421
10859_8_147	LILRB1	EXON	-	chr19:54633290-54633310	ACGAGCUCCAGGGGGUCACU	10422
10859_8_149	LILRB1	EXON	-	chr19:54633291-54633311	CACGAGCUCCAGGGGGUCAC	10423
10859_8_151	LILRB1	EXON	-	chr19:54633298-54633318	CUGAGACCACGAGCUCCAGG	10424
10859_8_152	LILRB1	EXON	-	chr19:54633299-54633319	CCUGAGACCACGAGCUCCAG	10425

10859_8_153	LILRB1	EXON	-	chr19:54633300-54633320	ACCUGAGACCACGAGCUCCA	10426
10859_8_156	LILRB1	EXON	-	chr19:54633301-54633321	CACCUGAGACCACGAGCUCC	10427
10859_9_2	LILRB1	EXON	+	chr19:54633624-54633644	UUCUUUUACCCAGGACCGUC	10428
10859_9_5	LILRB1	EXON	+	chr19:54633625-54633645	UCUUUUACCCAGGACCGUCU	10429
10859_9_6	LILRB1	EXON	+	chr19:54633626-54633646	CUUUUACCCAGGACCGUCUG	10430
10859_9_7	LILRB1	EXON	+	chr19:54633627-54633647	UUUUACCCAGGACCGUCUGG	10431
10859_9_12	LILRB1	EXON	+	chr19:54633648-54633668	GGCCCCAGCUCCCCGACAAC	10432
10859_9_13	LILRB1	EXON	+	chr19:54633666-54633686	ACAGGCCCCACCUCCACAUC	10433
10859_9_16	LILRB1	EXON	+	chr19:54633679-54633699	CCACAUCUGGUGAGUCCCUG	10434
10859_9_17	LILRB1	EXON	-	chr19:54633620-54633640	GUCCUGGGUAAAAGAAUGAG	10435
10859_9_21	LILRB1	EXON	-	chr19:54633635-54633655	UGGGGCCCCCAGACGGUCCU	10436
10859_9_22	LILRB1	EXON	-	chr19:54633636-54633656	CUGGGGCCCCCAGACGGUCC	10437
10859_9_25	LILRB1	EXON	-	chr19:54633642-54633662	GGGGAGCUGGGGCCCCCAGA	10438
10859_9_26	LILRB1	EXON	-	chr19:54633653-54633673	GGCCUGUUGUCGGGGAGCUG	10439
10859_9_27	LILRB1	EXON	-	chr19:54633654-54633674	GGGCCUGUUGUCGGGGAGCU	10440
10859_9_28	LILRB1	EXON	-	chr19:54633655-54633675	GGGGCCUGUUGUCGGGGAGC	10441
10859_9_31	LILRB1	EXON	-	chr19:54633661-54633681	GGAGGUGGGGCCUGUUGUCG	10442
10859_9_34	LILRB1	EXON	-	chr19:54633662-54633682	UGGAGGUGGGGCCUGUUGUC	10443
10859_9_36	LILRB1	EXON	-	chr19:54633663-54633683	GUGGAGGUGGGGCCUGUUGU	10444
10859_9_38	LILRB1	EXON	-	chr19:54633674-54633694	ACUCACCAGAUGUGGAGGUG	10445
10859_9_39	LILRB1	EXON	-	chr19:54633675-54633695	GACUCACCAGAUGUGGAGGU	10446
10859_9_41	LILRB1	EXON	-	chr19:54633676-54633696	GGACUCACCAGAUGUGGAGG	10447
10859_9_43	LILRB1	EXON	-	chr19:54633679-54633699	CAGGGACUCACCAGAUGUGG	10448
10859_9_44	LILRB1	EXON	-	chr19:54633682-54633702	CCUCAGGGACUCACCAGAUG	10449
10859_10_1	LILRB1	EXON	+	chr19:54633951-54633971	CCUCCCCGUCCUGACCCAGC	10450

10859_10_4	LILRB1	EXON	+	chr19:54633959-54633979	UCCUGACCCAGCAGGCCCUG	10451
10859_10_6	LILRB1	EXON	+	chr19:54633981-54634001	GACCAGCCCCUCACCCCCAC	10452
10859_10_7	LILRB1	EXON	+	chr19:54633982-54634002	ACCAGCCCCUCACCCCCACC	10453
10859_10_9	LILRB1	EXON	+	chr19:54633986-54634006	GCCCCUCACCCCCACCGGGU	10454
10859_10_11	LILRB1	EXON	+	chr19:54633999-54634019	ACCGGGUCGGAUCCCCAGAG	10455
10859_10_14	LILRB1	EXON	+	chr19:54634009-54634029	AUCCCCAGAGUGGUGAGUGA	10456
10859_10_15	LILRB1	EXON	+	chr19:54634010-54634030	UCCCCAGAGUGGUGAGUGAC	10457
10859_10_18	LILRB1	EXON	+	chr19:54634020-54634040	GGUGAGUGACGGGCUCUGAG	10458
10859_10_21	LILRB1	EXON	+	chr19:54634021-54634041	GUGAGUGACGGGCUCUGAGU	10459
10859_10_22	LILRB1	EXON	+	chr19:54634024-54634044	AGUGACGGGCUCUGAGUGGG	10460
10859_10_24	LILRB1	EXON	+	chr19:54634027-54634047	GACGGGCUCUGAGUGGGAGG	10461
10859_10_25	LILRB1	EXON	+	chr19:54634028-54634048	ACGGGCUCUGAGUGGGAGGU	10462
10859_10_27	LILRB1	EXON	+	chr19:54634032-54634052	GCUCUGAGUGGGAGGUGGGC	10463
10859_10_28	LILRB1	EXON	+	chr19:54634033-54634053	CUCUGAGUGGGAGGUGGCA	10464
10859_10_29	LILRB1	EXON	-	chr19:54633954-54633974	CCUGCUGGGUCAGGACGGGG	10465
10859_10_30	LILRB1	EXON	-	chr19:54633957-54633977	GGGCCUGCUGGGUCAGGACG	10466
10859_10_32	LILRB1	EXON	-	chr19:54633958-54633978	AGGGCCUGCUGGGUCAGGAC	10467
10859_10_34	LILRB1	EXON	-	chr19:54633959-54633979	CAGGGCCUGCUGGGUCAGGA	10468
10859_10_37	LILRB1	EXON	-	chr19:54633963-54633983	UCCUCAGGGCCUGCUGGGUC	10469
10859_10_39	LILRB1	EXON	-	chr19:54633968-54633988	GCUGGUCCUCAGGGCCUGCU	10470
10859_10_40	LILRB1	EXON	-	chr19:54633969-54633989	GGCUGGUCCUCAGGGCCUGC	10471
10859_10_42	LILRB1	EXON	-	chr19:54633977-54633997	GGGUGAGGGGCUGGUCCUCA	10472
10859_10_43	LILRB1	EXON	-	chr19:54633978-54633998	GGGGUGAGGGGCUGGUCCUC	10473
10859_10_45	LILRB1	EXON	-	chr19:54633986-54634006	ACCCGGUGGGGGUGAGGGGC	10474
10859_10_46	LILRB1	EXON	-	chr19:54633990-54634010	UCCGACCCGGUGGGGGUGAG	10475

10859_10_47	LILRB1	EXON	-	chr19:54633991-54634011	AUCCGACCCGGUGGGGGUGA	10476
10859_10_48	LILRB1	EXON	-	chr19:54633992-54634012	GAUCCGACCCGGUGGGGGUG	10477
10859_10_52	LILRB1	EXON	-	chr19:54633997-54634017	CUGGGGAUCCGACCCGGUGG	10478
10859_10_53	LILRB1	EXON	-	chr19:54633998-54634018	UCUGGGGAUCCGACCCGGUG	10479
10859_10_55	LILRB1	EXON	-	chr19:54633999-54634019	CUCUGGGGAUCCGACCCGGU	10480
10859_10_57	LILRB1	EXON	-	chr19:54634000-54634020	ACUCUGGGGAUCCGACCCGG	10481
10859_10_59	LILRB1	EXON	-	chr19:54634003-54634023	ACCACUCUGGGGAUCCGACC	10482
10859_10_60	LILRB1	EXON	-	chr19:54634014-54634034	GCCCGUCACUCACCACUCUG	10483
10859_10_62	LILRB1	EXON	-	chr19:54634015-54634035	AGCCCGUCACUCACCACUCU	10484
10859_10_64	LILRB1	EXON	-	chr19:54634016-54634036	GAGCCCGUCACUCACCACUC	10485
10859_10_67	LILRB1	EXON	-	chr19:54634060-54634080	CUUGGGUGGGGACGGAGGGC	10486
10859_11_2	LILRB1	EXON	+	chr19:54634623-54634643	ACAUCAUCGUGCUCAAGGUC	10487
10859_11_4	LILRB1	EXON	+	chr19:54634624-54634644	CAUCAUCGUGCUCAAGGUCU	10488
10859_11_6	LILRB1	EXON	+	chr19:54634628-54634648	AUCGUGCUCAAGGUCUGGGA	10489
10859_11_9	LILRB1	EXON	+	chr19:54634635-54634655	UCAAGGUCUGGGAAGGCACC	10490
10859_11_11	LILRB1	EXON	+	chr19:54634636-54634656	CAAGGUCUGGGAAGGCACCU	10491
10859_11_12	LILRB1	EXON	+	chr19:54634637-54634657	AAGGUCUGGGAAGGCACCUG	10492
10859_11_13	LILRB1	EXON	+	chr19:54634638-54634658	AGGUCUGGGAAGGCACCUGG	10493
10859_11_14	LILRB1	EXON	+	chr19:54634648-54634668	AGGCACCUGGGGGUUGUGAU	10494
10859_11_15	LILRB1	EXON	+	chr19:54634656-54634676	GGGGGUUGUGAUCGGCAUCU	10495
10859_11_16	LILRB1	EXON	+	chr19:54634659-54634679	GGUUGUGAUCGGCAUCUUGG	10496
10859_11_20	LILRB1	EXON	+	chr19:54634722-54634742	CAUCCUCCGACAUCGACGUC	10497
10859_11_21	LILRB1	EXON	+	chr19:54634723-54634743	AUCCUCCGACAUCGACGUCA	10498
10859_11_23	LILRB1	EXON	+	chr19:54634733-54634753	AUCGACGUCAGGGCAAACAC	10499
10859_11_28	LILRB1	EXON	+	chr19:54634749-54634769	ACACUGGACAUCGAGUGAGU	10500

10859_11_29	LILRB1	EXON	+	chr19:54634750-54634770	CACUGGACAUCGAGUGAGUA	10501
10859_11_32	LILRB1	EXON	+	chr19:54634755-54634775	GACAUCGAGUGAGUAGGGAA	10502
10859_11_35	LILRB1	EXON	+	chr19:54634756-54634776	ACAUCGAGUGAGUAGGGAAU	10503
10859_11_36	LILRB1	EXON	+	chr19:54634757-54634777	CAUCGAGUGAGUAGGGAAUG	10504
10859_11_38	LILRB1	EXON	+	chr19:54634758-54634778	AUCGAGUGAGUAGGGAAUGG	10505
10859_11_40	LILRB1	EXON	+	chr19:54634759-54634779	UCGAGUGAGUAGGGAAUGGG	10506
10859_11_43	LILRB1	EXON	-	chr19:54634656-54634676	AGAUGCCGAUCACAACCCCC	10507
10859_11_44	LILRB1	EXON	-	chr19:54634685-54634705	CUCCUCCUCCAGUAGGAUGA	10508
10859_11_45	LILRB1	EXON	-	chr19:54634692-54634712	CCUCCUCCUCCUCCUCCAGU	10509
10859_12_4	LILRB1	EXON	+	chr19:54635092-54635112	UCUUCCCCCAGCCCAGAGAA	10510
10859_12_8	LILRB1	EXON	+	chr19:54635114-54635134	GCUGAUUUCCAACAUCCUGC	10511
10859_12_10	LILRB1	EXON	+	chr19:54635115-54635135	CUGAUUUCCAACAUCCUGCA	10512
10859_12_11	LILRB1	EXON	+	chr19:54635116-54635136	UGAUUUCCAACAUCCUGCAG	10513
10859_12_15	LILRB1	EXON	+	chr19:54635122-54635142	CCAACAUCCUGCAGGGGCUG	10514
10859_12_16	LILRB1	EXON	+	chr19:54635123-54635143	CAACAUCCUGCAGGGGCUGU	10515
10859_12_18	LILRB1	EXON	+	chr19:54635124-54635144	AACAUCCUGCAGGGGCUGUG	10516
10859_12_21	LILRB1	EXON	+	chr19:54635144-54635164	GGGCCAGAGCCCACAGACAG	10517
10859_12_24	LILRB1	EXON	+	chr19:54635154-54635174	CCACAGACAGAGGCCUGCAG	10518
10859_12_25	LILRB1	EXON	+	chr19:54635157-54635177	CAGACAGAGGCCUGCAGUGG	10519
10859_12_30	LILRB1	EXON	-	chr19:54635092-54635112	UUCUCUGGGCUGGGGGAAGA	10520
10859_12_35	LILRB1	EXON	-	chr19:54635099-54635119	UCAGCCUUUCUCUGGGCUGG	10521
10859_12_37	LILRB1	EXON	-	chr19:54635100-54635120	AUCAGCCUUUCUCUGGGCUG	10522
10859_12_40	LILRB1	EXON	-	chr19:54635101-54635121	AAUCAGCCUUUCUCUGGGCU	10523
10859_12_42	LILRB1	EXON	-	chr19:54635102-54635122	AAAUCAGCCUUUCUCUGGGC	10524
10859_12_44	LILRB1	EXON	-	chr19:54635106-54635126	UUGGAAAUCAGCCUUUCUCU	10525

10859_12_45	LILRB1	EXON	-	chr19:54635107-54635127	GUUGGAAAUCAGCCUUUCUC	10526
10859_12_48	LILRB1	EXON	-	chr19:54635125-54635145	CCACAGCCCCUGCAGGAUGU	10527
10859_12_50	LILRB1	EXON	-	chr19:54635132-54635152	UCUGGCCCCACAGCCCCUGC	10528
10859_12_52	LILRB1	EXON	-	chr19:54635150-54635170	AGGCCUCUGUCUGUGGGCUC	10529
10859_12_53	LILRB1	EXON	-	chr19:54635156-54635176	CACUGCAGGCCUCUGUCUGU	10530
10859_12_55	LILRB1	EXON	-	chr19:54635157-54635177	CCACUGCAGGCCUCUGUCUG	10531
10859_12_58	LILRB1	EXON	-	chr19:54635170-54635190	GGCAGAAUUACCUCCACUGC	10532
10859_13_5	LILRB1	EXON	+	chr19:54635261-54635281	CAGCCCAGCUGCCGAUGCCC	10533
10859_13_13	LILRB1	EXON	+	chr19:54635285-54635305	AGAAAACCUCUGUGAGUGAG	10534
10859_13_15	LILRB1	EXON	+	chr19:54635291-54635311	CCUCUGUGAGUGAGAGGAAG	10535
10859_13_16	LILRB1	EXON	-	chr19:54635245-54635265	GCUGGACCUGGGGGAAGAAU	10536
10859_13_19	LILRB1	EXON	-	chr19:54635246-54635266	GGCUGGACCUGGGGGAAGAA	10537
10859_13_23	LILRB1	EXON	-	chr19:54635254-54635274	GGCAGCUGGGCUGGACCUGG	10538
10859_13_25	LILRB1	EXON	-	chr19:54635255-54635275	CGGCAGCUGGGCUGGACCUG	10539
10859_13_27	LILRB1	EXON	-	chr19:54635256-54635276	UCGGCAGCUGGGCUGGACCU	10540
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10859_13_33	LILRB1	EXON	-	chr19:54635263-54635283	CUGGGCAUCGGCAGCUGGGC	10542
10859_13_37	LILRB1	EXON	-	chr19:54635267-54635287	CUUCCUGGGCAUCGGCAGCU	10543
10859_13_38	LILRB1	EXON	-	chr19:54635268-54635288	UCUUCCUGGGCAUCGGCAGC	10544
10859_13_40	LILRB1	EXON	-	chr19:54635275-54635295	GAGGUUUUCUUCCUGGGCAU	10545
10859_13_41	LILRB1	EXON	-	chr19:54635281-54635301	CUCACAGAGGUUUUCUUCCU	10546
10859_13_42	LILRB1	EXON	-	chr19:54635282-54635302	ACUCACAGAGGUUUUCUUCC	10547
10859_13_45	LILRB1	EXON	-	chr19:54635294-54635314	CCUCUUCCUCUCACUCACAG	10548
10859_14_5	LILRB1	EXON	+	chr19:54635563-54635583	CGUGAAGCACACACAGCCUG	10549
10859_14_7	LILRB1	EXON	+	chr19:54635567-54635587	AAGCACACACAGCCUGAGGA	10550

10859_14_9	LILRB1	EXON	+	chr19:54635568-54635588	AGCACACACAGCCUGAGGAU	10551
10859_14_10	LILRB1	EXON	+	chr19:54635569-54635589	GCACACACAGCCUGAGGAUG	10552
10859_14_12	LILRB1	EXON	+	chr19:54635572-54635592	CACACAGCCUGAGGAUGGGG	10553
10859_14_15	LILRB1	EXON	+	chr19:54635578-54635598	GCCUGAGGAUGGGGUGGAGA	10554
10859_14_17	LILRB1	EXON	+	chr19:54635586-54635606	AUGGGGUGGAGAUGGACACU	10555
10859_14_18	LILRB1	EXON	+	chr19:54635587-54635607	UGGGGUGGAGAUGGACACUC	10556
10859_14_20	LILRB1	EXON	-	chr19:54635539-54635559	CAUCUGCUGGGGCAGAGCAA	10557
10859_14_21	LILRB1	EXON	-	chr19:54635540-54635560	GCAUCUGCUGGGGCAGAGCA	10558
10859_14_25	LILRB1	EXON	-	chr19:54635550-54635570	CUUCACGGCAGCAUCUGCUG	10559
10859_14_26	LILRB1	EXON	-	chr19:54635551-54635571	GCUUCACGGCAGCAUCUGCU	10560
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10859_14_30	LILRB1	EXON	-	chr19:54635565-54635585	CUCAGGCUGUGUGUGCUUCA	10562
10859_14_31	LILRB1	EXON	-	chr19:54635582-54635602	UCCAUCUCCACCCCAUCCUC	10563
10859_15_3	LILRB1	EXON	+	chr19:54636498-54636518	CCCACACGAUGAAGACCCCC	10564
10859_15_5	LILRB1	EXON	+	chr19:54636516-54636536	CCAGGCAGUGACGUAUGCCG	10565
10859_15_8	LILRB1	EXON	+	chr19:54636536-54636556	AGGUGAAACACUCCAGACCU	10566
10859_15_13	LILRB1	EXON	+	chr19:54636546-54636566	CUCCAGACCUAGGAGAGAAA	10567
10859_15_15	LILRB1	EXON	+	chr19:54636571-54636591	UCUCCUCCUUCCCCACUGUC	10568
10859_15_17	LILRB1	EXON	+	chr19:54636572-54636592	CUCCUCCUUCCCCACUGUCU	10569
10859_15_20	LILRB1	EXON	+	chr19:54636573-54636593	UCCUCCUUCCCCACUGUCUG	10570
10859_15_23	LILRB1	EXON	+	chr19:54636582-54636602	CCCACUGUCUGGGGAAUUCC	10571
10859_15_25	LILRB1	EXON	+	chr19:54636591-54636611	UGGGGAAUUCCUGGACACAA	10572
10859_15_26	LILRB1	EXON	+	chr19:54636600-54636620	CCUGGACACAAAGGACAGAC	10573
10859_15_29	LILRB1	EXON	+	chr19:54636603-54636623	GGACACAAAGGACAGACAGG	10574
10859_15_33	LILRB1	EXON	+	chr19:54636609-54636629	AAAGGACAGACAGGCGGAAG	10575

10859_15_34	LILRB1	EXON	+	chr19:54636614-54636634	ACAGACAGGCGGAAGAGGAC	10576
10859_15_36	LILRB1	EXON	+	chr19:54636621-54636641	GGCGGAAGAGGACAGGCAGA	10577
10859_15_38	LILRB1	EXON	+	chr19:54636630-54636650	GGACAGGCAGAUGGACACUG	10578
10859_15_40	LILRB1	EXON	-	chr19:54636476-54636496	CUGCUGGAGAGAGACAGUGG	10579
10859_15_41	LILRB1	EXON	-	chr19:54636479-54636499	GCUCUGCUGGAGAGAGACAG	10580
10859_15_46	LILRB1	EXON	-	chr19:54636492-54636512	CUUCAUCGUGUGGGCUCUGC	10581
10859_15_48	LILRB1	EXON	-	chr19:54636501-54636521	CCUGGGGGUCUUCAUCGUGU	10582
10859_15_49	LILRB1	EXON	-	chr19:54636502-54636522	GCCUGGGGGUCUUCAUCGUG	10583
10859_15_51	LILRB1	EXON	-	chr19:54636516-54636536	CGGCAUACGUCACUGCCUGG	10584
10859_15_52	LILRB1	EXON	-	chr19:54636517-54636537	UCGGCAUACGUCACUGCCUG	10585
10859_15_55	LILRB1	EXON	-	chr19:54636518-54636538	CUCGGCAUACGUCACUGCCU	10586
10859_15_58	LILRB1	EXON	-	chr19:54636519-54636539	CCUCGGCAUACGUCACUGCC	10587
10859_15_60	LILRB1	EXON	-	chr19:54636536-54636556	AGGUCUGGAGUGUUUCACCU	10588
10859_15_63	LILRB1	EXON	-	chr19:54636551-54636571	GGCCAUUUCUCUCCUAGGUC	10589
10859_15_66	LILRB1	EXON	-	chr19:54636556-54636576	GGAGAGGCCAUUUCUCUCCU	10590
10859_15_68	LILRB1	EXON	-	chr19:54636572-54636592	AGACAGUGGGGAAGGAGGAG	10591
10859_15_70	LILRB1	EXON	-	chr19:54636577-54636597	UCCCCAGACAGUGGGGAAGG	10592
10859_15_74	LILRB1	EXON	-	chr19:54636580-54636600	AAUUCCCCAGACAGUGGGGA	10593
10859_15_76	LILRB1	EXON	-	chr19:54636584-54636604	CAGGAAUUCCCCAGACAGUG	10594
10859_15_80	LILRB1	EXON	-	chr19:54636585-54636605	CCAGGAAUUCCCCAGACAGU	10595
10859_15_82	LILRB1	EXON	-	chr19:54636586-54636606	UCCAGGAAUUCCCCAGACAG	10596
10859_15_87	LILRB1	EXON	-	chr19:54636603-54636623	CCUGUCUGUCCUUUGUGUCC	10597
10859_16_3	LILRB1	EXON	+	chr19:54636733-54636753	UGCUGCAUCUGAAGCCCCCC	10598
10859_16_6	LILRB1	EXON	+	chr19:54636774-54636794	UGCACAGCUUGACCCUCAGA	10599
10859_16_7	LILRB1	EXON	+	chr19:54636775-54636795	GCACAGCUUGACCCUCAGAC	10600

10859_16_9	LILRB1	EXON	+	chr19:54636778-54636798	CAGCUUGACCCUCAGACGGG	10601
10859_16_14	LILRB1	EXON	+	chr19:54636802-54636822	AACUGAGCCUCCUCCAUCCC	10602
10859_16_16	LILRB1	EXON	+	chr19:54636806-54636826	GAGCCUCCUCCAUCCCAGGA	10603
10859_16_17	LILRB1	EXON	+	chr19:54636807-54636827	AGCCUCCUCCAUCCCAGGAA	10604
10859_16_18	LILRB1	EXON	+	chr19:54636844-54636864	GCCCAGCAUCUACGCCACUC	10605
10859_16_21	LILRB1	EXON	+	chr19:54636861-54636881	CUCUGGCCAUCCACUAGCCC	10606
10859_16_22	LILRB1	EXON	+	chr19:54636862-54636882	UCUGGCCAUCCACUAGCCCA	10607
10859_16_25	LILRB1	EXON	+	chr19:54636863-54636883	CUGGCCAUCCACUAGCCCAG	10608
10859_16_27	LILRB1	EXON	+	chr19:54636864-54636884	UGGCCAUCCACUAGCCCAGG	10609
10859_16_28	LILRB1	EXON	+	chr19:54636865-54636885	GGCCAUCCACUAGCCCAGGG	10610
10859_16_30	LILRB1	EXON	+	chr19:54636866-54636886	GCCAUCCACUAGCCCAGGGG	10611
10859_16_32	LILRB1	EXON	+	chr19:54636888-54636908	GACGCAGACCCCACACUCCA	10612
10859_16_35	LILRB1	EXON	+	chr19:54636895-54636915	ACCCCACACUCCAUGGAGUC	10613
10859_16_38	LILRB1	EXON	+	chr19:54636904-54636924	UCCAUGGAGUCUGGAAUGCA	10614
10859_16_40	LILRB1	EXON	+	chr19:54636905-54636925	CCAUGGAGUCUGGAAUGCAU	10615
10859_16_43	LILRB1	EXON	+	chr19:54636922-54636942	CAUGGGAGCUGCCCCCCCAG	10616
10859_16_45	LILRB1	EXON	+	chr19:54636932-54636952	GCCCCCCCAGUGGACACCAU	10617
10859_16_47	LILRB1	EXON	+	chr19:54636948-54636968	CCAUUGGACCCCACCCAGCC	10618
10859_16_50	LILRB1	EXON	+	chr19:54636960-54636980	ACCCAGCCUGGAUCUACCCC	10619
10859_16_54	LILRB1	EXON	+	chr19:54636969-54636989	GGAUCUACCCCAGGAGACUC	10620
10859_16_55	LILRB1	EXON	+	chr19:54636970-54636990	GAUCUACCCCAGGAGACUCU	10621
10859_16_58	LILRB1	EXON	+	chr19:54636980-54637000	AGGAGACUCUGGGAACUUUU	10622
10859_16_60	LILRB1	EXON	+	chr19:54636981-54637001	GGAGACUCUGGGAACUUUUA	10623
10859_16_61	LILRB1	EXON	+	chr19:54636982-54637002	GAGACUCUGGGAACUUUUAG	10624
10859_16_70	LILRB1	EXON	-	chr19:54636722-54636742	GAUGCAGCAGCCUGCAGCGG	10625

10859_16_72	LILRB1	EXON	-	chr19:54636723-54636743	AGAUGCAGCAGCCUGCAGCG	10626
10859_16_74	LILRB1	EXON	-	chr19:54636724-54636744	CAGAUGCAGCAGCCUGCAGC	10627
10859_16_75	LILRB1	EXON	-	chr19:54636725-54636745	UCAGAUGCAGCAGCCUGCAG	10628
10859_16_78	LILRB1	EXON	-	chr19:54636750-54636770	GGCGUAGGUCACAUCCUGGG	10629
10859_16_79	LILRB1	EXON	-	chr19:54636751-54636771	GGGCGUAGGUCACAUCCUGG	10630
10859_16_81	LILRB1	EXON	-	chr19:54636752-54636772	UGGGCGUAGGUCACAUCCUG	10631
10859_16_83	LILRB1	EXON	-	chr19:54636753-54636773	CUGGGCGUAGGUCACAUCCU	10632
10859_16_84	LILRB1	EXON	-	chr19:54636754-54636774	GCUGGGCGUAGGUCACAUCC	10633
10859_16_87	LILRB1	EXON	-	chr19:54636765-54636785	CAAGCUGUGCAGCUGGGCGU	10634
10859_16_88	LILRB1	EXON	-	chr19:54636771-54636791	GAGGGUCAAGCUGUGCAGCU	10635
10859_16_89	LILRB1	EXON	-	chr19:54636772-54636792	UGAGGGUCAAGCUGUGCAGC	10636
10859_16_92	LILRB1	EXON	-	chr19:54636789-54636809	CUCAGUUGCCUCCCGUCUGA	10637
10859_16_93	LILRB1	EXON	-	chr19:54636790-54636810	GCUCAGUUGCCUCCCGUCUG	10638
10859_16_97	LILRB1	EXON	-	chr19:54636812-54636832	GGCCCUUCCUGGGAUGGAGG	10639
10859_16_98	LILRB1	EXON	-	chr19:54636815-54636835	GAGGGCCCUUCCUGGGAUGG	10640
10859_16_101	LILRB1	EXON	-	chr19:54636818-54636838	GGAGAGGGCCCUUCCUGGGA	10641
10859_16_104	LILRB1	EXON	-	chr19:54636822-54636842	AGCUGGAGAGGGCCCUUCCU	10642
10859_16_105	LILRB1	EXON	-	chr19:54636823-54636843	CAGCUGGAGAGGGCCCUUCC	10643
10859_16_108	LILRB1	EXON	-	chr19:54636833-54636853	AUGCUGGGCACAGCUGGAGA	10644
10859_16_109	LILRB1	EXON	-	chr19:54636834-54636854	GAUGCUGGGCACAGCUGGAG	10645
10859_16_112	LILRB1	EXON	-	chr19:54636839-54636859	GCGUAGAUGCUGGGCACAGC	10646
10859_16_115	LILRB1	EXON	-	chr19:54636848-54636868	GCCAGAGUGGCGUAGAUGCU	10647
10859_16_116	LILRB1	EXON	-	chr19:54636849-54636869	GGCCAGAGUGGCGUAGAUGC	10648
10859_16_118	LILRB1	EXON	-	chr19:54636861-54636881	GGGCUAGUGGAUGGCCAGAG	10649
10859_16_120	LILRB1	EXON	-	chr19:54636870-54636890	UCCCCCCCUGGGCUAGUGGA	10650

10859_16_121	LILRB1	EXON	-	chr19:54636874-54636894	UGCGUCCCCCCCUGGGCUAG	10651
10859_16_123	LILRB1	EXON	-	chr19:54636881-54636901	UGGGGUCUGCGUCCCCCCCU	10652
10859_16_124	LILRB1	EXON	-	chr19:54636882-54636902	GUGGGGUCUGCGUCCCCCCC	10653
10859_16_127	LILRB1	EXON	-	chr19:54636899-54636919	UCCAGACUCCAUGGAGUGUG	10654
10859_16_128	LILRB1	EXON	-	chr19:54636900-54636920	UUCCAGACUCCAUGGAGUGU	10655
10859_16_129	LILRB1	EXON	-	chr19:54636901-54636921	AUUCCAGACUCCAUGGAGUG	10656
10859_16_132	LILRB1	EXON	-	chr19:54636908-54636928	CCCAUGCAUUCCAGACUCCA	10657
10859_16_135	LILRB1	EXON	-	chr19:54636936-54636956	UCCAAUGGUGUCCACUGGGG	10658
10859_16_136	LILRB1	EXON	-	chr19:54636937-54636957	GUCCAAUGGUGUCCACUGGG	10659
10859_16_137	LILRB1	EXON	-	chr19:54636938-54636958	GGUCCAAUGGUGUCCACUGG	10660
10859_16_139	LILRB1	EXON	-	chr19:54636939-54636959	GGGUCCAAUGGUGUCCACUG	10661
10859_16_141	LILRB1	EXON	-	chr19:54636940-54636960	GGGGUCCAAUGGUGUCCACU	10662
10859_16_143	LILRB1	EXON	-	chr19:54636941-54636961	UGGGGUCCAAUGGUGUCCAC	10663
10859_16_146	LILRB1	EXON	-	chr19:54636951-54636971	CCAGGCUGGGUGGGGUCCAA	10664
10859_16_147	LILRB1	EXON	-	chr19:54636959-54636979	GGGUAGAUCCAGGCUGGGUG	10665
10859_16_148	LILRB1	EXON	-	chr19:54636960-54636980	GGGGUAGAUCCAGGCUGGGU	10666
10859_16_150	LILRB1	EXON	-	chr19:54636961-54636981	UGGGGUAGAUCCAGGCUGGG	10667
10859_16_152	LILRB1	EXON	-	chr19:54636964-54636984	UCCUGGGGUAGAUCCAGGCU	10668
10859_16_153	LILRB1	EXON	-	chr19:54636965-54636985	CUCCUGGGGUAGAUCCAGGC	10669
10859_16_156	LILRB1	EXON	-	chr19:54636969-54636989	GAGUCUCCUGGGGUAGAUCC	10670
10859_16_157	LILRB1	EXON	-	chr19:54636979-54636999	AAAGUUCCCAGAGUCUCCUG	10671
10859_16_158	LILRB1	EXON	-	chr19:54636980-54637000	AAAAGUUCCCAGAGUCUCCU	10672
10859_16_159	LILRB1	EXON	-	chr19:54636981-54637001	UAAAAGUUCCCAGAGUCUCC	10673

Table 6e. Exemplary preferred targeting domains for gRNA molecules targeting CD3E

Targeting Domain ID	Strand	Target Sequence Location (hg38)	Targeting domain sequence	SEQ ID NO:
CR002230	+	Chr11:118304702-118304724	AGGCCUCUCUACUUCCUGUG	10677
CR002231	+	Chr11:118304703-118304725	GGCCUCUCUACUUCCUGUGU	10678
CR002232	+	Chr11:118304704-118304726	GCCUCUCUACUUCCUGUGUG	10679
CR002233	-	Chr11:118304570-118304592	GACUCUGACAAUACCUGGAG	10680
CR002234	-	Chr11:118304571-118304593	GGACUCUGACAAUACCUGGA	10681
CR002235	-	Chr11:118304575-118304597	AAGAGGACUCUGACAAUACC	10682
CR002236	-	Chr11:118304592-118304614	UUCCUAGAAGGCCAAACAAG	10683
CR002237	-	Chr11:118304604-118304626	GGUCCCACAGCCUUCCUAGA	10684
CR002238	-	Chr11:118304625-118304647	UGGACUGGUUGAAGAAAGCU	10685
CR002239	-	Chr11:118304640-118304662	GCAGAGGCCUCCACCUGGAC	10686
CR002240	-	Chr11:118304656-118304678	CUUGGAAACGUUCAAGGCAG	10687
CR002241	-	Chr11:118304662-118304684	ACCUCACUUGGAAACGUUCA	10688
CR002242	-	Chr11:118304674-118304696	CCUGCGGGUUUUACCUCACU	10689
CR002243	-	Chr11:118304689-118304711	AGAGAGGCCUCUGGGCCUGC	10690
CR002244	-	Chr11:118304697-118304719	CAGGAAGUAGAGAGGCCUCU	10691
CR002245	-	Chr11:118304705-118304727	ACCCCACACAGGAAGUAGAG	10692
CR002246	-	Chr11:118304716-118304738	AGGGUUUCUGAACCCCACAC	10693
CR002247	-	Chr11:118304736-118304758	CCUGAGGCUGGGAGGGGAGG	10694
CR002248	-	Chr11:118304747-118304769	UGAAGCAGGCACCUGAGGCU	10695
CR002249	-	Chr11:118304748-118304770	CUGAAGCAGGCACCUGAGGC	10696

CR002250	-	Chr11:118304752-118304774	UUUUCUGAAGCAGGCACCUG	10697
CR002251	+	Chr11:118304889-118304911	UCCAGAAGUAGUAAGUCUGC	10698
CR002252	+	Chr11:118304940-118304962	CCAUGAAACAAAGAUGCAGU	10699
CR002253	+	Chr11:118304941-118304963	CAUGAAACAAAGAUGCAGUC	10700
CR002254	+	Chr11:118304951-118304973	AGAUGCAGUCGGGCACUCAC	10701
CR002255	+	Chr11:118304961-118304983	GGGCACUCACUGGAGAGUUC	10702
CR002256	+	Chr11:118304962-118304984	GGCACUCACUGGAGAGUUCU	10703
CR002257	-	Chr11:118304912-118304934	UUACUUUACUAAGAUGGCGG	10704
CR002258	-	Chr11:118304915-118304937	CUGUUACUUUACUAAGAUGG	10705
CR002259	-	Chr11:118304918-118304940	GGACUGUUACUUUACUAAGA	10706
CR002260	-	Chr11:118304939-118304961	CGACUGCAUCUUUGUUUCAU	10707
CR002261	-	Chr11:118304940-118304962	CCGACUGCAUCUUUGUUUCA	10708
CR002262	-	Chr11:118304985-118305007	ACUCACCUGAUAAGAGGCAG	10709
CR002263	-	Chr11:118304991-118305013	CAUCCUACUCACCUGAUAAG	10710
CR002264	+	Chr11:118307269-118307291	UUUCUUAUUUAUUUUCUAGU	10711
CR002265	+	Chr11:118307276-118307298	UUUAUUUUCUAGUUGGCGUU	10712
CR002266	+	Chr11:118307277-118307299	UUAUUUUCUAGUUGGCGUUU	10713
CR002267	+	Chr11:118307278-118307300	UAUUUUCUAGUUGGCGUUUG	10714
CR002268	+	Chr11:118307279-118307301	AUUUUCUAGUUGGCGUUUGG	10715
CR002269	+	Chr11:118308419-118308441	CUUUUCAGGUAAUGAAGAAA	10716
CR002270	+	Chr11:118312617-118312639	GCAUAUAAAGUCUCCAUCUC	10717

CR002271	+	Chr11:118312653-118312675	UUGACAUGCCCUCAGUAUCC	10718
CR002272	+	Chr11:118312669-118312691	AUCCUGGAUCUGAAAUACUA	10719
CR002273	+	Chr11:118312695-118312717	CACAAUGAUAAAAACAUAGG	10720
CR002274	+	Chr11:118312703-118312725	UAAAAACAUAGGCGGUGAUG	10721
CR002275	+	Chr11:118312719-118312741	GAUGAGGAUGAUAAAAACAU	10722
CR002276	+	Chr11:118312730-118312752	UAAAAACAUAGGCAGUGAUG	10723
CR002277	+	Chr11:118312748-118312770	UGAGGAUCACCUGUCACUGA	10724
CR002278	+	Chr11:118312763-118312785	ACUGAAGGAAUUUUCAGAAU	10725
CR002279	+	Chr11:118312773-118312795	UUUUCAGAAUUGGAGCAAAG	10726
CR002280	+	Chr11:118312838-118312860	GAACUUUUAUCUCUACCUGA	10727
CR002281	-	Chr11:118312630-118312652	UAUUACUGUGGUUCCAGAGA	10728
CR002282	-	Chr11:118312642-118312664	AGGGCAUGUCAAUAUUACUG	10729
CR002283	-	Chr11:118312661-118312683	UUUCAGAUCCAGGAUACUGA	10730
CR002284	-	Chr11:118312662-118312684	AUUUCAGAUCCAGGAUACUG	10731
CR002285	-	Chr11:118312671-118312693	UGCCAUAGUAUUUCAGAUCC	10732
CR002286	-	Chr11:118312757-118312779	CUGAAAAUUCCUUCAGUGAC	10733
CR002287	-	Chr11:118312811-118312833	CUUCUGGUUUGCUUCCUCUG	10734
CR002288	-	Chr11:118312812-118312834	UCUUCUGGUUUGCUUCCUCU	10735
CR002289	-	Chr11:118312813-118312835	AUCUUCUGGUUUGCUUCCUC	10736
CR002290	-	Chr11:118312827-118312849	AGAUAAAAGUUCGCAUCUUC	10737
CR002291	-	Chr11:118312853-118312875	CUGGAUUACCUCUUGCCCUC	10738

CR002292	+	Chr11:118313720-118313742	CAUGGAGAUGGAUGUGAUGU	10739
CR002293	+	Chr11:118313758-118313780	UAGUGGACAUCUGCAUCACU	10740
CR002294	+	Chr11:118313760-118313782	GUGGACAUCUGCAUCACUGG	10741
CR002295	+	Chr11:118313774-118313796	CACUGGGGGCUUGCUGCUGC	10742
CR002296	+	Chr11:118313801-118313823	CUACUGGAGCAAGAAUAGAA	10743
CR002297	+	Chr11:118313807-118313829	GAGCAAGAAUAGAAAGGCCA	10744
CR002298	+	Chr11:118313826-118313848	AAGGCCAAGCCUGUGACACG	10745
CR002299	+	Chr11:118313831-118313853	CAAGCCUGUGACACGAGGAG	10746
CR002300	-	Chr11:118313746-118313768	GAUGUCCACUAUGACAAUUG	10747
CR002301	-	Chr11:118313824-118313846	UCGUGUCACAGGCUUGGCCU	10748
CR002302	-	Chr11:118313830-118313852	CGCUCCUCGUGUCACAGGCU	10749
CR002303	-	Chr11:118313835-118313857	GCACCCGCUCCUCGUGUCAC	10750
CR002304	+	Chr11:118314442-118314464	CCGCAGGACAAAACAAGGAG	10751
CR002305	-	Chr11:118314465-118314487	UCUGGGUUGGGAACAGGUGG	10752
CR002306	-	Chr11:118314468-118314490	UAGUCUGGGUUGGGAACAGG	10753
CR002307	-	Chr11:118314471-118314493	UCAUAGUCUGGGUUGGGAAC	10754
CR002308	-	Chr11:118314477-118314499	GUUACCUCAUAGUCUGGGUU	10755
CR002309	-	Chr11:118314478-118314500	CGUUACCUCAUAGUCUGGGU	10756
CR002310	-	Chr11:118314482-118314504	CCCACGUUACCUCAUAGUCU	10757
CR002311	-	Chr11:118314483-118314505	UCCCACGUUACCUCAUAGUC	10758
CR002312	+	Chr11:118315472-118315494	UAUUUCACCCCCAGCCCAUC	10759

CR002313	+	Chr11:118315477-118315499	CACCCCCAGCCCAUCCGGAA	10760
CR002314	+	Chr11:118315484-118315506	AGCCCAUCCGGAAAGGCCAG	10761
CR002315	+	Chr11:118315485-118315507	GCCCAUCCGGAAAGGCCAGC	10762
CR002316	+	Chr11:118315498-118315520	GGCCAGCGGGACCUGUAUUC	10763
CR002317	+	Chr11:118315528-118315550	CAGAGACGCAUCUGACCCUC	10764

Table 6f. Exemplary preferred targeting domains for gRNA molecules targeting CD3G

Targeting Domain Id	Exon	Strand	Target Sequence Location (hg38)	Targeting Domain Sequence	SEQ ID NO:
CR005349	3	-	chr11:118349904-118349926	UUACACUGAUACAUCCCUCG	10765
CR005350	4	-	chr11:118350673-118350695	GCAUUCUUUUACCUCUCGAC	10766
CR005351	3	-	chr11:118349903-118349925	UACACUGAUACAUCCCUCGA	10767
CR005352	3	-	chr11:118349896-118349918	AUACAUCCCUCGAGGGUCCU	10768
CR005353	5	-	chr11:118351652-118351674	UACCUGGUAGAGCUGGUCAU	10769
CR005354	3	+	chr11:118349907-118349929	CGAGGGAUGUAUCAGUGUAA	10770
CR005355	4	+	chr11:118350640-118350662	GGUCUACUUCAUUGCUGGAC	10771
CR005356	3	+	chr11:118349890-118349912	GUAAUGCCAAGGACCCUCGA	10772
CR005357	5	-	chr11:118351651-118351673	ACCUGGUAGAGCUGGUCAUU	10773
CR005358	4	+	chr11:118350618-118350640	GCAUUUUCGUCCUUGCUGUU	10774
CR005359	4	+	chr11:118350635-118350657	GUUGGGGUCUACUUCAUUGC	10775
CR005360	6	-	chr11:118352405-118352427	GUCAUCUUCUCGAUCCUUGA	10776
CR005361	6	-	chr11:118352404-118352426	UCAUCUUCUCGAUCCUUGAG	10777

CR005362	3	+	chr11:118349760-118349782	GUGUAUGACUAUCAAGAAGA	10778
CR005363	3	+	chr11:118349738-118349760	UUCAGGAAACCACUUGGUUA	10779

Table 6g. Exemplary preferred targeting domains for gRNA molecules targeting CD3D

Targeting Domain ID	Exon	Strand	Target Sequence Location (hg38)	Targeting Domain Sequence	SEQ ID NO:
CR005334	2	+	chr11:118340373-118340395	ACUUCGAUAAUGAACUUGCA	10780
CR005335	5	+	chr11:118339204-118339226	AGCAUCAUCUCGAUCUCGGA	10781
CR005336	5	+	chr11:118339203-118339225	GAGCAUCAUCUCGAUCUCGG	10782
CR005337	2	-	chr11:118340453-118340475	GGACCUGGGAAAACGCAUCC	10783
CR005338	2	-	chr11:118340467-118340489	GACAUUACAAGACUGGACCU	10784
CR005339	2	-	chr11:118340443-118340465	AAACGCAUCCUGGACCCACG	10785
CR005340	5	+	chr11:118339004-118339026	GGCGAGAUCCCAAGCAAGUC	10786
CR005341	5	+	chr11:118339200-118339222	ACUGAGCAUCAUCUCGAUCU	10787
CR005342	5	+	chr11:118339205-118339227	GCAUCAUCUCGAUCUCGGAG	10788
CR005343	4	-	chr11:118339469-118339491	CCGACACACAAGCUCUGUUG	10789
CR005344	2	+	chr11:118340429-118340451	UACACCUAUAUAUUCCUCGU	10790
CR005345	2	-	chr11:118340558-118340580	GAUACCUAUAGAGGAACUUG	10791
CR005346	5	+	chr11:118339027-118339049	ACAACUCCCACGCCUUGCCC	10792
CR005347	2	+	chr11:118340428-118340450	UUACACCUAUAUAUUCCUCG	10793
CR005348	5	-	chr11:118339150-118339172	GGAACAAGUGAACCUGAGAC	10794

In aspects of the invention, a gRNA to TRAC which includes the targeting domain of CR00961 (SEQ ID NO: 5569, underlined below, or modified version thereof (also as underlined below)), e.g., one of the gRNA molecules described below, is used in the CRISPR systems, methods, cells and other aspects and embodiments of the invention (and combinations thereof), including in aspects involving more than one gRNA molecule, e.g., described herein:

sgRNA CR00961 #1:

AGAGUCUCUCAGCUGGUACAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7833)

sgRNA CR00961 #2:

mA*mG*mA*GUCUCUCAGCUGGUACAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCU*mU*mU*mU (SEQ ID NO: 7834)

sgRNA CR00961 #3:

mA*mG*mA*GUCUCUCAGCUGGUACAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U (SEQ ID NO: 7835)

dgRNA CR00961 #1:

crRNA: AGAGUCUCUCAGCUGGUACAGUUUUAGAGCUAUGCUGUUUUG (SEQ ID NO: 7836)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUUUUU (SEQ ID NO: 6660)

dgRNA CR00961 #2:

crRNA: mA*mG*mA*GUCUCUCAGCUGGUACAGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7837)

tracr:
mA*mA*mC*AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU*mU*mU*mU (SEQ ID NO: 10798)

dgRNA CR00961 #3:

crRNA: mA*mG*mA*GUCUCUCAGCUGGUACAGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7837)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA
GUCGGUGCUUUUUUU (SEQ ID NO: 6660).

In aspects of the invention, a gRNA to TRAC which includes the targeting domain of CR00984 (SEQ ID NO: 5592, underlined below, or modified version thereof (also as underlined below)), e.g., one of the gRNA molecules described below, is used in the CRISPR systems, methods, cells and other aspects and embodiments of the invention (and combinations thereof), including in aspects involving more than one gRNA molecule, e.g., described herein:

sgRNA CR00984 #1:

UUCGGAACCCAAUCACUGACGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGU
CCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7838)

sgRNA CR00984 #2:

mU*mU*mC*GGAACCCAAUCACUGACGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGG
CUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCU*mU*mU*mU (SEQ ID NO: 7839)

sgRNA CR00984 #3:

mU*mU*mC*GGAACCCAAUCACUGACGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGG
CUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U (SEQ ID NO: 7840)

dgRNA CR00984 #1:

crRNA: UUCGGAACCCAAUCACUGACGUUUUAGAGCUAUGCUGUUUUG (SEQ ID NO: 7841)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA
GUCGGUGCUUUUUUU (SEQ ID NO: 6660)

dgRNA CR00984 #2:

crRNA: mU*mU*mC*GGAACCCAAUCACUGACGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7842)

tracr:
mA*mA*mC*AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGC ACCGAGUCGGUGCUUUU*mU*mU*mU (SEQ ID NO: 10798)

dgRNA CR00984 #3:

crRNA: mU*mU*mC*GGAACCCAAUCACUGACGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7842)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA GUCGGUGCUUUUUUU (SEQ ID NO: 6660).

In aspects of the invention, a gRNA to TRBC which includes the targeting domain of CR00798 (SEQ ID NO: 5694, underlined below, or modified version thereof (also as underlined below)), e.g., one of the gRNA molecules described below, is used in the CRISPR systems, methods, cells and other aspects and embodiments of the invention (and combinations thereof), including in aspects involving more than one gRNA molecule, e.g., described herein:

sgRNA CR00798 #1:

UGGCUCAAACACAGCGACCUGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGU CCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7843)

sgRNA CR00798 #2:

mU*mG*mG*CUCAAACACAGCGACCUGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGG CUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCU*mU*mU*mU (SEQ ID NO: 7844)

sgRNA CR00798 #3:

mU*mG*mG*CUCAAACACAGCGACCUGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGG CUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U (SEQ ID NO: 7845)

dgRNA CR00798 #1:

crRNA: UGGCUCAAACACAGCGACCUGUUUUAGAGCUAUGCUGUUUUG (SEQ ID NO: 7846)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA
GUCGGUGCUUUUUUU (SEQ ID NO: 6660)

dgRNA CR00798 #2:

crRNA: mU*mG*mG*CUCAAACACAGCGACCUGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7847)

tracr:
mA*mA*mC*AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGC
ACCGAGUCGGUGCUUUU*mU*mU*mU (SEQ ID NO: 10798)

dgRNA CR00798 #3:

crRNA: mU*mG*mG*CUCAAACACAGCGACCUGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7847)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA
GUCGGUGCUUUUUUU (SEQ ID NO: 6660).

In aspects of the invention, a gRNA to TRBC which includes the targeting domain of CR00823 (SEQ ID NO: 5719, underlined below, or modified version thereof (also as underlined below)), e.g., one of the gRNA molecules described below, is used in the CRISPR systems, methods, cells and other aspects and embodiments of the invention (and combinations thereof), including in aspects involving more than one gRNA molecule, e.g., described herein:

sgRNA CR00823 #1:

UCCCUAGCAAGAUCUCAUAGGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGU
CCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7848)

sgRNA CR00823 #2:

mU*mC*mC*CUAGCAAGAUCUCAUAGGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGG
CUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCU*mU*mU*mU (SEQ ID NO: 7849)

sgRNA CR00823 #3:

mU*mC*mC*CUAGCAAGAUCUCAUAGGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGG CUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U (SEQ ID NO: 7850)

dgRNA CR00823 #1:

crRNA: UCCCUAGCAAGAUCUCAUAGGUUUUAGAGCUAUGCUGUUUUG (SEQ ID NO: 7851)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA GUCGGUGCUUUUUUU (SEQ ID NO: 6660)

dgRNA CR00823 #2:

crRNA: mU*mC*mC*CUAGCAAGAUCUCAUAGGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7852)

tracr:
mA*mA*mC*AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGC ACCGAGUCGGUGCUUUU*mU*mU*mU (SEQ ID NO: 10798)

dgRNA CR00823 #3:

crRNA: mU*mC*mC*CUAGCAAGAUCUCAUAGGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7852)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA GUCGGUGCUUUUUUU (SEQ ID NO: 6660).

In aspects of the invention, a gRNA to B2M which includes the targeting domain of CR00442 (SEQ ID NO: 5496, underlined below, or modified version thereof (also as underlined below)), e.g., one of the gRNA molecules described below, is used in the CRISPR systems, methods, cells and other aspects and embodiments of the invention (and combinations thereof), including in aspects involving more than one gRNA molecule, e.g., described herein:

sgRNA CR00442 #1:

GGCCACGGAGCGAGACAUCUGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGU CCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7853)

sgRNA CR00442 #2:

mG*mG*mC*CACGGAGCGAGACAUCUGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGG CUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCU*mU*mU*mU (SEQ ID NO: 7854)

sgRNA CR00442 #3:

mG*mG*mC*CACGGAGCGAGACAUCUGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGG CUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U (SEQ ID NO: 7855)

dgRNA CR00442 #1:

crRNA: GGCCACGGAGCGAGACAUCUGUUUUAGAGCUAUGCUGUUUUG (SEQ ID NO: 7856)

tracr: AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA GUCGGUGCUUUUUUU (SEQ ID NO: 6660)

dgRNA CR00442 #2:

crRNA: mG*mG*mC*CACGGAGCGAGACAUCUGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7857)

tracr: mA*mA*mC*AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGC ACCGAGUCGGUGCUUUU*mU*mU*mU (SEQ ID NO: 10798)

dgRNA CR00442 #3:

crRNA: mG*mG*mC*CACGGAGCGAGACAUCUGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7857)

tracr: AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA GUCGGUGCUUUUUUU (SEQ ID NO: 6660).

In aspects of the invention, a gRNA to B2M which includes the targeting domain of CR00444 (SEQ ID NO: 5498, underlined below, or modified version thereof (also as underlined below)), e.g., one of the gRNA molecules described below, is used in the CRISPR systems, methods, cells and other aspects and embodiments of the invention (and combinations thereof), including in aspects involving more than one gRNA molecule, e.g., described herein:

sgRNA CR00444 #1:

GAGUAGCGCGAGCACAGCUAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGU CCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7858)

sgRNA CR00444 #2:

mG*mA*mU*AGCGCGAGCACAGCUAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGC UAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCU*mU*mU*mU (SEQ ID NO: 7859)

sgRNA CR00444 #3:

mG*mA*mU*AGCGCGAGCACAGCUAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGC UAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U (SEQ ID NO: 7860)

dgRNA CR00444 #1:

crRNA: GAGUAGCGCGAGCACAGCUAGUUUUAGAGCUAUGCUGUUUUG (SEQ ID NO: 7861)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA GUCGGUGCUUUUUUU (SEQ ID NO: 6660)

dgRNA CR00444 #2:

crRNA: mG*mA*mU*AGCGCGAGCACAGCUAGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7862)

tracr:
mA*mA*mC*AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGC ACCGAGUCGGUGCUUUU*mU*mU*mU (SEQ ID NO: 10798)

dgRNA CR00444 #3:

crRNA: mG*mA*mU*AGCGCGAGCACAGCUAGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7862)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA GUCGGUGCUUUUUUU (SEQ ID NO: 6660).

In aspects of the invention, a gRNA to FKBP1A which includes the targeting domain of CR002097 (SEQ ID NO: 6705, underlined below, or modified version thereof (also as underlined below)), e.g., one of the gRNA molecules described below, is used in the CRISPR systems, methods, cells and other aspects and embodiments of the invention (and combinations thereof), including in aspects involving more than one gRNA molecule, e.g., described herein:

sgRNA CR002097 #1:

CAAGCGCGGCCAGACCUGCGGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7863)

sgRNA CR002097 #2:

mC*mA*mA*GCGCGGCCAGACCUGCGGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCU*mU*mU*mU (SEQ ID NO: 7864)

sgRNA CR002097 #3:

mC*mA*mA*GCGCGGCCAGACCUGCGGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U (SEQ ID NO: 7865)

dgRNA CR002097 #1:

crRNA: CAAGCGCGGCCAGACCUGCGGUUUUAGAGCUAUGCUGUUUUG (SEQ ID NO: 7866)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUUUUU (SEQ ID NO: 6660)

dgRNA CR002097 #2:

crRNA: mC*mA*mA*GCGCGGCCAGACCUGCGGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7867)

tracr:
mA*mA*mC*AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU*mU*mU*mU (SEQ ID NO: 10798)

dgRNA CR002097 #3:

crRNA: mC*mA*mA*GCGCGGCCAGACCUGCGGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7867)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA
GUCGGUGCUUUUUUU (SEQ ID NO: 6660).

In aspects of the invention, a gRNA to FKBP1A which includes the targeting domain of CR002100 (SEQ ID NO: 6708, underlined below, or modified version thereof (also as underlined below)), e.g., one of the gRNA molecules described below, is used in the CRISPR systems, methods, cells and other aspects and embodiments of the invention (and combinations thereof), including in aspects involving more than one gRNA molecule, e.g., described herein:

sgRNA CR002100 #1:

CCGCUGGGCCCCCGACUCACGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUC
CGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUU (SEQ ID NO: 7868)

sgRNA CR002100 #2:

mC*mC*mG*CUGGGCCCCCGACUCACGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGG
CUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCU*mU*mU*mU (SEQ ID NO: 7869)

sgRNA CR002100 #3:

mC*mC*mG*CUGGGCCCCCGACUCACGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGG
CUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U (SEQ ID NO: 7870)

dgRNA CR002100 #1:

crRNA: CCGCUGGGCCCCCGACUCACGUUUUAGAGCUAUGCUGUUUUG (SEQ ID NO: 7871)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA
GUCGGUGCUUUUUUU (SEQ ID NO: 6660)

dgRNA CR002100 #2:

crRNA: mC*mC*mG*CUGGGCCCCCGACUCACGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7872)

tracr:
mA*mA*mC*AGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGC ACCGAGUCGGUGCUUUU*mU*mU*mU (SEQ ID NO: 10798)

dgRNA CR002100 #3:

crRNA: mC*mC*mG*CUGGGCCCCCGACUCACGUUUUAGAGCUAUGCUGUU*mU*mU*mG (SEQ ID NO: 7872)

tracr:
AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGA GUCGGUGCUUUUUUU (SEQ ID NO: 6660).

In each of the gRNA molecules described above, a "*" denotes a phosphorothioate bond between the adjacent nucleotides, and "mN" (where N = A, G, C or U) denotes a 2'-OMe modified nucleotide. In embodiments, any of the gRNA molecules described herein, e.g., described above, is complexed with a Cas9 molecule, e.g., as described herein, to form a ribonuclear protein complex (RNP). Such RNPs are particularly useful in the methods, cells, and other aspects and embodiments of the invention, e.g., described herein.

III. Methods for Designing gRNAs

Methods for designing gRNAs are described herein, including methods for selecting, designing and validating target sequences. Exemplary targeting domains are also provided herein. Targeting Domains discussed herein can be incorporated into the gRNAs described herein.

Methods for selection and validation of target sequences as well as off-target analyses are described, e.g., in. Mali el al. , 2013 SCIENCE 339(6121): 823-826; Hsu et al , 2013 NAT BIOTECHNOL, 31 (9): 827-32; Fu et al , 2014 NAT BIOTECHNOL, doi: 10.1038/nbt.2808. PubMed PM ID: 24463574; Heigwer et al, 2014 NAT METHODS ll (2): 122-3. doi: 10.1038/nmeth.2812. PubMed PMID: 24481216; Bae el al , 2014 BIOINFORMATICS PubMed PMID: 24463181 ; Xiao A el al , 2014 BIOINFORMATICS PubMed PMID: 24389662.

For example, a software tool can be used to optimize the choice of gRNA within a user's target sequence, e.g., to minimize total off-target activity across the genome. Off target activity may be other than cleavage. For each possible gRNA choice e.g., using S. pyogenes Cas9, the tool can identify all off-target sequences (e.g., preceding either NAG or NGG PAMs) across the genome that contain up to certain number (e.g., 1 , 2, 3, 4, 5, 6, 7, 8, 9, or 10) of mismatched base-pairs. The cleavage efficiency at each

off-target sequence can be predicted, e.g., using an experimentally-derived weighting scheme. Each possible gRNA is then ranked according to its total predicted off-target cleavage; the top-ranked gRNAs represent those that are likely to have the greatest on-target and the least off-target cleavage. Other functions, e.g., automated reagent design for CRISPR construction, primer design for the on-target Surveyor assay, and primer design for high-throughput detection and quantification of off-target cleavage via next-gen sequencing, can also be included in the tool. Candidate gRNA molecules can be evaluated by art-known methods or as described herein.

Although software algorithms may be used to generate an initial list of potential gRNA molecules, cutting efficiency and specificity will not necessarily reflect the predicted values, and gRNA molecules typically require screening in specific cell lines, e.g., primary human cell lines, e.g., primary human immune effector cells, e.g., primary human T cells, to determine, for example, cutting efficiency, indel formation, cutting specificity and change in desired phenotype. These properties may be assayed by the methods described herein.

IV. Cas Molecules

Cas9 Molecules

In preferred embodiments, the Cas molecule is a Cas9 molecule. Cas9 molecules of a variety of species can be used in the methods and compositions described herein. While the S. pyogenes Cas9 molecule are the subject of much of the disclosure herein, Cas9 molecules of, derived from, or based on the Cas9 proteins of other species listed herein can be used as well. In other words, other Cas9 molecules, e.g., S. thermophilus, Staphylococcus aureus and/or Neisseria meningitidis Cas9 molecules, may be used in the systems, methods and compositions described herein. Additional Cas9 species include: Acidovorax avenae, Actinobacillus pleuropneumoniae, Actinobacillus succinogenes, Actinobacillus suis, Actinomyces sp., cycliphilus denitrificans, Aminomonas paucivorans, Bacillus cereus, Bacillus smithii, Bacillus thuringiensis, Bacteroides sp., Blastopirellula marina, Bradyrhiz' obium sp., Brevibacillus latemsporus, Campylobacter coli, Campylobacter jejuni, Campylobacter lad, Candidatus Puniceispirillum, Clostridiu cellulolyticum, Clostridium perfringens, Corynebacterium accolens, Corynebacterium diphtheria, Corynebacterium matruchotii, Dinoroseobacter sliibae, Eubacterium dolichum, gamma proteobacterium, Gluconacetobacler diazotrophicus, Haemophilus parainfluenzae, Haemophilus sputorum, Helicobacter canadensis, Helicobacter cinaedi, Helicobacter mustelae, Ilyobacler polytropus, Kingella kingae, Lactobacillus crispatus, Listeria ivanovii, Listeria monocytogenes, Listeriaceae bacterium, Methylocystis sp., Methylosinus trichosporium, Mobiluncus mulieris, Neisseria bacilliformis, Neisseria cinerea, Neisseria flavescens, Neisseria lactamica. Neisseria sp., Neisseria wadsworthii,

Nitrosomonas sp., Parvibaculum lavamentivorans, Pasteurella multocida, Phascolarctobacterium succinatutens, Ralstonia syzygii, Rhodopseudomonas palustris, Rhodovulum sp., Simonsiella muelleri, Sphingomonas sp., Sporolactobacillus vineae, Staphylococcus lugdunensis, Streptococcus sp., Subdoligranulum sp., Tislrella mobilis, Treponema sp., or Verminephrobacter eiseniae.

A Cas9 molecule, as that term is used herein, refers to a molecule that can interact with a gRNA molecule (e.g., sequence of a domain of a tracr) and, in concert with the gRNA molecule, localize (e.g., target or home) to a site which comprises a target sequence and PAM sequence.

In an embodiment, the Cas9 molecule is capable of cleaving a target nucleic acid molecule, which may be referred to herein as an active Cas9 molecule. In an embodiment, an active Cas9 molecule, comprises one or more of the following activities: a nickase activity, i.e., .the ability to cleave a single strand, e.g., the non-complementary strand or the complementary strand, of a nucleic acid molecule; a double stranded nuclease activity, i.e., the ability to cleave both strands of a double stranded nucleic acid and create a double stranded break, which in an embodiment is the presence of two nickase activities; an endonuclease activity; an exonuclease activity; and a helicase activity, i.e., the ability to unwind the helical structure of a double stranded nucleic acid.

In an embodiment, an enzymatically active Cas9 molecule cleaves both DNA strands and results in a double stranded break. In an embodiment, a Cas9 molecule cleaves only one strand, e.g., the strand to which the gRNA hybridizes to, or the strand complementary to the strand the gRNA hybridizes with. In an embodiment, an active Cas9 molecule comprises cleavage activity associated with an HNH-like domain. In an embodiment, an active Cas9 molecule comprises cleavage activity associated with an N-terminal RuvC-like domain. In an embodiment, an active Cas9 molecule comprises cleavage activity associated with an HNH-like domain and cleavage activity associated with an N-terminal RuvC-like domain. In an embodiment, an active Cas9 molecule comprises an active, or cleavage competent, HNH-like domain and an inactive, or cleavage incompetent, N-terminal RuvC-like domain. In an embodiment, an active Cas9 molecule comprises an inactive, or cleavage incompetent, HNH-like domain and an active, or cleavage competent, N-terminal RuvC-like domain.

In an embodiment, the ability of an active Cas9 molecule to interact with and cleave a target nucleic acid is PAM sequence dependent. A PAM sequence is a sequence in the target nucleic acid. In an embodiment, cleavage of the target nucleic acid occurs upstream from the PAM sequence. Active Cas9 molecules from different bacterial species can recognize different sequence motifs (e.g., PAM sequences). In an embodiment, an active Cas9 molecule of S. pyogenes recognizes the sequence motif NGG and directs cleavage of a target nucleic acid sequence 1 to 10, e.g., 3 to 5, base pairs upstream from that sequence.

See, e.g., Mali el ai, SCIENCE 2013; 339(6121): 823- 826. In an embodiment, an active Cas9 molecule of S. thermophilus recognizes the sequence motif NGGNG and NNAG AAW (W = A or T) and directs cleavage of a core target nucleic acid sequence 1 to 10, e.g., 3 to 5, base pairs upstream from these sequences. See, e.g., Horvath et al., SCIENCE 2010; 327(5962): 167- 170, and Deveau et al , J BACTERIOL 2008; 190(4): 1390- 1400. In an embodiment, an active Cas9 molecule of S. mulans recognizes the sequence motif NGG or NAAR (R - A or G) and directs cleavage of a core target nucleic acid sequence 1 to 10, e.g., 3 to 5 base pairs, upstream from this sequence. See, e.g., Deveau et al. , J BACTERIOL 2008; 190(4): 1 390- 1400.

In an embodiment, an active Cas9 molecule of S. aureus recognizes the sequence motif NNGRR (R = A or G) and directs cleavage of a target nucleic acid sequence 1 to 10, e.g., 3 to 5, base pairs upstream from that sequence. See, e.g., Ran F. et al., NATURE, vol. 520, 2015, pp. 186-191. In an embodiment, an active Cas9 molecule of N. meningitidis recognizes the sequence motif NNNNGATT and directs cleavage of a target nucleic acid sequence 1 to 10, e.g., 3 to 5, base pairs upstream from that sequence. See, e.g., Hou et al., PNAS EARLY EDITION 2013, 1 -6. The ability of a Cas9 molecule to recognize a PAM sequence can be determined, e.g., using a transformation assay described in Jinek et al , SCIENCE 2012, 337:816.

Some Cas9 molecules have the ability to interact with a gRNA molecule, and in conjunction with the gRNA molecule home (e.g., targeted or localized) to a core target domain, but are incapable of cleaving the target nucleic acid, or incapable of cleaving at efficient rates. Cas9 molecules having no, or no substantial, cleavage activity may be referred to herein as an inactive Cas9 (an enzymatically inactive Cas9), a dead Cas9, or a dCas9 molecule. For example, an inactive Cas9 molecule can lack cleavage activity or have substantially less, e.g., less than 20, 10, 5, 1 or 0.1 % of the cleavage activity of a reference Cas9 molecule, as measured by an assay described herein.

Exemplary naturally occurring Cas9 molecules are described in Chylinski et al , RNA Biology 2013; 10:5, 727-737. Such Cas9 molecules include Cas9 molecules of a cluster 1 bacterial family, cluster 2 bacterial family, cluster 3 bacterial family, cluster 4 bacterial family, cluster 5 bacterial family, cluster 6 bacterial family, a cluster 7 bacterial family, a cluster 8 bacterial family, a cluster 9 bacterial family, a cluster 10 bacterial family, a cluster 1 1 bacterial family, a cluster 12 bacterial family, a cluster 13 bacterial family, a cluster 14 bacterial family, a cluster 1 bacterial family, a cluster 16 bacterial family, a cluster 17 bacterial family, a cluster 1 8 bacterial family, a cluster 19 bacterial family, a cluster 20 bacterial family, a cluster 21 bacterial family, a cluster 22 bacterial family, a cluster 23 bacterial family, a cluster 24 bacterial family, a cluster 25 bacterial family, a cluster 26 bacterial family, a cluster 27 bacterial family, a cluster 28 bacterial family, a cluster 29 bacterial family, a cluster 30 bacterial family, a

cluster 31 bacterial family, a cluster 32 bacterial family, a cluster 33 bacterial family, a cluster 34 bacterial family, a cluster 35 bacterial family, a cluster 36 bacterial family, a cluster 37 bacterial family, a cluster 38 bacterial family, a cluster 39 bacterial family, a cluster 40 bacterial family, a cluster 41 bacterial family, a cluster 42 bacterial family, a cluster 43 bacterial family, a cluster 44 bacterial family, a cluster 45 bacterial family, a cluster 46 bacterial family, a cluster 47 bacterial family, a cluster 48 bacterial family,. a cluster 49 bacterial family, a cluster 50 bacterial family, a cluster 5 1 bacterial family, a cluster 52 bacterial family, a cluster 53 bacterial family, a cluster 54 bacterial family, a cluster 55 bacterial family, a cluster 56 bacterial family, a cluster 57 bacterial family, a cluster 58 bacterial family, a cluster 59 bacterial family, a cluster 60 bacterial family, a cluster 61 bacterial family, a cluster 62 bacterial family, a cluster 63 bacterial family, a cluster 64 bacterial family, a cluster 65 bacterial family, a cluster 66 bacterial family, a cluster 67 bacterial family, a cluster 68 bacterial family, a cluster 69 bacterial family, a cluster 70 bacterial family, a cluster 71 bacterial family, a cluster 72 bacterial family, a cluster 73 bacterial family, a cluster 74 bacterial family, a cluster 75 bacterial family, a cluster 76 bacterial family, a cluster 77 bacterial family, or a cluster 78 bacterial family.

Exemplary naturally occurring Cas9 molecules include a Cas9 molecule of a cluster 1 bacterial family. Examples include a Cas9 molecule of: S. pyogenes (e.g., strain SF370, MGAS 10270, MGAS 10750, MGAS2096, MGAS315, MGAS5005, MGAS6180, MGAS9429, NZ131 and SSI- 1), S. thermophilus (e.g., strain LMD-9), S. pseudoporcinus (e.g., strain SPIN 20026), S. mutans (e.g., strain UA 159, NN2025), S. macacae (e.g., strain NCTC1 1558), S. gallolylicus (e.g., strain UCN34, ATCC BAA-2069), S. equines (e.g., strain ATCC 9812, MGCS 124), S. dysdalactiae (e.g., strain GGS 124), S. bovis (e.g., strain ATCC 700338), S. cmginosus (e.g.; strain F021 1), S. agalactia* (e.g., strain NEM316, A909), Listeria monocytogenes (e.g., strain F6854), Listeria innocua (L. innocua, e.g., strain Clip l 1262), EtUerococcus italicus (e.g., strain DSM 15952), or Enterococcus faecium (e.g., strain 1,231 ,408). Additional exemplary Cas9 molecules are a Cas9 molecule of Neisseria meningitidis (Hou et al. PNAS Early Edition 2013, 1 -6) and a S. aureus Cas9 molecule.

In an embodiment, a Cas9 molecule, e.g., an active Cas9 molecule or inactive Cas9 molecule, comprises an amino acid sequence: having 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% homology with; differs at no more than 1%, 2%, 5%, 10%, 15%, 20%, 30%, or 40% of the amino acid residues when compared with; differs by at least 1, 2, 5, 10 or 20 amino acids but by no more than 100, 80, 70, 60, 50, 40 or 30 amino acids from; or is identical to; any Cas9 molecule sequence described herein or a naturally occurring Cas9 molecule sequence, e.g., a Cas9 molecule from a species listed herein or described in Chylinski et al. , RNA Biology 2013, 10:5, 12I-T,1 Hou et al. PNAS Early Edition 2013, 1-6.

In an embodiment, a Cas9 molecule comprises an amino acid sequence having 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% homology with; differs at no more than 1%, 2%, 5%, 10%, 15%, 20%, 30%, or 40% of the amino acid residues when compared with; differs by at least 1, 2, 5, 10 or 20 amino acids but by no more than 100, 80, 70, 60, 50, 40 or 30 amino acids from; or is identical to; *S. pyogenes* Cas9:

```
Met Asp Lys Lys Tyr Ser Ile Gly Leu Asp Ile Gly Thr Asn Ser Val
1               5                  10                  15
Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
            20                  25                  30
Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
        35                  40                  45
Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
    50                  55                  60
Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
65                  70                  75                  80
Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
                85                  90                  95
Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
            100                 105                 110
His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
        115                 120                 125
His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
    130                 135                 140
Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
145                 150                 155                 160
Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
                165                 170                 175
Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
            180                 185                 190
Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
        195                 200                 205
Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
    210                 215                 220
Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
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225 230 235 240
Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
245 250 255
Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
260 265 270
Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
275 280 285
Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
290 295 300
Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
305 310 315 320
Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
325 330 335
Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
340 345 350
Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
355 360 365
Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
370 375 380
Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
385 390 395 400
Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
405 410 415
Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
420 425 430
Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
435 440 445
Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
450 455 460
Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
465 470 475 480
Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
485 490 495
Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
515 520 525
Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
530 535 540
Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
545 550 555 560
Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
565 570 575
Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
580 585 590
Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
595 600 605
Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
610 615 620
Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
625 630 635 640
His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
645 650 655
Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
660 665 670
Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
675 680 685
Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
690 695 700
Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
705 710 715 720
His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
725 730 735
Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
740 745 750
Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
755 760 765
Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
770 775 780
Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro

785 790 795 800
Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
805 810 815
Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
820 825 830
Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
835 840 845
Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
850 855 860
Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
865 870 875 880
Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
885 890 895
Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
900 905 910
Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
915 920 925
Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
930 935 940
Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
945 950 955 960
Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
965 970 975
Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
980 985 990
Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
995 1000 1005
Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala Lys
1010 1015 1020
Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe Tyr Ser
1025 1030 1035 1040
Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala Asn Gly Glu
1045 1050 1055
Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu Thr Gly Glu Ile
1060 1065 1070

Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val Arg Lys Val Leu Ser
1075 1080 1085
Met Pro Gln Val Asn Ile Val Lys Lys Thr Glu Val Gln Thr Gly Gly
1090 1095 1100
Phe Ser Lys Glu Ser Ile Leu Pro Lys Arg Asn Ser Asp Lys Leu Ile
1105 1110 1115 1120
Ala Arg Lys Lys Asp Trp Asp Pro Lys Lys Tyr Gly Gly Phe Asp Ser
1125 1130 1135
Pro Thr Val Ala Tyr Ser Val Leu Val Val Ala Lys Val Glu Lys Gly
1140 1145 1150
Lys Ser Lys Lys Leu Lys Ser Val Lys Glu Leu Leu Gly Ile Thr Ile
1155 1160 1165
Met Glu Arg Ser Ser Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala
1170 1175 1180
Lys Gly Tyr Lys Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys
1185 1190 1195 1200
Tyr Ser Leu Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser
1205 1210 1215
Ala Gly Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr
1220 1225 1230
Val Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
1235 1240 1245
Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys His
1250 1255 1260
Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys Arg Val
1265 1270 1275 1280
Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala Tyr Asn Lys
1285 1290 1295
His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn Ile Ile His Leu
1300 1305 1310
Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala Phe Lys Tyr Phe Asp
1315 1320 1325
Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser Thr Lys Glu Val Leu Asp
1330 1335 1340
Ala Thr Leu Ile His Gln Ser Ile Thr Gly Leu Tyr Glu Thr Arg Ile

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1345                1350                1355                1360
Asp Leu Ser Gln Leu Gly Gly Asp
                1365
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(SEQ ID NO: 6611)

In embodiments, the Cas9 molecule is a *S. pyogenes* Cas9 variant of SEQ ID NO: 6611 that includes one or more mutations to positively charged amino acids (e.g., lysine, arginine or histidine) that introduce an uncharged or nonpolar amino acid, e.g., alanine, at said position. In embodiments, the mutation is to one or more positively charged amino acids in the nt-groove of Cas9. In embodiments, the Cas9 molecule is a *S. pyogenes* Cas9 variant of SEQ ID NO: 6611 that includes a mutatation at position 855 of SEQ ID NO: 6611, for example a mutation to an uncharged amino acid, e.g., alanine, at position 855 of SEQ ID NO: 6611. In embodiments, the Cas9 molecule has a mutation only at position 855 of SEQ ID NO: 6611, relative to SEQ ID NO: 6611, e.g., to an uncharged amino acid, e.g., alanine. In embodiments, the Cas9 molecule is a *S. pyogenes* Cas9 variant of SEQ ID NO: 6611 that includes a mutatation at position 810, a mutation at position 1003, and/or a mutation at position 1060 of SEQ ID NO: 6611, for example a mutation to alanine at position 810, position 1003, and/or position 1060 of SEQ ID NO: 6611. In embodiments, the Cas9 molecule has a mutation only at position 810, position 1003, and position 1060 of SEQ ID NO: 6611, relative to SEQ ID NO: 6611, e.g., where each mutation is to an uncharged amino acid, for example, alanine. In embodiments, the Cas9 molecule is a *S. pyogenes* Cas9 variant of SEQ ID NO: 6611 that includes a mutatation at position 848, a mutation at position 1003, and/or a mutation at position 1060 of SEQ ID NO: 6611, for example a mutation to alanine at position 848, position 1003, and/or position 1060 of SEQ ID NO: 6611. In embodiments, the Cas9 molecule has a mutation only at position 848, position 1003, and position 1060 of SEQ ID NO: 6611, relative to SEQ ID NO: 6611, e.g., where each mutation is to an uncharged amino acid, for example, alanine. In embodiments, the Cas9 molecule is a Cas9 molecule as described in Slaymaker et al., *Science Express*, available online December 1, 2015 at Science DOI: 10.1126/science.aad5227.

In embodiments, the Cas9 molecule is a *S. pyogenes* Cas9 variant of SEQ ID NO: 6611 that includes one or more mutations. In embodiments, the Cas9 variant comprises a mutation at position 80 of SEQ ID NO: 6611, e.g., includes a leucine at position 80 of SEQ ID NO: 6611 (i.e., comprises, e.g., consists of, SEQ ID NO: 6611 with a C80L mutation). In embodiments, the Cas9 variant comprises a mutation at position 574 of SEQ ID NO: 6611, e.g., includes a glutamic acid at position 574 of SEQ ID NO: 6611 (i.e., comprises, e.g., consists of, SEQ ID NO: 6611 with a C574E mutation). In embodiments, the Cas9 variant comprises a mutation at position 80 and a mutation at position 574 of SEQ ID NO: 6611, e.g., includes a leucine at position 80 of SEQ ID NO: 6611, and a glutamic acid at position 574 of SEQ ID

NO: 6611 (i.e., comprises, e.g., consists of, SEQ ID NO: 6611 with a C80L mutation and a C574E mutation). Without being bound by theory, it is believed that such mutations improve the solution properties of the Cas9 molecule.

In embodiments, the Cas9 molecule is a *S. pyogenes* Cas9 variant of SEQ ID NO: 6611 that includes one or more mutations. In embodiments, the Cas9 variant comprises a mutation at position 147 of SEQ ID NO: 6611, e.g., includes a tyrosine at position 147 of SEQ ID NO: 6611 (i.e., comprises, e.g., consists of, SEQ ID NO: 6611 with a D147Y mutation). In embodiments, the Cas9 variant comprises a mutation at position 411 of SEQ ID NO: 6611, e.g., includes a threonine at position 411 of SEQ ID NO: 6611 (i.e., comprises, e.g., consists of, SEQ ID NO: 6611 with a P411T mutation). In embodiments, the Cas9 variant comprises a mutation at position 147 and a mutation at position 411 of SEQ ID NO: 6611, e.g., includes a tyrosine at position 147 of SEQ ID NO: 6611, and a threonine at position 411 of SEQ ID NO: 6611 (i.e., comprises, e.g., consists of, SEQ ID NO: 6611 with a D147Y mutation and a P411T mutation). Without being bound by theory, it is believed that such mutations improve the targeting efficiency of the Cas9 molecule, e.g., in yeast.

In embodiments, the Cas9 molecule is a *S. pyogenes* Cas9 variant of SEQ ID NO: 6611 that includes one or more mutations. In embodiments, the Cas9 variant comprises a mutation at position 1135 of SEQ ID NO: 6611, e.g., includes a glutamic acid at position 1135 of SEQ ID NO: 6611 (i.e., comprises, e.g., consists of, SEQ ID NO: 6611 with a D1135E mutation). Without being bound by theory, it is believed that such mutations improve the selectivity of the Cas9 molecule for the NGG PAM sequence versus the NAG PAM sequence.

In embodiments, the Cas9 molecule is a *S. pyogenes* Cas9 variant of SEQ ID NO: 6611 that includes one or more mutations that introduce an uncharged or nonpolar amino acid, e.g., alanine, at certain positions. In embodiments, the Cas9 molecule is a *S. pyogenes* Cas9 variant of SEQ ID NO: 6611 that includes a mutatation at position 497, a mutation at position 661, a mutation at position 695 and/or a mutation at position 926 of SEQ ID NO: 6611, for example a mutation to alanine at position 497, position 661, position 695 and/or position 926 of SEQ ID NO: 6611. In embodiments, the Cas9 molecule has a mutation only at position 497, position 661, position 695, and position 926 of SEQ ID NO: 6611, relative to SEQ ID NO: 6611, e.g., where each mutation is to an uncharged amino acid, for example, alanine. Without being bound by theory, it is believed that such mutations reduce the cutting by the Cas9 molecule at off-target sites

It will be understood that the mutations described herein to the Cas9 molecule may be combined, and may be combined with any of the fusions or other modifications described herien, and the Cas9 molecule tested in the assays described herein.

Various types of Cas molecules can be used to practice the inventions disclosed herein. In some embodiments, Cas molecules of Type II Cas systems are used. In other embodiments, Cas molecules of other Cas systems are used. For example, Type I or Type III Cas molecules may be used. Exemplary Cas molecules (and Cas systems) are described, e.g., in Haft et ai, PLoS COMPUTATIONAL BIOLOGY 2005, 1(6): e60 and Makarova et al , NATURE REVIEW MICROBIOLOGY 201 1 , 9:467-477, the contents of both references are incorporated herein by reference in their entirety.

In an embodiment, the Cas9 molecule comprises one or more of the following activities: a nickase activity; a double stranded cleavage activity (e.g., an endonuclease and/or exonuclease activity); a helicase activity; or the ability, together with a gRNA molecule, to localize to a target nucleic acid.

Altered Cas9 Molecules

Naturally occurring Cas9 molecules possess a number of properties, including: nickase activity, nuclease activity (e.g., endonuclease and/or exonuclease activity); helicase activity; the ability to associate functionally with a gRNA molecule; and the ability to target (or localize to) a site on a nucleic acid (e.g., PAM recognition and specificity). In an embodiment, a Cas9 molecules can include all or a subset of these properties. In typical embodiments, Cas9 molecules have the ability to interact with a gRNA molecule and, in concert with the gRNA molecule, localize to a site in a nucleic acid. Other activities, e.g., PAM specificity, cleavage activity, or helicase activity can vary more widely in Cas9 molecules.

Cas9 molecules with desired properties can be made in a number of ways, e.g., by alteration of a parental, e.g., naturally occurring Cas9 molecules to provide an altered Cas9 molecule having a desired property. For example, one or more mutations or differences relative to a parental Cas9 molecule can be introduced. Such mutations and differences comprise: substitutions (e.g., conservative substitutions or substitutions of non-essential amino acids); insertions; or deletions. In an embodiment, a Cas9 molecule can comprises one or more mutations or differences, e.g., at least 1 , 2, 3, 4, 5, 10, 15, 20, 30, 40 or 50 mutations but less than 200, 100, or 80 mutations relative to a reference Cas9 molecule.

In an embodiment, a mutation or mutations do not have a substantial effect on a Cas9 activity, e.g. a Cas9 activity described herein. In an embodiment, a mutation or mutations have a substantial effect on a Cas9 activity, e.g. a Cas9 activity described herein. In an embodiment, exemplary activities comprise one or more of PAM specificity, cleavage activity, and helicase activity. A mutation(s) can be present, e.g., in: one or more RuvC-like domain, e.g., an N- terminal RuvC-like domain; an HNH-like domain; a region

outside the RuvC-like domains and the HNH-like domain. In some embodiments, a mutation(s) is present in an N-terminal RuvC- like domain. In some embodiments, a mutation(s) is present in an HNH-like domain. In some embodiments, mutations are present in both an N-terminal RuvC-like domain and an HNH-like domain.

Whether or not a particular sequence, e.g., a substitution, may affect one or more activity, such as targeting activity, cleavage activity, etc, can be evaluated or predicted, e.g., by evaluating whether the mutation is conservative or by the method described in Section III. In an embodiment, a "non-essential" amino acid residue, as used in the context of a Cas9 molecule, is a residue that can be altered from the wild-type sequence of a Cas9 molecule, e.g., a naturally occurring Cas9 molecule, e.g., an active Cas9 molecule, without abolishing or more preferably, without substantially altering a Cas9 activity (e.g., cleavage activity), whereas changing an "essential" amino acid residue results in a substantial loss of activity (e.g., cleavage activity).

Cas9 Molecules with altered PAM recognition or no PAM recognition

Naturally occurring Cas9 molecules can recognize specific PAM sequences, for example the PAM recognition sequences described above for S. pyogenes, S. thermophilus, S. mutans, S. aureus and N. meningitidis.

In an embodiment, a Cas9 molecule has the same PAM specificities as a naturally occurring Cas9 molecule. In other embodiments, a Cas9 molecule has a PAM specificity not associated with a naturally occurring Cas9 molecule, or a PAM specificity not associated with the naturally occurring Cas9 molecule to which it has the closest sequence homology. For example, a naturally occurring Cas9 molecule can be altered, e.g., to alter PAM recognition, e.g., to alter the PAM sequence that the Cas9 molecule recognizes to decrease off target sites and/or improve specificity; or eliminate a PAM recognition requirement. In an embodiment, a Cas9 molecule can be altered, e.g., to increase length of PAM recognition sequence and/or improve Cas9 specificity to high level of identity to decrease off target sites and increase specificity. In an embodiment, the length of the PAM recognition sequence is at least 4, 5, 6, 7, 8, 9, 10 or 15 amino acids in length. Cas9 molecules that recognize different PAM sequences and/or have reduced off- target activity can be generated using directed evolution. Exemplary methods and systems that can be used for directed evolution of Cas9 molecules are described, e.g., in Esvelt el al , Nature 2011, 472(7344): 499-503. Candidate Cas9 molecules can be evaluated, e.g., by methods described herein.

Non-Cleaving and Modified-Cleavage Cas9 Molecules

In an embodiment, a Cas9 molecule comprises a cleavage property that differs from naturally occurring Cas9 molecules, e.g., that differs from the naturally occurring Cas9 molecule having the closest

homology. For example, a Cas9 molecule can differ from naturally occurring Cas9 molecules, e.g., a Cas9 molecule of S. pyogenes, as follows: its ability to modulate, e.g., decreased or increased, cleavage of a double stranded break (endonuclease and/or exonuclease activity), e.g., as compared to a naturally occurring Cas9 molecule (e.g., a Cas9 molecule of S. pyogenes); its ability to modulate, e.g., decreased or increased, cleavage of a single strand of a nucleic acid, e.g., a non-complimentary strand of a nucleic acid molecule or a complementary strand of a nucleic acid molecule (nickase activity), e.g., as compared to a naturally occurring Cas9 molecule (e.g., a Cas9 molecule of S. pyogenes); or the ability to cleave a nucleic acid molecule, e.g., a double stranded or single stranded nucleic acid molecule, can be eliminated.

Modified Cleavage active Cas9 Molecules

In an embodiment, an active Cas9 molecule comprises one or more of the following activities: cleavage activity associated with an N-terminal RuvC-like domain; cleavage activity associated with an HNH-like domain; cleavage activity associated with an HNH domain and cleavage activity associated with an N-terminal RuvC-like domain.

In an embodiment, the Cas9 molecule is a Cas9 nickase, e.g., cleaves only a single strand of DNA. In an embodiment, the Cas9 nickase includes a mutation at position 10 and/or a mutation at position 840 of SEQ ID NO: 6611, e.g., comprises a D10A and/or H840A mutation to SEQ ID NO: 6611.

Non-Cleaving inactive Cas9 Molecules

In an embodiment, the altered Cas9 molecule is an inactive Cas9 molecule which does not cleave a nucleic acid molecule (either double stranded or single stranded nucleic acid molecules) or cleaves a nucleic acid molecule with significantly less efficiency, e.g., less than 20, 10, 5, 1 or 0.1 % of the cleavage activity of a reference Cas9 molecule, e.g., as measured by an assay described herein. The reference Cas9 molecule can by a naturally occurring unmodified Cas9 molecule, e.g., a naturally occurring Cas9 molecule such as a Cas9 molecule of S. pyogenes, S. thermophilus, S. aureus or N. meningitidis. In an embodiment, the reference Cas9 molecule is the naturally occurring Cas9 molecule having the closest sequence identity or homology. In an embodiment, the inactive Cas9 molecule lacks substantial cleavage activity associated with an N- terminal RuvC-like domain and cleavage activity associated with an HNH-like domain.

In an embodiment, the Cas9 molecule is dCas9. Tsai et al. (2014), Nat. Biotech. 32:569-577.

A catalytically inactive Cas9 molecule may be fused with a transcription repressor. An inactive Cas9 fusion protein complexes with a gRNA and localizes to a DNA sequence specified by gRNA's targeting domain, but, unlike an active Cas9, it will not cleave the target DNA. Fusion of an effector domain, such

as a transcriptional repression domain, to an inactive Cas9 enables recruitment of the effector to any DNA site specified by the gRNA. Site specific targeting of a Cas9 fusion protein to a promoter region of a gene can block or affect polymerase binding to the promoter region, for example, a Cas9 fusion with a transcription factor (e.g., a transcription activator) and/or a transcriptional enhancer binding to the nucleic acid to increase or inhibit transcription activation. Alternatively, site specific targeting of a a Cas9- fusion to a transcription repressor to a promoter region of a gene can be used to decrease transcription activation.

Transcription repressors or transcription repressor domains that may be fused to an inactive Cas9 molecule can include ruppel associated box (KRAB or SKD), the Mad mSIN3 interaction domain (SID) or the ERF repressor domain (ERD).

In another embodiment, an inactive Cas9 molecule may be fused with a protein that modifies chromatin. For example, an inactive Cas9 molecule may be fused to heterochromatin protein 1 (HPl), a histone lysine methyltransferase (e.g., SUV39H 1 , SUV39H2, G9A, ESET/SETDB l , Pr-SET7/8, SUV4-20H 1,RIZ1), a histone lysine demethylates (e.g., LSD1/BHC1 10, SpLsdl/Sw, l/Safl 10, Su(var)3-3, JMJD2A/JHDM3A, JMJD2B, JMJD2C/GASC1 , JMJD2D, Rph l , JARID 1 A/RBP2, JARI DIB/PLU-I, JAR1D 1C/SMCX, JARID1 D/SMCY, Lid, Jhn2, Jmj2), a histone lysine deacetylases (e.g., HDAC1, HDAC2, HDAC3, HDAC8, Rpd3, Hos l , Cir6, HDAC4, HDAC5, HDAC7, HDAC9, Hdal , Cir3, SIRT 1 , SIRT2, Sir2, Hst l , Hst2, Hst3, Hst4, HDAC 1 1) and a DNA methylases (DNMT1,DNMT2a/DMNT3b, MET1). An inactive Cas9-chomatin modifying molecule fusion protein can be used to alter chromatin status to reduce expression a target gene.

The heterologous sequence (e.g., the transcription repressor domain) may be fused to the N- or C-terminus of the inactive Cas9 protein. In an alternative embodiment, the heterologous sequence (e.g., the transcription repressor domain) may be fused to an internal portion (i.e., a portion other than the N-terminus or C-terminus) of the inactive Cas9 protein.

The ability of a Cas9 molecule/gRNA molecule complex to bind to and cleave a target nucleic acid can be evaluated, e.g., by the methods described herein in Section ΠΙ. The activity of a Cas9 molecule, e.g., either an active Cas9 or a inactive Cas9, alone or in a complex with a gRNA molecule may also be evaluated by methods well-known in the art, including, gene expression assays and chromatin-based assays, e.g., chromatin immunoprecipitation (ChiP) and chromatin in vivo assay (CiA).

Other Cas9 Molecule Fusions

In embodiments, the Cas9 molecule, e.g, a Cas9 of *S. pyogenes*, may additionally comprise one or more amino acid sequences that confer additional activity.

In some aspects, the Cas9 molecule may comprise one or more nuclear localization sequences (NLSs), such as at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more NLSs. In some embodiments, the Cas9 molecule comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more NLSs at or near the amino-terminus, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more NLSs at or near the carboxy-terminus, or a combination of these (e.g. one or more NLS at the amino-terminus and one or more NLS at the carboxy terminus). When more than one NLS is present, each may be selected independently of the others, such that a single NLS may be present in more than one copy and/or in combination with one or more other NLSs present in one or more copies. In some embodiments, an NLS is considered near the N- or C-terminus when the nearest amino acid of the NLS is within about 1, 2, 3, 4, 5, 10, 15, 20, 25, 30, 40, 50, or more amino acids along the polypeptide chain from the N- or C-terminus. Typically, an NLS consists of one or more short sequences of positively charged lysines or arginines exposed on the protein surface, but other types of NLS are known. Non-limiting examples of NLSs include an NLS sequence comprising or derived from: the NLS of the SV40 virus large T-antigen, having the amino acid sequence PKKKRKV (SEQ ID NO: 6612); the NLS from nucleoplasmin (e.g. the nucleoplasmin bipartite NLS with the sequence KRPAATKKAGQAKKKK (SEQ ID NO: 6613); the c-myc NLS having the amino acid sequence PAAKRVKLD (SEQ ID NO: 6614) or RQRRNELKRSP (SEQ ID NO: 6615); the hRNPA1 M9 NLS having the sequence NQSSNFGPMKGGNFGGRSSGPYGGGGQYFAKPRNQGGY (SEQ ID NO: 6616); the sequence RMRIZFKNKGKDTAELRRRRVEVSVELRKAKKDEQILKRRNV (SEQ ID NO: 6617) of the IBB domain from importin-alpha; the sequences VSRKRPRP (SEQ ID NO: 6618) and PPKKARED (SEQ ID NO: 6619) of the myoma T protein; the sequence PQPKKKPL (SEQ ID NO: 6620) of human p53; the sequence SALIKKKKKMAP (SEQ ID NO: 6621) of mouse c-ab1 IV; the sequences DRLRR (SEQ ID NO: 6622) and PKQKKRK (SEQ ID NO: 6623) of the influenza virus NS1; the sequence RKLKKKIKKL (SEQ ID NO: 6624) of the Hepatitis virus delta antigen; the sequence REKKKFLKRR (SEQ ID NO: 6625) of the mouse Mx1 protein; the sequence KRKGDEVDGVDEVAKKKSKK (SEQ ID NO: 6626) of the human poly(ADP-ribose) polymerase; and the sequence RKCLQAGMNLEARKTKK (SEQ ID NO: 6627) of the steroid hormone receptors (human) glucocorticoid. Other suitable NLS sequences are known in the art (e.g., Sorokin, Biochemistry (Moscow) (2007) 72:13, 1439-1457; Lange J Biol Chem. (2007) 282:8, 5101-5).

In some aspects, the Cas9 molecule may comprise one or more amino acid sequences that allow the Cas9 molecule to be specifically recognized, for example a tag. In one embodiment, the tag is a Histidine tag, e.g., a histidine tag comprising at least 3, 4, 5, 6, 7, 8, 9, 10 or more histidine amino acids (SEQ ID NO: 10800). In embodiments, the histidine tag is a His6 tag (six histidines) (SEQ ID NO: 10795). In other embodiments, the histidine tag is a His8 tag (eight histidines). In embodiments, the histidine tag may be

separated from one or more other portions of the Cas9 molecule by a linker. In embodiments, the linker is GGS. An example of such a fusion is the Cas9 molecule iProt106520.

In some aspects, the Cas9 molecule may comprise one or more amino acid sequences that are recognized by a protease (e.g., comprise a protease cleavage site). In embodiments, the cleavage site is the tobacco etch virus (TEV) cleavage site, e.g., comprises the sequence ENLYFQG (SEQ ID NO: 7810). In some aspects the protease cleavage site, e.g., the TEV cleavage site is disposed between a tag, e.g., a His tag, e.g., a His6 (SEQ ID NO: 10795) or His8 tag (SEQ ID NO: 10796), and the remainder of the Cas9 molecule. Without being bound by theory it is believed that such introduction will allow for the use of the tag for, e.g., purification of the Cas9 molecule, and then subsequent cleavage so the tag does not interfere with the Cas9 molecule function.

In embodiments, the Cas9 molecule (e.g., a Cas9 molecule as described herein) comprises an N-terminal NLS, and a C-terminal NLS (e.g., comprises, from N- to C-terminal NLS-Cas9-NLS), e.g., wherein each NLS is an SV40 NLS (PKKKRKV (SEQ ID NO: 6612)). In embodiments, the Cas9 molecule (e.g., a Cas9 molecule as described herein) comprises an N-terminal NLS, a C-terminal NLS, and a C-terminal His6 tag (SEQ ID NO: 10795) (e.g., comprises, from N- to C-terminal NLS-Cas9-NLS-His tag), e.g., wherein each NLS is an SV40 NLS (PKKKRKV (SEQ ID NO: 6612)). In embodiments, the Cas9 molecule (e.g., a Cas9 molecule as described herein) comprises an N-terminal His tag (e.g., His6 tag (SEQ ID NO: 10795)), an N-terminal NLS, and a C-terminal NLS (e.g., comprises, from N- to C-terminal His tag-NLS-Cas9-NLS), e.g., wherein each NLS is an SV40 NLS (PKKKRKV (SEQ ID NO: 6612)). In embodiments, the Cas9 molecule (e.g., a Cas9 molecule as described herein) comprises an N-terminal NLS and a C-terminal His tag (e.g., His6 tag (SEQ ID NO: 10795)) (e.g., comprises from N- to C-terminal His tag-Cas9-NLS), e.g., wherein the NLS is an SV40 NLS (PKKKRKV (SEQ ID NO: 6612)). In embodiments, the Cas9 molecule (e.g., a Cas9 molecule as described herein) comprises an N-terminal His tag (e.g., His6 tag (SEQ ID NO: 10795)) and a C-terminal NLS (e.g., comprises from N- to C-terminal NLS-Cas9-His tag), e.g., wherein the NLS is an SV40 NLS (PKKKRKV (SEQ ID NO: 6612)). In embodiments, the Cas9 molecule (e.g., a Cas9 molecule as described herein) comprises an N-terminal His tag (e.g., His8 tag (SEQ ID NO: 10796)), an N-terminal cleavage domain (e.g., a tobacco etch virus (TEV) cleavage domain (e.g., comprises the sequence ENLYFQG (SEQ ID NO: 7810))), an N-terminal NLS (e.g., an SV40 NLS; SEQ ID NO: 6612), and a C-terminal NLS (e.g., an SV40 NLS; SEQ ID NO: 6612) (e.g., comprises from N- to C- terminal His tag-TEV-NLS-Cas9-NLS). In any of the aforementioned embodiments the Cas9 has the sequence of SEQ ID NO: 6611. Alternatively, in any of the aforementioned embodiments, the Cas9 has a sequence of a Cas9 variant of SEQ ID NO: 6611, e.g., as described herein. In any of the aforementioned embodiments, the Cas9 molecule comprises a linker

between the His tag and another portion of the molecule, e.g., a GGS linker. Amino acid sequences of exemplary Cas9 molecules described above are provided below. "iProt" identifiers match those in Figure 60.

iProt105026 (also referred to as iProt106154, iProt106331, iProt106545, and PID426303, depending on the preparation of the protein) (SEQ ID NO: 7821):

MAPKKKRKVD KKYSIGLDIG TNSVGWAVIT DEYKVPSKKF KVLGNTDRHS IKKNLIGALL FDSGETAEAT RLKRTARRRY TRRKNRICYL QEIFSNEMAK VDDSFFHRLE ESFLVEEDKK HERHPIFGNI VDEVAYHEKY PTIYHLRKKL VDSTDKADLR LIYLALAHMI KFRGHFLIEG DLNPDNSDVD KLFIQLVQTY NQLFEENPIN ASGVDAKAIL SARLSKSRRL ENLIAQLPGE KKNGLFGNLI ALSLGLTPNF KSNFDLAEDA KLQLSKDTYD DDLDNLLAQI GDQYADLFLA AKNLSDAILL SDILRVNTEI TKAPLSASMI KRYDEHHQDL TLLKALVRQQ LPEKYKEIFF DQSKNGYAGY IDGGASQEEF YKFIKPILEK MDGTEELLVK LNREDLLRKQ RTFDNGSIPH QIHLGELHAI LRRQEDFYPF LKDNREKIEK ILTFRIPYYV GPLARGNSRF AWMTRKSEET ITPWNFEEVV DKGASAQSFI ERMTNFDKNL PNEKVLPKHS LLYEYFTVYN ELTKVKYVTE GMRKPAFLSG EQKKAIVDLL FKTNRKVTVK QLKEDYFKKI ECFDSVEISG VEDRFNASLG TYHDLLKIIK DKDFLDNEEN EDILEDIVLT LTLFEDREMI EERLKTYAHL FDDKVMKQLK RRRYTGWGRL SRKLINGIRD KQSGKTILDF LKSDGFANRN FMQLIHDDSL TFKEDIQKAQ VSGQGDSLHE HIANLAGSPA IKKGILQTVK VVDELVKVMG RHKPENIVIE MARENQTTQK GQKNSRERMK RIEEGIKELG SQILKEHPVE NTQLQNEKLY LYYLQNGRDM YVDQELDINR LSDYDVDHIV PQSFLKDDSI DNKVLTRSDK NRGKSDNVPS EEVVKKMKNY WRQLLNAKLI TQRKFDNLTK AERGGLSELD KAGFIKRQLV ETRQITKHVA QILDSRMNTK YDENDKLIRE VKVITLKSKL VSDFRKDFQF YKVREINNYH HAHDAYLNAV VGTALIKKYP KLESEFVYGD YKVYDVRKMI AKSEQEIGKA TAKYFFYSNI MNFFKTEITL ANGEIRKRPL IETNGETGEI VWDKGRDFAT VRKVLSMPQV NIVKKTEVQT GGFSKESILP KRNSDKLIAR KKDWDPKKYG GFDSPTVAYS VLVVAKVEKG KSKKLKSVKE LLGITIMERS SFEKNPIDFL EAKGYKEVKK DLIIKLPKYS LFELENGRKR MLASAGELQK GNELALPSKY VNFLYLASHY EKLKGSPEDN EQKQLFVEQH KHYLDEIIEQ ISEFSKRVIL ADANLDKVLS AYNKHRDKPI REQAENIIHL FTLTNLGAPA AFKYFDTTID RKRYTSTKEV LDATLIHQSI TGLYETRIDL SQLGGDSRAD PKKKRKVHHH HHH

iProt106518 (SEQ ID NO: 7822):

MAPKKKRKVD KKYSIGLDIG TNSVGWAVIT DEYKVPSKKF KVLGNTDRHS IKKNLIGALL FDSGETAEAT RLKRTARRRY TRRKNRILYL QEIFSNEMAK VDDSFFHRLE ESFLVEEDKK HERHPIFGNI VDEVAYHEKY PTIYHLRKKL VDSTDKADLR LIYLALAHMI KFRGHFLIEG DLNPDNSDVD KLFIQLVQTY NQLFEENPIN ASGVDAKAIL SARLSKSRRL ENLIAQLPGE KKNGLFGNLI ALSLGLTPNF KSNFDLAEDA KLQLSKDTYD DDLDNLLAQI GDQYADLFLA AKNLSDAILL SDILRVNTEI TKAPLSASMI KRYDEHHQDL TLLKALVRQQ LPEKYKEIFF DQSKNGYAGY IDGGASQEEF YKFIKPILEK MDGTEELLVK LNREDLLRKQ RTFDNGSIPH QIHLGELHAI LRRQEDFYPF LKDNREKIEK ILTFRIPYYV GPLARGNSRF AWMTRKSEET ITPWNFEEVV DKGASAQSFI ERMTNFDKNL PNEKVLPKHS LLYEYFTVYN ELTKVKYVTE GMRKPAFLSG EQKKAIVDLL FKTNRKVTVK QLKEDYFKKI EEFDSVEISG VEDRFNASLG TYHDLLKIIK DKDFLDNEEN EDILEDIVLT LTLFEDREMI EERLKTYAHL FDDKVMKQLK RRRYTGWGRL SRKLINGIRD KQSGKTILDF LKSDGFANRN FMQLIHDDSL TFKEDIQKAQ VSGQGDSLHE HIANLAGSPA IKKGILQTVK VVDELVKVMG RHKPENIVIE MARENQTTQK GQKNSRERMK RIEEGIKELG SQILKEHPVE NTQLQNEKLY LYYLQNGRDM YVDQELDINR LSDYDVDHIV PQSFLKDDSI DNKVLTRSDK NRGKSDNVPS EEVVKKMKNY WRQLLNAKLI TQRKFDNLTK AERGGLSELD KAGFIKRQLV ETRQITKHVA QILDSRMNTK YDENDKLIRE

VKVITLKSKL VSDFRKDFQF YKVREINNYH HAHDAYLNAV VGTALIKKYP KLESEFVYGD
YKVYDVRKMI AKSEQEIGKA TAKYFFYSNI MNFFKTEITL ANGEIRKRPL IETNGETGEI
VWDKGRDFAT VRKVLSMPQV NIVKKTEVQT GGFSKESILP KRNSDKLIAR KKDWDPKKYG
GFDSPTVAYS VLVVAKVEKG KSKKLKSVKE LLGITIMERS SFEKNPIDFL EAKGYKEVKK
DLIIKLPKYS LFELENGRKR MLASAGELQK GNELALPSKY VNFLYLASHY EKLKGSPEDN
EQKQLFVEQH KHYLDEIIEQ ISEFSKRVIL ADANLDKVLS AYNKHRDKPI REQAENIIHL
FTLTNLGAPA AFKYFDTTID RKRYTSTKEV LDATLIHQSI TGLYETRIDL SQLGGDSRAD
PKKKRKVHHH HHH

iProt106519 (SEQ ID NO: 7823):

MGSSHHHHHH HHENLYFQGS MDKKYSIGLD IGTNSVGWAV ITDEYKVPSK KFKVLGNTDR
HSIKKNLIGA LLFDSGETAE ATRLKRTARR RYTRRKNRIC YLQEIFSNEM AKVDDSFFHR
LEESFLVEED KKHERHPIFG NIVDEVAYHE KYPTIYHLRK KLVDSTDKAD LRLIYLALAH
MIKFRGHFLI EGDLNPDNSD VDKLFIQLVQ TYNQLFEENP INASGVDAKA ILSARLSKSR
RLENLIAQLP GEKKNGLFGN LIALSLGLTP NFKSNFDLAE DAKLQLSKDT YDDDLDNLLA
QIGDQYADLF LAAKNLSDAI LLSDILRVNT EITKAPLSAS MIKRYDEHHQ DLTLLKALVR
QQLPEKYKEI FFDQSKNGYA GYIDGGASQE EFYKFIKPIL EKMDGTEELL VKLNREDLLR
KQRTFDNGSI PHQIHLGELH AILRRQEDFY PFLKDNREKI EKILTFRIPY YVGPLARGNS
RFAWMTRKSE ETITPWNFEE VVDKGASAQS FIERMTNFDK NLPNEKVLPK HSLLYEYFTV
YNELTKVKYV TEGMRKPAFL SGEQKKAIVD LLFKTNRKVT VKQLKEDYFK KIECFDSVEI
SGVEDRFNAS LGTYHDLLKI IKDKDFLDNE ENEDILEDIV LTLTLFEDRE MIEERLKTYA
HLFDDKVMKQ LKRRRYTGWG RLSRKLINGI RDKQSGKTIL DFLKSDGFAN RNFMQLIHDD
SLTFKEDIQK AQVSGQGDSL HEHIANLAGS PAIKKGILQT VKVVDELVKV MGRHKPENIV
IEMARENQTT QKGQKNSRER MKRIEEGIKE LGSQILKEHP VENTQLQNEK LYLYYLQNGR
DMYVDQELDI NRLSDYDVDH IVPQSFLKDD SIDNKVLTRS DKNRGKSDNV PSEEVVKKMK
NYWRQLLNAK LITQRKFDNL TKAERGGLSE LDKAGFIKRQ LVETRQITKH VAQILDSRMN
TKYDENDKLI REVKVITLKS KLVSDFRKDF QFYKVREINN YHHAHDAYLN AVVGTALIKK
YPKLESEFVY GDYKVYDVRK MIAKSEQEIG KATAKYFFYS NIMNFFKTEI TLANGEIRKR
PLIETNGETG EIVWDKGRDF ATVRKVLSMP QVNIVKKTEV QTGGFSKESI LPKRNSDKLI
ARKKDWDPKK YGGFDSPTVA YSVLVVAKVE KGKSKKLKSV KELLGITIME RSSFEKNPID
FLEAKGYKEV KKDLIIKLPK YSLFELENGR KRMLASAGEL QKGNELALPS KYVNFLYLAS
HYEKLKGSPE DNEQKQLFVE QHKHYLDEII EQISEFSKRV ILADANLDKV LSAYNKHRDK
PIREQAENII HLFTLTNLGA PAAFKYFDTT IDRKRYTSTK EVLDATLIHQ SITGLYETRI
DLSQLGGDGG GSPKKKRKV

iProt106520 (SEQ ID NO: 7824):

MAHHHHHHGG SPKKKRKVDK KYSIGLDIGT NSVGWAVITD EYKVPSKKFK VLGNTDRHSI
KKNLIGALLF DSGETAEATR LKRTARRRYT RRKNRICYLQ EIFSNEMAKV DDSFFHRLEE
SFLVEEDKKH ERHPIFGNIV DEVAYHEKYP TIYHLRKKLV DSTDKADLRL IYLALAHMIK
FRGHFLIEGD LNPDNSDVDK LFIQLVQTYN QLFEENPINA SGVDAKAILS ARLSKSRRLE
NLIAQLPGEK KNGLFGNLIA LSLGLTPNFK SNFDLAEDAK LQLSKDTYDD DLDNLLAQIG
DQYADLFLAA KNLSDAILLS DILRVNTEIT KAPLSASMIK RYDEHHQDLT LLKALVRQQL
PEKYKEIFFD QSKNGYAGYI DGGASQEEFY KFIKPILEKM DGTEELLVKL NREDLLRKQR
TFDNGSIPHQ IHLGELHAIL RRQEDFYPFL KDNREKIEKI LTFRIPYYVG PLARGNSRFA
WMTRKSEETI TPWNFEEVVD KGASAQSFIE RMTNFDKNLP NEKVLPKHSL LYEYFTVYNE
LTKVKYVTEG MRKPAFLSGE QKKAIVDLLF KTNRKVTVKQ LKEDYFKKIE CFDSVEISGV
EDRFNASLGT YHDLLKIIKD KDFLDNEENE DILEDIVLTL TLFEDREMIE ERLKTYAHLF
DDKVMKQLKR RRYTGWGRLS RKLINGIRDK QSGKTILDFL KSDGFANRNF MQLIHDDSLT
FKEDIQKAQV SGQGDSLHEH IANLAGSPAI KKGILQTVKV VDELVKVMGR HKPENIVIEM
ARENQTTQKG QKNSRERMKR IEEGIKELGS QILKEHPVEN TQLQNEKLYL YYLQNGRDMY

VDQELDINRL SDYDVDHIVP QSFLKDDSID NKVLTRSDKN RGKSDNVPSE EVVKKMKNYW
RQLLNAKLIT QRKFDNLTKA ERGGLSELDK AGFIKRQLVE TRQITKHVAQ ILDSRMNTKY
DENDKLIREV KVITLKSKLV SDFRKDFQFY KVREINNYHH AHDAYLNAVV GTALIKKYPK
LESEFVYGDY KVYDVRKMIA KSEQEIGKAT AKYFFYSNIM NFFKTEITLA NGEIRKRPLI
ETNGETGEIV WDKGRDFATV RKVLSMPQVN IVKKTEVQTG GFSKESILPK RNSDKLIARK
KDWDPKKYGG FDSPTVAYSV LVVAKVEKGK SKKLKSVKEL LGITIMERSS FEKNPIDFLE
AKGYKEVKKD LIIKLPKYSL FELENGRKRM LASAGELQKG NELALPSKYV NFLYLASHYE
KLKGSPEDNE QKQLFVEQHK HYLDEIIEQI SEFSKRVILA DANLDKVLSA YNKHRDKPIR
EQAENIIHLF TLTNLGAPAA FKYFDTTIDR KRYTSTKEVL DATLIHQSIT GLYETRIDLS
QLGGDSRADP KKKRKV

iProt106521 (SEQ ID NO: 7825):

MAPKKKRKVD KKYSIGLDIG TNSVGWAVIT DEYKVPSKKF KVLGNTDRHS IKKNLIGALL
FDSGETAEAT RLKRTARRRY TRRKNRICYL QEIFSNEMAK VDDSFFHRLE ESFLVEEDKK
HERHPIFGNI VDEVAYHEKY PTIYHLRKKL VDSTDKADLR LIYLALAHMI KFRGHFLIEG
DLNPDNSDVD KLFIQLVQTY NQLFEENPIN ASGVDAKAIL SARLSKSRRL ENLIAQLPGE
KKNGLFGNLI ALSLGLTPNF KSNFDLAEDA KLQLSKDTYD DDLDNLLAQI GDQYADLFLA
AKNLSDAILL SDILRVNTEI TKAPLSASMI KRYDEHHQDL TLLKALVRQQ LPEKYKEIFF
DQSKNGYAGY IDGGASQEEF YKFIKPILEK MDGTEELLVK LNREDLLRKQ RTFDNGSIPH
QIHLGELHAI LRRQEDFYPF LKDNREKIEK ILTFRIPYYV GPLARGNSRF AWMTRKSEET
ITPWNFEEVV DKGASAQSFI ERMTNFDKNL PNEKVLPKHS LLYEYFTVYN ELTKVKYVTE
GMRKPAFLSG EQKKAIVDLL FKTNRKVTVK QLKEDYFKKI ECFDSVEISG VEDRFNASLG
TYHDLLKIIK DKDFLDNEEN EDILEDIVLT LTLFEDREMI EERLKTYAHL FDDKVMKQLK
RRRYTGWGRL SRKLINGIRD KQSGKTILDF LKSDGFANRN FMQLIHDDSL TFKEDIQKAQ
VSGQGDSLHE HIANLAGSPA IKKGILQTVK VVDELVKVMG RHKPENIVIE MARENQTTQK
GQKNSRERMK RIEEGIKELG SQILKEHPVE NTQLQNEKLY LYYLQNGRDM YVDQELDINR
LSDYDVDHIV PQSFLKDDSI DNKVLTRSDK NRGKSDNVPS EEVVKKMKNY WRQLLNAKLI
TQRKFDNLTK AERGGLSELD KAGFIKRQLV ETRQITKHVA QILDSRMNTK YDENDKLIRE
VKVITLKSKL VSDFRKDFQF YKVREINNYH HAHDAYLNAV VGTALIKKYP KLESEFVYGD
YKVYDVRKMI AKSEQEIGKA TAKYFFYSNI MNFFKTEITL ANGEIRKRPL IETNGETGEI
VWDKGRDFAT VRKVLSMPQV NIVKKTEVQT GGFSKESILP KRNSDKLIAR KKDWDPKKYG
GFDSPTVAYS VLVVAKVEKG KSKKLKSVKE LLGITIMERS SFEKNPIDFL EAKGYKEVKK
DLIIKLPKYS LFELENGRKR MLASAGELQK GNELALPSKY VNFLYLASHY EKLKGSPEDN
EQKQLFVEQH KHYLDEIIEQ ISEFSKRVIL ADANLDKVLS AYNKHRDKPI REQAENIIHL
FTLTNLGAPA AFKYFDTTID RKRYTSTKEV LDATLIHQSI TGLYETRIDL SQLGGDSRAD
HHHHHH

iProt106522 (SEQ ID NO: 7826):

MAHHHHHHGG SDKKYSIGLD IGTNSVGWAV ITDEYKVPSK KFKVLGNTDR HSIKKNLIGA
LLFDSGETAE ATRLKRTARR RYTRRKNRIC YLQEIFSNEM AKVDDSFFHR LEESFLVEED
KKHERHPIFG NIVDEVAYHE KYPTIYHLRK KLVDSTDKAD LRLIYLALAH MIKFRGHFLI
EGDLNPDNSD VDKLFIQLVQ TYNQLFEENP INASGVDAKA ILSARLSKSR RLENLIAQLP
GEKKNGLFGN LIALSLGLTP NFKSNFDLAE DAKLQLSKDT YDDDLDNLLA QIGDQYADLF
LAAKNLSDAI LLSDILRVNT EITKAPLSAS MIKRYDEHHQ DLTLLKALVR QQLPEKYKEI
FFDQSKNGYA GYIDGGASQE EFYKFIKPIL EKMDGTEELL VKLNREDLLR KQRTFDNGSI
PHQIHLGELH AILRRQEDFY PFLKDNREKI EKILTFRIPY YVGPLARGNS RFAWMTRKSE
ETITPWNFEE VVDKGASAQS FIERMTNFDK NLPNEKVLPK HSLLYEYFTV YNELTKVKYV
TEGMRKPAFL SGEQKKAIVD LLFKTNRKVT VKQLKEDYFK KIECFDSVEI SGVEDRFNAS
LGTYHDLLKI IKDKDFLDNE ENEDILEDIV LTLTLFEDRE MIEERLKTYA HLFDDKVMKQ
LKRRRYTGWG RLSRKLINGI RDKQSGKTIL DFLKSDGFAN RNFMQLIHDD SLTFKEDIQK

AQVSGQGDSL HEHIANLAGS PAIKKGILQT VKVVDELVKV MGRHKPENIV IEMARENQTT QKGQKNSRER MKRIEEGIKE LGSQILKEHP VENTQLQNEK LYLYYLQNGR DMYVDQELDI NRLSDYDVDH IVPQSFLKDD SIDNKVLTRS DKNRGKSDNV PSEEVVKKMK NYWRQLLNAK LITQRKFDNL TKAERGGLSE LDKAGFIKRQ LVETRQITKH VAQILDSRMN TKYDENDKLI REVKVITLKS KLVSDFRKDF QFYKVREINN YHHAHDAYLN AVVGTALIKK YPKLESEFVY GDYKVYDVRK MIAKSEQEIG KATAKYFFYS NIMNFFKTEI TLANGEIRKR PLIETNGETG EIVWDKGRDF ATVRKVLSMP QVNIVKKTEV QTGGFSKESI LPKRNSDKLI ARKKDWDPKK YGGFDSPTVA YSVLVVAKVE KGKSKKLKSV KELLGITIME RSSFEKNPID FLEAKGYKEV KKDLIIKLPK YSLFELENGR KRMLASAGEL QKGNELALPS KYVNFLYLAS HYEKLKGSPE DNEQKQLFVE QHKHYLDEII EQISEFSKRV ILADANLDKV LSAYNKHRDK PIREQAENII HLFTLTNLGA PAAFKYFDTT IDRKRYTSTK EVLDATLIHQ SITGLYETRI DLSQLGGDSR ADPKKKRKV

iProt106658 (SEQ ID NO: 7827):

MGSSHHHHHH HHENLYFQGS MDKKYSIGLD IGTNSVGWAV ITDEYKVPSK KFKVLGNTDR HSIKKNLIGA LLFDSGETAE ATRLKRTARR RYTRRKNRIC YLQEIFSNEM AKVDDSFFHR LEESFLVEED KKHERHPIFG NIVDEVAYHE KYPTIYHLRK KLVDSTDKAD LRLIYLALAH MIKFRGHFLI EGDLNPDNSD VDKLFIQLVQ TYNQLFEENP INASGVDAKA ILSARLSKSR RLENLIAQLP GEKKNGLFGN LIALSLGLTP NFKSNFDLAE DAKLQLSKDT YDDDLDNLLA QIGDQYADLF LAAKNLSDAI LLSDILRVNT EITKAPLSAS MIKRYDEHHQ DLTLLKALVR QQLPEKYKEI FFDQSKNGYA GYIDGGASQE EFYKFIKPIL EKMDGTEELL VKLNREDLLR KQRTFDNGSI PHQIHLGELH AILRRQEDFY PFLKDNREKI EKILTFRIPY YVGPLARGNS RFAWMTRKSE ETITPWNFEE VVDKGASAQS FIERMTNFDK NLPNEKVLPK HSLLYEYFTV YNELTKVKYV TEGMRKPAFL SGEQKKAIVD LLFKTNRKVT VKQLKEDYFK KIECFDSVEI SGVEDRFNAS LGTYHDLLKI IKDKDFLDNE ENEDILEDIV LTLTLFEDRE MIEERLKTYA HLFDDKVMKQ LKRRRYTGWG RLSRKLINGI RDKQSGKTIL DFLKSDGFAN RNFMQLIHDD SLTFKEDIQK AQVSGQGDSL HEHIANLAGS PAIKKGILQT VKVVDELVKV MGRHKPENIV IEMARENQTT QKGQKNSRER MKRIEEGIKE LGSQILKEHP VENTQLQNEK LYLYYLQNGR DMYVDQELDI NRLSDYDVDH IVPQSFLKDD SIDNKVLTRS DKNRGKSDNV PSEEVVKKMK NYWRQLLNAK LITQRKFDNL TKAERGGLSE LDKAGFIKRQ LVETRQITKH VAQILDSRMN TKYDENDKLI REVKVITLKS KLVSDFRKDF QFYKVREINN YHHAHDAYLN AVVGTALIKK YPKLESEFVY GDYKVYDVRK MIAKSEQEIG KATAKYFFYS NIMNFFKTEI TLANGEIRKR PLIETNGETG EIVWDKGRDF ATVRKVLSMP QVNIVKKTEV QTGGFSKESI LPKRNSDKLI ARKKDWDPKK YGGFDSPTVA YSVLVVAKVE KGKSKKLKSV KELLGITIME RSSFEKNPID FLEAKGYKEV KKDLIIKLPK YSLFELENGR KRMLASAGEL QKGNELALPS KYVNFLYLAS HYEKLKGSPE DNEQKQLFVE QHKHYLDEII EQISEFSKRV ILADANLDKV LSAYNKHRDK PIREQAENII HLFTLTNLGA PAAFKYFDTT IDRKRYTSTK EVLDATLIHQ SITGLYETRI DLSQLGGDGG GSPKKKRKV

iProt106745 (SEQ ID NO: 7828):

MAPKKKRKVD KKYSIGLDIG TNSVGWAVIT DEYKVPSKKF KVLGNTDRHS IKKNLIGALL FDSGETAEAT RLKRTARRRY TRRKNRICYL QEIFSNEMAK VDDSFFHRLE ESFLVEEDKK HERHPIFGNI VDEVAYHEKY PTIYHLRKKL VDSTDKADLR LIYLALAHMI KFRGHFLIEG DLNPDNSDVD KLFIQLVQTY NQLFEENPIN ASGVDAKAIL SARLSKSRRL ENLIAQLPGE KKNGLFGNLI ALSLGLTPNF KSNFDLAEDA KLQLSKDTYD DDLDNLLAQI GDQYADLFLA AKNLSDAILL SDILRVNTEI TKAPLSASMI KRYDEHHQDL TLLKALVRQQ LPEKYKEIFF DQSKNGYAGY IDGGASQEEF YKFIKPILEK MDGTEELLVK LNREDLLRKQ RTFDNGSIPH QIHLGELHAI LRRQEDFYPF LKDNREKIEK ILTFRIPYYV GPLARGNSRF AWMTRKSEET ITPWNFEEVV DKGASAQSFI ERMTNFDKNL PNEKVLPKHS LLYEYFTVYN ELTKVKYVTE GMRKPAFLSG EQKKAIVDLL FKTNRKVTVK QLKEDYFKKI ECFDSVEISG VEDRFNASLG

TYHDLLKIIK DKDFLDNEEN EDILEDIVLT LTLFEDREMI EERLKTYAHL FDDKVMKQLK
RRRYTGWGRL SRKLINGIRD KQSGKTILDF LKSDGFANRN FMQLIHDDSL TFKEDIQKAQ
VSGQGDSLHE HIANLAGSPA IKKGILQTVK VVDELVKVMG RHKPENIVIE MARENQTTQK
GQKNSRERMK RIEEGIKELG SQILKEHPVE NTQLQNEKLY LYYLQNGRDM YVDQELDINR
LSDYDVDHIV PQSFLKDDSI DNAVLTRSDK NRGKSDNVPS EEVVKKMKNY WRQLLNAKLI
TQRKFDNLTK AERGGLSELD KAGFIKRQLV ETRQITKHVA QILDSRMNTK YDENDKLIRE
VKVITLKSKL VSDFRKDFQF YKVREINNYH HAHDAYLNAV VGTALIKKYP KLESEFVYGD
YKVYDVRKMI AKSEQEIGKA TAKYFFYSNI MNFFKTEITL ANGEIRKRPL IETNGETGEI
VWDKGRDFAT VRKVLSMPQV NIVKKTEVQT GGFSKESILP KRNSDKLIAR KKDWDPKKYG
GFDSPTVAYS VLVVAKVEKG KSKKLKSVKE LLGITIMERS SFEKNPIDFL EAKGYKEVKK
DLIIKLPKYS LFELENGRKR MLASAGELQK GNELALPSKY VNFLYLASHY EKLKGSPEDN
EQKQLFVEQH KHYLDEIIEQ ISEFSKRVIL ADANLDKVLS AYNKHRDKPI REQAENIIHL
FTLTNLGAPA AFKYFDTTID RKRYTSTKEV LDATLIHQSI TGLYETRIDL SQLGGDSRAD
PKKKRKVHHH HHH

iProt106746 (SEQ ID NO: 7829):

MAPKKKRKVD KKYSIGLDIG TNSVGWAVIT DEYKVPSKKF KVLGNTDRHS IKKNLIGALL
FDSGETAEAT RLKRTARRRY TRRKNRICYL QEIFSNEMAK VDDSFFHRLE ESFLVEEDKK
HERHPIFGNI VDEVAYHEKY PTIYHLRKKL VDSTDKADLR LIYLALAHMI KFRGHFLIEG
DLNPDNSDVD KLFIQLVQTY NQLFEENPIN ASGVDAKAIL SARLSKSRRL ENLIAQLPGE
KKNGLFGNLI ALSLGLTPNF KSNFDLAEDA KLQLSKDTYD DDLDNLLAQI GDQYADLFLA
AKNLSDAILL SDILRVNTEI TKAPLSASMI KRYDEHHQDL TLLKALVRQQ LPEKYKEIFF
DQSKNGYAGY IDGGASQEEF YKFIKPILEK MDGTEELLVK LNREDLLRKQ RTFDNGSIPH
QIHLGELHAI LRRQEDFYPF LKDNREKIEK ILTFRIPYYV GPLARGNSRF AWMTRKSEET
ITPWNFEEVV DKGASAQSFI ERMTNFDKNL PNEKVLPKHS LLYEYFTVYN ELTKVKYVTE
GMRKPAFLSG EQKKAIVDLL FKTNRKVTVK QLKEDYFKKI ECFDSVEISG VEDRFNASLG
TYHDLLKIIK DKDFLDNEEN EDILEDIVLT LTLFEDREMI EERLKTYAHL FDDKVMKQLK
RRRYTGWGRL SRKLINGIRD KQSGKTILDF LKSDGFANRN FMQLIHDDSL TFKEDIQKAQ
VSGQGDSLHE HIANLAGSPA IKKGILQTVK VVDELVKVMG RHKPENIVIE MARENQTTQK
GQKNSRERMK RIEEGIKELG SQILKEHPVE NTQLQNEALY LYYLQNGRDM YVDQELDINR
LSDYDVDHIV PQSFLKDDSI DNKVLTRSDK NRGKSDNVPS EEVVKKMKNY WRQLLNAKLI
TQRKFDNLTK AERGGLSELD KAGFIKRQLV ETRQITKHVA QILDSRMNTK YDENDKLIRE
VKVITLKSKL VSDFRKDFQF YKVREINNYH HAHDAYLNAV VGTALIKKYP ALESEFVYGD
YKVYDVRKMI AKSEQEIGKA TAKYFFYSNI MNFFKTEITL ANGEIRKAPL IETNGETGEI
VWDKGRDFAT VRKVLSMPQV NIVKKTEVQT GGFSKESILP KRNSDKLIAR KKDWDPKKYG
GFDSPTVAYS VLVVAKVEKG KSKKLKSVKE LLGITIMERS SFEKNPIDFL EAKGYKEVKK
DLIIKLPKYS LFELENGRKR MLASAGELQK GNELALPSKY VNFLYLASHY EKLKGSPEDN
EQKQLFVEQH KHYLDEIIEQ ISEFSKRVIL ADANLDKVLS AYNKHRDKPI REQAENIIHL
FTLTNLGAPA AFKYFDTTID RKRYTSTKEV LDATLIHQSI TGLYETRIDL SQLGGDSRAD
PKKKRKVHHH HHH

iProt106747 (SEQ ID NO: 7830):

MAPKKKRKVD KKYSIGLDIG TNSVGWAVIT DEYKVPSKKF KVLGNTDRHS IKKNLIGALL
FDSGETAEAT RLKRTARRRY TRRKNRICYL QEIFSNEMAK VDDSFFHRLE ESFLVEEDKK
HERHPIFGNI VDEVAYHEKY PTIYHLRKKL VDSTDKADLR LIYLALAHMI KFRGHFLIEG
DLNPDNSDVD KLFIQLVQTY NQLFEENPIN ASGVDAKAIL SARLSKSRRL ENLIAQLPGE
KKNGLFGNLI ALSLGLTPNF KSNFDLAEDA KLQLSKDTYD DDLDNLLAQI GDQYADLFLA
AKNLSDAILL SDILRVNTEI TKAPLSASMI KRYDEHHQDL TLLKALVRQQ LPEKYKEIFF
DQSKNGYAGY IDGGASQEEF YKFIKPILEK MDGTEELLVK LNREDLLRKQ RTFDNGSIPH
QIHLGELHAI LRRQEDFYPF LKDNREKIEK ILTFRIPYYV GPLARGNSRF AWMTRKSEET

ITPWNFEEVV DKGASAQSFI ERMTNFDKNL PNEKVLPKHS LLYEYFTVYN ELTKVKYVTE
GMRKPAFLSG EQKKAIVDLL FKTNRKVTVK QLKEDYFKKI ECFDSVEISG VEDRFNASLG
TYHDLLKIIK DKDFLDNEEN EDILEDIVLT LTLFEDREMI EERLKTYAHL FDDKVMKQLK
RRRYTGWGRL SRKLINGIRD KQSGKTILDF LKSDGFANRN FMQLIHDDSL TFKEDIQKAQ
VSGQGDSLHE HIANLAGSPA IKKGILQTVK VVDELVKVMG RHKPENIVIE MARENQTTQK
GQKNSRERMK RIEEGIKELG SQILKEHPVE NTQLQNEKLY LYYLQNGRDM YVDQELDINR
LSDYDVDHIV PQSFLADDSI DNKVLTRSDK NRGKSDNVPS EEVVKKMKNY WRQLLNAKLI
TQRKFDNLTK AERGGLSELD KAGFIKRQLV ETRQITKHVA QILDSRMNTK YDENDKLIRE
VKVITLKSKL VSDFRKDFQF YKVREINNYH HAHDAYLNAV VGTALIKKYP ALESEFVYGD
YKVYDVRKMI AKSEQEIGKA TAKYFFYSNI MNFFKTEITL ANGEIRKAPL IETNGETGEI
VWDKGRDFAT VRKVLSMPQV NIVKKTEVQT GGFSKESILP KRNSDKLIAR KKDWDPKKYG
GFDSPTVAYS VLVVAKVEKG KSKKLKSVKE LLGITIMERS SFEKNPIDFL EAKGYKEVKK
DLIIKLPKYS LFELENGRKR MLASAGELQK GNELALPSKY VNFLYLASHY EKLKGSPEDN
EQKQLFVEQH KHYLDEIIEQ ISEFSKRVIL ADANLDKVLS AYNKHRDKPI REQAENIIHL
FTLTNLGAPA AFKYFDTTID RKRYTSTKEV LDATLIHQSI TGLYETRIDL SQLGGDSRAD
PKKKRKVHHH HHH

iProt106884 (SEQ ID NO: 7831):

MAPKKKRKVD KKYSIGLDIG TNSVGWAVIT DEYKVPSKKF KVLGNTDRHS IKKNLIGALL
FDSGETAEAT RLKRTARRRY TRRKNRICYL QEIFSNEMAK VDDSFFHRLE ESFLVEEDKK
HERHPIFGNI VDEVAYHEKY PTIYHLRKKL VDSTDKADLR LIYLALAHMI KFRGHFLIEG
DLNPDNSDVD KLFIQLVQTY NQLFEENPIN ASGVDAKAIL SARLSKSRRL ENLIAQLPGE
KKNGLFGNLI ALSLGLTPNF KSNFDLAEDA KLQLSKDTYD DDLDNLLAQI GDQYADLFLA
AKNLSDAILL SDILRVNTEI TKAPLSASMI KRYDEHHQDL TLLKALVRQQ LPEKYKEIFF
DQSKNGYAGY IDGGASQEEF YKFIKPILEK MDGTEELLVK LNREDLLRKQ RTFDNGSIPH
QIHLGELHAI LRRQEDFYPF LKDNREKIEK ILTFRIPYYV GPLARGNSRF AWMTRKSEET
ITPWNFEEVV DKGASAQSFI ERMTAFDKNL PNEKVLPKHS LLYEYFTVYN ELTKVKYVTE
GMRKPAFLSG EQKKAIVDLL FKTNRKVTVK QLKEDYFKKI ECFDSVEISG VEDRFNASLG
TYHDLLKIIK DKDFLDNEEN EDILEDIVLT LTLFEDREMI EERLKTYAHL FDDKVMKQLK
RRRYTGWGAL SRKLINGIRD KQSGKTILDF LKSDGFANRN FMALIHDDSL TFKEDIQKAQ
VSGQGDSLHE HIANLAGSPA IKKGILQTVK VVDELVKVMG RHKPENIVIE MARENQTTQK
GQKNSRERMK RIEEGIKELG SQILKEHPVE NTQLQNEKLY LYYLQNGRDM YVDQELDINR
LSDYDVDHIV PQSFLKDDSI DNKVLTRSDK NRGKSDNVPS EEVVKKMKNY WRQLLNAKLI
TQRKFDNLTK AERGGLSELD KAGFIKRQLV ETRAITKHVA QILDSRMNTK YDENDKLIRE
VKVITLKSKL VSDFRKDFQF YKVREINNYH HAHDAYLNAV VGTALIKKYP KLESEFVYGD
YKVYDVRKMI AKSEQEIGKA TAKYFFYSNI MNFFKTEITL ANGEIRKRPL IETNGETGEI
VWDKGRDFAT VRKVLSMPQV NIVKKTEVQT GGFSKESILP KRNSDKLIAR KKDWDPKKYG
GFDSPTVAYS VLVVAKVEKG KSKKLKSVKE LLGITIMERS SFEKNPIDFL EAKGYKEVKK
DLIIKLPKYS LFELENGRKR MLASAGELQK GNELALPSKY VNFLYLASHY EKLKGSPEDN
EQKQLFVEQH KHYLDEIIEQ ISEFSKRVIL ADANLDKVLS AYNKHRDKPI REQAENIIHL
FTLTNLGAPA AFKYFDTTID RKRYTSTKEV LDATLIHQSI TGLYETRIDL SQLGGDSRAD
PKKKRKVHHH HHH

Nucleic Acids Encoding Cas9 Molecules

Nucleic acids encoding the Cas9 molecules, e.g., an active Cas9 molecule or an inactive Cas9 molecule are provided herein.

Exemplary nucleic acids encoding Cas9 molecules are described in Cong et al , SCIENCE 2013, 399(6121):819-823; Wang et al , CELL 2013, 153(4):910-918; Mali et al. , SCIENCE 2013, 399(6121):823-826; Jinek et al, SCIENCE 2012, 337(6096):816-821.

In an embodiment, a nucleic acid encoding a Cas9 molecule can be a synthetic nucleic acid sequence. For example, the synthetic nucleic acid molecule can be chemically modified, e.g., as described in Section XIII. In an embodiment, the Cas9 mRNA has one or more of, e.g., all of the following properties: it is capped, polyadenylated, substituted with 5-methylcytidine and/or pseudouridine.

In addition or alternatively, the synthetic nucleic acid sequence can be codon optimized, e.g., at least one non-common codon or less-common codon has been replaced by a common codon. For example, the synthetic nucleic acid can direct the synthesis of an optimized messenger mRNA, e.g., optimized for expression in a mammalian expression system, e.g., described herein.

Provided below is an exemplary codon optimized nucleic acid sequence encoding a Cas9 molecule of S. pyogenes.

atggataaaa agtacagcat cgggctggac atcggtacaa actcagtggg gtgggccgtg 60

attacggacg agtacaaggt accctccaaa aaatttaaag tgctgggtaa cacggacaga 120

cactctataa agaaaaatct tattggagcc ttgctgttcg actcaggcga gacagccgaa 180

gccacaaggt tgaagcggac cgccaggagg cggtatacca ggagaaagaa ccgcatatgc 240

tacctgcaag aaatcttcag taacgagatg gcaaaggttg acgatagctt tttccatcgc 300

ctggaagaat cctttcttgt tgaggaagac aagaagcacg aacggcaccc catctttggc 360

aatattgtcg acgaagtggc atatcacgaa aagtacccga ctatctacca cctcaggaag 420

aagctggtgg actctaccga taaggcggac ctcagactta tttatttggc actcgcccac 480

atgattaaat ttagaggaca tttcttgatc gagggcgacc tgaacccgga caacagtgac 540

gtcgataagc tgttcatcca acttgtgcag acctacaatc aactgttcga agaaaaccct 600

ataaatgctt caggagtcga cgctaaagca atcctgtccg cgcgcctctc aaaatctaga 660

agacttgaga atctgattgc tcagttgccc ggggaaaaga aaaatggatt gtttggcaac 720

ctgatcgccc tcagtctcgg actgacccca aatttcaaaa gtaacttcga cctggccgaa 780

gacgctaagc tccagctgtc caaggacaca tacgatgacg acctcgacaa tctgctggcc 840

cagattgggg atcagtacgc cgatctcttt ttggcagcaa agaacctgtc cgacgccatc 900

ctgttgagcg atatcttgag agtgaacacc gaaattacta aagcacccct tagcgcatct 960

atgatcaagc ggtacgacga gcatcatcag gatctgaccc tgctgaaggc tcttgtgagg 1020

caacagctcc ccgaaaaata caaggaaatc ttctttgacc agagcaaaaa cggctacgct 1080

ggctatatag atggtggggc cagtcaggag gaattctata aattcatcaa gcccattctc 1140

gagaaaatgg acggcacaga ggagttgctg gtcaaactta acagggagga cctgctgcgg 1200

aagcagcgga cctttgacaa cgggtctatc ccccaccaga ttcatctggg cgaactgcac 1260

gcaatcctga ggaggcagga ggatttttat cctttttctta aagataaccg cgagaaaata 1320

gaaaagattc ttacattcag gatcccgtac tacgtgggac ctctcgcccg gggcaattca 1380

cggtttgcct ggatgacaag gaagtcagag gagactatta caccttggaa cttcgaagaa 1440

gtggtggaca agggtgcatc tgcccagtct ttcatcgagc ggatgacaaa ttttgacaag 1500

aacctcccta atgagaaggt gctgcccaaa cattctctgc tctacgagta ctttaccgtc 1560

tacaatgaac tgactaaagt caagtacgtc accgagggaa tgaggaagcc ggcattcctt 1620

agtggagaac agaagaaggc gattgtagac ctgttgttca agaccaacag gaaggtgact 1680

gtgaagcaac ttaaagaaga ctactttaag aagatcgaat gttttgacag tgtggaaatt 1740

tcaggggttg aagaccgctt caatgcgtca ttggggactt accatgatct tctcaagatc 1800

ataaaggaca aagacttcct ggacaacgaa gaaaatgagg atattctcga agacatcgtc 1860

ctcaccctga ccctgttcga agacagggaa atgatagaag agcgcttgaa aacctatgcc 1920

cacctcttcg acgataaagt tatgaagcag ctgaagcgca ggagatacac aggatgggga 1980

agattgtcaa ggaagctgat caatggaatt agggataaac agagtggcaa gaccatactg 2040

gatttcctca aatctgatgg cttcgccaat aggaacttca tgcaactgat tcacgatgac 2100

tctcttacct tcaaggagga cattcaaaag gctcaggtga gcgggcaggg agactccctt 2160

catgaacaca tcgcgaattt ggcaggttcc cccgctatta aaaagggcat ccttcaaact 2220

gtcaaggtgg tggatgaatt ggtcaaggta atgggcagac ataagccaga aaatattgtg 2280

atcgagatgg cccgcgaaaa ccagaccaca cagaagggcc agaaaaatag tagagagcgg 2340

atgaagagga tcgaggaggg catcaaagag ctgggatctc agattctcaa agaacacccc 2400

gtagaaaaca cacagctgca gaacgaaaaa ttgtacttgt actatctgca gaacggcaga 2460

gacatgtacg tcgaccaaga acttgatatt aatagactgt ccgactatga cgtagaccat 2520

atcgtgcccc agtccttcct gaaggacgac tccattgata acaaagtctt gacaagaagc 2580

gacaagaaca ggggtaaaag tgataatgtg cctagcgagg aggtggtgaa aaaaatgaag 2640

aactactggc gacagctgct taatgcaaag ctcattacac aacggaagtt cgataatctg 2700

acgaaagcag agagaggtgg cttgtctgag ttggacaagg cagggtttat taagcggcag 2760

ctggtggaaa ctaggcagat cacaaagcac gtggcgcaga ttttggacag ccggatgaac 2820

acaaaatacg acgaaaatga taaactgata cgagaggtca aagttatcac gctgaaaagc 2880

aagctggtgt ccgattttcg gaaagacttc cagttctaca aagttcgcga gattaataac 2940

taccatcatg ctcacgatgc gtacctgaac gctgttgtcg ggaccgcctt gataaagaag 3000

tacccaaagc tggaatccga gttcgtatac ggggattaca aagtgtacga tgtgaggaaa 3060

atgatagcca agtccgagca ggagattgga aaggccacag ctaagtactt cttttattct 3120

aacatcatga attttttaa gacggaaatt accctggcca acggagagat cagaaagcgg 3180

ccccttatag agacaaatgg tgaaacaggt gaaatcgtct gggataaggg cagggatttc 3240

gctactgtga ggaaggtgct gagtatgcca caggtaaata tcgtgaaaaa aaccgaagta 3300

cagaccggag gattttccaa ggaaagcatt ttgcctaaaa gaaactcaga caagctcatc 3360

gcccgcaaga aagattggga ccctaagaaa tacgggggat ttgactcacc caccgtagcc 3420

tattctgtgc tggtggtagc taaggtggaa aaaggaaagt ctaagaagct gaagtccgtg 3480

aaggaactct tgggaatcac tatcatggaa agatcatcct ttgaaaagaa ccctatcgat 3540

ttcctggagg ctaagggtta caaggaggtc aagaaagacc tcatcattaa actgccaaaa 3600

tactctctct tcgagctgga aaatggcagg aagagaatgt tggccagcgc cggagagctg 3660

caaaagggaa acgagcttgc tctgccctcc aaatatgtta attttctcta tctcgcttcc 3720

cactatgaaa agctgaaagg gtctcccgaa gataacgagc agaagcagct gttcgtcgaa 3780

cagcacaagc actatctgga tgaaataatc gaacaaataa gcgagttcag caaaagggtt 3840

atcctggcgg atgctaattt ggacaaagta ctgtctgctt ataacaagca ccgggataag 3900

cctattaggg aacaagccga gaatataatt cacctcttta cactcacgaa tctcggagcc 3960

cccgccgcct tcaaatactt tgatacgact atcgaccgga aacggtatac cagtaccaaa 4020

gaggtcctcg atgccaccct catccaccag tcaattactg gcctgtacga aacacggatc 4080

gacctctctc aactgggcgg cgactag 4107

(SEQ ID NO: 6628)

If the above Cas9 sequences are fused with a peptide or polypeptide at the C-terminus (e.g., an inactive Cas9 fused with a transcription repressor at the C-terminus), it is understood that the stop codon will be removed.

V. Chimeric Antigen Receptors

The invention provides for gRNA molecules and CRISPR systems for use in connection wth adoptive immunotherapy methods and reagents such as chimeric antigen receptor (CAR) immune effector cells, e.g., T cells, or chimeric TCR-transduced immune effector cells, e.g., T cells. The gRNA molecules and CRISPR systems of the invention can be used to create adoptive immunotherapy cells and compositions with improved properties, such as efficacy and safety. This section describes CAR technology generally that is useful in conjunction with the gRNA molecules and CRISPR systems of the invention, and describes improved CAR reagents, e.g., cells and compositions, and methods.

In general, aspects of the invention pertain to or include an isolated nucleic acid molecule encoding a chimeric antigen receptor (CAR), wherein the CAR comprises an antigen binding domain (e.g., antibody or antibody fragment, TCR or TCR fragment) that binds to a tumor antigen as described herein, a transmembrane domain (e.g., a transmembrane domain described herein), and an intracellular signaling domain (e.g., an intracellular signaling domain described herein) (e.g., an intracellular signaling domain comprising a costimulatory domain (e.g., a costimulatory domain described herein) and/or a primary signaling domain (e.g., a primary signaling domain described herein). In other aspects, the invention includes: host cells containing the above nucleic acids and isolated proteins encoded by such nucleic acid molecules. CAR nucleic acid constructs, encoded proteins, containing vectors, host cells, pharmaceutical compositions, and methods of administration and treatment related to the present invention are disclosed

in detail in International Patent Application Publication No. WO2015142675, which is incorporated by reference in its entirety.

In one aspect, the invention pertains to an isolated nucleic acid molecule encoding a chimeric antigen receptor (CAR), wherein the CAR comprises an antigen binding domain (e.g., antibody or antibody fragment, TCR or TCR fragment) that binds to a tumor-supporting antigen (e.g., a tumor-supporting antigen as described herein), a transmembrane domain (e.g., a transmembrane domain described herein), and an intracellular signaling domain (e.g., an intracellular signaling domain described herein) (e.g., an intracellular signaling domain comprising a costimulatory domain (e.g., a costimulatory domain described herein) and/or a primary signaling domain (e.g., a primary signaling domain described herein). In some embodiments, the tumor-supporting antigen is an antigen present on a stromal cell or a myeloid-derived suppressor cell (MDSC). In other aspects, the invention features polypeptides encoded by such nucleic acids and host cells containing such nucleic acids and/or polypeptides.

Alternatively, aspects of the invention pertain to isolated nucleic acid encoding a chimeric T cell receptor (TCR) comprising a TCR alpha and/or TCR beta variable domain with specificity for a cancer antigen described herein. See for example, Dembic et al., Nature, 320, 232-238 (1986), Schumacher, *Nat. Rev. Immunol.*, 2, 512-519 (2002), Kershaw et al., *Nat. Rev. Immunol.*, 5, 928-940 (2005), Xue et al., *Clin. Exp. Immunol.*, 139, 167-172 (2005), Rossig et al., *Mol. Ther.*, 10, 5-18 (2004), and Murphy et al., *Immunity*, 22, 403-414 (2005); (Morgan et al. *J. Immunol.*, 171, 3287-3295 (2003), Hughes et al., *Hum. Gene Ther.*, 16, 1-16 (2005), Zhao et al., *J. Immunol.*, 174, 4415-4423 (2005), Roszkowski et al., *Cancer Res.*, 65, 1570-1576 (2005), and Engels et al., *Hum. Gene Ther.*, 16, 799-810 (2005); US2009/03046557, the contents of which are hereby incorporated by reference in their entirety. Such chimeric TCRs may recognize, for example, cancer antigens such as MART-1, gp-100, p53, and NY-ESO-1, MAGE A3/A6, MAGEA3, SSX2, HPV-16 E6 or HPV-16 E7. In other aspects, the invention features polypeptides encoded by such nucleic acids and host cells containing such nucleic acids and/or polypeptides.

Targets

The present invention provides cells, e.g., immune effector cells (e.g., T cells, NK cells), that comprise or at any time comprised a gRNA molecule or CRISPR system as described herein, that are further engineered to contain one or more CARs that direct the immune effector cells to undesired cells (e.g., cancer cells). This is achieved through an antigen binding domain on the CAR that is specific for a cancer associated antigen. There are two classes of cancer associated antigens (tumor antigens) that can be targeted by the CARs of the instant invention: (1) cancer associated antigens that are expressed on the surface of cancer cells; and (2) cancer associated antigens that itself is intracellar, however, a fragment of

such antigen (peptide) is presented on the surface of the cancer cells by MHC (major histocompatibility complex).

In some embodiments, the tumor antigen is chosen from one or more of: CD19; CD123; CD22; CD30; CD171; CS-1 (also referred to as CD2 subset 1, CRACC, SLAMF7, CD319, and 19A24); C-type lectin-like molecule-1 (CLL-1 or CLECL1); CD33; epidermal growth factor receptor variant III (EGFRvIII); ganglioside G2 (GD2); ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); TNF receptor family member B cell maturation (BCMA); Tn antigen ((Tn Ag) or (GalNAcα-Ser/Thr)); prostate-specific membrane antigen (PSMA); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Fms-Like Tyrosine Kinase 3 (FLT3); Tumor-associated glycoprotein 72 (TAG72); CD38; CD44v6; Carcinoembryonic antigen (CEA); Epithelial cell adhesion molecule (EPCAM); B7H3 (CD276); KIT (CD117); Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Mesothelin; Interleukin 11 receptor alpha (IL-11Ra); prostate stem cell antigen (PSCA); Protease Serine 21 (Testisin or PRSS21); vascular endothelial growth factor receptor 2 (VEGFR2); Lewis(Y) antigen; CD24; Platelet-derived growth factor receptor beta (PDGFR-beta); Stage-specific embryonic antigen-4 (SSEA-4); CD20; Folate receptor alpha; Receptor tyrosine-protein kinase ERBB2 (Her2/neu); Mucin 1, cell surface associated (MUC1); epidermal growth factor receptor (EGFR); neural cell adhesion molecule (NCAM); Prostase; prostatic acid phosphatase (PAP); elongation factor 2 mutated (ELF2M); Ephrin B2; fibroblast activation protein alpha (FAP); insulin-like growth factor 1 receptor (IGF-I receptor), carbonic anhydrase IX (CAIX); Proteasome (Prosome, Macropain) Subunit, Beta Type, 9 (LMP2); glycoprotein 100 (gp100); oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); tyrosinase; ephrin type-A receptor 2 (EphA2); Fucosyl GM1; sialyl Lewis adhesion molecule (sLe); ganglioside GM3 (aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); transglutaminase 5 (TGS5); high molecular weight-melanoma-associated antigen (HMWMAA); o-acetyl-GD2 ganglioside (OAcGD2); Folate receptor beta; tumor endothelial marker 1 (TEM1/CD248); tumor endothelial marker 7-related (TEM7R); claudin 6 (CLDN6); thyroid stimulating hormone receptor (TSHR); G protein-coupled receptor class C group 5, member D (GPRC5D); chromosome X open reading frame 61 (CXORF61); CD97; CD179a; anaplastic lymphoma kinase (ALK); Polysialic acid; placenta-specific 1 (PLAC1); hexasaccharide portion of globoH glycoceramide (GloboH); mammary gland differentiation antigen (NY-BR-1); uroplakin 2 (UPK2); Hepatitis A virus cellular receptor 1 (HAVCR1); adrenoceptor beta 3 (ADRB3); pannexin 3 (PANX3); G protein-coupled receptor 20 (GPR20); lymphocyte antigen 6 complex, locus K 9 (LY6K); Olfactory receptor 51E2 (OR51E2); TCR Gamma Alternate Reading Frame Protein (TARP); Wilms tumor protein (WT1); Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Melanoma-associated antigen 1 (MAGE-A1); ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML); sperm protein 17 (SPA17); X

Antigen Family, Member 1A (XAGE1); angiopoietin-binding cell surface receptor 2 (Tie 2); melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2); Fos-related antigen 1; tumor protein p53 (p53); p53 mutant; prostein; surviving; telomerase; prostate carcinoma tumor antigen-1 (PCTA-1 or Galectin 8), melanoma antigen recognized by T cells 1 (MelanA or MART1); Rat sarcoma (Ras) mutant; human Telomerase reverse transcriptase (hTERT); sarcoma translocation breakpoints; melanoma inhibitor of apoptosis (ML-IAP); ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene); N-Acetyl glucosaminyl-transferase V (NA17); paired box protein Pax-3 (PAX3); Androgen receptor; Cyclin B1; v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Ras Homolog Family Member C (RhoC); Tyrosinase-related protein 2 (TRP-2); Cytochrome P450 1B1 (CYP1B1); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites), Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Paired box protein Pax-5 (PAX5); proacrosin binding protein sp32 (OY-TES1); lymphocyte-specific protein tyrosine kinase (LCK); A kinase anchor protein 4 (AKAP-4); synovial sarcoma, X breakpoint 2 (SSX2); Receptor for Advanced Glycation Endproducts (RAGE-1); renal ubiquitous 1 (RU1); renal ubiquitous 2 (RU2); legumain; human papilloma virus E6 (HPV E6); human papilloma virus E7 (HPV E7); intestinal carboxyl esterase; heat shock protein 70-2 mutated (mut hsp70-2); CD79a; CD79b; CD72; Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Fc fragment of IgA receptor (FCAR or CD89); Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); CD300 molecule-like family member f (CD300LF); C-type lectin domain family 12 member A (CLEC12A); bone marrow stromal cell antigen 2 (BST2); EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2); lymphocyte antigen 75 (LY75); Glypican-3 (GPC3); Fc receptor-like 5 (FCRL5); and immunoglobulin lambda-like polypeptide 1 (IGLL1).

A CAR described herein can comprise an antigen binding domain (e.g., antibody or antibody fragment, TCR or TCR fragment) that binds to a tumor-supporting antigen (e.g., a tumor-supporting antigen as described herein). In some embodiments, the tumor-supporting antigen is an antigen present on a stromal cell or a myeloid-derived suppressor cell (MDSC). Stromal cells can secrete growth factors to promote cell division in the microenvironment. MDSC cells can inhibit T cell proliferation and activation. Without wishing to be bound by theory, in some embodiments, the CAR-expressing cells destroy the tumor-supporting cells, thereby indirectly inhibiting tumor growth or survival.

In embodiments, the stromal cell antigen is chosen from one or more of: bone marrow stromal cell antigen 2 (BST2), fibroblast activation protein (FAP) and tenascin. In an embodiment, the FAP-specific antibody is, competes for binding with, or has the same CDRs as, sibrotuzumab. In embodiments, the MDSC antigen is chosen from one or more of: CD33, CD11b, C14, CD15, and CD66b. Accordingly, in

some embodiments, the tumor-supporting antigen is chosen from one or more of: bone marrow stromal cell antigen 2 (BST2), fibroblast activation protein (FAP) or tenascin, CD33, CD11b, C14, CD15, and CD66b.

Antigen Binding Domain Structures

In some embodiments, the antigen binding domain of the encoded CAR molecule comprises an antibody, an antibody fragment, an scFv, a Fv, a Fab, a (Fab')2, a single domain antibody (SDAB), a VH or VL domain, a camelid VHH domain or a bi-functional (e.g. bi-specific) hybrid antibody (e.g., Lanzavecchia et al., Eur. J. Immunol. 17, 105 (1987)).

In some instances, scFvs can be prepared according to method known in the art (see, for example, Bird et al., (1988) Science 242:423-426 and Huston et al., (1988) Proc. Natl. Acad. Sci. USA 85:5879-5883). ScFv molecules can be produced by linking VH and VL regions together using flexible polypeptide linkers. The scFv molecules comprise a linker (e.g., a Ser-Gly linker) with an optimized length and/or amino acid composition. The linker length can greatly affect how the variable regions of a scFv fold and interact. In fact, if a short polypeptide linker is employed (e.g., between 5-10 amino acids) intrachain folding is prevented. Interchain folding is also required to bring the two variable regions together to form a functional epitope binding site. For examples of linker orientation and size see, e.g., Hollinger et al. 1993 Proc Natl Acad. Sci. U.S.A. 90:6444-6448, U.S. Patent Application Publication Nos. 2005/0100543, 2005/0175606, 2007/0014794, and PCT publication Nos. WO2006/020258 and WO2007/024715, is incorporated herein by reference.

An scFv can comprise a linker of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45, 50, or more amino acid residues between its VL and VH regions. The linker sequence may comprise any naturally occurring amino acid. In some embodiments, the linker sequence comprises amino acids glycine and serine. In another embodiment, the linker sequence comprises sets of glycine and serine repeats such as $(Gly_4Ser)n$, where n is a positive integer equal to or greater than 1 (SEQ ID NO:6629). In one embodiment, the linker can be $(Gly_4Ser)_4$ (SEQ ID NO:6593) or $(Gly_4Ser)_3$(SEQ ID NO:6594). Variation in the linker length may retain or enhance activity, giving rise to superior efficacy in activity studies.

In another aspect, the antigen binding domain is a T cell receptor ("TCR"), or a fragment thereof, for example, a single chain TCR (scTCR). Methods to make such TCRs are known in the art. See, e.g., Willemsen RA et al, Gene Therapy 7: 1369–1377 (2000); Zhang T et al, Cancer Gene Ther 11: 487–496 (2004); Aggen et al, Gene Ther. 19(4):365-74 (2012) (references are incorporated herein by its entirety). For example, scTCR can be engineered that contains the Vα and Vβ genes from a T cell clone linked by a linker (e.g., a flexible peptide). This approach is very useful to cancer associated target that itself is

intracellar, however, a fragment of such antigen (peptide) is presented on the surface of the cancer cells by MHC.

In certain embodiments, the encoded antigen binding domain has a binding affinity KD of 10^{-4} M to 10^{-8} M.

In one embodiment, the encoded CAR molecule comprises an antigen binding domain that has a binding affinity KD of 10^{-4} M to 10^{-8} M, e.g., 10^{-5} M to 10^{-7} M, e.g., 10^{-6} M or 10^{-7} M, for the target antigen. In one embodiment, the antigen binding domain has a binding affinity that is at least five-fold, 10-fold, 20-fold, 30-fold, 50-fold, 100-fold or 1,000-fold less than a reference antibody, e.g., an antibody described herein. In one embodiment, the encoded antigen binding domain has a binding affinity at least 5-fold less than a reference antibody (e.g., an antibody from which the antigen binding domain is derived). In one aspect such antibody fragments are functional in that they provide a biological response that can include, but is not limited to, activation of an immune response, inhibition of signal-transduction origination from its target antigen, inhibition of kinase activity, and the like, as will be understood by a skilled artisan.

In one aspect, the antigen binding domain of the CAR is a scFv antibody fragment that is humanized compared to the murine sequence of the scFv from which it is derived.

In one aspect, the antigen binding domain of a CAR of the invention (e.g., a scFv) is encoded by a nucleic acid molecule whose sequence has been codon optimized for expression in a mammalian cell. In one aspect, entire CAR construct of the invention is encoded by a nucleic acid molecule whose entire sequence has been codon optimized for expression in a mammalian cell. Codon optimization refers to the discovery that the frequency of occurrence of synonymous codons (i.e., codons that code for the same amino acid) in coding DNA is biased in different species. Such codon degeneracy allows an identical polypeptide to be encoded by a variety of nucleotide sequences. A variety of codon optimization methods is known in the art, and include, e.g., methods disclosed in at least US Patent Numbers 5,786,464 and 6,114,148.

Antigen bidning domains (and the targeted antigens)

In one embodiment, an antigen binding domain against CD19 is an antigen binding portion, e.g., CDRs, of a CAR, antibody or antigen-binding fragment thereof described in, e.g., PCT publication WO2012/079000; PCT publication WO2014/153270; Kochenderfer, J.N. et al., J. Immunother. 32 (7), 689-702 (2009); Kochenderfer, J.N., et al., Blood, 116 (20), 4099-4102 (2010); PCT publication WO2014/031687; Bejcek, Cancer Research, 55, 2346-2351, 1995; or U.S. Patent No. 7,446,190.

In one embodiment, an antigen binding domain against mesothelin is an antigen binding portion, e.g., CDRs, of an antibody, antigen-binding fragment or CAR described in, e.g., PCT publication

WO2015/090230. In one embodiment, an antigen binding domain against mesothelin is an antigen binding portion, e.g., CDRs, of an antibody, antigen-binding fragment, or CAR described in, e.g., PCT publication WO1997/025068, WO1999/028471, WO2005/014652, WO2006/099141, WO2009/045957, WO2009/068204, WO2013/142034, WO2013/040557, or WO2013/063419. In one embodiment, an antigen binding domain against mesothelin is an antigen binding portion, e.g., CDRs, of an antibody, antigen-binding fragment, or CAR described in WO/2015/090230.

In one embodiment, an antigen binding domain against CD123 is an antigen binding portion, e.g., CDRs, of an antibody, antigen-binding fragment or CAR described in, e.g., PCT publication WO2014/130635. In one embodiment, an antigen binding domain against CD123 is an antigen binding portion, e.g., CDRs, of an antibody, antigen-binding fragment, or CAR described in, e.g., PCT publication WO2014/138805, WO2014/138819, WO2013/173820, WO2014/144622, WO2001/66139, WO2010/126066, WO2014/144622, or US2009/0252742. In one embodiment, an antigen binding domain against CD123 is an antigen binding portion, e.g., CDRs, of an antibody, antigen-binding fragment, or CAR described in WO/2016/028896.

Examples include CAR molecules which include an antigen binding domain, or a VL and VH (in the sequences below, separated by a (G4S)3 linker (SEQ ID NO: 6594)) of:

CD123-1:
QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGGTNYA
QKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARDMNILATVPFDIWGQGTMVTVSSGGG
GSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISTYLNWYQQKPGKAPNLLIYAAFS
LQSGVPSRFSGSGSGTDFTLTINSLQPEDFATYYCQQGDSVPLTFGGGTKLEIK (SEQ ID NO: 7812);

CD123-2:

QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGGTNYA
QKFQGRVTLTRDTSISTVYMELSRLRSDDTAVYYCARDMNILATVPFDIWGQGTMVTVSSGGGG
SGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSL
QSGVPSRFSGSGSGTDFTLTVNSLQPEDFATYYCQQGDSVPLTFGGGTRLEIK (SEQ ID NO: 7813);

CD123-3:

QVQLVQSGAEVKKPGASVKVSCKASGYIFTGYYIHWVRQAPGQGLEWMGWINPNSGGTNYAQ
KFQGRVTMTRDTSISTAYMELSGLRSDDPAVYYCARDMNILATVPFDIWGQGTLVTVSSGGGGS
GGGGSGGGGSDIQLTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQS

GVPSRFSGSGSGTDFTLTVNSLQPEDFATYYCQQGDSVPLTFGGGTKVEIK (SEQ ID NO: 7814); OR

CD123-4:

QVQLQQSGAEVKKSGASVKVSCKASGYTFTDYYMHWLRQAPGQGLEWMGWINPNSGDTNYA QKFQGRVTLTRDTSISTVYMELSRLRSDDTAVYYCARDMNILATVPFDIWGQGTMVTVSSASGG GGSGGRASGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAAS SLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGDSVPLTFGGGTKVEIK (SEQ ID NO: 7815), from WO2016/0028896.

The CAR comprising said anti-CD123 binding domain may comprise, for example, the amino acid sequence of:

CAR123-2:
MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAP GQGLEWMGWINPNSGGTNYAQKFQGRVTLTRDTSISTVYMELSRLRSDDTAVYYCARDMNILA TVPFDIWGQGTMVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYL NWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTVNSLQPEDFATYYCQQGDSVPLTF GGGTRLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCG VLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPA YKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 7816);

CAR123-3:

MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVSCKASGYIFTGYYIHWVRQAPG QGLEWMGWINPNSGGTNYAQKFQGRVTMTRDTSISTAYMELSGLRSDDPAVYYCARDMNILAT VPFDIWGQGTLVTVSSGGGGSGGGGSGGGGSDIQLTQSPSSLSASVGDRVTITCRASQSISSYLN WYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTVNSLQPEDFATYYCQQGDSVPLTFG GGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGV LLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY KQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 7817);

CAR123-4:

MALPVTALLLPLALLLHAARPQVQLQQSGAEVKKSGASVKVSCKASGYTFTDYYMHWLRQAP GQGLEWMGWINPNSGDTNYAQKFQGRVTLTRDTSISTVYMELSRLRSDDTAVYYCARDMNILA

TVPFDIWGQGTMVTVSSASGGGGSGGRASGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISS YLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGDSVPL TFGGGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGT CGVLLLSLVITLYCK (SEQ ID NO: 7818); OR

CAR123-1: malpvtalllplalllhaarpqvqlvqsgaevkkpgasvkvsckasgytftgyymhwvrqapgqglewmgwinpnsggtnyaqkfqgrvtmtr dtsistaymelsrlrsddtavyycardmnilatvpfdiwgqgtmvtvssggggsggggsggggsdiqmtqspsslsasvgdrvtitcrasqsistyln wyqqkpgkapnlliyaafslqsgvpsrfsgsgsgtdftltinslqpedfatyycqqgdsvpltfgggtkleikttttpaprpptpaptiasqplslrpeacr paaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapaykqg qnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeayseigmkgerrrgkghdglyqglstatkdtydalhmqalp pr (SEQ ID NO: 7819). In each case, the CAR may optionally comprise or not comprise the leader sequence included in each of the above sequences (MALPVTALLLPLALLLHAARP; SEQ ID NO: 6640).

In one embodiment, an antigen binding domain against EGFRvIII is an antigen binding portion, e.g., CDRs, of an antibody, antigen-binding fragment or CAR described in, e.g.,WO/2014/130657.

In one embodiment, an antigen binding domain against CD22 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Haso et al., Blood, 121(7): 1165-1174 (2013); Wayne et al., Clin Cancer Res 16(6): 1894-1903 (2010); Kato et al., Leuk Res 37(1):83-88 (2013); Creative BioMart (creativebiomart.net): MOM-18047-S(P).

In one embodiment, an antigen binding domain against CS-1 is an antigen binding portion, e.g., CDRs, of Elotuzumab (BMS), see e.g., Tai et al., 2008, Blood 112(4):1329-37; Tai et al., 2007, Blood. 110(5):1656-63.

In one embodiment, an antigen binding domain against CLL-1 is an antigen binding portion, e.g., CDRs, of an antibody available from R&D, ebiosciences, Abcam, for example, PE-CLL1-hu Cat# 353604 (BioLegend); and PE-CLL1 (CLEC12A) Cat# 562566 (BD). In one embodiment, an antigen binding domain against CLL-1 is an antigen binding portion, e.g., CDRs, of an antibody, antigen-binding fragment, or CAR described in WO/2016/014535.

In one embodiment, an antigen binding domain against CD33 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Bross et al., Clin Cancer Res 7(6):1490-1496 (2001) (Gemtuzumab Ozogamicin, hP67.6),Caron et al., Cancer Res 52(24):6761-6767 (1992) (Lintuzumab, HuM195), Lapusan et al., Invest New Drugs 30(3):1121-1131 (2012) (AVE9633), Aigner et al., Leukemia 27(5): 1107-1115 (2013) (AMG330, CD33 BiTE), Dutour et al., Adv hematol 2012:683065 (2012), and

Pizzitola et al., Leukemia doi:10.1038/Lue.2014.62 (2014). In one embodiment, an antigen binding domain against CD33 is an antigen binding portion, e.g., CDRs, of an antibody, antigen-binding fragment, or CAR described in WO/2016/014576.

In one embodiment, an antigen binding domain against GD2 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Mujoo et al., Cancer Res. 47(4):1098-1104 (1987); Cheung et al., Cancer Res 45(6):2642-2649 (1985), Cheung et al., J Clin Oncol 5(9):1430-1440 (1987), Cheung et al., J Clin Oncol 16(9):3053-3060 (1998), Handgretinger et al., Cancer Immunol Immunother 35(3):199-204 (1992). In some embodiments, an antigen binding domain against GD2 is an antigen binding portion of an antibody selected from mAb 14.18, 14G2a, ch14.18, hu14.18, 3F8, hu3F8, 3G6, 8B6, 60C3, 10B8, ME36.1, and 8H9, see e.g., WO2012033885, WO2013040371, WO2013192294, WO2013061273, WO2013123061, WO2013074916, and WO201385552. In some embodiments, an antigen binding domain against GD2 is an antigen binding portion of an antibody described in US Publication No.: 20100150910 or PCT Publication No.: WO 2011160119.

In one embodiment, an antigen binding domain against BCMA is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., WO2012163805, WO200112812, and WO2003062401. In one embodiment, an antigen binding domain against BCMA is an antigen binding portion, e.g., CDRs, of an antibody, antigen-binding fragment, or CAR described in WO/2016/014565.

In one embodiment, an antigen binding domain against Tn antigen is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., US8,440,798, Brooks et al., PNAS 107(22):10056-10061 (2010), and Stone et al., OncoImmunology 1(6):863-873(2012).

In one embodiment, an antigen binding domain against PSMA is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Parker et al., Protein Expr Purif 89(2):136-145 (2013), US 20110268656 (J591 ScFv); Frigerio et al, European J Cancer 49(9):2223-2232 (2013) (scFvD2B); WO 2006125481 (mAbs 3/A12, 3/E7 and 3/F11) and single chain antibody fragments (scFv A5 and D7).

In one embodiment, an antigen binding domain against ROR1 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Hudecek et al., Clin Cancer Res 19(12):3153-3164 (2013); WO 2011159847; and US20130101607.

In one embodiment, an antigen binding domain against FLT3 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., WO2011076922, US5777084, EP0754230, US20090297529, and several commercial catalog antibodies (R&D, ebiosciences, Abcam).

In one embodiment, an antigen binding domain against TAG72 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Hombach et al., Gastroenterology 113(4):1163-1170 (1997); and Abcam ab691.

In one embodiment, an antigen binding domain against FAP is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Ostermann et al., Clinical Cancer Research 14:4584-4592 (2008) (FAP5), US Pat. Publication No. 2009/0304718; sibrotuzumab (see e.g., Hofheinz et al., Oncology Research and Treatment 26(1), 2003); and Tran et al., J Exp Med 210(6):1125-1135 (2013).

In one embodiment, an antigen binding domain against CD38 is an antigen binding portion, e.g., CDRs, of daratumumab (see, e.g., Groen et al., Blood 116(21):1261-1262 (2010); MOR202 (see, e.g., US8,263,746); or antibodies described in US8,362,211.

In one embodiment, an antigen binding domain against CD44v6 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Casucci et al., Blood 122(20):3461-3472 (2013).

In one embodiment, an antigen binding domain against CEA is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Chmielewski et al., Gastoenterology 143(4):1095-1107 (2012).

In one embodiment, an antigen binding domain against EPCAM is an antigen binding portion, e.g., CDRS, of an antibody selected from MT110, EpCAM-CD3 bispecific Ab (see, e.g., clinicaltrials.gov/ct2/show/NCT00635596); Edrecolomab; 3622W94; ING-1; and adecatumumab (MT201).

In one embodiment, an antigen binding domain against PRSS21 is an antigen binding portion, e.g., CDRs, of an antibody described in US Patent No.: 8,080,650.

In one embodiment, an antigen binding domain against B7H3 is an antigen binding portion, e.g., CDRs, of an antibody MGA271 (Macrogenics).

In one embodiment, an antigen binding domain against KIT is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., US7915391, US20120288506 , and several commercial catalog antibodies.

In one embodiment, an antigen binding domain against IL-13Ra2 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., WO2008/146911, WO2004087758, several commercial catalog antibodies, and WO2004087758.

In one embodiment, an antigen binding domain against CD30 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., US7090843 B1, and EP0805871.

In one embodiment, an antigen binding domain against GD3 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., US7253263; US 8,207,308; US 20120276046; EP1013761; WO2005035577; and US6437098.

In one embodiment, an antigen binding domain against CD171 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Hong et al., J Immunother 37(2):93-104 (2014).

In one embodiment, an antigen binding domain against IL-11Ra is an antigen binding portion, e.g., CDRs, of an antibody available from Abcam (cat# ab55262) or Novus Biologicals (cat# EPR5446). In another embodiment, an antigen binding domain again IL-11Ra is a peptide, see, e.g., Huang et al., Cancer Res 72(1):271-281 (2012).

In one embodiment, an antigen binding domain against PSCA is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Morgenroth et al., Prostate 67(10):1121-1131 (2007) (scFv 7F5); Nejatollahi et al., J of Oncology 2013(2013), article ID 839831 (scFv C5-II); and US Pat Publication No. 20090311181.

In one embodiment, an antigen binding domain against VEGFR2 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Chinnasamy et al., J Clin Invest 120(11):3953-3968 (2010).

In one embodiment, an antigen binding domain against LewisY is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Kelly et al., Cancer Biother Radiopharm 23(4):411-423 (2008) (hu3S193 Ab (scFvs)); Dolezal et al., Protein Engineering 16(1):47-56 (2003) (NC10 scFv).

In one embodiment, an antigen binding domain against CD24 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Maliar et al., Gastroenterology 143(5):1375-1384 (2012).

In one embodiment, an antigen binding domain against PDGFR-beta is an antigen binding portion, e.g., CDRs, of an antibody Abcam ab32570.

In one embodiment, an antigen binding domain against SSEA-4 is an antigen binding portion, e.g., CDRs, of antibody MC813 (Cell Signaling), or other commercially available antibodies.

In one embodiment, an antigen binding domain against CD20 is an antigen binding portion, e.g., CDRs, of the antibody Rituximab, Ofatumumab, Ocrelizumab, Veltuzumab, or GA101.

In one embodiment, an antigen binding domain against Folate receptor alpha is an antigen binding portion, e.g., CDRs, of the antibody IMGN853, or an antibody described in US20120009181; US4851332, LK26: US5952484.

In one embodiment, an antigen binding domain against ERBB2 (Her2/neu) is an antigen binding portion, e.g., CDRs, of the antibody trastuzumab, or pertuzumab.

In one embodiment, an antigen binding domain against MUC1 is an antigen binding portion, e.g., CDRs, of the antibody SAR566658.

In one embodiment, the antigen binding domain against EGFR is antigen binding portion, e.g., CDRs, of the antibody cetuximab, panitumumab, zalutumumab, nimotuzumab, or matuzumab.

In one embodiment, an antigen binding domain against NCAM is an antigen binding portion, e.g., CDRs, of the antibody clone 2-2B: MAB5324 (EMD Millipore).

In one embodiment, an antigen binding domain against Ephrin B2 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Abengozar et al., Blood 119(19):4565-4576 (2012).

In one embodiment, an antigen binding domain against IGF-I receptor is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., US8344112 B2; EP2322550 A1; WO 2006/138315, or PCT/US2006/022995.

In one embodiment, an antigen binding domain against CAIX is an antigen binding portion, e.g., CDRs, of the antibody clone 303123 (R&D Systems).

In one embodiment, an antigen binding domain against LMP2 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., US7,410,640, or US20050129701.

In one embodiment, an antigen binding domain against gp100 is an antigen binding portion, e.g., CDRs, of the antibody HMB45, NKIbetaB, or an antibody described in WO2013165940, or US20130295007

In one embodiment, an antigen binding domain against tyrosinase is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., US5843674; or US19950504048.

In one embodiment, an antigen binding domain against EphA2 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Yu et al., Mol Ther 22(1):102-111 (2014).

In one embodiment, an antigen binding domain against GD3 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., US7253263; US 8,207,308; US 20120276046; EP1013761 A3; 20120276046; WO2005035577; or US6437098.

In one embodiment, an antigen binding domain against fucosyl GM1 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., US20100297138; or WO2007/067992.

In one embodiment, an antigen binding domain against sLe is an antigen binding portion, e.g., CDRs, of the antibody G193 (for lewis Y), see Scott AM et al, Cancer Res 60: 3254-61 (2000), also as described in Neeson et al, J Immunol May 2013 190 (Meeting Abstract Supplement) 177.10.

In one embodiment, an antigen binding domain against GM3 is an antigen binding portion, e.g., CDRs, of the antibody CA 2523449 (mAb 14F7).

In one embodiment, an antigen binding domain against HMWMAA is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Kmiecik et al., Oncoimmunology 3(1):e27185 (2014) (PMID: 24575382) (mAb9.2.27); US6528481; WO2010033866; or US 20140004124.

In one embodiment, an antigen binding domain against o-acetyl-GD2 is an antigen binding portion, e.g., CDRs, of the antibody 8B6.

In one embodiment, an antigen binding domain against TEM1/CD248 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Marty et al., Cancer Lett 235(2):298-308 (2006); Zhao et al., J Immunol Methods 363(2):221-232 (2011).

In one embodiment, an antigen binding domain against CLDN6 is an antigen binding portion, e.g., CDRs, of the antibody IMAB027 (Ganymed Pharmaceuticals), see e.g., clinicaltrial.gov/show/NCT02054351.

In one embodiment, an antigen binding domain against TSHR is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., US8,603,466; US8,501,415; or US8,309,693.

In one embodiment, an antigen binding domain against GPRC5D is an antigen binding portion, e.g., CDRs, of the antibody FAB6300A (R&D Systems); or LS-A4180 (Lifespan Biosciences).

In one embodiment, an antigen binding domain against CD97 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., US6,846,911;de Groot et al., J Immunol 183(6):4127-4134 (2009); or an antibody from R&D:MAB3734.

In one embodiment, an antigen binding domain against ALK is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Mino-Kenudson et al., Clin Cancer Res 16(5):1561-1571 (2010).

In one embodiment, an antigen binding domain against polysialic acid is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Nagae et al., J Biol Chem 288(47):33784-33796 (2013).

In one embodiment, an antigen binding domain against PLAC1 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Ghods et al., Biotechnol Appl Biochem 2013 doi:10.1002/bab.1177.

In one embodiment, an antigen binding domain against GloboH is an antigen binding portion of the antibody VK9; or an antibody described in, e.g., Kudryashov V et al, Glycoconj J.15(3):243-9 (1998), Lou et al., Proc Natl Acad Sci USA 111(7):2482-2487 (2014) ; MBr1: Bremer E-G et al. J Biol Chem 259:14773–14777 (1984).

In one embodiment, an antigen binding domain against NY-BR-1 is an antigen binding portion, e.g., CDRs of an antibody described in, e.g., Jager et al., Appl Immunohistochem Mol Morphol 15(1):77-83 (2007).

In one embodiment, an antigen binding domain against WT-1 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Dao et al., Sci Transl Med 5(176):176ra33 (2013); or WO2012/135854.

In one embodiment, an antigen binding domain against MAGE-A1 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Willemsen et al., J Immunol 174(12):7853-7858 (2005) (TCR-like scFv).

In one embodiment, an antigen binding domain against sperm protein 17 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Song et al., Target Oncol 2013 Aug 14 (PMID: 23943313); Song et al., Med Oncol 29(4):2923-2931 (2012).

In one embodiment, an antigen binding domain against Tie 2 is an antigen binding portion, e.g., CDRs, of the antibody AB33 (Cell Signaling Technology).

In one embodiment, an antigen binding domain against MAD-CT-2 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., PMID: 2450952; US7635753.

In one embodiment, an antigen binding domain against Fos-related antigen 1 is an antigen binding portion, e.g., CDRs, of the antibody 12F9 (Novus Biologicals).

In one embodiment, an antigen binding domain against MelanA/MART1 is an antigen binding portion, e.g., CDRs, of an antibody described in, EP2514766 A2; or US 7,749,719.

In one embodiment, an antigen binding domain against sarcoma translocation breakpoints is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Luo et al, EMBO Mol. Med. 4(6):453-461 (2012).

In one embodiment, an antigen binding domain against TRP-2 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Wang et al, J Exp Med. 184(6):2207-16 (1996).

In one embodiment, an antigen binding domain against CYP1B1 is an antigen binding portion, e.g., CDRs, of an antibody described in, e.g., Maecker et al, Blood 102 (9): 3287-3294 (2003).

In one embodiment, an antigen binding domain against RAGE-1 is an antigen binding portion, e.g., CDRs, of the antibody MAB5328 (EMD Millipore).

In one embodiment, an antigen binding domain against human telomerase reverse transcriptase is an antigen binding portion, e.g., CDRs, of the antibody cat no: LS-B95-100 (Lifespan Biosciences)

In one embodiment, an antigen binding domain against intestinal carboxyl esterase is an antigen binding portion, e.g., CDRs, of the antibody 4F12: cat no: LS-B6190-50 (Lifespan Biosciences).

In one embodiment, an antigen binding domain against mut hsp70-2 is an antigen binding portion, e.g., CDRs, of the antibody Lifespan Biosciences: monoclonal: cat no: LS-C133261-100 (Lifespan Biosciences).

In one embodiment, an antigen binding domain against CD79a is an antigen binding portion, e.g., CDRs, of the antibody Anti-CD79a antibody [HM47/A9] (ab3121), available from Abcam; antibody CD79A Antibody #3351 available from Cell Signalling Technology; or antibody HPA017748 - Anti-CD79A antibody produced in rabbit, available from Sigma Aldrich.

In one embodiment, an antigen binding domain against CD79b is an antigen binding portion, e.g., CDRs, of the antibody polatuzumab vedotin, anti-CD79b described in Dornan et al., "Therapeutic potential of an anti-CD79b antibody-drug conjugate, anti-CD79b-vc-MMAE, for the treatment of non-Hodgkin lymphoma" Blood. 2009 Sep 24;114(13):2721-9. doi: 10.1182/blood-2009-02-205500. Epub 2009 Jul 24, or the bispecific antibody Anti-CD79b/CD3 described in "4507 Pre-Clinical Characterization of T Cell-Dependent Bispecific Antibody Anti-CD79b/CD3 As a Potential Therapy for B Cell Malignancies" Abstracts of 56th ASH Annual Meeting and Exposition, San Francisco, CA December 6-9 2014.

In one embodiment, an antigen binding domain against CD72 is an antigen binding portion, e.g., CDRs, of the antibody J3-109 described in Myers, and Uckun, "An anti-CD72 immunotoxin against therapy-refractory B-lineage acute lymphoblastic leukemia." Leuk Lymphoma. 1995 Jun;18(1-2):119-22, or anti-CD72 (10D6.8.1, mIgG1) described in Polson et al., "Antibody-Drug Conjugates for the Treatment of Non–Hodgkin's Lymphoma: Target and Linker-Drug Selection" Cancer Res March 15, 2009 69; 2358.

In one embodiment, an antigen binding domain against LAIR1 is an antigen binding portion, e.g., CDRs, of the antibody ANT-301 LAIR1 antibody, available from ProSpec; or anti-human CD305 (LAIR1) Antibody, available from BioLegend.

In one embodiment, an antigen binding domain against FCAR is an antigen binding portion, e.g., CDRs, of the antibody CD89/FCARAntibody (Catalog#10414-H08H), available from Sino Biological Inc.

In one embodiment, an antigen binding domain against LILRA2 is an antigen binding portion, e.g., CDRs, of the antibody LILRA2 monoclonal antibody (M17), clone 3C7, available from Abnova, or Mouse Anti-LILRA2 antibody, Monoclonal (2D7), available from Lifespan Biosciences..

In one embodiment, an antigen binding domain against CD300LF is an antigen binding portion, e.g., CDRs, of the antibody Mouse Anti-CMRF35-like molecule 1 antibody, Monoclonal[UP-D2, available

from BioLegend, or Rat Anti-CMRF35-like molecule 1 antibody, Monoclonal[234903], available from R&D Systems.

In one embodiment, an antigen binding domain against CLEC12A is an antigen binding portion, e.g., CDRs, of the antibody Bispecific T cell Engager (BiTE) scFv-antibody and ADC described in Noordhuis et al., "Targeting of CLEC12A In Acute Myeloid Leukemia by Antibody-Drug-Conjugates and Bispecific CLL-1xCD3 BiTE Antibody" 53rd ASH Annual Meeting and Exposition, December 10-13, 2011, and MCLA-117 (Merus).

In one embodiment, an antigen binding domain against BST2 (also called CD317) is an antigen binding portion, e.g., CDRs, of the antibody Mouse Anti-CD317 antibody, Monoclonal[3H4], available from Antibodies-Online or Mouse Anti-CD317 antibody, Monoclonal [696739], available from R&D Systems.

In one embodiment, an antigen binding domain against EMR2 (also called CD312) is an antigen binding portion, e.g., CDRs, of the antibody Mouse Anti-CD312 antibody, Monoclonal[LS-B8033] available from Lifespan Biosciences, or Mouse Anti-CD312 antibody, Monoclonal [494025] available from R&D Systems.

In one embodiment, an antigen binding domain against LY75 is an antigen binding portion, e.g., CDRs, of the antibody Mouse Anti-Lymphocyte antigen 75 antibody, Monoclonal[HD30] available from EMD Millipore or Mouse Anti-Lymphocyte antigen 75 antibody, Monoclonal[A15797] available from Life Technologies.

In one embodiment, an antigen binding domain against GPC3 is an antigen binding portion, e.g., CDRs, of the antibody hGC33 described in Nakano K, Ishiguro T, Konishi H, et al. Generation of a humanized anti-glypican 3 antibody by CDR grafting and stability optimization. Anticancer Drugs. 2010 Nov;21(10):907–916, or MDX-1414, HN3, or YP7, all three of which are described in Feng et al., "Glypican-3 antibodies: a new therapeutic target for liver cancer." FEBS Lett. 2014 Jan 21;588(2):377-82.

In one embodiment, an antigen binding domain against FCRL5 is an antigen binding portion, e.g., CDRs, of the anti-FcRL5 antibody described in Elkins et al., "FcRL5 as a target of antibody-drug conjugates for the treatment of multiple myeloma" Mol Cancer Ther. 2012 Oct;11(10):2222-32. In one embodiment, an antigen binding domain against FCRL5 is an antigen binding portion, e.g., CDRs, of the anti-FcRL5 antibody described in, for example, WO2001/038490, WO/2005/117986, WO2006/039238, WO2006/076691, WO2010/114940, WO2010/120561, or WO2014/210064.

In one embodiment, an antigen binding domain against IGLL1 is an antigen binding portion, e.g., CDRs, of the antibody Mouse Anti-Immunoglobulin lambda-like polypeptide 1 antibody, Monoclonal[AT1G4]

available from Lifespan Biosciences, Mouse Anti-Immunoglobulin lambda-like polypeptide 1 antibody, Monoclonal[HSL11] available from BioLegend.

In one embodiment, the antigen binding domain comprises one, two three (e.g., all three) heavy chain CDRs, HC CDR1, HC CDR2 and HC CDR3, from an antibody listed above, and/or one, two, three (e.g., all three) light chain CDRs, LC CDR1, LC CDR2 and LC CDR3, from an antibody listed above. In one embodiment, the antigen binding domain comprises a heavy chain variable region and/or a variable light chain region of an antibody listed above.

In another aspect, the antigen binding domain comprises a humanized antibody or an antibody fragment. In some aspects, a non-human antibody is humanized, where specific sequences or regions of the antibody are modified to increase similarity to an antibody naturally produced in a human or fragment thereof. In one aspect, the antigen binding domain is humanized.

In an embodiment, the antigen-binding domain of a CAR, e.g., a CAR expressed by a cell of the invention, binds to CD19. CD19 is found on B cells throughout differentiation of the lineage from the pro/pre-B cell stage through the terminally differentiated plasma cell stage. In an embodiment, the antigen binding domain is a murine scFv domain that binds to human CD19, e.g., the antigen binding domain of CTL019 (e.g., SEQ ID NO: 7895). In an embodiment, the antigen binding domain is a humanized antibody or antibody fragment, e.g., scFv domain, derived from the murine CTL019 scFv. In an embodiment, the antigen binding domain is a human antibody or antibody fragment that binds to human CD19. Exemplary scFv domains (and their sequences, e.g., CDRs, VL and VH sequences) that bind to CD19 are provided in Table 14. The scFv domain sequences provided in Table 14 include a light chain variable region (VL) and a heavy chain variable region (VH). The VL and VH are attached by a linker comprising the sequence GGGGSGGGGSGGGGS (SEQ ID NO: 6594), e.g., in the following orientation: VL-linker-VH.

Table 14. Antigen Binding domains that bind CD19

Antigen	Name	Amino Acid Sequence	SEQ ID NO:
CD19	muCTL019	DIQMTQTTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGGSYAMDYWGQGTSVTVSS	7895
CD19	huscFv1	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPY	7883

		TFGQGTKLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSLTC TVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYSSSLKSRVTIS KDNSKNQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTV SS	
CD19	huscFv2	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLI YHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPY TFGQGTKLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSLTC TVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYQSSLKSRVTIS KDNSKNQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTV SS	7884
CD19	huscFv3	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWI GVIWGSETTYYSSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCA KHYYYGGSYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSEIVMTQSPA TLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSG IPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQGTKLE IK	7885
CD19	huscFv4	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWI GVIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCA KHYYYGGSYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSEIVMTQSPA TLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSG IPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQGTKLE IK	7886
CD19	huscFv5	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLI YHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPY TFGQGTKLEIKGGGGSGGGGSGGGGSGGGGSQVQLQESGPGLVKPSET LSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYSSSLKS RVTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQG TLVTVSS	7887
CD19	huscFv6	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLI YHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPY TFGQGTKLEIKGGGGSGGGGSGGGGSGGGGSQVQLQESGPGLVKPSET LSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYQSSLKS RVTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQG TLVTVSS	7888
CD19	huscFv7	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWI GVIWGSETTYYSSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCA KHYYYGGSYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSGGGGSEIVM TQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLIYHTS RLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQ GTKLEIK	7889
CD19	huscFv8	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWI GVIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCA KHYYYGGSYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSGGGGSEIVM TQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLIYHTS RLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQ	7890

		GTKLEIK	
CD19	huscFv9	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLI YHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPY TFGQGTKLEIKGGGGSGGGGSGGGGSGGGGSQVQLQESGPGLVKPSET LSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYNSSLKS RVTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQG TLVTVSS	7891
CD19	Hu scFv10	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWI GVIWGSETTYYNSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCA KHYYYGGSYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVM TQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLIYHTS RLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQ GTKLEIK	7892
CD19	Hu scFv11	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLI YHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPY TFGQGTKLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSLTC TVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYNSSLKSRVTIS KDNSKNQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTV SS	7893
CD19	Hu scFv12	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWI GVIWGSETTYYNSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCA KHYYYGGSYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVMTQSPA TLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSG IPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQGTKLE IK	7894

The sequences of the CDR sequences of the scFv domains of the CD19 antigen binding domains provided in Table 14 are shown in Table 15 for the heavy chain variable domains and in Table 16 for the light chain variable domains. "ID" stands for the respective SEQ ID NO for each CDR.

Table 15. Heavy Chain Variable Domain CDRs

Description	FW	HCDR1	ID	HCDR2	ID	HCDR3	ID
murine_CART19		GVSLPDYGVS	7899	VIWGSETTYYNSALKS	7900	HYYYGGSYAMDY	7904
humanized_CART19 a	VH4	GVSLPDYGVS	7899	VIWGSETTYY***S***S***S***LKS	7901	HYYYGGSYAMDY	7904
humanized_CART19 b	VH4	GVSLPDYGVS	7899	VIWGSETTYY***Q***S***S***LKS	7902	HYYYGGSYAMDY	7904
humanized_CART19 c	VH4	GVSLPDYGVS	7899	VIWGSETTYYNS***S***LKS	7903	HYYYGGSYAMDY	7904

Table 16. Light Chain Variable Domain CDRs

Description	FW	LCDR1	ID	LCDR2	ID	LCDR3	ID
murine_CART19		RASQDISKYLN	7905	HTSRLHS	7906	QQGNTLPYT	7907
humanized_CART19 a	VK3	RASQDISKYLN	7905	HTSRLHS	7906	QQGNTLPYT	7907
humanized_CART19 b	VK3	RASQDISKYLN	7905	HTSRLHS	7906	QQGNTLPYT	7907
humanized_CART19 c	VK3	RASQDISKYLN	7905	HTSRLHS	7906	QQGNTLPYT	7907

In an embodiment, the antigen binding domain comprises an anti-CD19 antibody, or fragment thereof, e.g., an scFv. For example, the antigen binding domain comprises a variable heavy chain and a variable light chain listed in Table 17. The linker sequence joining the variable heavy and variable light chains can be any of the linker sequences described herein, or alternatively, can be GSTSGSGKPGSGEGSTKG (SEQ ID NO: 8167). The light chain variable region and heavy chain variable region of a scFv can be, e.g., in any of the following orientations: light chain variable region-linker-heavy chain variable region or heavy chain variable region-linker-light chain variable region.

Table 17. Additional Anti-CD19 antibody binding domains

Ab Name	VH Sequence	VL Sequence
SJ25-C1	QVQLLESGAELVRPGSSVKISCKASG YAFSSYWMNWVKQRPGQGLEWIGQIY PGDGDTNYNGKFKGQATLTADKSSST AYMQLSGLTSEDSAVYSCARKTISSV VDFYFDYWGQGTTVT (SEQ ID NO: 7896)	ELVLTQSPKFMSTSVGDRVSVTCKASQNV GTNVAWYQQKPGQSPKPLIYSATYRNSGV PDRFTGSGSGTDFTLTITNVQSKDLADYF YFCQYNRYPYTSGGGTKLEIKRRS (SEQ ID NO: 7897)
	ScFv Sequence	
SJ25-C1 scFv	QVQLLESGAELVRPGSSVKISCKASGYAFSSYWMNWVKQRPGQGLEWIGQIYPGDGD TNYNGKFKGQATLTADKSSSTAYMQLSGLTSEDSAVYSCARKTISSVVDFYFDYWGQ GTTVTGSTSGSGKPGSGEGSTKGELVLTQSPKFMSTSVGDRVSVTCKASQNVGTNVA WYQQKPGQSPKPLIYSATYRNSGVPDRFTGSGSGTDFTLTITNVQSKDLADYFYFCQ YNRYPYTSGGGTKLEIKRRS (SEQ ID NO: 7898)	

In one embodiment, the CD19 binding domain comprises one or more (e.g., all three) light chain complementary determining region 1 (LC CDR1), light chain complementary determining region 2 (LC CDR2), and light chain complementary determining region 3 (LC CDR3) of a CD19 binding domain described herein, e.g., provided in Table 14 or 15, and/or one or more (e.g., all three) heavy chain

complementary determining region 1 (HC CDR1), heavy chain complementary determining region 2 (HC CDR2), and heavy chain complementary determining region 3 (HC CDR3) of a CD19 binding domain described herein, e.g., provided in Table 14 or 16. In one embodiment, the CD19 binding domain comprises one, two, or all of LC CDR1, LC CDR2, and LC CDR3 of any amino acid sequences as provided in Table 16, incorporated herein by reference; and one, two or all of HC CDR1, HC CDR2, and HC CDR3 of any amino acid sequences as provided in Table 15.

In one embodiment, the CD19 antigen binding domain comprises:

(i) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 7905, a LC CDR2 amino acid sequence of SEQ ID NO: 7906, and a LC CDR3 amino acid sequence of SEQ ID NO: 7907; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 7899, a HC CDR2 amino acid sequence of SEQ ID NO: 7900, and a HC CDR3 amino acid sequence of SEQ ID NO: 7904

(ii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 7905, a LC CDR2 amino acid sequence of SEQ ID NO: 7906, and a LC CDR3 amino acid sequence of SEQ ID NO: 7907; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 7899, a HC CDR2 amino acid sequence of SEQ ID NO: 7901, and a HC CDR3 amino acid sequence of SEQ ID NO: 7904;

(iii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 7905, a LC CDR2 amino acid sequence of SEQ ID NO: 7906, and a LC CDR3 amino acid sequence of SEQ ID NO: 7907; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 7899, a HC CDR2 amino acid sequence of SEQ ID NO: 7902, and a HC CDR3 amino acid sequence of SEQ ID NO: 7904; or

(iv) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 7905, a LC CDR2 amino acid sequence of SEQ ID NO: 7906, and a LC CDR3 amino acid sequence of SEQ ID NO: 7907; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 7899, a HC CDR2 amino acid sequence of SEQ ID NO: 7903, and a HC CDR3 amino acid sequence of SEQ ID NO: 7904.

In one embodiment, the CD19 binding domain comprises a light chain variable region described herein (e.g., in Table 14 or 17) and/or a heavy chain variable region described herein (e.g., in Table 14 or 17). In one embodiment, the CD19 binding domain is a scFv comprising a light chain and a heavy chain of an amino acid sequence listed in Table 14 or 17. In an embodiment, the CD19 binding domain (e.g., an scFv) comprises: a light chain variable region comprising an amino acid sequence having at least one, two or three modifications (e.g., substitutions, e.g., conservative substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions, e.g., conservative substitutions) of an amino acid sequence of a light chain variable region provided in Table 14 or 17, or a sequence with 95-99% identity with an amino acid sequence provided in Table 14 or 17; and/or a heavy chain variable region comprising an amino acid sequence having at least one, two or three modifications (e.g., substitutions, e.g., conservative

substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions, e.g., conservative substitutions) of an amino acid sequence of a heavy chain variable region provided in Table 14 or 17, or a sequence with 95-99% identity to an amino acid sequence provided in Table 14 or 17.

In one embodiment, the CD19 binding domain comprises an amino acid sequence selected from a group consisting of SEQ ID NO: 7883; SEQ ID NO: 7884, SEQ ID NO: 7885; SEQ ID NO: 7886; SEQ ID NO: 7887; SEQ ID NO: 7888; SEQ ID NO: 7889, SEQ ID NO: 7890, SEQ ID NO: 7891, SEQ ID NO: 7892, SEQ ID NO: 7893, SEQ ID NO: 7894, SEQ ID NO: 7895, and SEQ ID NO: 7898; or an amino acid sequence having at least one, two or three modifications (e.g., substitutions, e.g., conservative substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions, e.g., conservative substitutions) to any of the aforesaid sequences; or a sequence with 95-99% identity to any of the aforesaid sequences. In one embodiment, the CD19 binding domain is a scFv, and a light chain variable region comprising an amino acid sequence described herein, e.g., in Table 14 or 17, is attached to a heavy chain variable region comprising an amino acid sequence described herein, e.g., in Table 14 or 17, via a linker, e.g., a linker described herein. In one embodiment, the CD19 binding domain includes a (Gly4-Ser)n linker, wherein n is 1, 2, 3, 4, 5, or 6, preferably 3 (SEQ ID NO: 10801). The light chain variable region and heavy chain variable region of a scFv can be, e.g., in any of the following orientations: light chain variable region-linker-heavy chain variable region or heavy chain variable region-linker-light chain variable region.

Any known CD19 CAR, e.g., the CD19 antigen binding domain of any known CD19 CAR, in the art can be used in accordance with the instant invention to construct a CAR. For example, LG-740; CD19 CAR described in the US Pat. No. 8,399,645; US Pat. No. 7,446,190; Xu et al., Leuk Lymphoma. 2013 54(2):255-260(2012); Cruz et al., Blood 122(17):2965-2973 (2013); Brentjens et al., Blood, 118(18):4817-4828 (2011); Kochenderfer et al., Blood 116(20):4099-102 (2010); Kochenderfer et al., Blood 122 (25):4129-39(2013); and 16th Annu Meet Am Soc Gen Cell Ther (ASGCT) (May 15-18, Salt Lake City) 2013, Abst 10. In one embodiment, an antigen binding domain against CD19 is an antigen binding portion, e.g., CDRs, of a CAR, antibody or antigen-binding fragment thereof described in, e.g., PCT publication WO2012/079000; PCT publication WO2014/153270; Kochenderfer, J.N. et al., J. Immunother. 32 (7), 689-702 (2009); Kochenderfer, J.N., et al., Blood, 116 (20), 4099-4102 (2010); PCT publication WO2014/031687; Bejcek, Cancer Research, 55, 2346-2351, 1995; or U.S. Patent No. 7,446,190.

In an embodiment, the antigen-binding domain of CAR, e.g., a CAR expressed by a cell of the invention, binds to BCMA. BCMA is found preferentially expressed in mature B lymphocytes. In an

embodiment, the antigen binding domain is a murine scFv domain that binds to human BCMA. In an embodiment, the antigen binding domain is a humanized antibody or antibody fragment, e.g., scFv domain, that binds human BCMA. In an embodiment, the antigen binding domain is a human antibody or antibody fragment that binds to human BCMA. Exemplary scFv domains (and their sequences, e.g., CDRs, VL and VH sequences) that bind to BCMA are provided in Table 18, Table 19, Table 20 and Table 21. The scFv domain sequences provided in Table 18 and Table 19 include a light chain variable region (VL) and a heavy chain variable region (VH). The VL and VH are attached by a linker, e.g., in the following orientation: VH-linker-VL.

Table 18. Antigen Binding domains that bind BCMA

The amino acid sequences variable heavy chain and variable light chain sequences for each scFv is also provided.

Name/ Description	SEQ ID NO:	Sequence
139109		
139109- aa ScFv domain	7949	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSSASGGGGSGGRASGGGGSDIQLTQSPSSLSASVGDR VTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSG TDFTLTISSLQPEDFATYYCQQSYSTPYTFGQGTKVEIK
139109- nt ScFv domain	7964	GAAGTGCAATTGGTGGAATCAGGGGGAGGACTTGTGCAGCCTGGAGGATC GCTGAGACTGTCATGTGCCGTGTCCGGCTTTGCCCTGTCCAACCACGGGA TGTCCTGGGTCCGCCGCGCGCCTGGAAAGGGCCTCGAATGGGTGTCGGGT ATTGTGTACAGCGGTAGCACCTACTATGCCGCATCCGTGAAGGGGAGATT CACCATCAGCCGGGACAACTCCAGGAACACTCTGTACCTCCAAATGAATT CGCTGAGGCCAGAGGACACTGCCATCTACTACTGCTCCGCGCATGGCGGA GAGTCCGACGTCTGGGGACAGGGGACCACCGTGACCGTGTCTAGCGCGTC CGGCGGAGGCGGCAGCGGGGGTCGGGCATCAGGGGGCGGCGGATCGGACA TCCAGCTCACCCAGTCCCCGAGCTCGCTGTCCGCCTCCGTGGGAGATCGG GTCACCATCACGTGCCGCGCCAGCCAGTCGATTTCCTCCTACCTGAACTG GTACCAACAGAAGCCCGGAAAAGCCCCGAAGCTTCTCATCTACGCCGCCT CGAGCCTGCAGTCAGGAGTGCCCTCACGGTTCTCCGGCTCCGGTTCCGGT ACTGATTTCACCCTGACCATTTCCTCCCTGCAACCGGAGGACTTCGCTAC TTACTACTGCCAGCAGTCGTACTCCACCCCCTACACTTTCGGACAAGGCA CCAAGGTCGAAATCAAG
139109- aa VH	7979	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSS
139109- aa	7994	DIQLTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYA

VL		ASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPYTFGQ GTKVEIK
139103		
139103- aa ScFv domain	7939	QVQLVESGGGLVQPGRSLRLSCAASGFTFSNYAMSWVRQAPGKGLGWVSG ISRSGENTYYADSVKGRFTISRDNSKNTLYLQMNSLRDEDTAVYYCARSP AHYYGGMDVWGQGTTVTVSSASGGGGSGGRASGGGGSDIVLTQSPGTLSL SPGERATLSCRASQSISSSFLAWYQQKPGQAPRLLIYGASRRATGIPDRF SGSGSGTDFTLTISRLEPEDSAVYYCQQYHSSPSWTFGQGTKLEIK
139103- nt ScFv domain	7954	CAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGTGCAACCCGGAAGATC GCTTAGACTGTCGTGTGCCGCCAGCGGGTTCACTTTCTCGAACTACGCGA TGTCCTGGGTCCGCCAGGCACCCGGAAAGGGACTCGGTTGGGTGTCCGGC ATTTCCCGGTCCGGCGAAAATACCTACTACGCCGACTCCGTGAAGGGCCG CTTCACCATCTCAAGGGACAACAGCAAAAACACCCTGTACTTGCAAATGA ACTCCCTGCGGGATGAAGATACAGCCGTGTACTATTGCGCCCGGTCGCCT GCCCATTACTACGGCGGAATGGACGTCTGGGGACAGGGAACCACTGTGAC TGTCAGCAGCGCGTCGGGTGGCGGCGGCTCAGGGGGTCGGGCCTCCGGGG GGGGAGGGTCCGACATCGTGCTGACCCAGTCCCCGGGAACCCTGAGCCTG AGCCCGGGAGAGCGCGCGACCCTGTCATGCCGGGCATCCCAGAGCATTAG CTCCTCCTTTCTCGCCTGGTATCAGCAGAAGCCCGGACAGGCCCCGAGGC TGCTGATCTACGGCGCTAGCAGAAGGGCTACCGGAATCCCAGACCGGTTC TCCGGCTCCGGTTCCGGGACCGATTTCACCCTTACTATCTCGCGCCTGGA ACCTGAGGACTCCGCCGTCTACTACTGCCAGCAGTACCACTCATCCCCGT CGTGGACGTTCGGACAGGGCACCAAGCTGGAGATTAAG
139103- aa VH	7969	QVQLVESGGGLVQPGRSLRLSCAASGFTFSNYAMSWVRQAPGKGLGWVSG ISRSGENTYYADSVKGRFTISRDNSKNTLYLQMNSLRDEDTAVYYCARSP AHYYGGMDVWGQGTTVTVSS
139103- aa VL	7984	DIVLTQSPGTLSLSPGERATLSCRASQSISSSFLAWYQQKPGQAPRLLIY GASRRATGIPDRFSGSGSGTDFTLTISRLEPEDSAVYYCQQYHSSPSWTF GQGTKLEIK
139105		
139105- aa ScFv domain	7940	QVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSG ISWNSGSIGYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTALYYCSVHS FLAYWGQGTLVTVSSASGGGGSGGRASGGGGSDIVMTQTPLSLPVTPGEP ASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFS GSGSGTDFTLKISRVEAEDVGVYYCMQALQTPYTFGQGTKVEIK
139105- nt ScFv domain	7955	CAAGTGCAACTCGTCGAATCCGGTGGAGGTCTGGTCCAACCTGGTAGAAG CCTGAGACTGTCGTGTGCGGCCAGCGGATTCACCTTTGATGACTATGCTA TGCACTGGGTGCGGCAGGCCCCAGGAAAGGGCCTGGAATGGGTGTCGGGA ATTAGCTGGAACTCCGGGTCCATTGGCTACGCCGACTCCGTGAAGGGCCG CTTCACCATCTCCCGCGACAACGCAAAGAACTCCCTGTACTTGCAAATGA ACTCGCTCAGGGCTGAGGATACCGCGCTGTACTACTGCTCCGTGCATTCC TTCCTGGCCTACTGGGGACAGGGAACTCTGGTCACCGTGTCGAGCGCCTC CGGCGGCGGGGGCTCGGGTGGACGGGCCTCGGGCGGAGGGGGGTCCGACA TCGTGATGACCCAGACCCCGCTGAGCTTGCCCGTGACTCCCGGAGAGCCT GCATCCATCTCCTGCCGGTCATCCCAGTCCCTTCTCCACTCCAACGGATA

		CAACTACCTCGACTGGTACCTCCAGAAGCCGGGACAGAGCCCTCAGCTTC TGATCTACCTGGGGTCAAATAGAGCCTCAGGAGTGCCGGATCGGTTCAGC GGATCTGGTTCGGGAACTGATTTCACTCTGAAGATTTCCCGCGTGGAAGC CGAGGACGTGGGCGTCTACTACTGTATGCAGGCGCTGCAGACCCCCTATA CCTTCGGCCAAGGGACGAAAGTGGAGATCAAG
139105- aa **VH**	7970	QVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSG ISWNSGSIGYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTALYYCSVHS FLAYWGQGTLVTVSS
139105- aa **VL**	7985	DIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQ LLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP YTFGQGTKVEIK
139111		
139111- aa **ScFv domain**	7941	EVQLLESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSSASGGGGSGGRASGGGGSDIVMTQTPLSLSVTPGQP ASISCKSSQSLLRNDGKTPLYWYLQKAGQPPQLLIYEVSNRFSGVPDRFS GSGSGTDFTLKISRVEAEDVGAYYCMQNIQFPSFGGGTKLEIK
139111- nt **ScFv domain**	7956	GAAGTGCAATTGTTGGAATCTGGAGGAGGACTTGTGCAGCCTGGAGGATC ACTGAGACTTTCGTGTGCGGTGTCAGGCTTCGCCCTGAGCAACCACGGCA TGAGCTGGGTGCGGAGAGCCCCGGGGAAGGGTCTGGAATGGGTGTCCGGG ATCGTCTACTCCGGTTCAACTTACTACGCCGCAAGCGTGAAGGGTCGCTT CACCATTTCCCGCGATAACTCCCGGAACACCCTGTACCTCCAAATGAACT CCCTGCGGCCCGAGGACACCGCCATCTACTACTGTTCCGCGCATGGAGGA GAGTCCGATGTCTGGGGACAGGGCACTACCGTGACCGTGTCGAGCGCCTC GGGGGGAGGAGGCTCCGGCGGTCGCGCCTCCGGGGGGGGTGGCAGCGACA TTGTGATGACGCAGACTCCACTCTCGCTGTCCGTGACCCCGGGACAGCCC GCGTCCATCTCGTGCAAGAGCTCCCAGAGCCTGCTGAGGAACGACGGAAA GACTCCTCTGTATTGGTACCTCCAGAAGGCTGGACAGCCCCCGCAACTGC TCATCTACGAAGTGTCAAATCGCTTCTCCGGGGTGCCGGATCGGTTTTCC GGCTCGGGATCGGGCACCGACTTCACCCTGAAAATCTCCAGGGTCGAGGC CGAGGACGTGGGAGCCTACTACTGCATGCAAAACATCCAGTTCCCTTCCT TCGGCGGCGGCACAAAGCTGGAGATTAAG
139111- aa **VH**	7971	EVQLLESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSS
139111- aa **VL**	7986	DIVMTQTPLSLSVTPGQPASISCKSSQSLLRNDGKTPLYWYLQKAGQPPQ LLIYEVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGAYYCMQNIQFP SFGGGTKLEIK
139100		
139100- aa **ScFv domain**	7942	QVQLVQSGAEVRKTGASVKVSCKASGYIFDNFGINWVRQAPGQGLEWMGW INPKNNNTNYAQKFQGRVTITADESTNTAYMEVSSLRSEDTAVYYCARGP YYYQSYMDVWGQGTMVTVSSASGGGGSGGRASGGGGSDIVMTQTPLSLPV TPGEPASISCRSSQSLLHSNGYNYLNWYLQKPGQSPQLLIYLGSKRASGV

		PDRFSGSGSGTDFTLHITRVGAEDVGVYYCMQALQTPYTFGQGTKLEIK
139100- nt **ScFv domain**	7957	CAAGTCCAACTCGTCCAGTCCGGCGCAGAAGTCAGAAAAACCGGTGCTAG CGTGAAAGTGTCCTGCAAGGCCTCCGGCTACATTTTCGATAACTTCGGAA TCAACTGGGTCAGACAGGCCCCGGGCCAGGGGCTGGAATGGATGGGATGG ATCAACCCCAAGAACAACAACACCAACTACGCACAGAAGTTCCAGGGCCG CGTGACTATCACCGCCGATGAATCGACCAATACCGCCTACATGGAGGTGT CCTCCCTGCGGTCGGAGGACACTGCCGTGTATTACTGCGCGAGGGGCCCA TACTACTACCAAAGCTACATGGACGTCTGGGGACAGGGAACCATGGTGAC CGTGTCATCCGCCTCCGGTGGTGGAGGCTCCGGGGGGCGGGCTTCAGGAG GCGGAGGAAGCGATATTGTGATGACCCAGACTCCGCTTAGCCTGCCCGTG ACTCCTGGAGAACCGGCCTCCATTTCCTGCCGGTCCTCGCAATCACTCCT GCATTCCAACGGTTACAACTACCTGAATTGGTACCTCCAGAAGCCTGGCC AGTCGCCCCAGTTGCTGATCTATCTGGGCTCGAAGCGCGCCTCCGGGGTG CCTGACCGGTTTAGCGGATCTGGGAGCGGCACGGACTTCACTCTCCACAT CACCCGCGTGGGAGCGGAGGACGTGGGAGTGTACTACTGTATGCAGGCGC TGCAGACTCCGTACACATTCGGACAGGGCACCAAGCTGGAGATCAAG
139100- aa **VH**	7972	QVQLVQSGAEVRKTGASVKVSCKASGYIFDNFGINWVRQAPGQGLEWMGW INPKNNNTNYAQKFQGRVTITADESTNTAYMEVSSLRSEDTAVYYCARGP YYYQSYMDVWGQGTMVTVSS
139100- aa **VL**	7987	DIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYLNWYLQKPGQSPQ LLIYLGSKRASGVPDRFSGSGSGTDFTLHITRVGAEDVGVYYCMQALQTP YTFGQGTKLEIK
139101		
139101- aa **ScFv domain**	7943	QVQLQESGGGLVQPGGSLRLSCAASGFTFSSDAMTWVRQAPGKGLEWVSV ISGSGGTTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKLD SSGYYYARGPRYWGQGTLVTVSSASGGGGSGGRASGGGGSDIQLTQSPSS LSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYGASTLASGVPA RFSGSGSGTHFTLTINSLQSEDSATYYCQQSYKRASFGQGTKVEIK
139101- nt **ScFv domain**	7958	CAAGTGCAACTTCAAGAATCAGGCGGAGGACTCGTGCAGCCCGGAGGATC ATTGCGGCTCTCGTGCGCCGCCTCGGGCTTCACCTTCTCGAGCGACGCCA TGACCTGGGTCCGCCAGGCCCCGGGGAAGGGGCTGGAATGGGTGTCTGTG ATTTCCGGCTCCGGGGGAACTACGTACTACGCCGATTCCGTGAAAGGTCG CTTCACTATCTCCCGGGACAACAGCAAGAACACCCTTTATCTGCAAATGA ATTCCCTCCGCGCCGAGGACACCGCCGTGTACTACTGCGCCAAGCTGGAC TCCTCGGGCTACTACTATGCCCGGGGTCCGAGATACTGGGGACAGGGAAC CCTCGTGACCGTGTCCTCCGCGTCCGGCGGAGGAGGGTCGGGAGGGCGGG CCTCCGGCGGCGGCGGTTCGGACATCCAGCTGACCCAGTCCCCATCCTCA CTGAGCGCAAGCGTGGGCGACAGAGTCACCATTACATGCAGGGCGTCCCA GAGCATCAGCTCCTACCTGAACTGGTACCAACAGAAGCCTGGAAAGGCTC CTAAGCTGTTGATCTACGGGGCTTCGACCCTGGCATCCGGGGTGCCCGCG AGGTTTAGCGGAAGCGGTAGCGGCACTCACTTCACTCTGACCATTAACAG CCTCCAGTCCGAGGATTCAGCCACTTACTACTGTCAGCAGTCCTACAAGC GGGCCAGCTTCGGACAGGGCACTAAGGTCGAGATCAAG
139101- aa	7973	QVQLQESGGGLVQPGGSLRLSCAASGFTFSSDAMTWVRQAPGKGLEWVSV ISGSGGTTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKLD

VH		SSGYYYARGPRYWGQGTLVTVSS
139101- aa VL	7988	DIQLTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYG ASTLASGVPARFSGSGSGTHFTLTINSLQSEDSATYYCQQSYKRASFGQG TKVEIK
139102		
139102- aa ScFv domain	7944	QVQLVQSGAEVKKPGASVKVSCKASGYTFSNYGITWVRQAPGQGLEWMGW ISAYNGNTNYAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCARGP YYYYMDVWGKGTMVTVSSASGGGGSGGRASGGGGSEIVMTQSPLSLPVTP GEPASISCRSSQSLLYSNGYNYVDWYLQKPGQSPQLLIYLGSNRASGVPD RFSGSGSGTDFKLQISRVEAEDVGIYYCMQGRQFPYSFGQGTKVEIK
139102- nt ScFv domain	7959	CAAGTCCAACTGGTCCAGAGCGGTGCAGAAGTGAAGAAGCCCGGAGCGAG CGTGAAAGTGTCCTGCAAGGCTTCCGGGTACACCTTCTCCAACTACGGCA TCACTTGGGTGCGCCAGGCCCCGGGACAGGGCCTGGAATGGATGGGGTGG ATTTCCGCGTACAACGGCAATACGAACTACGCTCAGAAGTTCCAGGGTAG AGTGACCATGACTAGGAACACCTCCATTTCCACCGCCTACATGGAACTGT CCTCCCTGCGGAGCGAGGACACCGCCGTGTACTATTGCGCCCGGGGACCA TACTACTACTACATGGATGTCTGGGGGAAGGGGACTATGGTCACCGTGTC ATCCGCCTCGGGAGGCGGCGGATCAGGAGGACGCGCCTCTGGTGGTGGAG GATCGGAGATCGTGATGACCCAGAGCCCTCTCTCCTTGCCCGTGACTCCT GGGGAGCCCGCATCCATTTCATGCCGGAGCTCCCAGTCACTTCTCTACTC CAACGGCTATAACTACGTGGATTGGTACCTCCAAAAGCCGGGCCAGAGCC CGCAGCTGCTGATCTACCTGGGCTCGAACAGGGCCAGCGGAGTGCCTGAC CGGTTCTCCGGGTCGGGAAGCGGGACCGACTTCAAGCTGCAAATCTCGAG AGTGGAGGCCGAGGACGTGGGAATCTACTACTGTATGCAGGGCCGCCAGT TTCCGTACTCGTTCGGACAGGGCACCAAAGTGGAAATCAAG
139102- aa VH	7974	QVQLVQSGAEVKKPGASVKVSCKASGYTFSNYGITWVRQAPGQGLEWMGW ISAYNGNTNYAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCARGP YYYYMDVWGKGTMVTVSS
139102- aa VL	7989	EIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYVDWYLQKPGQSPQ LLIYLGSNRASGVPDRFSGSGSGTDFKLQISRVEAEDVGIYYCMQGRQFP YSFGQGTKVEIK
139104		
139104- aa ScFv domain	7945	EVQLLETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSSASGGGGSGGRASGGGGSEIVLTQSPATLSVSPGES ATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRASGIPDRFSGSGSG TDFTLTISSLQAEDVAVYYCQQYGSSLTFGGGTKVEIK
139104- nt ScFv domain	7960	GAAGTGCAATTGCTCGAAACTGGAGGAGGTCTGGTGCAACCTGGAGGATC ACTTCGCCTGTCCTGCGCCGTGTCGGGCTTTGCCCTGTCCAACCATGGAA TGAGCTGGGTCCGCCGCGCGCCGGGGAAGGGCCTCGAATGGGTGTCCGGC ATCGTCTACTCCGGCTCCACCTACTACGCCGCGTCCGTGAAGGGCCGGTT CACGATTTCACGGGACAACTCGCGGAACACCCTGTACCTCCAAATGAATT CCCTTCGGCCGGAGGATACTGCCATCTACTACTGCTCCGCCCACGGTGGC GAATCCGACGTCTGGGGCCAGGGAACCACCGTGACCGTGTCCAGCGCGTC

		CGGGGGAGGAGGAAGCGGGGGTAGAGCATCGGGTGGAGGCGGATCAGAGA TCGTGCTGACCCAGTCCCCCGCCACCTTGAGCGTGTCACCAGGAGAGTCC GCCACCCTGTCATGCCGCGCCAGCCAGTCCGTGTCCTCCAACCTGGCTTG GTACCAGCAGAAGCCGGGGCAGGCCCCTAGACTCCTGATCTATGGGGCGT CGACCCGGGCATCTGGAATTCCCGATAGGTTCAGCGGATCGGGCTCGGGC ACTGACTTCACTCTGACCATCTCCTCGCTGCAAGCCGAGGACGTGGCTGT GTACTACTGTCAGCAGTACGGAAGCTCCCTGACTTTCGGTGGCGGGACCA AAGTCGAGATTAAG
139104- aa **VH**	7975	EVQLLETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSS
139104- aa **VL**	7990	EIVLTQSPATLSVSPGESATLSCRASQSVSSNLAWYQQKPGQAPRLLIYG ASTRASGIPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYGSSLTFGGG TKVEIK
139106		
139106- aa **ScFv domain**	7946	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSSASGGGGSGGRASGGGGSEIVMTQSPATLSVSPGER ATLSCRASQSVSSKLAWYQQKPGQAPRLLMYGASIRATGIPDRFSGSGSG TEFTLTISSLEPEDFAVYYCQQYGSSSWTFGQGTKVEIK
139106- nt **ScFv domain**	7961	GAAGTGCAATTGGTGGAAACTGGAGGAGGACTTGTGCAACCTGGAGGATC ATTGAGACTGAGCTGCGCAGTGTCGGGATTCGCCCTGAGCAACCATGGAA TGTCCTGGGTCAGAAGGGCCCCTGGAAAAGGCCTCGAATGGGTGTCAGGG ATCGTGTACTCCGGTTCCACTTACTACGCCGCCTCCGTGAAGGGGCGCTT CACTATCTCACGGGATAACTCCCGCAATACCCTGTACCTCCAAATGAACA GCCTGCGGCCGGAGGATACCGCCATCTACTACTGTTCCGCCCACGGTGGA GAGTCTGACGTCTGGGGCCAGGGAACTACCGTGACCGTGTCCTCCGCGTC CGGCGGTGGAGGGAGCGGCGGCCGCGCCAGCGGCGGCGGAGGCTCCGAGA TCGTGATGACCCAGAGCCCCGCTACTCTGTCGGTGTCGCCCGGAGAAAGG GCGACCCTGTCCTGCCGGGCGTCGCAGTCCGTGAGCAGCAAGCTGGCTTG GTACCAGCAGAAGCCGGGCCAGGCACCACGCCTGCTTATGTACGGTGCCT CCATTCGGGCCACCGGAATCCCGGACCGGTTCTCGGGGTCGGGGTCCGGT ACCGAGTTCACACTGACCATTTCCTCGCTCGAGCCCGAGGACTTTGCCGT CTATTACTGCCAGCAGTACGGCTCCTCCTCATGGACGTTCGGCCAGGGGA CCAAGGTCGAAATCAAG
139106- aa **VH**	7976	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSS
139106- aa **VL**	7991	EIVMTQSPATLSVSPGERATLSCRASQSVSSKLAWYQQKPGQAPRLLMYG ASIRATGIPDRFSGSGSGTEFTLTISSLEPEDFAVYYCQQYGSSSWTFGQ GTKVEIK
139107		
139107- aa	7947	EVQLVETGGGVVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG

ScFv domain		ESDVWGQGTTVTVSSASGGGGSGGRASGGGGSEIVLTQSPGTLSLSPGER ATLSCRASQSVGSTNLAWYQQKPGQAPRLLIYDASNRATGIPDRFSGGGS GTDFTLTISRLEPEDFAVYYCQQYGSSPPWTFGQGTKVEIK
139107- nt **ScFv domain**	7962	GAAGTGCAATTGGTGGAGACTGGAGGAGGAGTGGTGCAACCTGGAGGAAG CCTGAGACTGTCATGCGCGGTGTCGGGCTTCGCCCTCTCCAACCACGGAA TGTCCTGGGTCCGCCGGGCCCCTGGGAAAGGACTTGAATGGGTGTCCGGC ATCGTGTACTCGGGTTCCACCTACTACGCGGCCTCAGTGAAGGGCCGGTT TACTATTAGCCGCGACAACTCCAGAAACACACTGTACCTCCAAATGAACT CGCTGCGGCCGGAAGATACCGCTATCTACTACTGCTCCGCCCATGGGGGA GAGTCGGACGTCTGGGGACAGGGCACCACTGTCACTGTGTCCAGCGCTTC CGGCGGTGGTGGAAGCGGGGGACGGGCCTCAGGAGGCGGTGGCAGCGAGA TTGTGCTGACCCAGTCCCCCGGGACCCTGAGCCTGTCCCCGGGAGAAAGG GCCACCCTCTCCTGTCGGGCATCCCAGTCCGTGGGGTCTACTAACCTTGC ATGGTACCAGCAGAAGCCCGGCCAGGCCCCTCGCCTGCTGATCTACGACG CGTCCAATAGAGCCACCGGCATCCCGGATCGCTTCAGCGGAGGCGGATCG GGCACCGACTTCACCCTCACCATTTCAAGGCTGGAACCGGAGGACTTCGC CGTGTACTACTGCCAGCAGTATGGTTCGTCCCCACCCTGGACGTTCGGCC AGGGGACTAAGGTCGAGATCAAG
139107- aa **VH**	7977	EVQLVETGGGVVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSS
139107- aa **VL**	7992	EIVLTQSPGTLSLSPGERATLSCRASQSVGSTNLAWYQQKPGQAPRLLIY DASNRATGIPDRFSGGGSGTDFTLTISRLEPEDFAVYYCQQYGSSPPWTF GQGTKVEIK
139108		
139108- aa **ScFv domain**	7948	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSY ISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARES GDGMDVWGQGTTVTVSSASGGGGSGGRASGGGGSDIQMTQSPSSLSASVG DRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSG SGTDFTLTISSLQPEDFATYYCQQSYTLAFGQGTKVDIK
139108- nt **ScFv domain**	7963	CAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGTGAAACCTGGAGGATC ATTGAGACTGTCATGCGCGGCCTCGGGATTCACGTTCTCCGATTACTACA TGAGCTGGATTCGCCAGGCTCCGGGGAAGGGACTGGAATGGGTGTCCTAC ATTTCCTCATCCGGCTCCACCATCTACTACGCGGACTCCGTGAAGGGGAG ATTCACCATTAGCCGCGATAACGCCAAGAACAGCCTGTACCTTCAGATGA ACTCCCTGCGGGCTGAAGATACTGCCGTCTACTACTGCGCAAGGGAGAGC GGAGATGGGATGGACGTCTGGGGACAGGGTACCACTGTGACCGTGTCGTC GGCCTCCGGCGGAGGGGGTTCGGGTGGAAGGGCCAGCGGCGGCGGAGGCA GCGACATCCAGATGACCCAGTCCCCCTCATCGCTGTCCGCCTCCGTGGGC GACCGCGTCACCATCACATGCCGGGCCTCACAGTCGATCTCCTCCTACCT CAATTGGTATCAGCAGAAGCCCGGAAAGGCCCCTAAGCTTCTGATCTACG CAGCGTCCTCCCTGCAATCCGGGGTCCCATCTCGGTTCTCCGGCTCGGGC AGCGGTACCGACTTCACTCTGACCATCTCGAGCCTGCAGCCGGAGGACTT CGCCACTTACTACTGTCAGCAAAGCTACACCCTCGCGTTTGGCCAGGGCA CCAAAGTGGACATCAAG

139108- aa VH	7978	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSY ISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARES GDGMDVWGQGTTVTVSS
139108- aa VL	7993	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYA ASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYTLAFGQGT KVDIK
139110		
139110- aa ScFv domain	7950	QVQLVQSGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSY ISSSGNTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARST MVREDYWGQGTLVTVSSASGGGGSGGRASGGGGSDIVLTQSPLSLPVTLG QPASISCKSSESLVHNSGKTYLNWFHQRPGQSPRRLIYEVSNRDSGVPDR FTGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPGTFGQGTKLEIK
139110- nt ScFv domain	7965	CAAGTGCAACTGGTGCAAAGCGGAGGAGGATTGGTCAAACCCGGAGGAAG CCTGAGACTGTCATGCGCGGCCTCTGGATTCACCTTCTCCGATTACTACA TGTCATGGATCAGACAGGCCCCGGGGAAGGGCCTCGAATGGGTGTCCTAC ATCTCGTCCTCCGGGAACACCATCTACTACGCCGACAGCGTGAAGGGCCG CTTTACCATTTCCCGCGACAACGCAAAGAACTCGCTGTACCTTCAGATGA ATTCCCTGCGGGCTGAAGATACCGCGGTGTACTATTGCGCCCGGTCCACT ATGGTCCGGGAGGACTACTGGGGACAGGGCACACTCGTGACCGTGTCCAG CGCGAGCGGGGGTGGAGGCAGCGGTGGACGCGCCTCCGGCGGCGGCGGTT CAGACATCGTGCTGACTCAGTCGCCCCTGTCGCTGCCGGTCACCCTGGGC CAACCGGCCTCAATTAGCTGCAAGTCCTCGGAGAGCCTGGTGCACAACTC AGGAAAGACTTACCTGAACTGGTTCCATCAGCGGCCTGGACAGTCCCCAC GGAGGCTCATCTATGAAGTGTCCAACAGGGATTCGGGGGTGCCCGACCGC TTCACTGGCTCCGGGTCCGGCACCGACTTCACCTTGAAAATCTCCAGAGT GGAAGCCGAGGACGTGGGCGTGTACTACTGTATGCAGGGTACCCACTGGC CTGGAACCTTTGGACAAGGAACTAAGCTCGAGATTAAG
139110- aa VH	7980	QVQLVQSGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSY ISSSGNTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARST MVREDYWGQGTLVTVSS
139110- aa VL	7995	DIVLTQSPLSLPVTLGQPASISCKSSESLVHNSGKTYLNWFHQRPGQSPR RLIYEVSNRDSGVPDRFTGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWP GTFGQGTKLEIK
139112		
139112- aa ScFv domain	7951	QVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSSASGGGGSGGRASGGGGSDIRLTQSPSPLSASVGDR VTITCQASEDINKFLNWYHQTPGKAPKLLIYDASTLQTGVPSRFSGSGSG TDFTLTINSLQPEDIGTYYCQQYESLPLTFGGGTKVEIK
139112- nt ScFv domain	7966	CAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGTGCAACCCGGTGGAAG CCTTAGGCTGTCGTGCGCCGTCAGCGGGTTTGCTCTGAGCAACCATGGAA TGTCCTGGGTCCGCCGGGCACCGGGAAAAGGGCTGGAATGGGTGTCCGGC ATCGTGTACAGCGGGTCAACCTATTACGCCGCGTCCGTGAAGGGCAGATT CACTATCTCAAGAGACAACAGCCGGAACACCCTGTACTTGCAAATGAATT

		CCCTGCGCCCCGAGGACACCGCCATCTACTACTGCTCCGCCCACGGAGGA GAGTCGGACGTGTGGGGCCAGGGAACGACTGTGACTGTGTCCAGCGCATC AGGAGGGGGTGGTTCGGGCGGCCGGGCCTCGGGGGGAGGAGGTTCCGACA TTCGGCTGACCCAGTCCCCGTCCCCACTGTCGGCCTCCGTCGGCGACCGC GTGACCATCACTTGTCAGGCGTCCGAGGACATTAACAAGTTCCTGAACTG GTACCACCAGACCCCTGGAAAGGCCCCCAAGCTGCTGATCTACGATGCCT CGACCCTTCAAACTGGAGTGCCTAGCCGGTTCTCCGGGTCCGGCTCCGGC ACTGATTTCACTCTGACCATCAACTCATTGCAGCCGGAAGATATCGGGAC CTACTATTGCCAGCAGTACGAATCCCTCCCGCTCACATTCGGCGGGGGAA CCAAGGTCGAGATTAAG
139112- aa VH	7981	QVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSS
139112- aa VL	7996	DIRLTQSPSPLSASVGDRVTITCQASEDINKFLNWYHQTPGKAPKLLIYD ASTLQTGVPSRFSGSGSGTDFTLTINSLQPEDIGTYYCQQYESLPLTFGG GTKVEIK
139113		
139113- aa ScFv domain	7952	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSSASGGGGSGGRASGGGGSETTLTQSPATLSVSPGER ATLSCRASQSVGSNLAWYQQKPGQGPRLLIYGASTRATGIPARFSGSGSG TEFTLTISSLQPEDFAVYYCQQYNDWLPVTFGQGTKVEIK
139113- nt ScFv domain	7967	GAAGTGCAATTGGTGGAAACTGGAGGAGGACTTGTGCAACCTGGAGGATC ATTGCGGCTCTCATGCGCTGTCTCCGGCTTCGCCCTGTCAAATCACGGGA TGTCGTGGGTCAGACGGGCCCCGGGAAAGGGTCTGGAATGGGTGTCGGGG ATTGTGTACAGCGGCTCCACCTACTACGCCGCTTCGGTCAAGGGCCGCTT CACTATTTCACGGGACAACAGCCGCAACACCCTCTATCTGCAAATGAACT CTCTCCGCCCGGAGGATACCGCCATCTACTACTGCTCCGCACACGGCGGC GAATCCGACGTGTGGGGACAGGGAACCACTGTCACCGTGTCGTCCGCATC CGGTGGCGGAGGATCGGGTGGCCGGGCCTCCGGGGGCGGCGGCAGCGAGA CTACCCTGACCCAGTCCCCTGCCACTCTGTCCGTGAGCCCGGGAGAGAGA GCCACCCTTAGCTGCCGGGCCAGCCAGAGCGTGGGCTCCAACCTGGCCTG GTACCAGCAGAAGCCAGGACAGGGTCCCAGGCTGCTGATCTACGGAGCCT CCACTCGCGCGACCGGCATCCCCGCGAGGTTCTCCGGGTCGGGTTCCGGG ACCGAGTTCACCCTGACCATCTCCTCCCTCCAACCGGAGGACTTCGCGGT GTACTACTGTCAGCAGTACAACGATTGGCTGCCCGTGACATTTGGACAGG GGACGAAGGTGGAAATCAAA
139113- aa VH	7982	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSS
139113- aa VL	7997	ETTLTQSPATLSVSPGERATLSCRASQSVGSNLAWYQQKPGQGPRLLIYG ASTRATGIPARFSGSGSGTEFTLTISSLQPEDFAVYYCQQYNDWLPVTFG QGTKVEIK
139114		

139114- aa **ScFv domain**	7953	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSSASGGGGSGGRASGGGGSEIVLTQSPGTLSLSPGER ATLSCRASQSIGSSSLAWYQQKPGQAPRLLMYGASSRASGIPDRFSGSGS GTDFTLTISRLEPEDFAVYYCQQYAGSPPFTFGQGTKVEIK
139114- nt **ScFv domain**	7968	GAAGTGCAATTGGTGGAATCTGGTGGAGGACTTGTGCAACCTGGAGGATC ACTGAGACTGTCATGCGCGGTGTCCGGTTTTGCCCTGAGCAATCATGGGA TGTCGTGGGTCCGGCGCGCCCCCGGAAAGGGTCTGGAATGGGTGTCGGGT ATCGTCTACTCCGGGAGCACTTACTACGCCGCGAGCGTGAAGGGCCGCTT CACCATTTCCCGCGATAACTCCCGCAACACCCTGTACTTGCAAATGAACT CGCTCCGGCCTGAGGACACTGCCATCTACTACTGCTCCGCACACGGAGGA GAATCCGACGTGTGGGGCCAGGGAACTACCGTGACCGTCAGCAGCGCCTC CGGCGGCGGGGGCTCAGGCGGACGGGCTAGCGGCGGCGGTGGCTCCGAGA TCGTGCTGACCCAGTCGCCTGGCACTCTCTCGCTGAGCCCCGGGGAAAGG GCAACCCTGTCCTGTCGGGCCAGCCAGTCCATTGGATCATCCTCCCTCGC CTGGTATCAGCAGAAACCGGGACAGGCTCCGCGGCTGCTTATGTATGGGG CCAGCTCAAGAGCCTCCGGCATTCCCGACCGGTTCTCCGGGTCCGGTTCC GGCACCGATTTCACCCTGACTATCTCGAGGCTGGAGCCAGAGGACTTCGC CGTGTACTACTGCCAGCAGTACGCGGGGTCCCCGCCGTTCACGTTCGGAC AGGGAACCAAGGTCGAGATCAAG
139114- aa **VH**	7983	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVSG IVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAHGG ESDVWGQGTTVTVSS
139114- aa **VL**	7998	EIVLTQSPGTLSLSPGERATLSCRASQSIGSSSLAWYQQKPGQAPRLLMY GASSRASGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYAGSPPFTF GQGTKVEIK
149362		
149362-aa **ScFv domain**	8029	QVQLQESGPGLVKPSETLSLTCTVSGGSISSSYYYWGWIRQPPGKGLEWI GSIYYSGSAYYNPSLKSRVTISVDTSKNQFSLRLSSVTAADTAVYYCARH WQEWPDAFDIWGQGTMVTVSSGGGGSGGGGSGGGGSETTLTQSPAFMSAT PGDKVIISCKASQDIDDAMNWYQQKPGEAPLFIIQSATSPVPGIPPRFSG SGFGTDFSLTINNIESEDAAYYFCLQHDNFPLTFGQGTKLEIK
149362-nt **ScFv domain**	8050	CAAGTGCAGCTTCAGGAAAGCGGACCGGGCCTGGTCAAGCCATCCGAAAC TCTCTCCCTGACTTGCACTGTGTCTGGCGGTTCCATCTCATCGTCGTACT ACTACTGGGGCTGGATTAGGCAGCCGCCCGGAAAGGGACTGGAGTGGATC GGAAGCATCTACTATTCCGGCTCGGCGTACTACAACCCTAGCCTCAAGTC GAGAGTGACCATCTCCGTGGATACCTCCAAGAACCAGTTTTCCCTGCGCC TGAGCTCCGTGACCGCCGCTGACACCGCCGTGTACTACTGTGCTCGGCAT TGGCAGGAATGGCCCGATGCCTTCGACATTTGGGGCCAGGGCACTATGGT CACTGTGTCATCCGGGGGTGGAGGCAGCGGGGGAGGAGGGTCCGGGGGGG GAGGTTCAGAGACAACCTTGACCCAGTCACCCGCATTCATGTCCGCCACT CCGGGAGACAAGGTCATCATCTCGTGCAAAGCGTCCCAGGATATCGACGA TGCCATGAATTGGTACCAGCAGAAGCCTGGCGAAGCGCCGCTGTTCATTA TCCAATCCGCAACCTCGCCCGTGCCTGGAATCCCACCGCGGTTCAGCGGC AGCGGTTTCGGAACCGACTTTTCCCTGACCATTAACAACATTGAGTCCGA GGACGCCGCCTACTACTTCTGCCTGCAACACGACAACTTCCCTCTCACGT

		TCGGCCAGGGAACCAAGCTGGAAATCAAG
149362-aa VH	8071	QVQLQESGPGLVKPSETLSLTCTVSGGSISSSYYYWGWIRQPPGKGLEWI GSIYYSGSAYYNPSLKSRVTISVDTSKNQFSLRLSSVTAADTAVYYCARH WQEWPDAFDIWGQGTMVTVSS
149362-aa VL	8092	ETTLTQSPAFMSATPGDKVIISCKASQDIDDAMNWYQQKPGEAPLFIIQS ATSPVPGIPPRFSGSGFGTDFSLTINNIESEDAAYYFCLQHDNFPLTFGQ GTKLEIK
149363		
149363-aa ScFv domain	8030	QVNLRESGPALVKPTQTLTLTCTFSGFSLRTSGMCVSWIRQPPGKALEWL ARIDWDEDKFYSTSLKTRLTISKDTSDNQVVLRMTNMDPADTATYYCARS GAGGTSATAFDIWGPGTMVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLS ASVGDRVTITCRASQDIYNNLAWFQLKPGSAPRSLMYAANKSQSGVPSRF SGSASGTDFTLTISSLQPEDFATYYCQHYYRFPYSFGQGTKLEIK
149363-nt ScFv domain	8051	CAAGTCAATCTGCGCGAATCCGGCCCCGCCTTGGTCAAGCCTACCCAGAC CCTCACTCTGACCTGTACTTTCTCCGGCTTCTCCCTGCGGACTTCCGGGA TGTGCGTGTCCTGGATCAGACAGCCTCCGGGAAAGGCCCTGGAGTGGCTC GCTCGCATTGACTGGGATGAGGACAAGTTCTACTCCACCTCACTCAAGAC CAGGCTGACCATCAGCAAAGATACCTCTGACAACCAAGTGGTGCTCCGCA TGACCAACATGGACCCAGCCGACACTGCCACTTACTACTGCGCGAGGAGC GGAGCGGGCGGAACCTCCGCCACCGCCTTCGATATTTGGGGCCCGGGTAC CATGGTCACCGTGTCAAGCGGAGGAGGGGGGTCCGGGGGCGGCGGTTCCG GGGGAGGCGGATCGGACATTCAGATGACTCAGTCACCATCGTCCCTGAGC GCTAGCGTGGGCGACAGAGTGACAATCACTTGCCGGGCATCCCAGGACAT CTATAACAACCTTGCGTGGTTCCAGCTGAAGCCTGGTTCCGCACCGCGGT CACTTATGTACGCCGCCAACAAGAGCCAGTCGGGAGTGCCGTCCCGGTTT TCCGGTTCGGCCTCGGGAACTGACTTCACCCTGACGATCTCCAGCCTGCA ACCCGAGGATTTCGCCACCTACTACTGCCAGCACTACTACCGCTTTCCCT ACTCGTTCGGACAGGGAACCAAGCTGGAAATCAAG
149363-aa VH	8072	QVNLRESGPALVKPTQTLTLTCTFSGFSLRTSGMCVSWIRQPPGKALEWL ARIDWDEDKFYSTSLKTRLTISKDTSDNQVVLRMTNMDPADTATYYCARS GAGGTSATAFDIWGPGTMVTVSS
149363-aa VL	8093	DIQMTQSPSSLSASVGDRVTITCRASQDIYNNLAWFQLKPGSAPRSLMYA ANKSQSGVPSRFSGSASGTDFTLTISSLQPEDFATYYCQHYYRFPYSFGQ GTKLEIK
149364		
149364-aa ScFv domain	8031	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSS ISSSSSYIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAKTI AAVYAFDIWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPLSLPVTPE EPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDR FSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPYTFGQGTKLEIK
149364-nt ScFv domain	8052	GAAGTGCAGCTTGTCGAATCCGGGGGGGGACTGGTCAAGCCGGGCGGATC ACTGAGACTGTCCTGCGCCGCGAGCGGCTTCACGTTCTCCTCCTACTCCA TGAACTGGGTCCGCCAAGCCCCCGGGAAGGGACTGGAATGGGTGTCCTCT

		ATCTCCTCGTCGTCGTCCTACATCTACTACGCCGACTCCGTGAAGGGAAG ATTCACCATTTCCCGCGACAACGCAAAGAACTCACTGTACTTGCAAATGA ACTCACTCCGGGCCGAAGATACTGCTGTGTACTATTGCGCCAAGACTATT GCCGCCGTCTACGCTTTCGACATCTGGGGCCAGGGAACCACCGTGACTGT GTCGTCCGGTGGTGGTGGCTCGGGCGGAGGAGGAAGCGGCGGCGGGGGGT CCGAGATTGTGCTGACCCAGTCGCCACTGAGCCTCCCTGTGACCCCCGAG GAACCCGCCAGCATCAGCTGCCGGTCCAGCCAGTCCCTGCTCCACTCCAA CGGATACAATTACCTCGATTGGTACCTTCAGAAGCCTGGACAAAGCCCGC AGCTGCTCATCTACTTGGGATCAAACCGCGCGTCAGGAGTGCCTGACCGG TTCTCCGGCTCGGGCAGCGGTACCGATTTCACCCTGAAAATCTCCAGGGT GGAGGCAGAGGACGTGGGAGTGTATTACTGTATGCAGGCGCTGCAGACTC CGTACACATTTGGGCAGGGCACCAAGCTGGAGATCAAG
149364-aa VH	8073	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSS ISSSSSYIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAKTI AAVYAFDIWGQGTTVTVSS
149364-aa VL	8094	EIVLTQSPLSLPVTPEEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQ LLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP YTFGQGTKLEIK
149365		
149365-aa ScFv domain	8032	EVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSY ISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDL RGAFDIWGQGTMVTVSSGGGGSGGGGSGGGGSSYVLTQSPSVSAAPGYTA TISCGGNNIGTKSVHWYQQKPGQAPLLVIRDDSVRPSKIPGRFSGSNSGN MATLTISGVQAGDEADFYCQVWDSDSEHVVFGGGTKLTVL
149365-nt ScFv domain	8053	GAAGTCCAGCTCGTGGAGTCCGGCGGAGGCCTTGTGAAGCCTGGAGGTTC GCTGAGACTGTCCTGCGCCGCCTCCGGCTTCACCTTCTCCGACTACTACA TGTCCTGGATCAGACAGGCCCCGGGAAAGGGCCTGGAATGGGTGTCCTAC ATCTCGTCATCGGGCAGCACTATCTACTACGCGGACTCAGTGAAGGGGCG GTTCACCATTTCCCGGGATAACGCGAAGAACTCGCTGTATCTGCAAATGA ACTCACTGAGGGCCGAGGACACCGCCGTGTACTACTGCGCCCGCGATCTC CGCGGGGCATTTGACATCTGGGGACAGGGAACCATGGTCACAGTGTCCAG CGGAGGGGGAGGATCGGGTGGCGGAGGTTCCGGGGGTGGAGGCTCCTCCT ACGTGCTGACTCAGAGCCCAAGCGTCAGCGCTGCGCCCGGTTACACGGCA ACCATCTCCTGTGGCGGAAACAACATTGGGACCAAGTCTGTGCACTGGTA TCAGCAGAAGCCGGGCCAAGCTCCCCTGTTGGTGATCCGCGATGACTCCG TGCGGCCTAGCAAAATTCCGGGACGGTTCTCCGGCTCCAACAGCGGCAAT ATGGCCACTCTCACCATCTCGGGAGTGCAGGCCGGAGATGAAGCCGACTT CTACTGCCAAGTCTGGGACTCAGACTCCGAGCATGTGGTGTTCGGGGGCG GAACCAAGCTGACTGTGCTC
149365-aa VH	8074	EVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSY ISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDL RGAFDIWGQGTMVTVSS
149365-aa VL	8095	SYVLTQSPSVSAAPGYTATISCGGNNIGTKSVHWYQQKPGQAPLLVIRDD SVRPSKIPGRFSGSNSGNMATLTISGVQAGDEADFYCQVWDSDSEHVVFG GGTKLTVL

149366		
149366-aa ScFv domain	8033	QVQLVQSGAEVKKPGASVKVSCKPSGYTVTSHYIHWVRRAPGQGLEWMGM INPSGGVTAYSQTLQGRVTMTSDTSSSTVYMELSSLRSEDTAMYYCAREG SGSGWYFDFWGRGTLVTVSSGGGGSGGGGSGGGGSSYVLTQPPSVSVSPG QTASITCSGDGLSKKYVSWYQQKAGQSPVVLISRDKERPSGIPDRFSGSN SADTATLTISGTQAMDEADYYCQAWDDTTVVFGGGTKLTVL
149366-nt ScFv domain	8054	CAAGTGCAGCTGGTGCAGAGCGGGGCCGAAGTCAAGAAGCCGGGAGCCTC CGTGAAAGTGTCCTGCAAGCCTTCGGGATACACCGTGACCTCCCACTACA TTCATTGGGTCCGCCGCGCCCCCGGCCAAGGACTCGAGTGGATGGGCATG ATCAACCCTAGCGGCGGAGTGACCGCGTACAGCCAGACGCTGCAGGGACG CGTGACTATGACCTCGGATACCTCCTCCTCCACCGTCTATATGGAACTGT CCAGCCTGCGGTCCGAGGATACCGCCATGTACTACTGCGCCCGGGAAGGA TCAGGCTCCGGGTGGTATTTCGACTTCTGGGGAAGAGGCACCCTCGTGAC TGTGTCATCTGGGGGAGGGGGTTCCGGTGGTGGCGGATCGGGAGGAGGCG GTTCATCCTACGTGCTGACCCAGCCACCCTCCGTGTCCGTGAGCCCCGGC CAGACTGCATCGATTACATGTAGCGGCGACGGCCTCTCCAAGAAATACGT GTCGTGGTACCAGCAGAAGGCCGGACAGAGCCCGGTGGTGCTGATCTCAA GAGATAAGGAGCGGCCTAGCGGAATCCCGGACAGGTTCTCGGGTTCCAAC TCCGCGGACACTGCTACTCTGACCATCTCGGGGACCCAGGCTATGGACGA AGCCGATTACTACTGCCAAGCCTGGGACGACACTACTGTCGTGTTTGGAG GGGGCACCAAGTTGACCGTCCTT
149366-aa VH	8075	QVQLVQSGAEVKKPGASVKVSCKPSGYTVTSHYIHWVRRAPGQGLEWMGM INPSGGVTAYSQTLQGRVTMTSDTSSSTVYMELSSLRSEDTAMYYCAREG SGSGWYFDFWGRGTLVTVSS
149366-aa VL	8096	SYVLTQPPSVSVSPGQTASITCSGDGLSKKYVSWYQQKAGQSPVVLISRD KERPSGIPDRFSGSNSADTATLTISGTQAMDEADYYCQAWDDTTVVFGGG TKLTVL
149367		
149367-aa ScFv domain	8034	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHPGKGLEWI GYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARA GIAARLRGAFDIWGQGTMVTVSSGGGGSGGGGSGGGGSDIVMTQSPSSVS ASVGDRVIITCRASQGIRNWLAWYQQKPGKAPNLLIYAASNLQSGVPSRF SGSGSGADFTLTISSLQPEDVATYYCQKYNSAPFTFGPGTKVDIK
149367-nt ScFv domain	8055	CAAGTGCAGCTTCAGGAGAGCGGCCCGGGACTCGTGAAGCCGTCCCAGAC CCTGTCCCTGACTTGCACCGTGTCGGGAGGAAGCATCTCGAGCGGAGGCT ACTATTGGTCGTGGATTCGGCAGCACCCTGGAAAGGGCCTGGAATGGATC GGCTACATCTACTACTCCGGCTCGACCTACTACAACCCATCGCTGAAGTC CAGAGTGACAATCTCAGTGGACACGTCCAAGAATCAGTTCAGCCTGAAGC TCTCTTCCGTGACTGCGGCCGACACCGCCGTGTACTACTGCGCACGCGCT GGAATTGCCGCCCGGCTGAGGGGTGCCTTCGACATTTGGGGACAGGGCAC CATGGTCACCGTGTCCTCCGGCGGCGGAGGTTCCGGGGGTGGAGGCTCAG GAGGAGGGGGGTCCGACATCGTCATGACTCAGTCGCCCTCAAGCGTCAGC GCGTCCGTCGGGGACAGAGTGATCATCACCTGTCGGGCGTCCCAGGGAAT TCGCAACTGGCTGGCCTGGTATCAGCAGAAGCCCGGAAAGGCCCCCAACC TGTTGATCTACGCCGCCTCAAACCTCCAATCCGGGGTGCCGAGCCGCTTC

		AGCGGCTCCGGTTCGGGTGCCGATTTCACTCTGACCATCTCCTCCCTGCA ACCTGAAGATGTGGCTACCTACTACTGCCAAAAGTACAACTCCGCACCTT TTACTTTCGGACCGGGGACCAAAGTGGACATTAAG
149367-aa VH	8076	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHPGKGLEWI GYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARA GIAARLRGAFDIWGQGTMVTVSS
149367-aa VL	8097	DIVMTQSPSSVSASVGDRVIITCRASQGIRNWLAWYQQKPGKAPNLLIYA ASNLQSGVPSRFSGSGSGADFTLTISSLQPEDVATYYCQKYNSAPFTFGP GTKVDIK
149368		
149368-aa ScFv domain	8035	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGG IIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARRG GYQLLRWDVGLLRSAFDIWGQGTMVTVSSGGGGSGGGGSGGGGSSYVLTQ PPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVLYGKNNRPSG VPDRFSGSRSGTTASLTITGAQAEDEADYYCSSRDSSGDHLRVFGTGTKV TVL
149368-nt ScFv domain	8056	CAAGTGCAGCTGGTCCAGTCGGGCGCCGAGGTCAAGAAGCCCGGGAGCTC TGTGAAAGTGTCCTGCAAGGCCTCCGGGGGCACCTTTAGCTCCTACGCCA TCTCCTGGGTCCGCCAAGCACCGGGTCAAGGCCTGGAGTGGATGGGGGGA ATTATCCCTATCTTCGGCACTGCCAACTACGCCCAGAAGTTCCAGGGACG CGTGACCATTACCGCGGACGAATCCACCTCCACCGCTTATATGGAGCTGT CCAGCTTGCGCTCGGAAGATACCGCCGTGTACTACTGCGCCCGGAGGGGT GGATACCAGCTGCTGAGATGGGACGTGGGCCTCCTGCGGTCGGCGTTCGA CATCTGGGGCCAGGGCACTATGGTCACTGTGTCCAGCGGAGGAGGCGGAT CGGGAGGCGGCGGATCAGGGGGAGGCGGTTCCAGCTACGTGCTTACTCAA CCCCCTTCGGTGTCCGTGGCCCCGGGACAGACCGCCAGAATCACTTGCGG AGGAAACAACATTGGGTCCAAGAGCGTGCATTGGTACCAGCAGAAGCCAG GACAGGCCCCTGTGCTGGTGCTCTACGGGAAGAACAATCGGCCCAGCGGA GTGCCGGACAGGTTCTCGGGTTCACGCTCCGGTACAACCGCTTCACTGAC TATCACCGGGGCCCAGGCAGAGGATGAAGCGGACTACTACTGTTCCTCCC GGGATTCATCCGGCGACCACCTCCGGGTGTTCGGAACCGGAACGAAGGTC ACCGTGCTG
149368-aa VH	8077	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGG IIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARRG GYQLLRWDVGLLRSAFDIWGQGTMVTVSS
149368-aa VL	8098	SYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVLYGK NNRPSGVPDRFSGSRSGTTASLTITGAQAEDEADYYCSSRDSSGDHLRVF GTGTKVTVL
149369		
149369-aa ScFv domain	8036	EVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPSRGLEWL GRTYYRSKWYSFYAISLKSRIIINPDTSKNQFSLQLKSVTPEDTAVYYCA RSSPEGLFLYWFDPWGQGTLVTVSSGGDGSGGGGSGGGGSSSELTQDPAV SVALGQTIRITCQGDSLGNYYATWYQQKPGQAPVLVIYGTNNRPSGIPDR

		FSASSSGNTASLTITGAQAEDEADYYCNSRDSSGHHLLFGTGTKVTVL
149369-nt ScFv domain	8057	GAAGTGCAGCTCCAACAGTCAGGACCGGGGCTCGTGAAGCCATCCCAGAC CCTGTCCCTGACTTGTGCCATCTCGGGAGATAGCGTGTCATCGAACTCCG CCGCCTGGAACTGGATTCGGCAGAGCCCGTCCCGCGGACTGGAGTGGCTT GGAAGGACCTACTACCGGTCCAAGTGGTACTCTTTCTACGCGATCTCGCT GAAGTCCCGCATTATCATTAACCCTGATACCTCCAAGAATCAGTTCTCCC TCCAACTGAAATCCGTCACCCCCGAGGACACAGCAGTGTATTACTGCGCA CGGAGCAGCCCCGAAGGACTGTTCCTGTATTGGTTTGACCCCTGGGGCCA GGGGACTCTTGTGACCGTGTCGAGCGGCGGAGATGGGTCCGGTGGCGGTG GTTCGGGGGGCGGCGGATCATCATCCGAACTGACCCAGGACCCGGCTGTG TCCGTGGCGCTGGGACAAACCATCCGCATTACGTGCCAGGGAGACTCCCT GGGCAACTACTACGCCACTTGGTACCAGCAGAAGCCGGGCCAAGCCCCTG TGTTGGTCATCTACGGGACCAACAACAGACCTTCCGGCATCCCCGACCGG TTCAGCGCTTCGTCCTCCGGCAACACTGCCAGCCTGACCATCACTGGAGC GCAGGCCGAAGATGAGGCCGACTACTACTGCAACAGCAGAGACTCCTCGG GTCATCACCTCTTGTTCGGAACTGGAACCAAGGTCACCGTGCTG
149369-aa VH	8078	EVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPSRGLEWL GRTYYRSKWYSFYAISLKSRIIINPDTSKNQFSLQLKSVTPEDTAVYYCA RSSPEGLFLYWFDPWGQGTLVTVSS
149369-aa VL	8099	SSELTQDPAVSVALGQTIRITCQGDSLGNYYATWYQQKPGQAPVLVIYGT NNRPSGIPDRFSASSSGNTASLTITGAQAEDEADYYCNSRDSSGHHLLFG TGTKVTVL
BCMA_EBB-C1978-A4		
BCMA_EBB-C1978-A4 - aa **ScFv domain**	8037	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVE GSGSLDYWGQGTLVTVSSGGGGSGGGGSGGGGSEIVMTQSPGTLSLSPGE RATLSCRASQSVSSAYLAWYQQKPGQPPRLLISGASTRATGIPDRFGGSG SGTDFTLTISRLEPEDFAVYYCQHYGSSFNGSSLFTFGQGTRLEIK
BCMA_EBB-C1978-A4 - nt **ScFv domain**	8058	GAAGTGCAGCTCGTGGAGTCAGGAGGCGGCCTGGTCCAGCCGGGAGGGTC CCTTAGACTGTCATGCGCCGCAAGCGGATTCACTTTCTCCTCCTATGCCA TGAGCTGGGTCCGCCAAGCCCCCGGAAAGGGACTGGAATGGGTGTCCGCC ATCTCGGGGTCTGGAGGCTCAACTTACTACGCTGACTCCGTGAAGGGACG GTTCACCATTAGCCGCGACAACTCCAAGAACACCCTCTACCTCCAAATGA ACTCCCTGCGGGCCGAGGATACCGCCGTCTACTACTGCGCCAAAGTGGAA GGTTCAGGATCGCTGGACTACTGGGGACAGGGTACTCTCGTGACCGTGTC ATCGGGCGGAGGAGGTTCCGGCGGTGGCGGCTCCGGCGGCGGAGGGTCGG AGATCGTGATGACCCAGAGCCCTGGTACTCTGAGCCTTTCGCCGGGAGAA AGGGCCACCCTGTCCTGCCGCGCTTCCCAATCCGTGTCCTCCGCGTACTT GGCGTGGTACCAGCAGAAGCCGGGACAGCCCCCTCGGCTGCTGATCAGCG GGGCCAGCACCCGGGCAACCGGAATCCCAGACAGATTCGGGGGTTCCGGC AGCGGCACAGATTTCACCCTGACTATTTCGAGGTTGGAGCCCGAGGACTT TGCGGTGTATTACTGTCAGCACTACGGGTCGTCCTTTAATGGCTCCAGCC TGTTCACGTTCGGACAGGGGACCCGCCTGGAAATCAAG
BCMA_EBB-	8079	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVE

C1978-A4 - aa **VH**		GSGSLDYWGQGTLVTVSS
BCMA_EBB-C1978-A4 - aa **VL**	8100	EIVMTQSPGTLSLSPGERATLSCRASQSVSSAYLAWYQQKPGQPPRLLIS GASTRATGIPDRFGGSGSGTDFTLTISRLEPEDFAVYYCQHYGSSFNGSS LFTFGQGTRLEIK
BCMA_EBB-C1978-G1		
BCMA_EBB-C1978-G1 - aa **ScFv domain**	8038	EVQLVETGGGLVQPGGSLRLSCAASGITFSRYPMSWVRQAPGKGLEWVSG ISDSGVSTYYADSAKGRFTISRDNSKNTLFLQMSSLRDEDTAVYYCVTRA GSEASDIWGQGTMVTVSSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGE RATLSCRASQSVSNSLAWYQQKPGQAPRLLIYDASSRATGIPDRFSGSGS GTDFTLTISRLEPEDFAIYYCQQFGTSSGLTFGGGTKLEIK
BCMA_EBB-C1978-G1 - nt **ScFv domain**	8059	GAAGTGCAACTGGTGGAAACCGGTGGCGGCCTGGTGCAGCCTGGAGGATC ATTGAGGCTGTCATGCGCGGCCAGCGGTATTACCTTCTCCCGGTACCCCA TGTCCTGGGTCAGACAGGCCCCGGGGAAAGGGCTTGAATGGGTGTCCGGG ATCTCGGACTCCGGTGTCAGCACTTACTACGCCGACTCCGCCAAGGGACG CTTCACCATTTCCCGGGACAACTCGAAGAACACCCTGTTCCTCCAAATGA GCTCCCTCCGGGACGAGGATACTGCAGTGTACTACTGCGTGACCCGCGCC GGGTCCGAGGCGTCTGACATTTGGGGACAGGGCACTATGGTCACCGTGTC GTCCGGCGGAGGGGGCTCGGGAGGCGGTGGCAGCGGAGGAGGAGGGTCCG AGATCGTGCTGACCCAATCCCCGGCCACCCTCTCGCTGAGCCCTGGAGAA AGGGCAACCTTGTCCTGTCGCGCGAGCCAGTCCGTGAGCAACTCCCTGGC CTGGTACCAGCAGAAGCCCGGACAGGCTCCGAGACTTCTGATCTACGACG CTTCGAGCCGGGCCACTGGAATCCCCGACCGCTTTTCGGGGTCCGGCTCA GGAACCGATTTCACCCTGACAATCTCACGGCTGGAGCCAGAGGATTTCGC CATCTATTACTGCCAGCAGTTCGGTACTTCCTCCGGCCTGACTTTCGGAG GCGGCACGAAGCTCGAAATCAAG
BCMA_EBB-C1978-G1 - aa **VH**	8080	EVQLVETGGGLVQPGGSLRLSCAASGITFSRYPMSWVRQAPGKGLEWVSG ISDSGVSTYYADSAKGRFTISRDNSKNTLFLQMSSLRDEDTAVYYCVTRA GSEASDIWGQGTMVTVSS
BCMA_EBB-C1978-G1 - aa **VL**	8101	EIVLTQSPATLSLSPGERATLSCRASQSVSNSLAWYQQKPGQAPRLLIYD ASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAIYYCQQFGTSSGLTFG GGTKLEIK
BCMA_EBB-C1979-C1		
BCMA_EBB-C1979-C1 - aa **ScFv domain**	8039	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAIYYCARAT YKRELRYYYGMDVWGQGTMVTVSSGGGGSGGGGSGGGGSEIVMTQSPGTV SLSPGERATLSCRASQSVSSSFLAWYQQKPGQAPRLLIYGASSRATGIPD RFSGSGSGTDFTLTISRLEPEDSAVYYCQQYHSSPSWTFGQGTRLEIK

BCMA_EBB-C1979-C1 - nt **ScFv domain**	8060	CAAGTGCAGCTCGTGGAATCGGGTGGCGGACTGGTGCAGCCGGGGGGCTC ACTTAGACTGTCCTGCGCGGCCAGCGGATTCACTTTCTCCTCCTACGCCA TGTCCTGGGTCAGACAGGCCCCTGGAAAGGGCCTGGAATGGGTGTCCGCA ATCAGCGGCAGCGGCGGCTCGACCTATTACGCGGATTCAGTGAAGGGCAG ATTCACCATTTCCCGGGACAACGCCAAGAACTCCTTGTACCTTCAAATGA ACTCCCTCCGCGCGGAAGATACCGCAATCTACTACTGCGCTCGGGCCACT TACAAGAGGGAACTGCGCTACTACTACGGGATGGACGTCTGGGGCCAGGG AACCATGGTCACCGTGTCCAGCGGAGGAGGAGGATCGGGAGGAGGCGGTA GCGGGGGTGGAGGGTCGGAGATCGTGATGACCCAGTCCCCCGGCACTGTG TCGCTGTCCCCCGGCGAACGGGCCACCCTGTCATGTCGGGCCAGCCAGTC AGTGTCGTCAAGCTTCCTCGCCTGGTACCAGCAGAAACCGGGACAAGCTC CCCGCCTGCTGATCTACGGAGCCAGCAGCCGGGCCACCGGTATTCCTGAC CGGTTCTCCGGTTCGGGGTCCGGGACCGACTTTACTCTGACTATCTCTCG CCTCGAGCCAGAGGACTCCGCCGTGTATTACTGCCAGCAGTACCACTCCT CCCCGTCCTGGACGTTCGGACAGGGCACAAGGCTGGAGATTAAG
BCMA_EBB-C1979-C1 - aa **VH**	8081	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAIYYCARAT YKRELRYYYGMDVWGQGTMVTVSS
BCMA_EBB-C1979-C1 - aa **VL**	8102	EIVMTQSPGTVSLSPGERATLSCRASQSVSSSFLAWYQQKPGQAPRLLIY GASSRATGIPDRFSGSGSGTDFTLTISRLEPEDSAVYYCQQYHSSPSWTF GQGTRLEIK
BCMA_EBB-C1978-C7		
BCMA_EBB-C1978-C7 - aa **ScFv domain**	8040	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNTLKAEDTAVYYCARAT YKRELRYYYGMDVWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPSTL SLSPGESATLSCRASQSVSTTFLAWYQQKPGQAPRLLIYGSSNRATGIPD RFSGSGSGTDFTLTIRRLEPEDFAVYYCQQYHSSPSWTFGQGTKVEIK
BCMA_EBB-C1978-C7 - nt **ScFv domain**	8061	GAGGTGCAGCTTGTGGAAACCGGTGGCGGACTGGTGCAGCCCGGAGGAAG CCTCAGGCTGTCCTGCGCCGCGTCCGGCTTCACCTTCTCCTCGTACGCCA TGTCCTGGGTCCGCCAGGCCCCCGGAAAGGGCCTGGAATGGGTGTCCGCC ATCTCTGGAAGCGGAGGTTCCACGTACTACGCGGACAGCGTCAAGGGAAG GTTCACAATCTCCCGCGATAATTCGAAGAACACTCTGTACCTTCAAATGA ACACCCTGAAGGCCGAGGACACTGCTGTGTACTACTGCGCACGGGCCACC TACAAGAGAGAGCTCCGGTACTACTACGGAATGGACGTCTGGGGCCAGGG AACTACTGTGACCGTGTCCTCGGGAGGGGGTGGCTCCGGGGGGGGCGGCT CCGGCGGAGGCGGTTCCGAGATTGTGCTGACCCAGTCACCTTCAACTCTG TCGCTGTCCCCGGGAGAGAGCGCTACTCTGAGCTGCCGGGCCAGCCAGTC CGTGTCCACCACCTTCCTCGCCTGGTATCAGCAGAAGCCGGGGCAGGCAC CACGGCTCTTGATCTACGGGTCAAGCAACAGAGCGACCGGAATTCCTGAC CGCTTCTCGGGGAGCGGTTCAGGCACCGACTTCACCCTGACTATCCGGCG CCTGGAACCCGAAGATTTCGCCGTGTATTACTGTCAACAGTACCACTCCT CGCCGTCCTGGACCTTTGGCCAAGGAACCAAAGTGGAAATCAAG
BCMA_EBB-	8082	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNTLKAEDTAVYYCARAT

C1978-C7 - aa **VH**		YKRELRYYYGMDVWGQGTTVTVSS
BCMA_EBB-C1978-C7 - aa **VL**	8103	EIVLTQSPSTLSLSPGESATLSCRASQSVSTTFLAWYQQKPGQAPRLLIY GSSNRATGIPDRFSGSGSGTDFTLTIRRLEPEDFAVYYCQQYHSSPSWTF GQGTKVEIK
BCMA_EBB-C1978-D10		
BCMA_EBB-C1978-D10 - aa **ScFv domain**	8041	EVQLVETGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSG ISWNSGSIGYADSVKGRFTISRDNAKNSLYLQMNSLRDEDTAVYYCARVG KAVPDVWGQGTTVTVSSGGGGSGGGGSGGGGSDIVMTQTPSSLSASVGDR VTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSG TDFTLTISSLQPEDFATYYCQQSYSTPYSFGQGTRLEIK
BCMA_EBB-C1978-D10- nt **ScFv domain**	8062	GAAGTGCAGCTCGTGGAAACTGGAGGTGGACTCGTGCAGCCTGGACGGTC GCTGCGGCTGAGCTGCGCTGCATCCGGCTTCACCTTCGACGATTATGCCA TGCACTGGGTCAGACAGGCGCCAGGGAAGGGACTTGAGTGGGTGTCCGGT ATCAGCTGGAATAGCGGCTCAATCGGATACGCGGACTCCGTGAAGGGAAG GTTCACCATTTCCCGCGACAACGCCAAGAACTCCCTGTACTTGCAAATGA ACAGCCTCCGGGATGAGGACACTGCCGTGTACTACTGCGCCCGCGTCGGA AAAGCTGTGCCCGACGTCTGGGGCCAGGGAACCACTGTGACCGTGTCCAG CGGCGGGGGTGGATCGGGCGGTGGAGGGTCCGGTGGAGGGGGCTCAGATA TTGTGATGACCCAGACCCCCTCGTCCCTGTCCGCCTCGGTCGGCGACCGC GTGACTATCACATGTAGAGCCTCGCAGAGCATCTCCAGCTACCTGAACTG GTATCAGCAGAAGCCGGGGAAGGCCCCGAAGCTCCTGATCTACGCGGCAT CATCACTGCAATCGGGAGTGCCGAGCCGGTTTTCCGGGTCCGGCTCCGGC ACCGACTTCACGCTGACCATTTCTTCCCTGCAACCCGAGGACTTCGCCAC TTACTACTGCCAGCAGTCCTACTCCACCCCTTACTCCTTCGGCCAAGGAA CCAGGCTGGAAATCAAG
BCMA_EBB-C1978-D10 - aa **VH**	8083	EVQLVETGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSG ISWNSGSIGYADSVKGRFTISRDNAKNSLYLQMNSLRDEDTAVYYCARVG KAVPDVWGQGTTVTVSS
BCMA_EBB-C1978-D10- aa **VL**	8104	DIVMTQTPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYA ASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPYSFGQ GTRLEIK
BCMA_EBB-C1979-C12		
BCMA_EBB-C1979-C12- aa **ScFv domain**	8042	EVQLVESGGGLVQPGRSLRLSCTASGFTFDDYAMHWVRQRPGKGLEWVAS INWKGNSLAYGDSVKGRFAISRDNAKNTVFLQMNSLRTEDTAVYYCASHQ GVAYYNYAMDVWGRGTLVTVSSGGGGSGGGGSGGGGSEIVLTQSPGTLSL SPGERATLSCRATQSIGSSFLAWYQQRPGQAPRLLIYGASQRATGIPDRF SGRGSGTDFTLTISRVEPEDSAVYYCQHYESSPSWTFGQGTKVEIK

BCMA_EBB-C1979-C12 - nt **ScFv domain**	8063	GAAGTGCAGCTCGTGGAGAGCGGGGGAGGATTGGTGCAGCCCGGAAGGTC CCTGCGGCTCTCCTGCACTGCGTCTGGCTTCACCTTCGACGACTACGCGA TGCACTGGGTCAGACAGCGCCCGGGAAAGGGCCTGGAATGGGTCGCCTCA ATCAACTGGAAGGGAAACTCCCTGGCCTATGGCGACAGCGTGAAGGGCCG CTTCGCCATTTCGCGCGACAACGCCAAGAACACCGTGTTTCTGCAAATGA ATTCCCTGCGGACCGAGGATACCGCTGTGTACTACTGCGCCAGCCACCAG GGCGTGGCATACTATAACTACGCCATGGACGTGTGGGGAAGAGGGACGCT CGTCACCGTGTCCTCCGGGGGCGGTGGATCGGGTGGAGGAGGAAGCGGTG GCGGGGGCAGCGAAATCGTGCTGACTCAGAGCCCGGGAACTCTTTCACTG TCCCCGGGAGAACGGGCCACTCTCTCGTGCCGGGCCACCCAGTCCATCGG CTCCTCCTTCCTTGCCTGGTACCAGCAGAGGCCAGGACAGGCGCCCCGCC TGCTGATCTACGGTGCTTCCCAACGCGCCACTGGCATTCCTGACCGGTTC AGCGGCAGAGGGTCGGGAACCGATTTCACACTGACCATTTCCCGGGTGGA GCCCGAAGATTCGGCAGTCTACTACTGTCAGCATTACGAGTCCTCCCCTT CATGGACCTTCGGTCAAGGGACCAAAGTGGAGATCAAG
BCMA_EBB-C1979-C12 - aa **VH**	8084	EVQLVESGGGLVQPGRSLRLSCTASGFTFDDYAMHWVRQRPGKGLEWVAS INWKGNSLAYGDSVKGRFAISRDNAKNTVFLQMNSLRTEDTAVYYCASHQ GVAYYNYAMDVWGRGTLVTVSS
BCMA_EBB-C1979-C12 - aa **VL**	8105	EIVLTQSPGTLSLSPGERATLSCRATQSIGSSFLAWYQQRPGQAPRLLIY GASQRATGIPDRFSGRGSGTDFTLTISRVEPEDSAVYYCQHYESSPSWTF GQGTKVEIK
BCMA_EBB-C1980-G4		
BCMA_EBB-C1980-G4- aa **ScFv domain**	8043	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVV RDGMDVWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGER ATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGNGS GTDFTLTISRLEPEDFAVYYCQQYGSPPRFTFGPGTKVDIK
BCMA_EBB-C1980-G4- nt **ScFv domain**	8064	GAGGTGCAGTTGGTCGAAAGCGGGGGCGGGCTTGTGCAGCCTGGCGGATC ACTGCGGCTGTCCTGCGCGGCATCAGGCTTCACGTTTTCTTCCTACGCCA TGTCCTGGGTGCGCCAGGCCCCTGGAAAGGGACTGGAATGGGTGTCCGCG ATTTCGGGGTCCGGCGGGAGCACCTACTACGCCGATTCCGTGAAGGGCCG CTTCACTATCTCGCGGGACAACTCCAAGAACACCCTCTACCTCCAAATGA ATAGCCTGCGGGCCGAGGATACCGCCGTCTACTATTGCGCTAAGGTCGTG CGCGACGGAATGGACGTGTGGGGACAGGGTACCACCGTGACAGTGTCCTC GGGGGGAGGCGGTAGCGGCGGAGGAGGAAGCGGTGGTGGAGGTTCCGAGA TTGTGCTGACTCAATCACCCGCGACCCTGAGCCTGTCCCCCGGCGAAAGG GCCACTCTGTCCTGTCGGGCCAGCCAATCAGTCTCCTCCTCGTACCTGGC CTGGTACCAGCAGAAGCCAGGACAGGCTCCGAGACTCCTTATCTATGGCG CATCCTCCCGCGCCACCGGAATCCCGGATAGGTTCTCGGGAAACGGATCG GGGACCGACTTCACTCTCACCATCTCCCGGCTGGAACCGGAGGACTTCGC CGTGTACTACTGCCAGCAGTACGGCAGCCCGCCTAGATTCACTTTCGGCC CCGGCACCAAAGTGGACATCAAG

BCMA_EBB-C1980-G4- aa VH	8085	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVV RDGMDVWGQGTTVTVSS
BCMA_EBB-C1980-G4- aa VL	8106	EIVLTQSPATLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIY GASSRATGIPDRFSGNGSGTDFTLTISRLEPEDFAVYYCQQYGSPPRFTF GPGTKVDIK
BCMA_EBB-C1980-D2		
BCMA_EBB-C1980-D2- aa ScFv domain	8044	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKIP QTGTFDYWGQGTLVTVSSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGE RATLSCRASQSVSSSYLAWYQQRPGQAPRLLIYGASSRATGIPDRFSGSG SGTDFTLTISRLEPEDFAVYYCQHYGSSPSWTFGQGTRLEIK
BCMA_EBB-C1980-D2- nt ScFv domain	8065	GAAGTGCAGCTGCTGGAGTCCGGCGGTGGATTGGTGCAACCGGGGGGATC GCTCAGACTGTCCTGTGCGGCGTCAGGCTTCACCTTCTCGAGCTACGCCA TGTCATGGGTCAGACAGGCCCCTGGAAAGGGTCTGGAATGGGTGTCCGCC ATTTCCGGGAGCGGGGGATCTACATACTACGCCGATAGCGTGAAGGGCCG CTTCACCATTTCCCGGGACAACTCCAAGAACACTCTCTATCTGCAAATGA ACTCCCTCCGCGCTGAGGACACTGCCGTGTACTACTGCGCCAAAATCCCT CAGACCGGCACCTTCGACTACTGGGGACAGGGGACTCTGGTCACCGTCAG CAGCGGTGGCGGAGGTTCGGGGGGAGGAGGAAGCGGCGGCGGAGGGTCCG AGATTGTGCTGACCCAGTCACCCGGCACTTTGTCCCTGTCGCCTGGAGAA AGGGCCACCCTTTCCTGCCGGGCATCCCAATCCGTGTCCTCCTCGTACCT GGCCTGGTACCAGCAGAGGCCCGGACAGGCCCCACGGCTTCTGATCTACG GAGCAAGCAGCCGCGCGACCGGTATCCCGGACCGGTTTTCGGGCTCGGGC TCAGGAACTGACTTCACCCTCACCATCTCCCGCCTGGAACCCGAAGATTT CGCTGTGTATTACTGCCAGCACTACGGCAGCTCCCCGTCCTGGACGTTCG GCCAGGGAACTCGGCTGGAGATCAAG
BCMA_EBB-C1980-D2- aa VH	8086	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKIP QTGTFDYWGQGTLVTVSS
BCMA_EBB-C1980-D2- aa VL	8107	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQRPGQAPRLLIY GASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYGSSPSWTF GQGTRLEIK
BCMA_EBB-C1978-A10		
BCMA_EBB-C1978-A10- aa ScFv domain	8045	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTMSRENDKNSVFLQMNSLRVEDTGVYYCARAN YKRELRYYYGMDVWGQGTMVTVSSGGGGSGGGGSGGGGSEIVMTQSPGTL SLSPGESATLSCRASQRVASNYLAWYQHKPGQAPSLLISGASSRATGVPD RFSGSGSGTDFTLAISRLEPEDSAVYYCQHYDSSPSWTFGQGTKVEIK

BCMA_EBB-C1978-A10- nt **ScFv domain**	8066	GAAGTGCAACTGGTGGAAACCGGTGGAGGACTCGTGCAGCCTGGCGGCAG CCTCCGGCTGAGCTGCGCCGCTTCGGGATTCACCTTTTCCTCCTACGCGA TGTCTTGGGTCAGACAGGCCCCCGGAAAGGGGCTGGAATGGGTGTCAGCC ATCTCCGGCTCCGGCGGATCAACGTACTACGCCGACTCCGTGAAAGGCCG GTTCACCATGTCGCGCGAGAATGACAAGAACTCCGTGTTCCTGCAAATGA ACTCCCTGAGGGTGGAGGACACCGGAGTGTACTATTGTGCGCGCGCCAAC TACAAGAGAGAGCTGCGGTACTACTACGGAATGGACGTCTGGGGACAGGG AACTATGGTGACCGTGTCATCCGGTGGAGGGGGAAGCGGCGGTGGAGGCA GCGGGGGCGGGGGTTCAGAAATTGTCATGACCCAGTCCCCGGGAACTCTT TCCCTCTCCCCCGGGGAATCCGCGACTTTGTCCTGCCGGGCCAGCCAGCG CGTGGCCTCGAACTACCTCGCATGGTACCAGCATAAGCCAGGCCAAGCCC CTTCCCTGCTGATTTCCGGGGCTAGCAGCCGCGCCACTGGCGTGCCGGAT AGGTTCTCGGGAAGCGGCTCGGGTACCGATTTCACCCTGGCAATCTCGCG GCTGGAACCGGAGGATTCGGCCGTGTACTACTGCCAGCACTATGACTCAT CCCCCTCCTGGACATTCGGACAGGGCACCAAGGTCGAGATCAAG
BCMA_EBB-C1978-A10- aa **VH**	8087	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTMSRENDKNSVFLQMNSLRVEDTGVYYCARAN YKRELRYYYGMDVWGQGTMVTVSS
BCMA_EBB-C1978-A10- aa **VL**	8108	EIVMTQSPGTLSLSPGESATLSCRASQRVASNYLAWYQHKPGQAPSLLIS GASSRATGVPDRFSGSGSGTDFTLAISRLEPEDSAVYYCQHYDSSPSWTF GQGTKVEIK
BCMA_EBB-C1978-D4		
BCMA_EBB-C1978-D4- aa **ScFv domain**	8046	EVQLLETGGGLVQPGGSLRLSCAASGFSFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKAL VGATGAFDIWGQGTLVTVSSGGGGSGGGGSGGGGSEIVLTQSPGTLSLSP GERATLSCRASQSLSSNFLAWYQQKPGQAPGLLIYGASNWATGTPDRFSG SGSGTDFTLTITRLEPEDFAVYYCQYYGTSPMYTFGQGTKVEIK
BCMA_EBB-C1978-D4- nt **ScFv domain**	8067	GAAGTGCAGCTGCTCGAAACCGGTGGAGGGCTGGTGCAGCCAGGGGGCTC CCTGAGGCTTTCATGCGCCGCTAGCGGATTCTCCTTCTCCTCTTACGCCA TGTCGTGGGTCCGCCAAGCCCCTGGAAAAGGCCTGGAATGGGTGTCCGCG ATTTCCGGGAGCGGAGGTTCGACCTATTACGCCGACTCCGTGAAGGGCCG CTTTACCATCTCCCGGGATAACTCCAAGAACACTCTGTACCTCCAAATGA ACTCGCTGAGAGCCGAGGACACCGCCGTGTATTACTGCGCGAAGGCGCTG GTCGGCGCGACTGGGGCATTCGACATCTGGGGACAGGGAACTCTTGTGAC CGTGTCGAGCGGAGGCGGCGGCTCCGGCGGAGGAGGGAGCGGGGGCGGTG GTTCCGAAATCGTGTTGACTCAGTCCCCGGGAACCCTGAGCTTGTCACCC GGGGAGCGGGCCACTCTCTCCTGTCGCGCCTCCCAATCGCTCTCATCCAA TTTCCTGGCCTGGTACCAGCAGAAGCCCGGACAGGCCCCGGGCCTGCTCA TCTACGGCGCTTCAAACTGGGCAACGGGAACCCCTGATCGGTTCAGCGGA AGCGGATCGGGTACTGACTTTACCCTGACCATCACCAGACTGGAACCGGA GGACTTCGCCGTGTACTACTGCCAGTACTACGGCACCTCCCCCATGTACA CATTCGGACAGGGTACCAAGGTCGAGATTAAG
BCMA_EBB-	8088	EVQLLETGGGLVQPGGSLRLSCAASGFSFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKAL

C1978-D4- aa VH		VGATGAFDIWGQGTLVTVSS
BCMA_EBB-C1978-D4- aa VL	8109	EIVLTQSPGTLSLSPGERATLSCRASQSLSSNFLAWYQQKPGQAPGLLIY GASNWATGTPDRFSGSGSGTDFTLTITRLEPEDFAVYYCQYYGTSPMYTF GQGTKVEIK
BCMA_EBB-C1980-A2		
BCMA_EBB-C1980-A2- aa ScFv domain	8047	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCVLWF GEGFDPWGQGTLVTVSSGGGGSGGGGSGGGGSDIVLTQSPLSLPVTPGEP ASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFS GSGSGTDFTLKISRVEAEDVGVYYCMQALQTPLTFGGGTKVDIK
BCMA_EBB-C1980-A2- nt ScFv domain	8068	GAAGTGCAGCTGCTTGAGAGCGGTGGAGGTCTGGTGCAGCCCGGGGGATC ACTGCGCCTGTCCTGTGCCGCGTCCGGTTTCACTTTCTCCTCGTACGCCA TGTCGTGGGTCAGACAGGCACCGGGAAAGGGACTGGAATGGGTGTCAGCC ATTTCGGGTTCGGGGGGCAGCACCTACTACGCTGACTCCGTGAAGGGCCG GTTCACCATTTCCCGCGACAACTCCAAGAACACCTTGTACCTCCAAATGA ACTCCCTGCGGGCCGAAGATACCGCCGTGTATTACTGCGTGCTGTGGTTC GGAGAGGGATTCGACCCGTGGGGACAAGGAACACTCGTGACTGTGTCATC CGGCGGAGGCGGCAGCGGTGGCGGCGGTTCCGGCGGCGGCGGATCTGACA TCGTGTTGACCCAGTCCCCTCTGAGCCTGCCGGTCACTCCTGGCGAACCA GCCAGCATCTCCTGCCGGTCGAGCCAGTCCCTCCTGCACTCCAATGGGTA CAACTACCTCGATTGGTATCTGCAAAAGCCGGGCCAGAGCCCCCAGCTGC TGATCTACCTTGGGTCAAACCGCGCTTCCGGGGTGCCTGATAGATTCTCC GGGTCCGGGAGCGGAACCGACTTTACCCTGAAAATCTCGAGGGTGGAGGC CGAGGACGTCGGAGTGTACTACTGCATGCAGGCGCTCCAGACTCCCCTGA CCTTCGGAGGAGGAACGAAGGTCGACATCAAGA
BCMA_EBB-C1980-A2- aa VH	8089	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCVLWF GEGFDPWGQGTLVTVSS
BCMA_EBB-C1980-A2- aa VL	8110	DIVLTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQ LLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP LTFGGGTKVDIK
BCMA_EBB-C1981-C3		
BCMA_EBB-C1981-C3- aa ScFv domain	8048	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVG YDSSGYYRDYYGMDVWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPG TLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGTSSRATGI SDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYGNSPPKFTFGPGTKLEI K

BCMA_EBB-C1981-C3- nt **ScFv domain**	8069	CAAGTGCAGCTCGTGGAGTCAGGCGGAGGACTGGTGCAGCCCGGGGGCTC CCTGAGACTTTCCTGCGCGGCATCGGGTTTTACCTTCTCCTCCTATGCTA TGTCCTGGGTGCGCCAGGCCCCGGGAAAGGGACTGGAATGGGTGTCCGCA ATCAGCGGTAGCGGGGGCTCAACATACTACGCCGACTCCGTCAAGGGTCG CTTCACTATTTCCCGGGACAACTCCAAGAATACCCTGTACCTCCAAATGA ACAGCCTCAGGGCCGAGGATACTGCCGTGTACTACTGCGCCAAAGTCGGA TACGATAGCTCCGGTTACTACCGGGACTACTACGGAATGGACGTGTGGGG ACAGGGCACCACCGTGACCGTGTCAAGCGGCGGAGGCGGTTCAGGAGGGG GAGGCTCCGGCGGTGGAGGGTCCGAAATCGTCCTGACTCAGTCGCCTGGC ACTCTGTCGTTGTCCCCGGGGGAGCGCGCTACCCTGTCGTGTCGGGCGTC GCAGTCCGTGTCGAGCTCCTACCTCGCGTGGTACCAGCAGAAGCCCGGAC AGGCCCCTAGACTTCTGATCTACGGCACTTCTTCACGCGCCACCGGGATC AGCGACAGGTTCAGCGGCTCCGGCTCCGGGACCGACTTCACCCTGACCAT TAGCCGGCTGGAGCCTGAAGATTTCGCCGTGTATTACTGCCAACACTACG GAAACTCGCCGCCAAAGTTCACGTTCGGACCCGGAACCAAGCTGGAAATC AAG
BCMA_EBB-C1981-C3- aa **VH**	8090	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVG YDSSGYYRDYYGMDVWGQGTTVTVSS
BCMA_EBB-C1981-C3- aa **VL**	8111	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIY GTSSRATGISDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYGNSPPKFT FGPGTKLEIK
BCMA_EBB-C1978-G4		
BCMA_EBB-C1978-G4- aa **ScFv domain**	8049	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKMG WSSGYLGAFDIWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPGTLSL SPGERATLSCRASQSVASSFLAWYQQKPGQAPRLLIYGASGRATGIPDRF SGSGSGTDFTLTISRLEPEDFAVYYCQHYGGSPRLTFGGGTKVDIK
BCMA_EBB-C1978-G4- nt **ScFv domain**	8070	GAAGTCCAACTGGTGGAGTCCGGGGGAGGGCTCGTGCAGCCCGGAGGCAG CCTTCGGCTGTCGTGCGCCGCCTCCGGGTTCACGTTCTCATCCTACGCGA TGTCGTGGGTCAGACAGGCACCAGGAAAGGGACTGGAATGGGTGTCCGCC ATTAGCGGCTCCGGCGGTAGCACCTACTATGCCGACTCAGTGAAGGGAAG GTTCACTATCTCCCGCGACAACAGCAAGAACACCCTGTACCTCCAAATGA ACTCTCTGCGGGCCGAGGATACCGCGGTGTACTATTGCGCCAAGATGGGT TGGTCCAGCGGATACTTGGGAGCCTTCGACATTTGGGGACAGGGCACTAC TGTGACCGTGTCCTCCGGGGGTGGCGGATCGGGAGGCGGCGGCTCGGGTG GAGGGGGTTCCGAAATCGTGTTGACCCAGTCACCGGGAACCCTCTCGCTG TCCCCGGGAGAACGGGCTACACTGTCATGTAGAGCGTCCCAGTCCGTGGC TTCCTCGTTCCTGGCCTGGTACCAGCAGAAGCCGGGACAGGCACCCCGCC TGCTCATCTACGGAGCCAGCGGCCGGGCGACCGGCATCCCTGACCGCTTC TCCGGTTCCGGCTCGGGCACCGACTTTACTCTGACCATTAGCAGGCTTGA GCCCGAGGATTTTGCCGTGTACTACTGCCAACACTACGGGGGGAGCCCTC GCCTGACCTTCGGAGGCGGAACTAAGGTCGATATCAAAA

BCMA_EBB-C1978-G4- aa VH	8091	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSA ISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKMG WSSGYLGAFDIWGQGTTVTVSS
BCMA_EBB-C1978-G4- aa VL	8112	EIVLTQSPGTLSLSPGERATLSCRASQSVASSFLAWYQQKPGQAPRLLIY GASGRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYGGSPRLTF GGGTKVDIK

In embodiments, additional exemplary BCMA CAR constructs are generated using the VH and VL sequences from PCT Publication WO2012/0163805 (the contents of which are hereby incorporated by reference in its entirety). In embodiments, additional exemplary BCMA CAR constructs are generated using the VH and VL sequences from PCT Publication WO2016/014565 (the contents of which are hereby incorporated by reference in its entirety). In embodiments, additional exemplary BCMA CAR constructs are generated using the VH and VL sequences from PCT Publication WO2014/122144 (the contents of which are hereby incorporated by reference in its entirety). In embodiments, additional exemplary BCMA CAR constructs are generated using the CAR molecules, and/or the VH and VL sequences from PCT Publication WO2016/014789 (the contents of which are hereby incorporated by reference in its entirety). In embodiments, additional exemplary BCMA CAR constructs are generated using the CAR molecules, and/or the VH and VL sequences from PCT Publication WO2014/089335 (the contents of which are hereby incorporated by reference in its entirety). In embodiments, additional exemplary BCMA CAR constructs are generated using the CAR molecules, and/or the VH and VL sequences from PCT Publication WO2014/140248 (the contents of which are hereby incorporated by reference in its entirety).

In embodiments, additional exemplary BCMA CAR constructs can also be generated using the VH and VL sequences found in Table 19. The amino acid sequences of exemplary scFv domains comprising the VH and VL domains and a linker sequence, and full-length CARs are also found in Table 19.

Table 19. Additional exemplary BCMA binding domain sequences

Name	Sequence	SEQ ID NO:
A7D12.2 VH	QIQLVQSGPDLKKPGETVKLSCKASGYTFTNFGMNWVKQAPGKGFKWMAWINTY TGESYFADDFKGRFAFSVETSATTAYLQINNLKTEDTATYFCARGEIYYGYDGG FAYWGQGTLVTVSA	8155
A7D12.2 VL	DVVMTQSHRFMSTSVGDRVSITCRASQDVNTAVSWYQQKPGQSPKLLIFSASYR YTGVPDRFTGSGSGADFTLTISSVQAEDLAVYYCQQHYSTPWTFGGGTKLDIK	8159

A7D12.2 scFv domain	QIQLVQSGPDLKKPGETVKLSCKASGYTFTNFGMNWVKQAPGKGFKWMAWINTY TGESYFADDFKGRFAFSVETSATTAYLQINNLKTEDTATYFCARGEIYYGYDGG FAYWGQGTLVTVSAGGGGSGGGGSGGGGSDVVMTQSHRFMSTSVGDRVSITCRA SQDVNTAVSWYQQKPGQSPKLLIFSASYRYTGVPDRFTGSGSGADFTLTISSVQ AEDLAVYYCQQHYSTPWTFGGGTKLDIK	8163
C11D5.3 VH	QIQLVQSGPELKKPGETVKISCKASGYTFTDYSINWVKRAPGKGLKWMGWINTE TREPAYAYDFRGRFAFSLETSASTAYLQINNLKYEDTATYFCALDYSYAMDYWG QGTSVTVSS	8156
C11D5.3 VL	DIVLTQSPASLAMSLGKRATISCRASESVSVIGAHLIHWYQQKPGQPPKLLIYL ASNLETGVPARFSGSGSGTDFTLTIDPVEEDDVAIYSCLQSRIFPRTFGGGTKL EIK	8160
C11D5.3 scFv domain	QIQLVQSGPELKKPGETVKISCKASGYTFTDYSINWVKRAPGKGLKWMGWINTE TREPAYAYDFRGRFAFSLETSASTAYLQINNLKYEDTATYFCALDYSYAMDYWG QGTSVTVSSGGGGSGGGGSGGGGSQIQLVQSGPELKKPGETVKISCKASGYTFT DYSINWVKRAPGKGLKWMGWINTETREPAYAYDFRGRFAFSLETSASTAYLQIN NLKYEDTATYFCALDYSYAMDYWGQGTSVTVSS	8164
C12A3.2 VH	QIQLVQSGPELKKPGETVKISCKASGYTFRHYSMNWVKQAPGKGLKWMGRINTE SGVPIYADDFKGRFAFSVETSASTAYLVINNLKDEDTASYFCSNDYLYSLDFWG QGTALTVSS	8157
C12A3.2 VL	DIVLTQSPPSLAMSLGKRATISCRASESVTILGSHLIYWYQQKPGQPPTLLIQL ASNVQTGVPARFSGSGSRTDFTLTIDPVEEDDVAVYYCLQSRTIPRTFGGGTKL EIK	8161
C12A3.2 scFv domain	QIQLVQSGPELKKPGETVKISCKASGYTFRHYSMNWVKQAPGKGLKWMGRINTE SGVPIYADDFKGRFAFSVETSASTAYLVINNLKDEDTASYFCSNDYLYSLDFWG QGTALTVSSGGGGSGGGGSGGGGSDIVLTQSPPSLAMSLGKRATISCRASESVT ILGSHLIYWYQQKPGQPPTLLIQLASNVQTGVPARFSGSGSRTDFTLTIDPVEE DDVAVYYCLQSRTIPRTFGGGTKLEIK	8165
C13F12.1 VH	QIQLVQSGPELKKPGETVKISCKASGYTFTHYSMNWVKQAPGKGLKWMGRINTE TGEPLYADDFKGRFAFSLETSASTAYLVINNLKNEDTATFFCSNDYLYSCDYWG QGTTLTVSS	8158
C13F12.1 VL	DIVLTQSPPSLAMSLGKRATISCRASESVTILGSHLIYWYQQKPGQPPTLLIQL ASNVQTGVPARFSGSGSRTDFTLTIDPVEEDDVAVYYCLQSRTIPRTFGGGTKL EIK	8162
C13F12.1 scFv domain	QIQLVQSGPELKKPGETVKISCKASGYTFTHYSMNWVKQAPGKGLKWMGRINTE TGEPLYADDFKGRFAFSLETSASTAYLVINNLKNEDTATFFCSNDYLYSCDYWG QGTTLTVSSGGGGSGGGGSGGGGSDIVLTQSPPSLAMSLGKRATISCRASESVT ILGSHLIYWYQQKPGQPPTLLIQLASNVQTGVPARFSGSGSRTDFTLTIDPVEE DDVAVYYCLQSRTIPRTFGGGTKLEIK	8166

The sequences of human CDR sequences of the scFv domains are shown in Table 20 for the heavy chain variable domains and in Table 21 for the light chain variable domains. "ID" stands for the respective SEQ ID NO for each CDR. The CDRs are shown according to the Kabat definition, however, the CDRs under other convention, for example, Chothia or the combined Kabat/Chothia definitions may be readily deduced based on the VH and VL sequences above.

Table 20: Heavy Chain Variable Domain CDRs according to the Kabat numbering scheme (Kabat et al. (1991), "Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD)

Candidate	HCDR1	ID	HCDR2	ID	HCDR3	ID
139109	NHGMS	8294	GIVYSGSTYYAASVKG	8334	HGGESDV	8374
139103	NYAMS	8284	GISRSGENTYYADSVKG	8324	SPAHYYGGMDV	8364
139105	DYAMH	8285	GISWNSGSIGYADSVKG	8325	HSFLAY	8365
139111	NHGMS	8286	GIVYSGSTYYAASVKG	8326	HGGESDV	8366
139100	NFGIN	8287	WINPKNNNTNYAQKFQG	8327	GPYYYQSYMDV	8367
139101	SDAMT	8288	VISGSGGTTYYADSVKG	8328	LDSSGYYYARGPRY	8368
139102	NYGIT	8289	WISAYNGNTNYAQKFQG	8329	GPYYYYMDV	8369
139104	NHGMS	8290	GIVYSGSTYYAASVKG	8330	HGGESDV	8370
139106	NHGMS	8291	GIVYSGSTYYAASVKG	8331	HGGESDV	8371
139107	NHGMS	8292	GIVYSGSTYYAASVKG	8332	HGGESDV	8372
139108	DYYMS	8293	YISSSGSTIYYADSVKG	8333	ESGDGMDV	8373
139110	DYYMS	8295	YISSSGNTIYYADSVKG	8335	STMVREDY	8375
139112	NHGMS	8296	GIVYSGSTYYAASVKG	8336	HGGESDV	8376
139113	NHGMS	8297	GIVYSGSTYYAASVKG	8337	HGGESDV	8377
139114	NHGMS	8298	GIVYSGSTYYAASVKG	8338	HGGESDV	8378

149362	SSYYYWG	8299	SIYYSGSAYYNPSLKS	8339	HWQEWPDAFDI	8379
149363	TSGMCVS	8300	RIDWDEDKFYSTSLKT	8340	SGAGGTSATAFDI	8380
149364	SYSMN	8301	SISSSSSYIYYADSVKG	8341	TIAAVYAFDI	8381
149365	DYYMS	8302	YISSSGSTIYYADSVKG	8342	DLRGAFDI	8382
149366	SHYIH	8303	MINPSGGVTAYSQTLQG	8343	EGSGSGWYFDF	8383
149367	SGGYYWS	8304	YIYYSGSTYYNPSLKS	8344	AGIAARLRGAFDI	8384
149368	SYAIS	8305	GIIPIFGTANYAQKFQG	8345	RGGYQLLRWDVGLLRSAFDI	8385
149369	SNSAAWN	8306	RTYYRSKWYSFYAISLKS	8346	SSPEGLFLYWFDP	8386
BCMA_EBB-C1978-A4	SYAMS	8307	AISGSGGSTYYADSVKG	8347	VEGSGSLDY	8387
BCMA_EBB-C1978-G1	RYPMS	8308	GISDSGVSTYYADSAKG	8348	RAGSEASDI	8388
BCMA_EBB-C1979-C1	SYAMS	8309	AISGSGGSTYYADSVKG	8349	ATYKRELRYYYGMDV	8389
BCMA_EBB-C1978-C7	SYAMS	8310	AISGSGGSTYYADSVKG	8350	ATYKRELRYYYGMDV	8390
BCMA_EBB-C1978-D10	DYAMH	8311	GISWNSGSIGYADSVKG	8351	VGKAVPDV	8391
BCMA_EBB-C1979-C12	DYAMH	8312	SINWKGNSLAYGDSVKG	8352	HQGVAYYNYAMDV	8392
BCMA_EBB-C1980-G4	SYAMS	8313	AISGSGGSTYYADSVKG	8353	VVRDGMDV	8393

BCMA_EBB-C1980-D2	SYAMS	8314	AISGSGGSTYYADSVKG	8354	IPQTGTFDY	8394
BCMA_EBB-C1978-A10	SYAMS	8315	AISGSGGSTYYADSVKG	8355	ANYKRELRYYYGMDV	8395
BCMA_EBB-C1978-D4	SYAMS	8316	AISGSGGSTYYADSVKG	8356	ALVGATGAFDI	8396
BCMA_EBB-C1980-A2	SYAMS	8317	AISGSGGSTYYADSVKG	8357	WFGEGFDP	8397
BCMA_EBB-C1981-C3	SYAMS	8318	AISGSGGSTYYADSVKG	8358	VGYDSSGYYRDYYGMDV	8398
BCMA_EBB-C1978-G4	SYAMS	8319	AISGSGGSTYYADSVKG	8359	MGWSSGYLGAFDI	8399
A7D12.2	NFGMN	8320	WINTYTGESYFADDFKG	8360	GEIYYGYDGGFAY	8400
C11D5.3	DYSIN	8321	WINTETREPAYAYDFRG	8361	DYSYAMDY	8401
C12A3.2	HYSMN	8322	RINTESGVPIYADDFKG	8362	DYLYSLDF	8402
C13F12.1	HYSMN	8323	RINTETGEPLYADDFKG	8363	DYLYSCDY	8403

Table 21: Light Chain Variable Domain CDRs according to the Kabat numbering scheme (Kabat et al. (1991), "Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD)

Candidate	**LCDR1**	**ID**	**LCDR2**	**ID**	**LCDR3**	**ID**
139109	RASQSISSYLN	8414	AASSLQS	8454	QQSYSTPYT	8494
139103	RASQSISSSFLA	8404	GASRRAT	8444	QQYHSSPSWT	8484
139105	RSSQSLLHSNGYNY	8405	LGSNRAS	8445	MQALQTPYT	8485

	LD					
139111	KSSQSLLRNDGKTPLY	8406	EVSNRFS	8446	MQNIQFPS	8486
139100	RSSQSLLHSNGYNYLN	8407	LGSKRAS	8447	MQALQTPYT	8487
139101	RASQSISSYLN	8408	GASTLAS	8448	QQSYKRAS	8488
139102	RSSQSLLYSNGYNYVD	8409	LGSNRAS	8449	MQGRQFPYS	8489
139104	RASQSVSSNLA	8410	GASTRAS	8450	QQYGSSLT	8490
139106	RASQSVSSKLA	8411	GASIRAT	8451	QQYGSSSWT	8491
139107	RASQSVGSTNLA	8412	DASNRAT	8452	QQYGSSPPWT	8492
139108	RASQSISSYLN	8413	AASSLQS	8453	QQSYTLA	8493
139110	KSSESLVHNSGKTYLN	8415	EVSNRDS	8455	MQGTHWPGT	8495
139112	QASEDINKFLN	8416	DASTLQT	8456	QQYESLPLT	8496
139113	RASQSVGSNLA	8417	GASTRAT	8457	QQYNDWLPVT	8497
139114	RASQSIGSSSLA	8418	GASSRAS	8458	QQYAGSPPFT	8498
149362	KASQDIDDAMN	8419	SATSPVP	8459	LQHDNFPLT	8499
149363	RASQDIYNNLA	8420	AANKSQS	8460	QHYYRFPYS	8500
149364	RSSQSLLHSNGYNYLD	8421	LGSNRAS	8461	MQALQTPYT	8501
149365	GGNNIGTKSVH	8422	DDSVRPS	8462	QVWDSDSEHVV	8502
149366	SGDGLSKKYVS	8423	RDKERPS	8463	QAWDDTTVV	8503
149367	RASQGIRNWLA	8424	AASNLQS	8464	QKYNSAPFT	8504
149368	GGNNIGSKSVH	8425	GKNNRPS	8465	SSRDSSGDHLRV	8505
149369	QGDSLGNYYAT	8426	GTNNRPS	8466	NSRDSSGHHLL	8506
BCMA_EBB-C1978-A4	RASQSVSSAYLA	8427	GASTRAT	8467	QHYGSSFNGSSLFT	8507
BCMA_E	RASQSVSNSLA	8428	DASSRAT	8468	QQFGTSSGLT	8508

BB-C1978-G1						
BCMA_EBB-C1979-C1	RASQSVSSSFLA	8429	GASSRAT	8469	QQYHSSPSWT	8509
BCMA_EBB-C1978-C7	RASQSVSTTFLA	8430	GSSNRAT	8470	QQYHSSPSWT	8510
BCMA_EBB-C1978-D10	RASQSISSYLN	8431	AASSLQS	8471	QQSYSTPYS	8511
BCMA_EBB-C1979-C12	RATQSIGSSFLA	8432	GASQRAT	8472	QHYESSPSWT	8512
BCMA_EBB-C1980-G4	RASQSVSSSYLA	8433	GASSRAT	8473	QQYGSPPRFT	8513
BCMA_EBB-C1980-D2	RASQSVSSSYLA	8434	GASSRAT	8474	QHYGSSPSWT	8514
BCMA_EBB-C1978-A10	RASQRVASNYLA	8435	GASSRAT	8475	QHYDSSPSWT	8515
BCMA_EBB-C1978-D4	RASQSLSSNFLA	8436	GASNWAT	8476	QYYGTSPMYT	8516
BCMA_EBB-C1980-A2	RSSQSLLHSNGYNYLD	8437	LGSNRAS	8477	MQALQTPLT	8517
BCMA_EBB-C1981-C3	RASQSVSSSYLA	8438	GTSSRAT	8478	QHYGNSPPKFT	8518
BCMA_EBB-C1978-G4	RASQSVASSFLA	8439	GASGRAT	8479	QHYGGSPRLT	8519
A7D12.2	RASQDVNTAVS	8440	SASYRYT	8480	QQHYSTPWT	8520

C11D5.3	RASESVSVIGAHLIH	8441	LASNLET	8481	LQSRIFPRT	8521
C12A3.2	RASESVTILGSHLIY	8442	LASNVQT	8482	LQSRTIPRT	8522
C13F12.1	RASESVTILGSHLIY	8443	LASNVQT	8483	LQSRTIPRT	8523

In one embodiment, the BCMA binding domain comprises one or more (e.g., all three) light chain complementary determining region 1 (LC CDR1), light chain complementary determining region 2 (LC CDR2), and light chain complementary determining region 3 (LC CDR3) of a BCMA binding domain described herein, e.g., provided in Table 18, 19 or 21, and/or one or more (e.g., all three) heavy chain complementary determining region 1 (HC CDR1), heavy chain complementary determining region 2 (HC CDR2), and heavy chain complementary determining region 3 (HC CDR3) of a BCMA binding domain described herein, e.g., provided in Table 18, 19 or 20. In one embodiment, the BCMA binding domain comprises one, two, or all of LC CDR1, LC CDR2, and LC CDR3 of any amino acid sequences as provided in Table 18, incorporated herein by reference; and one, two or all of HC CDR1, HC CDR2, and HC CDR3 of any amino acid sequences as provided in Table 18.

In one embodiment, the BCMA antigen binding domain comprises:

(i) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8414, a LC CDR2 amino acid sequence of SEQ ID NO: 8454, and a LC CDR3 amino acid sequence of SEQ ID NO: 8494; and
(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8294, a HC CDR2 amino acid sequence of SEQ ID NO: 8334, and a HC CDR3 amino acid sequence of SEQ ID NO: 8374

(ii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8404, a LC CDR2 amino acid sequence of SEQ ID NO: 8444, and a LC CDR3 amino acid sequence of SEQ ID NO: 8484; and
(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8284, a HC CDR2 amino acid sequence of SEQ ID NO: 8324, and a HC CDR3 amino acid sequence of SEQ ID NO: 8364

(iii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8405, a LC CDR2 amino acid sequence of SEQ ID NO: 8445, and a LC CDR3 amino acid sequence of SEQ ID NO: 8485; and
(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8285, a HC CDR2 amino acid sequence of SEQ ID NO: 8325, and a HC CDR3 amino acid sequence of SEQ ID NO: 8365

(iv) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8406, a LC CDR2 amino acid sequence of SEQ ID NO: 8446, and a LC CDR3 amino acid sequence of SEQ ID NO: 8486; and
(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8286, a HC CDR2 amino acid sequence of SEQ ID NO: 8326, and a HC CDR3 amino acid sequence of SEQ ID NO: 8366

(v) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8407, a LC CDR2 amino acid sequence of SEQ ID NO: 8447, and a LC CDR3 amino acid sequence of SEQ ID NO: 8487; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 8287, a HC CDR2 amino acid sequence of SEQ ID NO: 8327, and a HC CDR3 amino acid sequence of SEQ ID NO: 8367

(vi) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8408, a LC CDR2 amino acid sequence of SEQ ID NO: 8448, and a LC CDR3 amino acid sequence of SEQ ID NO: 8488; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 8288, a HC CDR2 amino acid sequence of SEQ ID NO: 8328, and a HC CDR3 amino acid sequence of SEQ ID NO: 8368

(vii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8409, a LC CDR2 amino acid sequence of SEQ ID NO: 8449, and a LC CDR3 amino acid sequence of SEQ ID NO: 8489; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 8289, a HC CDR2 amino acid sequence of SEQ ID NO: 8329, and a HC CDR3 amino acid sequence of SEQ ID NO: 8369

(viii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8410, a LC CDR2 amino acid sequence of SEQ ID NO: 8450, and a LC CDR3 amino acid sequence of SEQ ID NO: 8490; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 8290, a HC CDR2 amino acid sequence of SEQ ID NO: 8330, and a HC CDR3 amino acid sequence of SEQ ID NO: 8370

(ix) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8411, a LC CDR2 amino acid sequence of SEQ ID NO: 8451, and a LC CDR3 amino acid sequence of SEQ ID NO: 8491; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 8291, a HC CDR2 amino acid sequence of SEQ ID NO: 8331, and a HC CDR3 amino acid sequence of SEQ ID NO: 8371

(x) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8412, a LC CDR2 amino acid sequence of SEQ ID NO: 8452, and a LC CDR3 amino acid sequence of SEQ ID NO: 8492; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 8292, a HC CDR2 amino acid sequence of SEQ ID NO: 8332, and a HC CDR3 amino acid sequence of SEQ ID NO: 8372

(xi) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8413, a LC CDR2 amino acid sequence of SEQ ID NO: 8453, and a LC CDR3 amino acid sequence of SEQ ID NO: 8493; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 8293, a HC CDR2 amino acid sequence of SEQ ID NO: 8333, and a HC CDR3 amino acid sequence of SEQ ID NO: 8373

(xii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8415, a LC CDR2 amino acid sequence of SEQ ID NO: 8455, and a LC CDR3 amino acid sequence of SEQ ID NO: 8495; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 8295, a HC CDR2 amino acid sequence of SEQ ID NO: 8335, and a HC CDR3 amino acid sequence of SEQ ID NO: 8375

(xiii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8416, a LC CDR2 amino acid sequence of SEQ ID NO: 8456, and a LC CDR3 amino acid sequence of SEQ ID NO: 8496; and

(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8296, a HC CDR2 amino acid sequence of SEQ ID NO: 8336, and a HC CDR3 amino acid sequence of SEQ ID NO: 8376

(xiv) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8417, a LC CDR2 amino acid sequence of SEQ ID NO: 8457, and a LC CDR3 amino acid sequence of SEQ ID NO: 8497; and

(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8297, a HC CDR2 amino acid sequence of SEQ ID NO: 8337, and a HC CDR3 amino acid sequence of SEQ ID NO: 8377

(xv) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8418, a LC CDR2 amino acid sequence of SEQ ID NO: 8458, and a LC CDR3 amino acid sequence of SEQ ID NO: 8498; and

(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8298, a HC CDR2 amino acid sequence of SEQ ID NO: 8338, and a HC CDR3 amino acid sequence of SEQ ID NO: 8378

(xvi) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8419, a LC CDR2 amino acid sequence of SEQ ID NO: 8459, and a LC CDR3 amino acid sequence of SEQ ID NO: 8499; and

(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8299, a HC CDR2 amino acid sequence of SEQ ID NO: 8339, and a HC CDR3 amino acid sequence of SEQ ID NO: 8379

(xvii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8420, a LC CDR2 amino acid sequence of SEQ ID NO: 8460, and a LC CDR3 amino acid sequence of SEQ ID NO: 8500; and

(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8300, a HC CDR2 amino acid sequence of SEQ ID NO: 8340, and a HC CDR3 amino acid sequence of SEQ ID NO: 8380

(xviii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8421, a LC CDR2 amino acid sequence of SEQ ID NO: 8461, and a LC CDR3 amino acid sequence of SEQ ID NO: 8501; and

(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8301, a HC CDR2 amino acid sequence of SEQ ID NO: 8341, and a HC CDR3 amino acid sequence of SEQ ID NO: 8381

(xix) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8422, a LC CDR2 amino acid sequence of SEQ ID NO: 8462, and a LC CDR3 amino acid sequence of SEQ ID NO: 8502; and

(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8302, a HC CDR2 amino acid sequence of SEQ ID NO: 8342, and a HC CDR3 amino acid sequence of SEQ ID NO: 8382

(xx) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8423, a LC CDR2 amino acid sequence of SEQ ID NO: 8463, and a LC CDR3 amino acid sequence of SEQ ID NO: 8503; and

(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8303, a HC CDR2 amino acid sequence of SEQ ID NO: 8343, and a HC CDR3 amino acid sequence of SEQ ID NO: 8383

(xxi) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8424, a LC CDR2 amino acid sequence of SEQ ID NO: 8464, and a LC CDR3 amino acid sequence of SEQ ID NO: 8504; and

(b) a HC CDR1 amino acid sequence of SEQ ID NO: 8304, a HC CDR2 amino acid sequence of SEQ ID NO: 8344, and a HC CDR3 amino acid sequence of SEQ ID NO: 8384

(xxii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8425, a LC CDR2 amino acid sequence of SEQ ID NO: 8465, and a LC CDR3 amino acid sequence of SEQ ID NO: 8505; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 8305, a HC CDR2 amino acid sequence of SEQ ID NO: 8345, and a HC CDR3 amino acid sequence of SEQ ID NO: 8385 or

(xxiii) (a) a LC CDR1 amino acid sequence of SEQ ID NO: 8426, a LC CDR2 amino acid sequence of SEQ ID NO: 8466, and a LC CDR3 amino acid sequence of SEQ ID NO: 8506; and (b) a HC CDR1 amino acid sequence of SEQ ID NO: 8306, a HC CDR2 amino acid sequence of SEQ ID NO: 8346, and a HC CDR3 amino acid sequence of SEQ ID NO: 8386.

In one embodiment, the BCMA binding domain comprises a light chain variable region described herein (e.g., in Table 18 or 19) and/or a heavy chain variable region described herein (e.g., in Table 18 or 19). In one embodiment, the BCMA binding domain is a scFv comprising a light chain and a heavy chain of an amino acid sequence listed in Table 18 or 19. In an embodiment, the BCMA binding domain (e.g., an scFv) comprises: a light chain variable region comprising an amino acid sequence having at least one, two or three modifications (e.g., substitutions, e.g., conservative substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions, e.g., conservative substitutions) of an amino acid sequence of a light chain variable region provided in Table 18 or 19, or a sequence with 95-99% identity with an amino acid sequence provided in Table 18 or 19; and/or a heavy chain variable region comprising an amino acid sequence having at least one, two or three modifications (e.g., substitutions, e.g., conservative substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions, e.g., conservative substitutions) of an amino acid sequence of a heavy chain variable region provided in Table 18 or 19, or a sequence with 95-99% identity to an amino acid sequence provided in Table 18 or 19.

In one embodiment, the BCMA binding domain comprises an amino acid sequence selected from a group consisting of SEQ ID NO: 7949; SEQ ID NO: 7939, SEQ ID NO: 7940; SEQ ID NO: 7941; SEQ ID NO: 7942; SEQ ID NO: 7943; SEQ ID NO: 7944, SEQ ID NO: 7945, SEQ ID NO: 7946, SEQ ID NO: 7947, SEQ ID NO: 7948, SEQ ID NO: 7950, SEQ ID NO: 7951, SEQ ID NO: 7952, SEQ ID NO: 7953, SEQ ID NO: 8029, SEQ ID NO: 8030, SEQ ID NO: 8031, SEQ ID NO: 8032, SEQ ID NO: 8033, SEQ ID NO: 8034, SEQ ID NO: 8035, SEQ ID NO: 8036, SEQ ID NO: 8037, SEQ ID NO: 8038, SEQ ID NO: 8039, SEQ ID NO: 8040, SEQ ID NO: 8041, SEQ ID NO: 8042, SEQ ID NO: 8043, SEQ ID NO: 8044, SEQ ID NO: 8045, SEQ ID NO: 8046, SEQ ID NO: 8047, SEQ ID NO: 8048, SEQ ID NO: 8049, SEQ ID NO: 8163, SEQ ID NO: 8164, SEQ ID NO: 8165 and SEQ ID NO: 8166; or an amino acid sequence having at least one, two or three modifications (e.g., substitutions, e.g., conservative substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions, e.g., conservative substitutions) to any of the aforesaid sequences; or a sequence with 95-99% identity to any of the

aforesaid sequences. In one embodiment, the BCMA binding domain is a scFv, and a light chain variable region comprising an amino acid sequence described herein, e.g., in Table 18 or 19, is attached to a heavy chain variable region comprising an amino acid sequence described herein, e.g., in Table 18 or 19, via a linker, e.g., a linker described herein. In one embodiment, the BCMA binding domain includes a (Gly4-Ser)n linker, wherein n is 1, 2, 3, 4, 5, or 6, preferably 3 (SEQ ID NO: 10801). The light chain variable region and heavy chain variable region of a scFv can be, e.g., in any of the following orientations: light chain variable region-linker-heavy chain variable region or heavy chain variable region-linker-light chain variable region.

Any known BCMA CAR, e.g., the BMCA antigen binding domain of any known BCMA CAR, in the art can be used in accordance with the instant invention. For example, those described herein.

Exemplary CAR Molecules

In one aspect, a CAR, e.g., a CAR expressed by the cell of the invention, comprises a CAR molecule comprising an antigen binding domain that binds to a B cell antigen, e.g., as described herein, such as CD19 or BCMA.

In one embodiment, the CAR comprises a CAR molecule comprising a CD19 antigen binding domain (e.g., a murine, human or humanized antibody or antibody fragment that specifically binds to CD19), a transmembrane domain, and an intracellular signaling domain (e.g., an intracellular signaling domain comprising a costimulatory domain and/or a primary signaling domain).

Exemplary CAR molecules described herein are provided in Table 22. The CAR molecules in Table 22 comprise a CD19 antigen binding domain, e.g., an amino acid sequence of any CD19 antigen binding domain provided in Table 14.

Table 22. Exemplary CD19 CAR molecules

Antigen	Name	Amino Acid Sequence	SEQ ID NO:
CD19	CTL019	MALPVTALLLPLALLLHAARPDIQMTQTTSSLSASLGDRVTISCRASQ DISKYLNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTI SNLEQEDIATYFCQQGNTLPYTFGGGTKLEITGGGGSGGGGSGGGGSE VKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLG VIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAK HYYYGGSYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPE ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGR KKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADA	7920

		PAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGL YNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR	
CD19	CAR 1	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERATLSCRASQ DISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTI SSLQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSQ VQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIG VIWGSETTYYSSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAK HYYYGGSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLRPE ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGR KKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADA PAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGL YNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR	**7908**
CD19	CAR 2	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERATLSCRASQ DISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTI SSLQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSQ VQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIG VIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAK HYYYGGSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLRPE ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGR KKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADA PAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGL YNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR	**7909**
CD19	CAR 3	MALPVTALLLPLALLLHAARPQVQLQESGPGLVKPSETLSLTCTVSGV SLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYSSSLKSRVTISKDNSK NQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTVSSGGG GSGGGGSGGGGSEIVMTQSPATLSLSPGERATLSCRASQDISKYLNWY QQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFA VYFCQQGNTLPYTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPE ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGR KKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADA PAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGL YNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR	**7910**
CD19	CAR 4	MALPVTALLLPLALLLHAARPQVQLQESGPGLVKPSETLSLTCTVSGV SLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYQSSLKSRVTISKDNSK NQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTVSSGGG GSGGGGSGGGGSEIVMTQSPATLSLSPGERATLSCRASQDISKYLNWY QQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFA VYFCQQGNTLPYTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPE ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGR KKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADA PAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGL YNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR	**7911**

CD19	CAR 5	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERATLSCRASQ DISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTI SSLQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSG GGGSQVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKG LEWIGVIWGSETTYYSSSLKSRVTISKDNSKNQVSLKLSSVTAADTAV YYCAKHYYYGGSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY CKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFS RSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKN PQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTY DALHMQALPPR	**7912**
CD19	CAR 6	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERATLSCRASQ DISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTI SSLQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSG GGGSQVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKG LEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSSVTAADTAV YYCAKHYYYGGSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY CKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFS RSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKN PQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTY DALHMQALPPR	**7913**
CD19	CAR 7	MALPVTALLLPLALLLHAARPQVQLQESGPGLVKPSETLSLTCTVSGV SLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYSSSLKSRVTISKDNSK NQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTVSSGGG GSGGGGSGGGGSGGGGSEIVMTQSPATLSLSPGERATLSCRASQDISK YLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQ PEDFAVYFCQQGNTLPYTFGQGTKLEIKTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY CKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFS RSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKN PQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTY DALHMQALPPR	**7914**
CD19	CAR 8	MALPVTALLLPLALLLHAARPQVQLQESGPGLVKPSETLSLTCTVSGV SLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYQSSLKSRVTISKDNSK NQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTVSSGGG GSGGGGSGGGGSGGGGSEIVMTQSPATLSLSPGERATLSCRASQDISK YLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQ PEDFAVYFCQQGNTLPYTFGQGTKLEIKTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY CKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFS RSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKN PQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTY DALHMQALPPR	**7915**
CD19	CAR 9	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERATLSCRASQ DISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTI SSLQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSG GGGSQVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKG	**7916**

		LEWIGVIWGSETTYYNSSLKSRVTISKDNSKNQVSLKLSSVTAADTAV YYCAKHYYYGGSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY CKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFS RSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKN PQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTY DALHMQALPPR	
CD19	CAR 10	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERATLSCRASQ DISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTI SSLQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSG GGGSQVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKG LEWIGVIWGSETTYYNSSLKSRVTISKDNSKNQVSLKLSSVTAADTAV YYCAKHYYYGGSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY CKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFS RSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKN PQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTY DALHMQALPPR	**7917**
CD19	CAR 11	MALPVTALLLPLALLLHAARPQVQLQESGPGLVKPSETLSLTCTVSGV SLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYNSSLKSRVTISKDNSK NQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTVSSGGG GSGGGGSGGGGSGGGGSEIVMTQSPATLSLSPGERATLSCRASQDISK YLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQ PEDFAVYFCQQGNTLPYTFGQGTKLEIKTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY CKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFS RSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKN PQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTY DALHMQALPPR	**7918**
CD19	CAR 12	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERATLSCRASQ DISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTI SSLQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSQ VQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIG VIWGSETTYYNSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAK HYYYGGSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLRPE ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGR KKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADA PAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGL YNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHM QALPPR	**7919**

In one embodiment, the CAR molecule comprises (e.g., consists of) an amino acid sequence as provided in Table 22, or in Table 3 of International Publication No. WO2014/153270, filed March 15, 2014; incorporated herein by reference. In one embodiment, the CAR molecule comprises (e.g., consists of) an amino acid sequence of SEQ ID NO: 7908, SEQ ID NO: 7909, SEQ ID NO: 7910, SEQ ID NO:

7911, SEQ ID NO: 7912, SEQ ID NO: 7913, SEQ ID NO: 7914, SEQ ID NO: 7915, SEQ ID NO: 7916, SEQ ID NO: 7917, SEQ ID NO: 7918, SEQ ID NO: 7919, or SEQ ID NO: 7920; or an amino acid sequence having at least one, two, three, four, five, 10, 15, 20 or 30 modifications (e.g., substitutions, e.g., conservative substitutions) but not more than 60, 50, or 40 modifications (e.g., substitutions, e.g., conservative substitutions) of an amino acid sequence of SEQ ID NO: 7908, SEQ ID NO: 7909, SEQ ID NO: 7910, SEQ ID NO: 7911, SEQ ID NO: 7912, SEQ ID NO: 7913, SEQ ID NO: 7914, SEQ ID NO: 7915, SEQ ID NO: 7916, SEQ ID NO: 7917, SEQ ID NO: 7918, SEQ ID NO: 7919, or SEQ ID NO: 7920; or an amino acid sequence having 85%, 90%, 95%, 96%, 97%, 98%, 99% identity to an amino acid sequence of SEQ ID NO: 7908, SEQ ID NO: 7909, SEQ ID NO: 7910, SEQ ID NO: 7911, SEQ ID NO: 7912, SEQ ID NO: 7913, SEQ ID NO: 7914, SEQ ID NO: 7915, SEQ ID NO: 7916, SEQ ID NO: 7917, SEQ ID NO: 7918, SEQ ID NO: 7919, or SEQ ID NO: 7920.

In one aspect, a CAR, e.g., a CAR expressed by the cell of the invention, comprises a CAR molecule comprising an antigen binding domain that binds to BCMA, e.g., comprises a BCMA antigen binding domain (e.g., a murine, human or humanized antibody or antibody fragment that specifically binds to BCMA, e.g., human BCMA), a transmembrane domain, and an intracellular signaling domain (e.g., an intracellular signaling domain comprising a costimulatory domain and/or a primary signaling domain).

Exemplary CAR molecules of a CAR described herein are provided in Table 23, or Table 1 of WO2016/014565, or as otherwise described herein. The CAR molecules in Table 23 comprise a BCMA antigen binding domain, e.g., an amino acid sequence of any BCMA antigen binding domain provided in Table 18 or 19.

Table 23. Exemplary BCMA CAR molecules. Sequences are provided with a leader sequence.

Name/ Description	SEQ ID NO:	Sequence
139109		
139109- aa Full CAR	8559	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAVSGFALS NHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNTLYLQ MNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRASGGGGS DIQLTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAA SSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPYTFGQGT KVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDI YIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGC SCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDK RRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDG

		LYQGLSTATKDTYDALHMQALPPR
139109- nt **Full CAR**	8574	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAATTGGTGGAATCAGGGGGAGGACTTGTGCAG CCTGGAGGATCGCTGAGACTGTCATGTGCCGTGTCCGGCTTTGCCCTGTCC AACCACGGGATGTCCTGGGTCCGCCGCGCGCCTGGAAAGGGCCTCGAATGG GTGTCGGGTATTGTGTACAGCGGTAGCACCTACTATGCCGCATCCGTGAAG GGGAGATTCACCATCAGCCGGGACAACTCCAGGAACACTCTGTACCTCCAA ATGAATTCGCTGAGGCCAGAGGACACTGCCATCTACTACTGCTCCGCGCAT GGCGGAGAGTCCGACGTCTGGGGACAGGGGACCACCGTGACCGTGTCTAGC GCGTCCGGCGGAGGCGGCAGCGGGGGTCGGGCATCAGGGGGCGGCGGATCG GACATCCAGCTCACCCAGTCCCCGAGCTCGCTGTCCGCCTCCGTGGGAGAT CGGGTCACCATCACGTGCCGCGCCAGCCAGTCGATTTCCTCCTACCTGAAC TGGTACCAACAGAAGCCCGGAAAAGCCCCGAAGCTTCTCATCTACGCCGCC TCGAGCCTGCAGTCAGGAGTGCCCTCACGGTTCTCCGGCTCCGGTTCCGGT ACTGATTTCACCCTGACCATTTCCTCCCTGCAACCGGAGGACTTCGCTACT TACTACTGCCAGCAGTCGTACTCCACCCCCTACACTTTCGGACAAGGCACC AAGGTCGAAATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCT CCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCC GCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATC TACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTC GTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTT AAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGT TCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAA TTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTC TACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAG CGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCC CAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTAT AGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGACGGA CTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCTCTTCAC ATGCAGGCCCTGCCGCCTCGG
139103		
139103- aa **Full CAR**	8549	MALPVTALLLPLALLLHAARPQVQLVESGGGLVQPGRSLRLSCAASGFTFS NYAMSWVRQAPGKGLGWVSGISRSGENTYYADSVKGRFTISRDNSKNTLYL QMNSLRDEDTAVYYCARSPAHYYGGMDVWGQGTTVTVSSASGGGGSGGRAS GGGGSDIVLTQSPGTLSLSPGERATLSCRASQSISSSFLAWYQQKPGQAPR LLIYGASRRATGIPDRFSGSGSGTDFTLTISRLEPEDSAVYYCQQYHSSPS WTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRG LDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQT TQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRRE EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERR RGKGHDGLYQGLSTATKDTYDALHMQALPPR
139103- nt **Full CAR**	8564	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGTGCAA CCCGGAAGATCGCTTAGACTGTCGTGTGCCGCCAGCGGGTTCACTTTCTCG AACTACGCGATGTCCTGGGTCCGCCAGGCACCCGGAAAGGGACTCGGTTGG GTGTCCGGCATTTCCCGGTCCGGCGAAAATACCTACTACGCCGACTCCGTG AAGGGCCGCTTCACCATCTCAAGGGACAACAGCAAAAACACCCTGTACTTG CAAATGAACTCCCTGCGGGATGAAGATACAGCCGTGTACTATTGCGCCCGG

		TCGCCTGCCCATTACTACGGCGGAATGGACGTCTGGGGACAGGGAACCACT GTGACTGTCAGCAGCGCGTCGGGTGGCGGCGGCTCAGGGGGTCGGGCCTCC GGGGGGGGAGGGTCCGACATCGTGCTGACCCAGTCCCCGGGAACCCTGAGC CTGAGCCCGGGAGAGCGCGCGACCCTGTCATGCCGGGCATCCCAGAGCATT AGCTCCTCCTTTCTCGCCTGGTATCAGCAGAAGCCCGGACAGGCCCCGAGG CTGCTGATCTACGGCGCTAGCAGAAGGGCTACCGGAATCCCAGACCGGTTC TCCGGCTCCGGTTCCGGGACCGATTTCACCCTTACTATCTCGCGCCTGGAA CCTGAGGACTCCGCCGTCTACTACTGCCAGCAGTACCACTCATCCCCGTCG TGGACGTTCGGACAGGGCACCAAGCTGGAGATTAAGACCACTACCCCAGCA CCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTG CGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGT CTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGC GGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGG AAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACT ACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGC GGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTAC AAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAG GAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGG AAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAG GATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGA AGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAG GACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139105		
139105- aa **Full CAR**	8550	MALPVTALLLPLALLLHAARPQVQLVESGGGLVQPGRSLRLSCAASGFTFD DYAMHWVRQAPGKGLEWVSGISWNSGSIGYADSVKGRFTISRDNAKNSLYL QMNSLRAEDTALYYCSVHSFLAYWGQGTLVTVSSASGGGGSGGRASGGGGS DIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQL LIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPYT FGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLD FACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQ EEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEY DVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRG KGHDGLYQGLSTATKDTYDALHMQALPPR
139105- nt **Full CAR**	8565	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAACTCGTCGAATCCGGTGGAGGTCTGGTCCAA CCTGGTAGAAGCCTGAGACTGTCGTGTGCGGCCAGCGGATTCACCTTTGAT GACTATGCTATGCACTGGGTGCGGCAGGCCCCAGGAAAGGGCCTGGAATGG GTGTCGGGAATTAGCTGGAACTCCGGGTCCATTGGCTACGCCGACTCCGTG AAGGGCCGCTTCACCATCTCCCGCGACAACGCAAAGAACTCCCTGTACTTG CAAATGAACTCGCTCAGGGCTGAGGATACCGCGCTGTACTACTGCTCCGTG CATTCCTTCCTGGCCTACTGGGGACAGGGAACTCTGGTCACCGTGTCGAGC GCCTCCGGCGGCGGGGGCTCGGGTGGACGGGCCTCGGGCGGAGGGGGGTCC GACATCGTGATGACCCAGACCCCGCTGAGCTTGCCCGTGACTCCCGGAGAG CCTGCATCCATCTCCTGCCGGTCATCCCAGTCCCTTCTCCACTCCAACGGA TACAACTACCTCGACTGGTACCTCCAGAAGCCGGGACAGAGCCCTCAGCTT CTGATCTACCTGGGGTCAAATAGAGCCTCAGGAGTGCCGGATCGGTTCAGC GGATCTGGTTCGGGAACTGATTTCACTCTGAAGATTTCCCGCGTGGAAGCC GAGGACGTGGGCGTCTACTACTGTATGCAGGCGCTGCAGACCCCCTATACC TTCGGCCAAGGGACGAAAGTGGAGATCAAGACCACTACCCCAGCACCGAGG

		CCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCG GAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGAC TTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTC CTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAG CTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAA GAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGC GAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAG GGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTAC GACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCG CGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAG ATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGC AAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACC TATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139111		
139111- aa **Full CAR**	8551	MALPVTALLLPLALLLHAARPEVQLLESGGGLVQPGGSLRLSCAVSGFALS NHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNTLYLQ MNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRASGGGGS DIVMTQTPLSLSVTPGQPASISCKSSQSLLRNDGKTPLYWYLQKAGQPPQL LIYEVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGAYYCMQNIQFPSF GGGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDF ACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQE EDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYD VLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGK GHDGLYQGLSTATKDTYDALHMQALPPR
139111- nt **Full CAR**	8566	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAATTGTTGGAATCTGGAGGAGGACTTGTGCAG CCTGGAGGATCACTGAGACTTTCGTGTGCGGTGTCAGGCTTCGCCCTGAGC AACCACGGCATGAGCTGGGTGCGGAGAGCCCCGGGGAAGGGTCTGGAATGG GTGTCCGGGATCGTCTACTCCGGTTCAACTTACTACGCCGCAAGCGTGAAG GGTCGCTTCACCATTTCCCGCGATAACTCCCGGAACACCCTGTACCTCCAA ATGAACTCCCTGCGGCCCGAGGACACCGCCATCTACTACTGTTCCGCGCAT GGAGGAGAGTCCGATGTCTGGGGACAGGGCACTACCGTGACCGTGTCGAGC GCCTCGGGGGGGAGGAGGCTCCGGCGGTCGCGCCTCCGGGGGGGGGTGGCAGC GACATTGTGATGACGCAGACTCCACTCTCGCTGTCCGTGACCCCGGGACAG CCCGCGTCCATCTCGTGCAAGAGCTCCCAGAGCCTGCTGAGGAACGACGGA AAGACTCCTCTGTATTGGTACCTCCAGAAGGCTGGACAGCCCCCGCAACTG CTCATCTACGAAGTGTCAAATCGCTTCTCCGGGGTGCCGGATCGGTTTTCC GGCTCGGGATCGGGCACCGACTTCACCCTGAAAATCTCCAGGGTCGAGGCC GAGGACGTGGGAGCCTACTACTGCATGCAAAACATCCAGTTCCCTTCCTTC GGCGGCGGCACAAAGCTGGAGATTAAGACCACTACCCCAGCACCGAGGCCA CCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAG GCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTC GCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTG CTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTG CTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAG GAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAA CTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGG CAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGAC GTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGC

		AGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATG GCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAA GGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTAT GACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139100		
139100- aa **Full CAR**	8552	MALPVTALLLPLALLLHAARPQVQLVQSGAEVRKTGASVKVSCKASGYIFD NFGINWVRQAPGQGLEWMGWINPKNNNTNYAQKFQGRVTITADESTNTAYM EVSSLRSEDTAVYYCARGPYYYQSYMDVWGQGTMVTVSSASGGGGSGGRAS GGGGSDIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYLNWYLQKPG QSPQLLIYLGSKRASGVPDRFSGSGSGTDFTLHITRVGAEDVGVYYCMQAL QTPYTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVH TRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRP VQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKG ERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139100- nt **Full CAR**	8567	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTCCAACTCGTCCAGTCCGGCGCAGAAGTCAGAAAA ACCGGTGCTAGCGTGAAAGTGTCCTGCAAGGCCTCCGGCTACATTTTCGAT AACTTCGGAATCAACTGGGTCAGACAGGCCCCGGGCCAGGGGCTGGAATGG ATGGGATGGATCAACCCCAAGAACAACAACACCAACTACGCACAGAAGTTC CAGGGCCGCGTGACTATCACCGCCGATGAATCGACCAATACCGCCTACATG GAGGTGTCCTCCCTGCGGTCGGAGGACACTGCCGTGTATTACTGCGCGAGG GGCCCATACTACTACCAAAGCTACATGGACGTCTGGGGACAGGGAACCATG GTGACCGTGTCATCCGCCTCCGGTGGTGGAGGCTCCGGGGGGGCGGGCTTCA GGAGGCGGAGGAAGCGATATTGTGATGACCCAGACTCCGCTTAGCCTGCCC GTGACTCCTGGAGAACCGGCCTCCATTTCCTGCCGGTCCTCGCAATCACTC CTGCATTCCAACGGTTACAACTACCTGAATTGGTACCTCCAGAAGCCTGGC CAGTCGCCCCAGTTGCTGATCTATCTGGGCTCGAAGCGCGCCTCCGGGGTG CCTGACCGGTTTAGCGGATCTGGGAGCGGCACGGACTTCACTCTCCACATC ACCCGCGTGGGAGCGGAGGACGTGGGAGTGTACTACTGTATGCAGGCGCTG CAGACTCCGTACACATTCGGACAGGGCACCAAGCTGGAGATCAAGACCACT ACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCT CTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCAT ACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCT GGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAG CGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCT GTGCAGACTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAG GAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCT CCAGCCTACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGT CGGAGAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAA ATGGGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAG CTCCAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGG GAACGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACC GCCACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139101		
139101- aa	8553	MALPVTALLLPLALLLHAARPQVQLQESGGGLVQPGGSLRLSCAASGFTFS SDAMTWVRQAPGKGLEWVSVISGSGGTTYYADSVKGRFTISRDNSKNTLYL

Full CAR		QMNSLRAEDTAVYYCAKLDSSGYYYARGPRYWGQGTLVTVSSASGGGGSGG RASGGGGSDIQLTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKA PKLLIYGASTLASGVPARFSGSGSGTHFTLTINSLQSEDSATYYCQQSYKR ASFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRG LDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQT TQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRRE EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERR RGKGHDGLYQGLSTATKDTYDALHMQALPPR
139101- nt **Full CAR**	8568	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAACTTCAAGAATCAGGCGGAGGACTCGTGCAG CCCGGAGGATCATTGCGGCTCTCGTGCGCCGCCTCGGGCTTCACCTTCTCG AGCGACGCCATGACCTGGGTCCGCCAGGCCCCGGGGAAGGGGCTGGAATGG GTGTCTGTGATTTCCGGCTCCGGGGGAACTACGTACTACGCCGATTCCGTG AAAGGTCGCTTCACTATCTCCCGGGACAACAGCAAGAACACCCTTTATCTG CAAATGAATTCCCTCCGCGCCGAGGACACCGCCGTGTACTACTGCGCCAAG CTGGACTCCTCGGGCTACTACTATGCCCGGGGTCCGAGATACTGGGGACAG GGAACCCTCGTGACCGTGTCCTCCGCGTCCGGCGGAGGAGGGTCGGGAGGG CGGGCCTCCGGCGGCGGCGGTTCGGACATCCAGCTGACCCAGTCCCCATCC TCACTGAGCGCAAGCGTGGGCGACAGAGTCACCATTACATGCAGGGCGTCC CAGAGCATCAGCTCCTACCTGAACTGGTACCAACAGAAGCCTGGAAAGGCT CCTAAGCTGTTGATCTACGGGGCTTCGACCCTGGCATCCGGGGTGCCCGCG AGGTTTAGCGGAAGCGGTAGCGGCACTCACTTCACTCTGACCATTAACAGC CTCCAGTCCGAGGATTCAGCCACTTACTACTGTCAGCAGTCCTACAAGCGG GCCAGCTTCGGACAGGGCACTAAGGTCGAGATCAAGACCACTACCCCAGCA CCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTG CGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGT CTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGC GGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGG AAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACT ACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGC GGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTAC AAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAG GAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGG AAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAG GATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGA AGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAG GACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139102		
139102- aa **Full CAR**	8554	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVSCKASGYTFS NYGITWVRQAPGQGLEWMGWISAYNGNTNYAQKFQGRVTMTRNTSISTAYM ELSSLRSEDTAVYYCARGPYYYYMDVWGKGTMVTVSSASGGGGSGGRASGG GGSEIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYVDWYLQKPGQS PQLLIYLGSNRASGVPDRFSGSGSGTDFKLQISRVEAEDVGIYYCMQGRQF PYSFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTR GLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQ TTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRR EEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGER RRGKGHDGLYQGLSTATKDTYDALHMQALPPR

139102- nt **Full CAR**	8569	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTCCAACTGGTCCAGAGCGGTGCAGAAGTGAAGAAG CCCGGAGCGAGCGTGAAAGTGTCCTGCAAGGCTTCCGGGTACACCTTCTCC AACTACGGCATCACTTGGGTGCGCCAGGCCCCGGGACAGGGCCTGGAATGG ATGGGGTGGATTTCCGCGTACAACGGCAATACGAACTACGCTCAGAAGTTC CAGGGTAGAGTGACCATGACTAGGAACACCTCCATTTCCACCGCCTACATG GAACTGTCCTCCCTGCGGAGCGAGGACACCGCCGTGTACTATTGCGCCCGG GGACCATACTACTACTACATGGATGTCTGGGGGAAGGGGACTATGGTCACC GTGTCATCCGCCTCGGGAGGCGGCGGATCAGGAGGACGCGCCTCTGGTGGT GGAGGATCGGAGATCGTGATGACCCAGAGCCCTCTCTCCTTGCCCGTGACT CCTGGGGAGCCCGCATCCATTTCATGCCGGAGCTCCCAGTCACTTCTCTAC TCCAACGGCTATAACTACGTGGATTGGTACCTCCAAAAGCCGGGCCAGAGC CCGCAGCTGCTGATCTACCTGGGCTCGAACAGGGCCAGCGGAGTGCCTGAC CGGTTCTCCGGGTCGGGAAGCGGGACCGACTTCAAGCTGCAAATCTCGAGA GTGGAGGCCGAGGACGTGGGAATCTACTACTGTATGCAGGGCCGCCAGTTT CCGTACTCGTTCGGACAGGGCACCAAAGTGGAAATCAAGACCACTACCCCA GCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCC CTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGG GGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACT TGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGT CGGAAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAG ACTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAA GGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCC TACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGA GAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGC GGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAA AAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGC AGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACC AAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139104		
139104- aa **Full CAR**	8555	MALPVTALLLPLALLLHAARPEVQLLETGGGLVQPGGSLRLSCAVSGFALS NHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNTLYLQ MNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRASGGGGS EIVLTQSPATLSVSPGESATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGA STRASGIPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYGSSLTFGGGTK VEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIY IWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCS CRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDKR RGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL YQGLSTATKDTYDALHMQALPPR
139104- nt **Full CAR**	8570	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAATTGCTCGAAACTGGAGGAGGTCTGGTGCAA CCTGGAGGATCACTTCGCCTGTCCTGCGCCGTGTCGGGCTTTGCCCTGTCC AACCATGGAATGAGCTGGGTCCGCCGCGCGCCGGGGAAGGGCCTCGAATGG GTGTCCGGCATCGTCTACTCCGGCTCCACCTACTACGCCGCGTCCGTGAAG GGCCGGTTCACGATTTCACGGGACAACTCGCGGAACACCCTGTACCTCCAA ATGAATTCCCTTCGGCCGGAGGATACTGCCATCTACTACTGCTCCGCCCAC GGTGGCGAATCCGACGTCTGGGGCCAGGGAACCACCGTGACCGTGTCCAGC GCGTCCGGGGGAGGAGGAAGCGGGGGTAGAGCATCGGGTGGAGGCGGATCA

		GAGATCGTGCTGACCCAGTCCCCCGCCACCTTGAGCGTGTCACCAGGAGAG TCCGCCACCCTGTCATGCCGCGCCAGCCAGTCCGTGTCCTCCAACCTGGCT TGGTACCAGCAGAAGCCGGGGCAGGCCCCTAGACTCCTGATCTATGGGGCG TCGACCCGGGCATCTGGAATTCCCGATAGGTTCAGCGGATCGGGCTCGGGC ACTGACTTCACTCTGACCATCTCCTCGCTGCAAGCCGAGGACGTGGCTGTG TACTACTGTCAGCAGTACGGAAGCTCCCTGACTTTCGGTGGCGGGACCAAA GTCGAGATTAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCT ACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCA GCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTAC ATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTG ATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAG CAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCA TGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTC AGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTCTAC AACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGCGG AGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCCCAA GAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAGC GAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGACGGACTG TACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCTCTTCACATG CAGGCCCTGCCGCCTCGG
139106		
139106- aa **Full CAR**	8556	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGGSLRLSCAVSGFALS NHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNTLYLQ MNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRASGGGGS EIVMTQSPATLSVSPGERATLSCRASQSVSSKLAWYQQKPGQAPRLLMYGA SIRATGIPDRFSGSGSGTEFTLTISSLEPEDFAVYYCQQYGSSSWTFGQGT KVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDI YIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGC SCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDK RRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDG LYQGLSTATKDTYDALHMQALPPR
139106- nt **Full CAR**	8571	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAATTGGTGGAAACTGGAGGAGGACTTGTGCAA CCTGGAGGATCATTGAGACTGAGCTGCGCAGTGTCGGGATTCGCCCTGAGC AACCATGGAATGTCCTGGGTCAGAAGGGCCCCTGGAAAAGGCCTCGAATGG GTGTCAGGGATCGTGTACTCCGGTTCCACTTACTACGCCGCCTCCGTGAAG GGGCGCTTCACTATCTCACGGGATAACTCCCGCAATACCCTGTACCTCCAA ATGAACAGCCTGCGGCCGGAGGATACCGCCATCTACTACTGTTCCGCCCAC GGTGGAGAGTCTGACGTCTGGGGCCAGGGAACTACCGTGACCGTGTCCTCC GCGTCCGGCGGTGGAGGGAGCGGCGGCCGCGCCAGCGGCGGCGGAGGCTCC GAGATCGTGATGACCCAGAGCCCCGCTACTCTGTCGGTGTCGCCCGGAGAA AGGGCGACCCTGTCCTGCCGGGCGTCGCAGTCCGTGAGCAGCAAGCTGGCT TGGTACCAGCAGAAGCCGGGCCAGGCACCACGCCTGCTTATGTACGGTGCC TCCATTCGGGCCACCGGAATCCCGGACCGGTTCTCGGGGTCGGGGTCCGGT ACCGAGTTCACACTGACCATTTCCTCGCTCGAGCCCGAGGACTTTGCCGTC TATTACTGCCAGCAGTACGGCTCCTCCTCATGGACGTTCGGCCAGGGGACC AAGGTCGAAATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCT CCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCC GCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATC

		TACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTC GTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTT AAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGT TCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAA TTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTC TACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAG CGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCC CAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTAT AGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGACGGA CTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCTCTTCAC ATGCAGGCCCTGCCGCCTCGG
139107		
139107- aa **Full CAR**	8557	MALPVTALLLPLALLLHAARPEVQLVETGGGVVQPGGSLRLSCAVSGFALS NHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNTLYLQ MNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRASGGGGS EIVLTQSPGTLSLSPGERATLSCRASQSVGSTNLAWYQQKPGQAPRLLIYD ASNRATGIPDRFSGGGSGTDFTLTISRLEPEDFAVYYCQQYGSSPPWTFGQ GTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFAC DIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEED GCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGH DGLYQGLSTATKDTYDALHMQALPPR
139107- nt **Full CAR**	8572	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAATTGGTGGAGACTGGAGGAGGAGTGGTGCAA CCTGGAGGAAGCCTGAGACTGTCATGCGCGGTGTCGGGCTTCGCCCTCTCC AACCACGGAATGTCCTGGGTCCGCCGGGCCCCTGGGAAAGGACTTGAATGG GTGTCCGGCATCGTGTACTCGGGTTCCACCTACTACGCGGCCTCAGTGAAG GGCCGGTTTACTATTAGCCGCGACAACTCCAGAAACACACTGTACCTCCAA ATGAACTCGCTGCGGCCGGAAGATACCGCTATCTACTACTGCTCCGCCCAT GGGGGAGAGTCGGACGTCTGGGGACAGGGCACCACTGTCACTGTGTCCAGC GCTTCCGGCGGTGGTGGAAGCGGGGGACGGGCCTCAGGAGGCGGTGGCAGC GAGATTGTGCTGACCCAGTCCCCCGGGACCCTGAGCCTGTCCCCGGGAGAA AGGGCCACCCTCTCCTGTCGGGCATCCCAGTCCGTGGGGTCTACTAACCTT GCATGGTACCAGCAGAAGCCCGGCCAGGCCCCTCGCCTGCTGATCTACGAC GCGTCCAATAGAGCCACCGGCATCCCGGATCGCTTCAGCGGAGGCGGATCG GGCACCGACTTCACCCTCACCATTTCAAGGCTGGAACCGGAGGACTTCGCC GTGTACTACTGCCAGCAGTATGGTTCGTCCCCACCCTGGACGTTCGGCCAG GGGACTAAGGTCGAGATCAAGACCACTACCCCAGCACCGAGGCCACCCACC CCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGC GATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTT TCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTAC ATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGAC GGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGC GTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAAC CAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTG GACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAG AATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAA GCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCAC

		GACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCT CTTCACATGCAGGCCCTGCCGCCTCGG
139108		
139108- aa **Full CAR**	8558	MALPVTALLLPLALLLHAARPQVQLVESGGGLVKPGGSLRLSCAASGFTFS DYYMSWIRQAPGKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYL QMNSLRAEDTAVYYCARESGDGMDVWGQGTTVTVSSASGGGGSGGRASGGG GSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIY AASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYTLAFGQGT KVDIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDI YIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGC SCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDK RRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDG LYQGLSTATKDTYDALHMQALPPR
139108- nt **Full CAR**	8573	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGTGAAA CCTGGAGGATCATTGAGACTGTCATGCGCGGCCTCGGGATTCACGTTCTCC GATTACTACATGAGCTGGATTCGCCAGGCTCCGGGGAAGGGACTGGAATGG GTGTCCTACATTTCCTCATCCGGCTCCACCATCTACTACGCGGACTCCGTG AAGGGGAGATTCACCATTAGCCGCGATAACGCCAAGAACAGCCTGTACCTT CAGATGAACTCCCTGCGGGCTGAAGATACTGCCGTCTACTACTGCGCAAGG GAGAGCGGAGATGGGATGGACGTCTGGGGACAGGGTACCACTGTGACCGTG TCGTCGGCCTCCGGCGGAGGGGGTTCGGGTGGAAGGGCCAGCGGCGGCGGA GGCAGCGACATCCAGATGACCCAGTCCCCCTCATCGCTGTCCGCCTCCGTG GGCGACCGCGTCACCATCACATGCCGGGCCTCACAGTCGATCTCCTCCTAC CTCAATTGGTATCAGCAGAAGCCCGGAAAGGCCCCTAAGCTTCTGATCTAC GCAGCGTCCTCCCTGCAATCCGGGGTCCCATCTCGGTTCTCCGGCTCGGGC AGCGGTACCGACTTCACTCTGACCATCTCGAGCCTGCAGCCGGAGGACTTC GCCACTTACTACTGTCAGCAAAGCTACACCCTCGCGTTTGGCCAGGGCACC AAAGTGGACATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCT CCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCC GCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATC TACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTC GTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTT AAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGT TCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAA TTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTC TACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAG CGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCC CAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTAT AGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGACGGA CTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCTCTTCAC ATGCAGGCCCTGCCGCCTCGG
139110		
139110- aa **Full CAR**	8560	MALPVTALLLPLALLLHAARPQVQLVQSGGGLVKPGGSLRLSCAASGFTFS DYYMSWIRQAPGKGLEWVSYISSSGNTIYYADSVKGRFTISRDNAKNSLYL QMNSLRAEDTAVYYCARSTMVREDYWGQGTLVTVSSASGGGGSGGRASGGG GSDIVLTQSPLSLPVTLGQPASISCKSSESLVHNSGKTYLNWFHQRPGQSP

		RRLIYEVSNRDSGVPDRFTGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWP GTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRG LDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQT TQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRRE EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERR RGKGHDGLYQGLSTATKDTYDALHMQALPPR
139110- nt **Full CAR**	8575	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAACTGGTGCAAAGCGGAGGAGGATTGGTCAAA CCCGGAGGAAGCCTGAGACTGTCATGCGCGGCCTCTGGATTCACCTTCTCC GATTACTACATGTCATGGATCAGACAGGCCCCGGGGAAGGGCCTCGAATGG GTGTCCTACATCTCGTCCTCCGGGAACACCATCTACTACGCCGACAGCGTG AAGGGCCGCTTTACCATTTCCCGCGACAACGCAAAGAACTCGCTGTACCTT CAGATGAATTCCCTGCGGGCTGAAGATACCGCGGTGTACTATTGCGCCCGG TCCACTATGGTCCGGGAGGACTACTGGGGACAGGGCACACTCGTGACCGTG TCCAGCGCGAGCGGGGGTGGAGGCAGCGGTGGACGCGCCTCCGGCGGCGGC GGTTCAGACATCGTGCTGACTCAGTCGCCCCTGTCGCTGCCGGTCACCCTG GGCCAACCGGCCTCAATTAGCTGCAAGTCCTCGGAGAGCCTGGTGCACAAC TCAGGAAAGACTTACCTGAACTGGTTCCATCAGCGGCCTGGACAGTCCCCA CGGAGGCTCATCTATGAAGTGTCCAACAGGGATTCGGGGGTGCCCGACCGC TTCACTGGCTCCGGGTCCGGCACCGACTTCACCTTGAAAATCTCCAGAGTG GAAGCCGAGGACGTGGGCGTGTACTACTGTATGCAGGGTACCCACTGGCCT GGAACCTTTGGACAAGGAACTAAGCTCGAGATTAAGACCACTACCCCAGCA CCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTG CGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGT CTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGC GGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGG AAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACT ACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGC GGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTAC AAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAG GAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGG AAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAG GATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGA AGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAG GACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139112		
139112- aa **Full CAR**	8561	MALPVTALLLPLALLLHAARPQVQLVESGGGLVQPGGSLRLSCAVSGFALS NHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNTLYLQ MNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRASGGGGS DIRLTQSPSPLSASVGDRVTITCQASEDINKFLNWYHQTPGKAPKLLIYDA STLQTGVPSRFSGSGSGTDFTLTINSLQPEDIGTYYCQQYESLPLTFGGGT KVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDI YIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGC SCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDK RRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDG LYQGLSTATKDTYDALHMQALPPR
139112- nt	8576	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGTGCAA

Full CAR		CCCGGTGGAAGCCTTAGGCTGTCGTGCGCCGTCAGCGGGTTTGCTCTGAGC AACCATGGAATGTCCTGGGTCCGCCGGGCACCGGGAAAAGGGCTGGAATGG GTGTCCGGCATCGTGTACAGCGGGTCAACCTATTACGCCGCGTCCGTGAAG GGCAGATTCACTATCTCAAGAGACAACAGCCGGAACACCCTGTACTTGCAA ATGAATTCCCTGCGCCCCGAGGACACCGCCATCTACTACTGCTCCGCCCAC GGAGGAGAGTCGGACGTGTGGGGCCAGGGAACGACTGTGACTGTGTCCAGC GCATCAGGAGGGGGTGGTTCGGGCGGCCGGGCCTCGGGGGGAGGAGGTTCC GACATTCGGCTGACCCAGTCCCCGTCCCCACTGTCGGCCTCCGTCGGCGAC CGCGTGACCATCACTTGTCAGGCGTCCGAGGACATTAACAAGTTCCTGAAC TGGTACCACCAGACCCCTGGAAAGGCCCCCAAGCTGCTGATCTACGATGCC TCGACCCTTCAAACTGGAGTGCCTAGCCGGTTCTCCGGGTCCGGCTCCGGC ACTGATTTCACTCTGACCATCAACTCATTGCAGCCGGAAGATATCGGGACC TACTATTGCCAGCAGTACGAATCCCTCCCGCTCACATTCGGCGGGGGAACC AAGGTCGAGATTAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCT CCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCC GCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATC TACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTC GTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTT AAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGT TCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAA TTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTC TACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAG CGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCC CAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTAT AGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGACGGA CTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCTCTTCAC ATGCAGGCCCTGCCGCCTCGG
139113		
139113- aa **Full CAR**	8562	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGGSLRLSCAVSGFALS NHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNTLYLQ MNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRASGGGGS ETTLTQSPATLSVSPGERATLSCRASQSVGSNLAWYQQKPGQGPRLLIYGA STRATGIPARFSGSGSGTEFTLTISSLQPEDFAVYYCQQYNDWLPVTFGQG TKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD IYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLD KRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHD GLYQGLSTATKDTYDALHMQALPPR
139113- nt **Full CAR**	8577	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAATTGGTGGAAACTGGAGGAGGACTTGTGCAA CCTGGAGGATCATTGCGGCTCTCATGCGCTGTCTCCGGCTTCGCCCTGTCA AATCACGGGATGTCGTGGGTCAGACGGGCCCCGGGAAAGGGTCTGGAATGG GTGTCGGGGATTGTGTACAGCGGCTCCACCTACTACGCCGCTTCGGTCAAG GGCCGCTTCACTATTTCACGGGACAACAGCCGCAACACCCTCTATCTGCAA ATGAACTCTCTCCGCCCGGAGGATACCGCCATCTACTACTGCTCCGCACAC GGCGGCGAATCCGACGTGTGGGGACAGGGAACCACTGTCACCGTGTCGTCC GCATCCGGTGGCGGAGGATCGGGTGGCCGGGCCTCCGGGGGCGGCGGCAGC GAGACTACCCTGACCCAGTCCCCTGCCACTCTGTCCGTGAGCCCGGGAGAG AGAGCCACCCTTAGCTGCCGGGCCAGCCAGAGCGTGGGCTCCAACCTGGCC

		TGGTACCAGCAGAAGCCAGGACAGGGTCCCAGGCTGCTGATCTACGGAGCC TCCACTCGCGCGACCGGCATCCCCGCGAGGTTCTCCGGGTCGGGTTCCGGG ACCGAGTTCACCCTGACCATCTCCTCCCTCCAACCGGAGGACTTCGCGGTG TACTACTGTCAGCAGTACAACGATTGGCTGCCCGTGACATTTGGACAGGGG ACGAAGGTGGAAATCAAAACCACTACCCCAGCACCGAGGCCACCCACCCCG GCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGA CCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGAT ATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCA CTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATC TTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGC TGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTG AAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAG CTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGAC AAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAAT CCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCC TATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGAC GGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCTCTT CACATGCAGGCCCTGCCGCCTCGG
139114		
139114- aa **Full CAR**	8563	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAVSGFALS NHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNTLYLQ MNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRASGGGGS EIVLTQSPGTLSLSPGERATLSCRASQSIGSSSLAWYQQKPGQAPRLLMYG ASSRASGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYAGSPPFTFGQ GTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFAC DIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEED GCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGH DGLYQGLSTATKDTYDALHMQALPPR
139114- nt **Full CAR**	8578	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAATTGGTGGAATCTGGTGGAGGACTTGTGCAA CCTGGAGGATCACTGAGACTGTCATGCGCGGTGTCCGGTTTTGCCCTGAGC AATCATGGGATGTCGTGGGTCCGGCGCGCCCCCGGAAAGGGTCTGGAATGG GTGTCGGGTATCGTCTACTCCGGGAGCACTTACTACGCCGCGAGCGTGAAG GGCCGCTTCACCATTTCCCGCGATAACTCCCGCAACACCCTGTACTTGCAA ATGAACTCGCTCCGGCCTGAGGACACTGCCATCTACTACTGCTCCGCACAC GGAGGAGAATCCGACGTGTGGGGCCAGGGAACTACCGTGACCGTCAGCAGC GCCTCCGGCGGCGGGGGCTCAGGCGGACGGGCTAGCGGCGGCGGTGGCTCC GAGATCGTGCTGACCCAGTCGCCTGGCACTCTCTCGCTGAGCCCCGGGGAA AGGGCAACCCTGTCCTGTCGGGCCAGCCAGTCCATTGGATCATCCTCCCTC GCCTGGTATCAGCAGAAACCGGGACAGGCTCCGCGGCTGCTTATGTATGGG GCCAGCTCAAGAGCCTCCGGCATTCCCGACCGGTTCTCCGGGTCCGGTTCC GGCACCGATTTCACCCTGACTATCTCGAGGCTGGAGCCAGAGGACTTCGCC GTGTACTACTGCCAGCAGTACGCGGGGTCCCCGCCGTTCACGTTCGGACAG GGAACCAAGGTCGAGATCAAGACCACTACCCCAGCACCGAGGCCACCCACC CCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGC GATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTT TCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTAC

		ATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGAC GGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGC GTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAAC CAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTG GACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAG AATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAA GCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCAC GACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCT CTTCACATGCAGGCCCTGCCGCCTCGG
149362		
149362-aa **Full CAR**	8579	MALPVTALLLPLALLLHAARPQVQLQESGPGLVKPSETLSLTCTVSGGSIS SSYYYWGWIRQPPGKGLEWIGSIYYSGSAYYNPSLKSRVTISVDTSKNQFS LRLSSVTAADTAVYYCARHWQEWPDAFDIWGQGTMVTVSSGGGGSGGGGSG GGGSETTLTQSPAFMSATPGDKVIISCKASQDIDDAMNWYQQKPGEAPLFI IQSATSPVPGIPPRFSGSGFGTDFSLTINNIESEDAAYYFCLQHDNFPLTF GQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDF ACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQE EDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYD VLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGK GHDGLYQGLSTATKDTYDALHMQALPPR
149362-nt **Full CAR**	8601	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAGCTTCAGGAAAGCGGACCGGGCCTGGTCAAG CCATCCGAAACTCTCTCCCTGACTTGCACTGTGTCTGGCGGTTCCATCTCA TCGTCGTACTACTACTGGGGCTGGATTAGGCAGCCGCCCGGAAAGGGACTG GAGTGGATCGGAAGCATCTACTATTCCGGCTCGGCGTACTACAACCCTAGC CTCAAGTCGAGAGTGACCATCTCCGTGGATACCTCCAAGAACCAGTTTTCC CTGCGCCTGAGCTCCGTGACCGCCGCTGACACCGCCGTGTACTACTGTGCT CGGCATTGGCAGGAATGGCCCGATGCCTTCGACATTTGGGGCCAGGGCACT ATGGTCACTGTGTCATCCGGGGGTGGAGGCAGCGGGGGAGGAGGGTCCGGG GGGGGAGGTTCAGAGACAACCTTGACCCAGTCACCCGCATTCATGTCCGCC ACTCCGGGAGACAAGGTCATCATCTCGTGCAAAGCGTCCCAGGATATCGAC GATGCCATGAATTGGTACCAGCAGAAGCCTGGCGAAGCGCCGCTGTTCATT ATCCAATCCGCAACCTCGCCCGTGCCTGGAATCCCACCGCGGTTCAGCGGC AGCGGTTTCGGAACCGACTTTTCCCTGACCATTAACAACATTGAGTCCGAG GACGCCGCCTACTACTTCTGCCTGCAACACGACAACTTCCCTCTCACGTTC GGCCAGGGAACCAAGCTGGAAATCAAGACCACTACCCCAGCACCGAGGCCA CCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAG GCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTC GCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTG CTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTG CTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAG GAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAA CTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGG CAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGAC GTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGC AGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATG GCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAA GGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTAT

		GACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
149363		
149363-aa Full CAR	8580	MALPVTALLLPLALLLHAARPQVNLRESGPALVKPTQTLTLTCTFSGFSLR TSGMCVSWIRQPPGKALEWLARIDWDEDKFYSTSLKTRLTISKDTSDNQVV LRMTNMDPADTATYYCARSGAGGTSATAFDIWGPGTMVTVSSGGGGSGGGG SGGGGSDIQMTQSPSSLSASVGDRVTITCRASQDIYNNLAWFQLKPGSAPR SLMYAANKSQSGVPSRFSGSASGTDFTLTISSLQPEDFATYYCQHYYRFPY SFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGL DFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTT QEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREE YDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRR GKGHDGLYQGLSTATKDTYDALHMQALPPR
149363-nt **Full CAR**	8602	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTCAATCTGCGCGAATCCGGCCCCGCCTTGGTCAAG CCTACCCAGACCCTCACTCTGACCTGTACTTTCTCCGGCTTCTCCCTGCGG ACTTCCGGGATGTGCGTGTCCTGGATCAGACAGCCTCCGGGAAAGGCCCTG GAGTGGCTCGCTCGCATTGACTGGGATGAGGACAAGTTCTACTCCACCTCA CTCAAGACCAGGCTGACCATCAGCAAAGATACCTCTGACAACCAAGTGGTG CTCCGCATGACCAACATGGACCCAGCCGACACTGCCACTTACTACTGCGCG AGGAGCGGAGCGGGCGGAACCTCCGCCACCGCCTTCGATATTTGGGGCCCG GGTACCATGGTCACCGTGTCAAGCGGAGGAGGGGGGTCCGGGGGCGGCGGT TCCGGGGGAGGCGGATCGGACATTCAGATGACTCAGTCACCATCGTCCCTG AGCGCTAGCGTGGGCGACAGAGTGACAATCACTTGCCGGGCATCCCAGGAC ATCTATAACAACCTTGCGTGGTTCCAGCTGAAGCCTGGTTCCGCACCGCGG TCACTTATGTACGCCGCCAACAAGAGCCAGTCGGGAGTGCCGTCCCGGTTT TCCGGTTCGGCCTCGGGAACTGACTTCACCCTGACGATCTCCAGCCTGCAA CCCGAGGATTTCGCCACCTACTACTGCCAGCACTACTACCGCTTTCCCTAC TCGTTCGGACAGGGAACCAAGCTGGAAATCAAGACCACTACCCCAGCACCG AGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGT CCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTT GACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGG GTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAG AAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACT CAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGC TGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAG CAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAG TACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAG CCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGAT AAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGA GGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGAC ACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
149364		
149364-aa Full CAR	8581	MALPVTALLLPLALLLHAARPEVQLVESGGGLVKPGGSLRLSCAASGFTFS SYSMNWVRQAPGKGLEWVSSISSSSSYIYYADSVKGRFTISRDNAKNSLYL QMNSLRAEDTAVYYCAKTIAAVYAFDIWGQGTTVTVSSGGGGSGGGGSGGG GSEIVLTQSPLSLPVTPEEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSP QLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP

		YTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRG LDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQT TQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRRE EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERR RGKGHDGLYQGLSTATKDTYDALHMQALPPR
149364-nt **Full CAR**	8603	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAGCTTGTCGAATCCGGGGGGGGACTGGTCAAG CCGGGCGGATCACTGAGACTGTCCTGCGCCGCGAGCGGCTTCACGTTCTCC TCCTACTCCATGAACTGGGTCCGCCAAGCCCCCGGGAAGGGACTGGAATGG GTGTCCTCTATCTCCTCGTCGTCGTCCTACATCTACTACGCCGACTCCGTG AAGGGAAGATTCACCATTTCCCGCGACAACGCAAAGAACTCACTGTACTTG CAAATGAACTCACTCCGGGCCGAAGATACTGCTGTGTACTATTGCGCCAAG ACTATTGCCGCCGTCTACGCTTTCGACATCTGGGGCCAGGGAACCACCGTG ACTGTGTCGTCCGGTGGTGGTGGCTCGGGCGGAGGAGGAAGCGGCGGCGGG GGGTCCGAGATTGTGCTGACCCAGTCGCCACTGAGCCTCCCTGTGACCCCC GAGGAACCCGCCAGCATCAGCTGCCGGTCCAGCCAGTCCCTGCTCCACTCC AACGGATACAATTACCTCGATTGGTACCTTCAGAAGCCTGGACAAAGCCCG CAGCTGCTCATCTACTTGGGATCAAACCGCGCGTCAGGAGTGCCTGACCGG TTCTCCGGCTCGGGCAGCGGTACCGATTTCACCCTGAAAATCTCCAGGGTG GAGGCAGAGGACGTGGGAGTGTATTACTGTATGCAGGCGCTGCAGACTCCG TACACATTTGGGCAGGGCACCAAGCTGGAGATCAAGACCACTACCCCAGCA CCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTG CGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGT CTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGC GGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGG AAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACT ACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGC GGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTAC AAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAG GAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGG AAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAG GATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGA AGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAG GACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
149365		
149365-aa **Full CAR**	8582	MALPVTALLLPLALLLHAARPEVQLVESGGGLVKPGGSLRLSCAASGFTFS DYYMSWIRQAPGKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKNSLYL QMNSLRAEDTAVYYCARDLRGAFDIWGQGTMVTVSSGGGGSGGGGSGGGGS SYVLTQSPSVSAAPGYTATISCGGNNIGTKSVHWYQQKPGQAPLLVIRDDS VRPSKIPGRFSGSNSGNMATLTISGVQAGDEADFYCQVWDSDSEHVVFGGG TKLTVLTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD IYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDG CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLD KRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHD GLYQGLSTATKDTYDALHMQALPPR
149365-nt	8604	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTCCAGCTCGTGGAGTCCGGCGGAGGCCTTGTGAAG CCTGGAGGTTCGCTGAGACTGTCCTGCGCCGCCTCCGGCTTCACCTTCTCC

Full CAR		GACTACTACATGTCCTGGATCAGACAGGCCCCGGGAAAGGGCCTGGAATGG GTGTCCTACATCTCGTCATCGGGCAGCACTATCTACTACGCGGACTCAGTG AAGGGGCGGTTCACCATTTCCCGGGATAACGCGAAGAACTCGCTGTATCTG CAAATGAACTCACTGAGGGCCGAGGACACCGCCGTGTACTACTGCGCCCGC GATCTCCGCGGGGCATTTGACATCTGGGGACAGGGAACCATGGTCACAGTG TCCAGCGGAGGGGGAGGATCGGGTGGCGGAGGTTCCGGGGGTGGAGGCTCC TCCTACGTGCTGACTCAGAGCCCAAGCGTCAGCGCTGCGCCCGGTTACACG GCAACCATCTCCTGTGGCGGAAACAACATTGGGACCAAGTCTGTGCACTGG TATCAGCAGAAGCCGGGCCAAGCTCCCCTGTTGGTGATCCGCGATGACTCC GTGCGGCCTAGCAAAATTCCGGGACGGTTCTCCGGCTCCAACAGCGGCAAT ATGGCCACTCTCACCATCTCGGGAGTGCAGGCCGGAGATGAAGCCGACTTC TACTGCCAAGTCTGGGACTCAGACTCCGAGCATGTGGTGTTCGGGGGCGGA ACCAAGCTGACTGTGCTCACCACTACCCCAGCACCGAGGCCACCCACCCCG GCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGA CCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGAT ATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCA CTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATC TTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGC TGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTG AAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAG CTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGAC AAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAAT CCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCC TATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGAC GGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCTCTT CACATGCAGGCCCTGCCGCCTCGG
149366		
149366-aa **Full CAR**	8583	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVSCKPSGYTVT SHYIHWVRRAPGQGLEWMGMINPSGGVTAYSQTLQGRVTMTSDTSSSTVYM ELSSLRSEDTAMYYCAREGSGSGWYFDFWGRGTLVTVSSGGGGSGGGGSGG GGSSYVLTQPPSVSVSPGQTASITCSGDGLSKKYVSWYQQKAGQSPVVLIS RDKERPSGIPDRFSGSNSADTATLTISGTQAMDEADYYCQAWDDTTVVFGG GTKLTVLTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFAC DIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEED GCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGH DGLYQGLSTATKDTYDALHMQALPPR
149366-nt **Full CAR**	8605	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAGCTGGTGCAGAGCGGGGCCGAAGTCAAGAAG CCGGGAGCCTCCGTGAAAGTGTCCTGCAAGCCTTCGGGATACACCGTGACC TCCCACTACATTCATTGGGTCCGCCGCGCCCCCGGCCAAGGACTCGAGTGG ATGGGCATGATCAACCCTAGCGGCGGAGTGACCGCGTACAGCCAGACGCTG CAGGGACGCGTGACTATGACCTCGGATACCTCCTCCTCCACCGTCTATATG GAACTGTCCAGCCTGCGGTCCGAGGATACCGCCATGTACTACTGCGCCCGG GAAGGATCAGGCTCCGGGTGGTATTTCGACTTCTGGGGAAGAGGCACCCTC GTGACTGTGTCATCTGGGGGAGGGGGTTCCGGTGGTGGCGGATCGGGAGGA GGCGGTTCATCCTACGTGCTGACCCAGCCACCCTCCGTGTCCGTGAGCCCC GGCCAGACTGCATCGATTACATGTAGCGGCGACGGCCTCTCCAAGAAATAC GTGTCGTGGTACCAGCAGAAGGCCGGACAGAGCCCGGTGGTGCTGATCTCA

		AGAGATAAGGAGCGGCCTAGCGGAATCCCGGACAGGTTCTCGGGTTCCAAC TCCGCGGACACTGCTACTCTGACCATCTCGGGGACCCAGGCTATGGACGAA GCCGATTACTACTGCCAAGCCTGGGACGACACTACTGTCGTGTTTGGAGGG GGCACCAAGTTGACCGTCCTTACCACTACCCCAGCACCGAGGCCACCCACC CCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGC GATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTT TCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTAC ATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGAC GGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGC GTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAAC CAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTG GACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAG AATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAA GCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCAC GACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCT CTTCACATGCAGGCCCTGCCGCCTCGG
149367		
149367-aa Full CAR	8584	MALPVTALLLPLALLLHAARPQVQLQESGPGLVKPSQTLSLTCTVSGGSIS SGGYYWSWIRQHPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFS LKLSSVTAADTAVYYCARAGIAARLRGAFDIWGQGTMVTVSSGGGGSGGGG SGGGGSDIVMTQSPSSVSASVGDRVIITCRASQGIRNWLAWYQQKPGKAPN LLIYAASNLQSGVPSRFSGSGSGADFTLTISSLQPEDVATYYCQKYNSAPF TFGPGTKVDIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGL DFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTT QEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREE YDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRR GKGHDGLYQGLSTATKDTYDALHMQALPPR
149367-nt **Full CAR**	8606	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAGCTTCAGGAGAGCGGCCCGGGACTCGTGAAG CCGTCCCAGACCCTGTCCCTGACTTGCACCGTGTCGGGAGGAAGCATCTCG AGCGGAGGCTACTATTGGTCGTGGATTCGGCAGCACCCTGGAAAGGGCCTG GAATGGATCGGCTACATCTACTACTCCGGCTCGACCTACTACAACCCATCG CTGAAGTCCAGAGTGACAATCTCAGTGGACACGTCCAAGAATCAGTTCAGC CTGAAGCTCTCTTCCGTGACTGCGGCCGACACCGCCGTGTACTACTGCGCA CGCGCTGGAATTGCCGCCCGGCTGAGGGGTGCCTTCGACATTTGGGGACAG GGCACCATGGTCACCGTGTCCTCCGGCGGCGGAGGTTCCGGGGGTGGAGGC TCAGGAGGAGGGGGGTCCGACATCGTCATGACTCAGTCGCCCTCAAGCGTC AGCGCGTCCGTCGGGGACAGAGTGATCATCACCTGTCGGGCGTCCCAGGGA ATTCGCAACTGGCTGGCCTGGTATCAGCAGAAGCCCGGAAAGGCCCCCAAC CTGTTGATCTACGCCGCCTCAAACCTCCAATCCGGGGTGCCGAGCCGCTTC AGCGGCTCCGGTTCGGGTGCCGATTTCACTCTGACCATCTCCTCCCTGCAA CCTGAAGATGTGGCTACCTACTACTGCCAAAAGTACAACTCCGCACCTTTT ACTTTCGGACCGGGGACCAAAGTGGACATTAAGACCACTACCCCAGCACCG AGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGT CCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTT GACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGG GTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAG AAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACT

		CAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGC TGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAG CAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAG TACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAG CCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGAT AAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGA GGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGAC ACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
149368		
149368-aa **Full CAR**	8585	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGSSVKVSCKASGGTFS SYAISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQGRVTITADESTSTAYM ELSSLRSEDTAVYYCARRGGYQLLRWDVGLLRSAFDIWGQGTMVTVSSGGG GSGGGGSGGGGSSYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKP GQAPVLVLYGKNNRPSGVPDRFSGSRSGTTASLTITGAQAEDEADYYCSSR DSSGDHLRVFGTGTKVTVLTTTPAPRPPTPAPTIASQPLSLRPEACRPAAG GAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQP FMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNE LNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
149368-nt **Full CAR**	8607	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAGCTGGTCCAGTCGGGCGCCGAGGTCAAGAAG CCCGGGAGCTCTGTGAAAGTGTCCTGCAAGGCCTCCGGGGGCACCTTTAGC TCCTACGCCATCTCCTGGGTCCGCCAAGCACCGGGTCAAGGCCTGGAGTGG ATGGGGGGAATTATCCCTATCTTCGGCACTGCCAACTACGCCCAGAAGTTC CAGGGACGCGTGACCATTACCGCGGACGAATCCACCTCCACCGCTTATATG GAGCTGTCCAGCTTGCGCTCGGAAGATACCGCCGTGTACTACTGCGCCCGG AGGGGTGGATACCAGCTGCTGAGATGGGACGTGGGCCTCCTGCGGTCGGCG TTCGACATCTGGGGCCAGGGCACTATGGTCACTGTGTCCAGCGGAGGAGGC GGATCGGGAGGCGGCGGATCAGGGGGAGGCGGTTCCAGCTACGTGCTTACT CAACCCCCTTCGGTGTCCGTGGCCCCGGGACAGACCGCCAGAATCACTTGC GGAGGAAACAACATTGGGTCCAAGAGCGTGCATTGGTACCAGCAGAAGCCA GGACAGGCCCCTGTGCTGGTGCTCTACGGGAAGAACAATCGGCCCAGCGGA GTGCCGGACAGGTTCTCGGGTTCACGCTCCGGTACAACCGCTTCACTGACT ATCACCGGGGCCCAGGCAGAGGATGAAGCGGACTACTACTGTTCCTCCCGG GATTCATCCGGCGACCACCTCCGGGTGTTCGGAACCGGAACGAAGGTCACC GTGCTGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATC GCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGT GGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGG GCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACT CTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCC TTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCATGCCGG TTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGC AGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTCTACAACGAA CTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGA CGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGC CTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATT GGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAG GGACTCAGCACCGCCACCAAGGACACCTATGACGCTCTTCACATGCAGGCC

		CTGCCGCCTCGG
149369		
149369-aa Full CAR	8586	MALPVTALLLPLALLLHAARPEVQLQQSGPGLVKPSQTLSLTCAISGDSVS SNSAAWNWIRQSPSRGLEWLGRTYYRSKWYSFYAISLKSRIIINPDTSKNQ FSLQLKSVTPEDTAVYYCARSSPEGLFLYWFDPWGQGTLVTVSSGGDGSGG GGSGGGGSSSELTQDPAVSVALGQTIRITCQGDSLGNYYATWYQQKPGQAP VLVIYGTNNRPSGIPDRFSASSSGNTASLTITGAQAEDEADYYCNSRDSSG HHLLFGTGTKVTVLTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHT RGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPV QTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGR REEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGE RRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
149369-nt **Full CAR**	8608	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAGCTCCAACAGTCAGGACCGGGGCTCGTGAAG CCATCCCAGACCCTGTCCCTGACTTGTGCCATCTCGGGAGATAGCGTGTCA TCGAACTCCGCCGCCTGGAACTGGATTCGGCAGAGCCCGTCCCGCGGACTG GAGTGGCTTGGAAGGACCTACTACCGGTCCAAGTGGTACTCTTTCTACGCG ATCTCGCTGAAGTCCCGCATTATCATTAACCCTGATACCTCCAAGAATCAG TTCTCCCTCCAACTGAAATCCGTCACCCCCGAGGACACAGCAGTGTATTAC TGCGCACGGAGCAGCCCCGAAGGACTGTTCCTGTATTGGTTTGACCCCTGG GGCCAGGGGACTCTTGTGACCGTGTCGAGCGGCGGAGATGGGTCCGGTGGC GGTGGTTCGGGGGGCGGCGGATCATCATCCGAACTGACCCAGGACCCGGCT GTGTCCGTGGCGCTGGGACAAACCATCCGCATTACGTGCCAGGGAGACTCC CTGGGCAACTACTACGCCACTTGGTACCAGCAGAAGCCGGGCCAAGCCCCT GTGTTGGTCATCTACGGGACCAACAACAGACCTTCCGGCATCCCCGACCGG TTCAGCGCTTCGTCCTCCGGCAACACTGCCAGCCTGACCATCACTGGAGCG CAGGCCGAAGATGAGGCCGACTACTACTGCAACAGCAGAGACTCCTCGGGT CATCACCTCTTGTTCGGAACTGGAACCAAGGTCACCGTGCTGACCACTACC CCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTG TCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACC CGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGT ACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGC GGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTG CAGACTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAG GAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCA GCCTACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGG AGAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATG GGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTC CAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAA CGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCC ACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1978-A4		
BCMA_EBB-C1978-A4 - aa **Full CAR**	8587	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAASGFTFS SYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCAKVEGSGSLDYWGQGTLVTVSSGGGGSGGGGSGGGG SEIVMTQSPGTLSLSPGERATLSCRASQSVSSAYLAWYQQKPGQPPRLLIS GASTRATGIPDRFGGSGSGTDFTLTISRLEPEDFAVYYCQHYGSSFNGSSL

		FTFGQGTRLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRG LDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQT TQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRRE EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERR RGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-A4 - nt **Full CAR**	8609	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAGCTCGTGGAGTCAGGAGGCGGCCTGGTCCAG CCGGGAGGGTCCCTTAGACTGTCATGCGCCGCAAGCGGATTCACTTTCTCC TCCTATGCCATGAGCTGGGTCCGCCAAGCCCCCGGAAAGGGACTGGAATGG GTGTCCGCCATCTCGGGGTCTGGAGGCTCAACTTACTACGCTGACTCCGTG AAGGGACGGTTCACCATTAGCCGCGACAACTCCAAGAACACCCTCTACCTC CAAATGAACTCCCTGCGGGCCGAGGATACCGCCGTCTACTACTGCGCCAAA GTGGAAGGTTCAGGATCGCTGGACTACTGGGGACAGGGTACTCTCGTGACC GTGTCATCGGGCGGAGGAGGTTCCGGCGGTGGCGGCTCCGGCGGCGGAGGG TCGGAGATCGTGATGACCCAGAGCCCTGGTACTCTGAGCCTTTCGCCGGGA GAAAGGGCCACCCTGTCCTGCCGCGCTTCCCAATCCGTGTCCTCCGCGTAC TTGGCGTGGTACCAGCAGAAGCCGGGACAGCCCCCTCGGCTGCTGATCAGC GGGGCCAGCACCCGGGCAACCGGAATCCCAGACAGATTCGGGGGTTCCGGC AGCGGCACAGATTTCACCCTGACTATTTCGAGGTTGGAGCCCGAGGACTTT GCGGTGTATTACTGTCAGCACTACGGGTCGTCCTTTAATGGCTCCAGCCTG TTCACGTTCGGACAGGGGACCCGCCTGGAAATCAAGACCACTACCCCAGCA CCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTG CGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGT CTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGC GGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGG AAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACT ACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGC GGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTAC AAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAG GAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGG AAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAG GATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGA AGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAG GACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1978-G1		
BCMA_EBB-C1978-G1 - aa **Full CAR**	8588	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGGSLRLSCAASGITFS RYPMSWVRQAPGKGLEWVSGISDSGVSTYYADSAKGRFTISRDNSKNTLFL QMSSLRDEDTAVYYCVTRAGSEASDIWGQGTMVTVSSGGGGSGGGGSGGGG SEIVLTQSPATLSLSPGERATLSCRASQSVSNSLAWYQQKPGQAPRLLIYD ASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAIYYCQQFGTSSGLTFGG GTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFAC DIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEED GCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGH DGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-G1 -	8610	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAACTGGTGGAAACCGGTGGCGGCCTGGTGCAG CCTGGAGGATCATTGAGGCTGTCATGCGCGGCCAGCGGTATTACCTTCTCC

nt **Full CAR**		CGGTACCCCATGTCCTGGGTCAGACAGGCCCCGGGGAAAGGGCTTGAATGG GTGTCCGGGATCTCGGACTCCGGTGTCAGCACTTACTACGCCGACTCCGCC AAGGGACGCTTCACCATTTCCCGGGACAACTCGAAGAACACCCTGTTCCTC CAAATGAGCTCCCTCCGGGACGAGGATACTGCAGTGTACTACTGCGTGACC CGCGCCGGGTCCGAGGCGTCTGACATTTGGGGACAGGGCACTATGGTCACC GTGTCGTCCGGCGGAGGGGGCTCGGGAGGCGGTGGCAGCGGAGGAGGAGGG TCCGAGATCGTGCTGACCCAATCCCCGGCCACCCTCTCGCTGAGCCCTGGA GAAAGGGCAACCTTGTCCTGTCGCGCGAGCCAGTCCGTGAGCAACTCCCTG GCCTGGTACCAGCAGAAGCCCGGACAGGCTCCGAGACTTCTGATCTACGAC GCTTCGAGCCGGGCCACTGGAATCCCCGACCGCTTTTCGGGGTCCGGCTCA GGAACCGATTTCACCCTGACAATCTCACGGCTGGAGCCAGAGGATTTCGCC ATCTATTACTGCCAGCAGTTCGGTACTTCCTCCGGCCTGACTTTCGGAGGC GGCACGAAGCTCGAAATCAAGACCACTACCCCAGCACCGAGGCCACCCACC CCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGC GATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTT TCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTAC ATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGAC GGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGC GTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAAC CAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTG GACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAG AATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAA GCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCAC GACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCT CTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1979-C1		
BCMA_EBB-C1979-C1 - aa **Full CAR**	8589	MALPVTALLLPLALLLHAARPQVQLVESGGGLVQPGGSLRLSCAASGFTFS SYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNAKNSLYL QMNSLRAEDTAIYYCARATYKRELRYYYGMDVWGQGTMVTVSSGGGGSGGG GSGGGGSEIVMTQSPGTVSLSPGERATLSCRASQSVSSSFLAWYQQKPGQA PRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDSAVYYCQQYHSS PSWTFGQGTRLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHT RGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPV QTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGR REEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGE RRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1979-C1 - nt **Full CAR**	8611	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAGCTCGTGGAATCGGGTGGCGGACTGGTGCAG CCGGGGGGCTCACTTAGACTGTCCTGCGCGGCCAGCGGATTCACTTTCTCC TCCTACGCCATGTCCTGGGTCAGACAGGCCCCTGGAAAGGGCCTGGAATGG GTGTCCGCAATCAGCGGCAGCGGCGGCTCGACCTATTACGCGGATTCAGTG AAGGGCAGATTCACCATTTCCCGGGACAACGCCAAGAACTCCTTGTACCTT CAAATGAACTCCCTCCGCGCGGAAGATACCGCAATCTACTACTGCGCTCGG GCCACTTACAAGAGGGAACTGCGCTACTACTACGGGATGGACGTCTGGGGC CAGGGAACCATGGTCACCGTGTCCAGCGGAGGAGGAGGATCGGGAGGAGGC GGTAGCGGGGGTGGAGGGTCGGAGATCGTGATGACCCAGTCCCCCGGCACT GTGTCGCTGTCCCCCGGCGAACGGGCCACCCTGTCATGTCGGGCCAGCCAG TCAGTGTCGTCAAGCTTCCTCGCCTGGTACCAGCAGAAACCGGGACAAGCT

		CCCCGCCTGCTGATCTACGGAGCCAGCAGCCGGGCCACCGGTATTCCTGAC CGGTTCTCCGGTTCGGGGTCCGGGACCGACTTTACTCTGACTATCTCTCGC CTCGAGCCAGAGGACTCCGCCGTGTATTACTGCCAGCAGTACCACTCCTCC CCGTCCTGGACGTTCGGACAGGGCACAAGGCTGGAGATTAAGACCACTACC CCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTG TCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACC CGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGT ACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGC GGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTG CAGACTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAG GAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCA GCCTACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGG AGAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATG GGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTC CAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAA CGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCC ACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1978-C7		
BCMA_EBB-C1978-C7 - aa **Full CAR**	8590	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGGSLRLSCAASGFTFS SYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYL QMNTLKAEDTAVYYCARATYKRELRYYYGMDVWGQGTTVTVSSGGGGSGGG GSGGGGSEIVLTQSPSTLSLSPGESATLSCRASQSVSTTFLAWYQQKPGQA PRLLIYGSSNRATGIPDRFSGSGSGTDFTLTIRRLEPEDFAVYYCQQYHSS PSWTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHT RGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPV QTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGR REEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGE RRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-C7 - nt **Full CAR**	8612	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAGGTGCAGCTTGTGGAAACCGGTGGCGGACTGGTGCAG CCCGGAGGAAGCCTCAGGCTGTCCTGCGCCGCGTCCGGCTTCACCTTCTCC TCGTACGCCATGTCCTGGGTCCGCCAGGCCCCCGGAAAGGGCCTGGAATGG GTGTCCGCCATCTCTGGAAGCGGAGGTTCCACGTACTACGCGGACAGCGTC AAGGGAAGGTTCACAATCTCCCGCGATAATTCGAAGAACACTCTGTACCTT CAAATGAACACCCTGAAGGCCGAGGACACTGCTGTGTACTACTGCGCACGG GCCACCTACAAGAGAGAGCTCCGGTACTACTACGGAATGGACGTCTGGGGC CAGGGAACTACTGTGACCGTGTCCTCGGGAGGGGGTGGCTCCGGGGGGGGC GGCTCCGGCGGAGGCGGTTCCGAGATTGTGCTGACCCAGTCACCTTCAACT CTGTCGCTGTCCCCGGGAGAGAGCGCTACTCTGAGCTGCCGGGCCAGCCAG TCCGTGTCCACCACCTTCCTCGCCTGGTATCAGCAGAAGCCGGGGCAGGCA CCACGGCTCTTGATCTACGGGTCAAGCAACAGAGCGACCGGAATTCCTGAC CGCTTCTCGGGGAGCGGTTCAGGCACCGACTTCACCCTGACTATCCGGCGC CTGGAACCCGAAGATTTCGCCGTGTATTACTGTCAACAGTACCACTCCTCG CCGTCCTGGACCTTTGGCCAAGGAACCAAAGTGGAAATCAAGACCACTACC CCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTG TCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACC CGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGT ACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGC GGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTG

		CAGACTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAG GAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCA GCCTACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGG AGAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATG GGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTC CAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAA CGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCC ACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1978-D10		
BCMA_EBB-C1978-D10 - aa **Full CAR**	8591	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGRSLRLSCAASGFTFD DYAMHWVRQAPGKGLEWVSGISWNSGSIGYADSVKGRFTISRDNAKNSLYL QMNSLRDEDTAVYYCARVGKAVPDVWGQGTTVTVSSGGGGSGGGGSGGGGS DIVMTQTPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAA SSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPYSFGQGT RLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDI YIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGC SCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDK RRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDG LYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-D10 - nt **Full CAR**	8613	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAGCTCGTGGAAACTGGAGGTGGACTCGTGCAG CCTGGACGGTCGCTGCGGCTGAGCTGCGCTGCATCCGGCTTCACCTTCGAC GATTATGCCATGCACTGGGTCAGACAGGCGCCAGGGAAGGGACTTGAGTGG GTGTCCGGTATCAGCTGGAATAGCGGCTCAATCGGATACGCGGACTCCGTG AAGGGAAGGTTCACCATTTCCCGCGACAACGCCAAGAACTCCCTGTACTTG CAAATGAACAGCCTCCGGGATGAGGACACTGCCGTGTACTACTGCGCCCGC GTCGGAAAAGCTGTGCCCGACGTCTGGGGCCAGGGAACCACTGTGACCGTG TCCAGCGGCGGGGGTGGATCGGGCGGTGGAGGGTCCGGTGGAGGGGGCTCA GATATTGTGATGACCCAGACCCCCTCGTCCCTGTCCGCCTCGGTCGGCGAC CGCGTGACTATCACATGTAGAGCCTCGCAGAGCATCTCCAGCTACCTGAAC TGGTATCAGCAGAAGCCGGGGAAGGCCCCGAAGCTCCTGATCTACGCGGCA TCATCACTGCAATCGGGAGTGCCGAGCCGGTTTTCCGGGTCCGGCTCCGGC ACCGACTTCACGCTGACCATTTCTTCCCTGCAACCCGAGGACTTCGCCACT TACTACTGCCAGCAGTCCTACTCCACCCCTTACTCCTTCGGCCAAGGAACC AGGCTGGAAATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCT CCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCC GCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATC TACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTC GTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTT AAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGT TCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAA TTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTC TACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAG CGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCC CAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTAT AGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGACGGA CTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCTCTTCAC ATGCAGGCCCTGCCGCCTCGG

BCMA_EBB-C1979-C12		
BCMA_EBB-C1979-C12 - aa **Full CAR**	8592	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGRSLRLSCTASGFTFD DYAMHWVRQRPGKGLEWVASINWKGNSLAYGDSVKGRFAISRDNAKNTVFL QMNSLRTEDTAVYYCASHQGVAYYNYAMDVWGRGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRATQSIGSSFLAWYQQRPGQAPR LLIYGASQRATGIPDRFSGRGSGTDFTLTISRVEPEDSAVYYCQHYESSPS WTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRG LDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQT TQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRRE EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERR RGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1979-C12 - nt **Full CAR**	8614	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAGCTCGTGGAGAGCGGGGGAGGATTGGTGCAG CCCGGAAGGTCCCTGCGGCTCTCCTGCACTGCGTCTGGCTTCACCTTCGAC GACTACGCGATGCACTGGGTCAGACAGCGCCCGGGAAAGGGCCTGGAATGG GTCGCCTCAATCAACTGGAAGGGAAACTCCCTGGCCTATGGCGACAGCGTG AAGGGCCGCTTCGCCATTTCGCGCGACAACGCCAAGAACACCGTGTTTCTG CAAATGAATTCCCTGCGGACCGAGGATACCGCTGTGTACTACTGCGCCAGC CACCAGGGCGTGGCATACTATAACTACGCCATGGACGTGTGGGGAAGAGGG ACGCTCGTCACCGTGTCCTCCGGGGGCGGTGGATCGGGTGGAGGAGGAAGC GGTGGCGGGGGCAGCGAAATCGTGCTGACTCAGAGCCCGGGAACTCTTTCA CTGTCCCCGGGAGAACGGGCCACTCTCTCGTGCCGGGCCACCCAGTCCATC GGCTCCTCCTTCCTTGCCTGGTACCAGCAGAGGCCAGGACAGGCGCCCCGC CTGCTGATCTACGGTGCTTCCCAACGCGCCACTGGCATTCCTGACCGGTTC AGCGGCAGAGGGTCGGGAACCGATTTCACACTGACCATTTCCCGGGTGGAG CCCGAAGATTCGGCAGTCTACTACTGTCAGCATTACGAGTCCTCCCCTTCA TGGACCTTCGGTCAAGGGACCAAAGTGGAGATCAAGACCACTACCCCAGCA CCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTG CGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGT CTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGC GGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGG AAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACT ACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGC GGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTAC AAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAG GAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGG AAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAG GATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGA AGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAG GACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1980-G4		
BCMA_EBB-C1980-G4-aa **Full CAR**	8593	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAASGFTFS SYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCAKVVRDGMDVWGQGTTVTVSSGGGGSGGGGSGGGGS EIVLTQSPATLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYG ASSRATGIPDRFSGNGSGTDFTLTISRLEPEDFAVYYCQQYGSPPRFTFGP GTKVDIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFAC DIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEED

		GCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGH DGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1980-G4-nt **Full CAR**	8615	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAGGTGCAGTTGGTCGAAAGCGGGGGCGGGCTTGTGCAG CCTGGCGGATCACTGCGGCTGTCCTGCGCGGCATCAGGCTTCACGTTTTCT TCCTACGCCATGTCCTGGGTGCGCCAGGCCCCTGGAAAGGGACTGGAATGG GTGTCCGCGATTTCGGGGTCCGGCGGGAGCACCTACTACGCCGATTCCGTG AAGGGCCGCTTCACTATCTCGCGGGACAACTCCAAGAACACCCTCTACCTC CAAATGAATAGCCTGCGGGCCGAGGATACCGCCGTCTACTATTGCGCTAAG GTCGTGCGCGACGGAATGGACGTGTGGGGACAGGGTACCACCGTGACAGTG TCCTCGGGGGGAGGCGGTAGCGGCGGAGGAGGAAGCGGTGGTGGAGGTTCC GAGATTGTGCTGACTCAATCACCCGCGACCCTGAGCCTGTCCCCCGGCGAA AGGGCCACTCTGTCCTGTCGGGCCAGCCAATCAGTCTCCTCCTCGTACCTG GCCTGGTACCAGCAGAAGCCAGGACAGGCTCCGAGACTCCTTATCTATGGC GCATCCTCCCGCGCCACCGGAATCCCGGATAGGTTCTCGGGAAACGGATCG GGGACCGACTTCACTCTCACCATCTCCCGGCTGGAACCGGAGGACTTCGCC GTGTACTACTGCCAGCAGTACGGCAGCCCGCCTAGATTCACTTTCGGCCCC GGCACCAAAGTGGACATCAAGACCACTACCCCAGCACCGAGGCCACCCACC CCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGC GATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTT TCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTAC ATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGAC GGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGC GTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAAC CAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTG GACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAG AATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAA GCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCAC GACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCT CTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1980-D2		
BCMA_EBB-C1980-D2-aa **Full CAR**	8594	MALPVTALLLPLALLLHAARPEVQLLESGGGLVQPGGSLRLSCAASGFTFS SYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCAKIPQTGTFDYWGQGTLVTVSSGGGGSGGGGSGGGG SEIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQRPGQAPRLLIY GASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYGSSPSWTFG QGTRLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFA CDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEE DGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDV LDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKG HDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1980-D2-nt	8616	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAGCTGCTGGAGTCCGGCGGTGGATTGGTGCAA CCGGGGGGATCGCTCAGACTGTCCTGTGCGGCGTCAGGCTTCACCTTCTCG AGCTACGCCATGTCATGGGTCAGACAGGCCCCTGGAAAGGGTCTGGAATGG GTGTCCGCCATTTCCGGGAGCGGGGGATCTACATACTACGCCGATAGCGTG

Full CAR		AAGGGCCGCTTCACCATTTCCCGGGACAACTCCAAGAACACTCTCTATCTG CAAATGAACTCCCTCCGCGCTGAGGACACTGCCGTGTACTACTGCGCCAAA ATCCCTCAGACCGGCACCTTCGACTACTGGGGACAGGGGACTCTGGTCACC GTCAGCAGCGGTGGCGGAGGTTCGGGGGGAGGAGGAAGCGGCGGCGGAGGG TCCGAGATTGTGCTGACCCAGTCACCCGGCACTTTGTCCCTGTCGCCTGGA GAAAGGGCCACCCTTTCCTGCCGGGCATCCCAATCCGTGTCCTCCTCGTAC CTGGCCTGGTACCAGCAGAGGCCCGGACAGGCCCCACGGCTTCTGATCTAC GGAGCAAGCAGCCGCGCGACCGGTATCCCGGACCGGTTTTCGGGCTCGGGC TCAGGAACTGACTTCACCCTCACCATCTCCCGCCTGGAACCCGAAGATTTC GCTGTGTATTACTGCCAGCACTACGGCAGCTCCCCGTCCTGGACGTTCGGC CAGGGAACTCGGCTGGAGATCAAGACCACTACCCCAGCACCGAGGCCACCC ACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCA TGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCC TGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTG CTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTG TACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAG GACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTG CGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAG AACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTG CTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGA AAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCA GAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGC CACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGAC GCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1978-A10		
BCMA_EBB-C1978-A10-aa **Full CAR**	8595	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGGSLRLSCAASGFTFS SYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTMSRENDKNSVFL QMNSLRVEDTGVYYCARANYKRELRYYYGMDVWGQGTMVTVSSGGGGSGGG GSGGGGSEIVMTQSPGTLSLSPGESATLSCRASQRVASNYLAWYQHKPGQA PSLLISGASSRATGVPDRFSGSGSGTDFTLAISRLEPEDSAVYYCQHYDSS PSWTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHT RGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPV QTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGR REEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGE RRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-A10-nt **Full CAR**	8617	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAACTGGTGGAAACCGGTGGAGGACTCGTGCAG CCTGGCGGCAGCCTCCGGCTGAGCTGCGCCGCTTCGGGATTCACCTTTTCC TCCTACGCGATGTCTTGGGTCAGACAGGCCCCCGGAAAGGGGCTGGAATGG GTGTCAGCCATCTCCGGCTCCGGCGGATCAACGTACTACGCCGACTCCGTG AAAGGCCGGTTCACCATGTCGCGCGAGAATGACAAGAACTCCGTGTTCCTG CAAATGAACTCCCTGAGGGTGGAGGACACCGGAGTGTACTATTGTGCGCGC GCCAACTACAAGAGAGAGCTGCGGTACTACTACGGAATGGACGTCTGGGGA CAGGGAACTATGGTGACCGTGTCATCCGGTGGAGGGGGAAGCGGCGGTGGA GGCAGCGGGGGCGGGGGTTCAGAAATTGTCATGACCCAGTCCCCGGGAACT CTTTCCCTCTCCCCCGGGGAATCCGCGACTTTGTCCTGCCGGGCCAGCCAG CGCGTGGCCTCGAACTACCTCGCATGGTACCAGCATAAGCCAGGCCAAGCC CCTTCCCTGCTGATTTCCGGGGCTAGCAGCCGCGCCACTGGCGTGCCGGAT AGGTTCTCGGGAAGCGGCTCGGGTACCGATTTCACCCTGGCAATCTCGCGG

		CTGGAACCGGAGGATTCGGCCGTGTACTACTGCCAGCACTATGACTCATCC CCCTCCTGGACATTCGGACAGGGCACCAAGGTCGAGATCAAGACCACTACC CCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTG TCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACC CGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGT ACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGC GGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTG CAGACTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAG GAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCA GCCTACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGG AGAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATG GGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTC CAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAA CGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCC ACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1978-D4		
BCMA_EBB-C1978-D4-aa **Full CAR**	8596	MALPVTALLLPLALLLHAARPEVQLLETGGGLVQPGGSLRLSCAASGFSFS SYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCAKALVGATGAFDIWGQGTLVTVSSGGGGSGGGGSGG GGSEIVLTQSPGTLSLSPGERATLSCRASQSLSSNFLAWYQQKPGQAPGLL IYGASNWATGTPDRFSGSGSGTDFTLTITRLEPEDFAVYYCQYYGTSPMYT FGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLD FACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQ EEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEY DVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRG KGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-D4-nt **Full CAR**	8618	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAGCTGCTCGAAACCGGTGGAGGGCTGGTGCAG CCAGGGGGCTCCCTGAGGCTTTCATGCGCCGCTAGCGGATTCTCCTTCTCC TCTTACGCCATGTCGTGGGTCCGCCAAGCCCCTGGAAAAGGCCTGGAATGG GTGTCCGCGATTTCCGGGAGCGGAGGTTCGACCTATTACGCCGACTCCGTG AAGGGCCGCTTTACCATCTCCCGGGATAACTCCAAGAACACTCTGTACCTC CAAATGAACTCGCTGAGAGCCGAGGACACCGCCGTGTATTACTGCGCGAAG GCGCTGGTCGGCGCGACTGGGGCATTCGACATCTGGGGACAGGGAACTCTT GTGACCGTGTCGAGCGGAGGCGGCGGCTCCGGCGGAGGAGGGAGCGGGGGC GGTGGTTCCGAAATCGTGTTGACTCAGTCCCCGGGAACCCTGAGCTTGTCA CCCGGGGAGCGGGCCACTCTCTCCTGTCGCGCCTCCCAATCGCTCTCATCC AATTTCCTGGCCTGGTACCAGCAGAAGCCCGGACAGGCCCCGGGCCTGCTC ATCTACGGCGCTTCAAACTGGGCAACGGGAACCCCTGATCGGTTCAGCGGA AGCGGATCGGGTACTGACTTTACCCTGACCATCACCAGACTGGAACCGGAG GACTTCGCCGTGTACTACTGCCAGTACTACGGCACCTCCCCCATGTACACA TTCGGACAGGGTACCAAGGTCGAGATTAAGACCACTACCCCAGCACCGAGG CCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCG GAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGAC TTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTC CTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAG CTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAA GAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGC GAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAG

		GGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTAC GACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCG CGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAG ATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGC AAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACC TATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1980-A2		
BCMA_EBB-C1980-A2-aa **Full CAR**	8597	MALPVTALLLPLALLLHAARPEVQLLESGGGLVQPGGSLRLSCAASGFTFS SYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCVLWFGEGFDPWGQGTLVTVSSGGGGSGGGGSGGGGS DIVLTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQL LIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPLT FGGGTKVDIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLD FACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQ EEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEY DVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRG KGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1980-A2-nt **Full CAR**	8619	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTGCAGCTGCTTGAGAGCGGTGGAGGTCTGGTGCAG CCCGGGGGATCACTGCGCCTGTCCTGTGCCGCGTCCGGTTTCACTTTCTCC TCGTACGCCATGTCGTGGGTCAGACAGGCACCGGGAAAGGGACTGGAATGG GTGTCAGCCATTTCGGGTTCGGGGGGCAGCACCTACTACGCTGACTCCGTG AAGGGCCGGTTCACCATTTCCCGCGACAACTCCAAGAACACCTTGTACCTC CAAATGAACTCCCTGCGGGCCGAAGATACCGCCGTGTATTACTGCGTGCTG TGGTTCGGAGAGGGATTCGACCCGTGGGGACAAGGAACACTCGTGACTGTG TCATCCGGCGGAGGCGGCAGCGGTGGCGGCGGTTCCGGCGGCGGCGGATCT GACATCGTGTTGACCCAGTCCCCTCTGAGCCTGCCGGTCACTCCTGGCGAA CCAGCCAGCATCTCCTGCCGGTCGAGCCAGTCCCTCCTGCACTCCAATGGG TACAACTACCTCGATTGGTATCTGCAAAAGCCGGGCCAGAGCCCCCAGCTG CTGATCTACCTTGGGTCAAACCGCGCTTCCGGGGTGCCTGATAGATTCTCC GGGTCCGGGAGCGGAACCGACTTTACCCTGAAAATCTCGAGGGTGGAGGCC GAGGACGTCGGAGTGTACTACTGCATGCAGGCGCTCCAGACTCCCCTGACC TTCGGAGGAGGAACGAAGGTCGACATCAAGACCACTACCCCAGCACCGAGG CCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCG GAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGAC TTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTC CTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAG CTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAA GAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGC GAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAG GGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTAC GACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCG CGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAG ATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGC AAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACC TATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1981-C3		

BCMA_EBB-C1981-C3-aa **Full CAR**	8598	MALPVTALLLPLALLLHAARPQVQLVESGGGLVQPGGSLRLSCAASGFTFS SYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCAKVGYDSSGYYRDYYGMDVWGQGTTVTVSSGGGGSG GGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPG QAPRLLIYGTSSRATGISDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYG NSPPKFTFGPGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGA VHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFM RPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELN LGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGM KGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1981-C3-nt **Full CAR**	8620	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCCAAGTGCAGCTCGTGGAGTCAGGCGGAGGACTGGTGCAG CCCGGGGGCTCCCTGAGACTTTCCTGCGCGGCATCGGGTTTTACCTTCTCC TCCTATGCTATGTCCTGGGTGCGCCAGGCCCCGGGAAAGGGACTGGAATGG GTGTCCGCAATCAGCGGTAGCGGGGGCTCAACATACTACGCCGACTCCGTC AAGGGTCGCTTCACTATTTCCCGGGACAACTCCAAGAATACCCTGTACCTC CAAATGAACAGCCTCAGGGCCGAGGATACTGCCGTGTACTACTGCGCCAAA GTCGGATACGATAGCTCCGGTTACTACCGGGACTACTACGGAATGGACGTG TGGGGACAGGGCACCACCGTGACCGTGTCAAGCGGCGGAGGCGGTTCAGGA GGGGGAGGCTCCGGCGGTGGAGGGTCCGAAATCGTCCTGACTCAGTCGCCT GGCACTCTGTCGTTGTCCCCGGGGGAGCGCGCTACCCTGTCGTGTCGGGCG TCGCAGTCCGTGTCGAGCTCCTACCTCGCGTGGTACCAGCAGAAGCCCGGA CAGGCCCCTAGACTTCTGATCTACGGCACTTCTTCACGCGCCACCGGGATC AGCGACAGGTTCAGCGGCTCCGGCTCCGGGACCGACTTCACCCTGACCATT AGCCGGCTGGAGCCTGAAGATTTCGCCGTGTATTACTGCCAACACTACGGA AACTCGCCGCCAAAGTTCACGTTCGGACCCGGAACCAAGCTGGAAATCAAG ACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCC CAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCC GTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCT CTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTAC TGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATG AGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCA GAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCA GATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAAT CTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGAC CCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTAC AACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATG AAAGGGGAACGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTC AGCACCGCCACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCG CCTCGG
BCMA_EBB-C1978-G4		
BCMA_EBB-C1978-G4-aa **Full CAR**	8599	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAASGFTFS SYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCAKMGWSSGYLGAFDIWGQGTTVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVASSFLAWYQQKPGQAPR LLIYGASGRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYGGSPR LTFGGGTKVDIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRG LDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQT TQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRRE

		EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERR RGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-G4-nt **Full CAR**	8621	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCAC GCCGCTCGGCCCGAAGTCCAACTGGTGGAGTCCGGGGGAGGGCTCGTGCAG CCCGGAGGCAGCCTTCGGCTGTCGTGCGCCGCCTCCGGGTTCACGTTCTCA TCCTACGCGATGTCGTGGGTCAGACAGGCACCAGGAAAGGGACTGGAATGG GTGTCCGCCATTAGCGGCTCCGGCGGTAGCACCTACTATGCCGACTCAGTG AAGGGAAGGTTCACTATCTCCCGCGACAACAGCAAGAACACCCTGTACCTC CAAATGAACTCTCTGCGGGCCGAGGATACCGCGGTGTACTATTGCGCCAAG ATGGGTTGGTCCAGCGGATACTTGGGAGCCTTCGACATTTGGGGACAGGGC ACTACTGTGACCGTGTCCTCCGGGGGTGGCGGATCGGGAGGCGGCGGCTCG GGTGGAGGGGGTTCCGAAATCGTGTTGACCCAGTCACCGGGAACCCTCTCG CTGTCCCCGGGAGAACGGGCTACACTGTCATGTAGAGCGTCCCAGTCCGTG GCTTCCTCGTTCCTGGCCTGGTACCAGCAGAAGCCGGGACAGGCACCCCGC CTGCTCATCTACGGAGCCAGCGGCCGGGCGACCGGCATCCCTGACCGCTTC TCCGGTTCCGGCTCGGGCACCGACTTTACTCTGACCATTAGCAGGCTTGAG CCCGAGGATTTTGCCGTGTACTACTGCCAACACTACGGGGGGAGCCCTCGC CTGACCTTCGGAGGCGGAACTAAGGTCGATATCAAAACCACTACCCCAGCA CCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTG CGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGT CTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGC GGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGG AAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACT ACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGC GGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTAC AAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAG GAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGG AAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAG GATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGA AGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAG GACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG

In one embodiment, the CAR molecule comprises (e.g., consists of) an amino acid sequence provided in Table 23, or Table 1 of WO2016/014565, or as otherwise described herein. In one embodiment, the CAR molecule comprises (e.g., consists of) an amino acid sequence of SEQ ID NO: 8549, SEQ ID NO: 8550, SEQ ID NO: 8551, SEQ ID NO: 8552, SEQ ID NO: 8553, SEQ ID NO: 8554, SEQ ID NO: 8555, SEQ ID NO: 8556, SEQ ID NO: 8557, SEQ ID NO: 8558, SEQ ID NO: 8559, SEQ ID NO: 8560, SEQ ID NO: 8561, SEQ ID NO: 8562, SEQ ID NO: 8563, SEQ ID NO: 8579, SEQ ID NO: 8580, SEQ ID NO: 8581, SEQ ID NO: 8582, SEQ ID NO: 8583, SEQ ID NO: 8584, SEQ ID NO: 8585, SEQ ID NO: 8586, SEQ ID NO: 8587, SEQ ID NO: 8588, SEQ ID NO: 8589, SEQ ID NO: 8590, SEQ ID NO: 8591, SEQ ID NO: 8592, SEQ ID NO: 8593, SEQ ID NO: 8594, SEQ ID NO: 8595, SEQ ID NO: 8596, SEQ ID NO: 8597, SEQ ID NO: 8598, or SEQ ID NO: 8599; or an amino acid sequence having at least one, two, three, four, five, 10, 15, 20 or 30 modifications (e.g., substitutions, e.g.,

conservative substitutions) but not more than 60, 50, or 40 modifications (e.g., substitutions, e.g., conservative substitutions) of an amino acid sequence of SEQ ID NO: 8549, SEQ ID NO: 8550, SEQ ID NO: 8551, SEQ ID NO: 8552, SEQ ID NO: 8553, SEQ ID NO: 8554, SEQ ID NO: 8555, SEQ ID NO: 8556, SEQ ID NO: 8557, SEQ ID NO: 8558, SEQ ID NO: 8559, SEQ ID NO: 8560, SEQ ID NO: 8561, SEQ ID NO: 8562, SEQ ID NO: 8563, SEQ ID NO: 8579, SEQ ID NO: 8580, SEQ ID NO: 8581, SEQ ID NO: 8582, SEQ ID NO: 8583, SEQ ID NO: 8584, SEQ ID NO: 8585, SEQ ID NO: 8586, SEQ ID NO: 8587, SEQ ID NO: 8588, SEQ ID NO: 8589, SEQ ID NO: 8590, SEQ ID NO: 8591, SEQ ID NO: 8592, SEQ ID NO: 8593, SEQ ID NO: 8594, SEQ ID NO: 8595, SEQ ID NO: 8596, SEQ ID NO: 8597, SEQ ID NO: 8598, or SEQ ID NO: 8599; or an amino acid sequence having 85%, 90%, 95%, 96%, 97%, 98%, 99% identity to an amino acid sequence of SEQ ID NO: 8549, SEQ ID NO: 8550, SEQ ID NO: 8551, SEQ ID NO: 8552, SEQ ID NO: 8553, SEQ ID NO: 8554, SEQ ID NO: 8555, SEQ ID NO: 8556, SEQ ID NO: 8557, SEQ ID NO: 8558, SEQ ID NO: 8559, SEQ ID NO: 8560, SEQ ID NO: 8561, SEQ ID NO: 8562, SEQ ID NO: 8563, SEQ ID NO: 8579, SEQ ID NO: 8580, SEQ ID NO: 8581, SEQ ID NO: 8582, SEQ ID NO: 8583, SEQ ID NO: 8584, SEQ ID NO: 8585, SEQ ID NO: 8586, SEQ ID NO: 8587, SEQ ID NO: 8588, SEQ ID NO: 8589, SEQ ID NO: 8590, SEQ ID NO: 8591, SEQ ID NO: 8592, SEQ ID NO: 8593, SEQ ID NO: 8594, SEQ ID NO: 8595, SEQ ID NO: 8596, SEQ ID NO: 8597, SEQ ID NO: 8598, or SEQ ID NO: 8599.

Transmembrane domains

With respect to the transmembrane domain, in various embodiments, a CAR can be designed to comprise a transmembrane domain that is attached to the extracellular domain of the CAR. A transmembrane domain can include one or more additional amino acids adjacent to the transmembrane region, e.g., one or more amino acid associated with the extracellular region of the protein from which the transmembrane was derived (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 up to 15 amino acids of the extracellular region) and/or one or more additional amino acids associated with the intracellular region of the protein from which the transmembrane protein is derived (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 up to 15 amino acids of the intracellular region). In one aspect, the transmembrane domain is one that is associated with one of the other domains of the CAR e.g., in one embodiment, the transmembrane domain may be from the same protein that the signaling domain, costimulatory domain or the hinge domain is derived from. In another aspect, the transmembrane domain is not derived from the same protein that any other domain of the CAR is derived from. In some instances, the transmembrane domain can be selected or modified by amino acid substitution to avoid binding of such domains to the transmembrane domains of the same or different surface membrane proteins, e.g., to minimize interactions with other members of the receptor complex. In one aspect, the transmembrane domain is capable of homodimerization with another CAR on the cell

surface of a CAR-expressing cell. In a different aspect, the amino acid sequence of the transmembrane domain may be modified or substituted so as to minimize interactions with the binding domains of the native binding partner present in the same CAR-expressing cell.

The transmembrane domain may be derived either from a natural or from a recombinant source. Where the source is natural, the domain may be derived from any membrane-bound or transmembrane protein. In one aspect the transmembrane domain is capable of signaling to the intracellular domain(s) whenever the CAR has bound to a target. A transmembrane domain of particular use in this invention may include at least the transmembrane region(s) of e.g., the alpha, beta or zeta chain of the T-cell receptor, CD28, CD27, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154. In some embodiments, a transmembrane domain may include at least the transmembrane region(s) of, e.g., KIRDS2, OX40, CD2, CD27, LFA-1 (CD11a, CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD40, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD160, CD19, IL2R beta, IL2R gamma, IL7R α, ITGA1, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, PAG/Cbp, NKG2D, NKG2C.

In some instances, the transmembrane domain can be attached to the extracellular region of the CAR, e.g., the antigen binding domain of the CAR, via a hinge, e.g., a hinge from a human protein. For example, in one embodiment, the hinge can be a human Ig (immunoglobulin) hinge (e.g., an IgG4 hinge, an IgD hinge), a GS linker (e.g., a GS linker described herein), a KIR2DS2 hinge or a CD8a hinge. In one embodiment, the hinge or spacer comprises (e.g., consists of) the amino acid sequence of SEQ ID NO:6642. In one aspect, the transmembrane domain comprises (e.g., consists of) a transmembrane domain of SEQ ID NO: 6644.

In certain embodiments, the encoded transmembrane domain comprises an amino acid sequence of a CD8 transmembrane domain having at least one, two or three modifications but not more than 20, 10 or 5 modifications of an amino acid sequence of SEQ ID NO: 6644, or a sequence with 95-99% identity to an amino acid sequence of SEQ ID NO: 6644. In one embodiment, the encoded transmembrane domain comprises the sequence of SEQ ID NO: 6644.

In other embodiments, the nucleic acid molecule encoding the CAR comprises a nucleotide sequence of a CD8 transmembrane domain, e.g., comprising the sequence of SEQ ID NO: 6645, or a sequence with 95-99% identity thereof.

In certain embodiments, the encoded antigen binding domain is connected to the transmembrane domain by a hinge region. In one embodiment, the encoded hinge region comprises the amino acid sequence of a CD8 hinge, e.g., SEQ ID NO: 6642; or the amino acid sequence of an IgG4 hinge, e.g., SEQ ID NO: 6630, or a sequence with 95-99% identity to SEQ ID NO: 6642 or 6630. In other embodiments, the nucleic acid sequence encoding the hinge region comprises a sequence of SEQ ID NO: 6643 or SEQ ID NO: 6631, corresponding to a CD8 hinge or an IgG4 hinge, respectively, or a sequence with 95-99% identity to SEQ ID NO:6643 or 6631.

In one aspect, the hinge or spacer comprises an IgG4 hinge. For example, in one embodiment, the hinge or spacer comprises a hinge of the amino acid sequence

ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVE
VHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQ
VYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTV
DKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKM (SEQ ID NO:6630). In some embodiments, the hinge or spacer comprises a hinge encoded by a nucleotide sequence of

GAGAGCAAGTACGGCCCTCCCTGCCCCCCTTGCCCTGCCCCCGAGTTCCTGGGCGGACCCAG
CGTGTTCCTGTTCCCCCCCAAGCCCAAGGACACCCTGATGATCAGCCGGACCCCCGAGGTGA
CCTGTGTGGTGGTGGACGTGTCCCAGGAGGACCCCGAGGTCCAGTTCAACTGGTACGTGGAC
GGCGTGGAGGTGCACAACGCCAAGACCAAGCCCCGGGAGGAGCAGTTCAATAGCACCTACC
GGGTGGTGTCCGTGCTGACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAATACAAGTG
TAAGGTGTCCAACAAGGGCCTGCCCAGCAGCATCGAGAAAACCATCAGCAAGGCCAAGGGC
CAGCCTCGGGAGCCCCAGGTGTACACCCTGCCCCCTAGCCAAGAGGAGATGACCAAGAACC
AGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCCAGCGACATCGCCGTGGAGTGGGAG
AGCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCCCCTGTGCTGGACAGCGACGGCA
GCTTCTTCCTGTACAGCCGGCTGACCGTGGACAAGAGCCGGTGGCAGGAGGGCAACGTCTTT
AGCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCCTGAGCCTGTC
CCTGGGCAAGATG (SEQ ID NO:6631).

In one aspect, the hinge or spacer comprises an IgD hinge. For example, in one embodiment, the hinge or spacer comprises a hinge of the amino acid sequence

RWPESPKAQASSVPTAQPQAEGSLAKATTAPATTRNTGRGGEEKKKEKEKEEQEERETKTPECP
SHTQPLGVYLLTPAVQDLWLRDKATFTCFVVGSDLKDAHLTWEVAGKVPTGGVEEGLLERHSN
GSQSQHSRLTLPRSLWNAGTSVTCTLNHPSLPPQRLMALREPAAQAPVKLSLNLLASSDPPEAAS
WLLCEVSGFSPPNILLMWLEDQREVNTSGFAPARPPPQPGSTTFWAWSVLRVPAPPSPQPATYTC
VVSHEDSRTLLNASRSLEVSYVTDH (SEQ ID NO:6632). In some embodiments, the hinge or spacer

comprises a hinge encoded by a nucleotide sequence of
AGGTGGCCCGAAAGTCCCAAGGCCCAGGCATCTAGTGTTCCTACTGCACAGCCCCAGGCAG
AAGGCAGCCTAGCCAAAGCTACTACTGCACCTGCCACTACGCGCAATACTGGCCGTGGCGG
GGAGGAGAAGAAAAAGGAGAAAGAGAAAGAAGAACAGGAAGAGAGGGAGACCAAGACCC
CTGAATGTCCATCCCATACCCAGCCGCTGGGCGTCTATCTCTTGACTCCCGCAGTACAGGAC
TTGTGGCTTAGAGATAAGGCCACCTTTACATGTTTCGTCGTGGGCTCTGACCTGAAGGATGC
CCATTTGACTTGGGAGGTTGCCGGAAAGGTACCCACAGGGGGGGTTGAGGAAGGGTTGCTG
GAGCGCCATTCCAATGGCTCTCAGAGCCAGCACTCAAGACTCACCCTTCCGAGATCCCTGTG
GAACGCCGGGACCTCTGTCACATGTACTCTAAATCATCCTAGCCTGCCCCCACAGCGTCTGA
TGGCCCTTAGAGAGCCAGCCGCCCAGGCACCAGTTAAGCTTAGCCTGAATCTGCTCGCCAGT
AGTGATCCCCCAGAGGCCGCCAGCTGGCTCTTATGCGAAGTGTCCGGCTTTAGCCCGCCCAA
CATCTTGCTCATGTGGCTGGAGGACCAGCGAGAAGTGAACACCAGCGGCTTCGCTCCAGCCC
GGCCCCCACCCCAGCCGGGTTCTACCACATTCTGGGCCTGGAGTGTCTTAAGGGTCCCAGCA
CCACCTAGCCCCCAGCCAGCCACATACACCTGTGTTGTGTCCCATGAAGATAGCAGGACCCT
GCTAAATGCTTCTAGGAGTCTGGAGGTTTCCTACGTGACTGACCATT (SEQ ID NO:6633).

In one aspect, the transmembrane domain may be recombinant, in which case it will comprise predominantly hydrophobic residues such as leucine and valine. In one aspect a triplet of phenylalanine, tryptophan and valine can be found at each end of a recombinant transmembrane domain.

Optionally, a short oligo- or polypeptide linker, between 2 and 10 amino acids in length may form the linkage between the transmembrane domain and the cytoplasmic region of the CAR. A glycine-serine doublet provides a particularly suitable linker. For example, in one aspect, the linker comprises the amino acid sequence of GGGGSGGGGS (SEQ ID NO:6634). In some embodiments, the linker is encoded by a nucleotide sequence of GGTGGCGGAGGTTCTGGAGGTGGAGGTTCC (SEQ ID NO:6635).

In one aspect, the hinge or spacer comprises a KIR2DS2 hinge.

Signaling domains

In embodiments of the invention having an intracellular signaling domain, such a domain can contain, e.g., one or more of a primary signaling domain and/or a costimulatory signaling domain. In some embodiments, the intracellular signaling domain comprises a sequence encoding a primary signaling domain. In some embodiments, the intracellular signaling domain comprises a costimulatory signaling domain. In some embodiments, the intracellular signaling domain comprises a primary signaling domain and a costimulatory signaling domain.

The intracellular signaling sequences within the cytoplasmic portion of the CAR of the invention may be linked to each other in a random or specified order. Optionally, a short oligo- or polypeptide linker, for example, between 2 and 10 amino acids (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids) in length may form the linkage between intracellular signaling sequences. In one embodiment, a glycine-serine doublet can be used as a suitable linker. In one embodiment, a single amino acid, e.g., an alanine, a glycine, can be used as a suitable linker.

In one aspect, the intracellular signaling domain is designed to comprise two or more, e.g., 2, 3, 4, 5, or more, costimulatory signaling domains. In an embodiment, the two or more, e.g., 2, 3, 4, 5, or more, costimulatory signaling domains, are separated by a linker molecule, e.g., a linker molecule described herein. In one embodiment, the intracellular signaling domain comprises two costimulatory signaling domains. In some embodiments, the linker molecule is a glycine residue. In some embodiments, the linker is an alanine residue.

Primary Signaling domains

A primary signaling domain regulates primary activation of the TCR complex either in a stimulatory way, or in an inhibitory way. Primary intracellular signaling domains that act in a stimulatory manner may contain signaling motifs which are known as immunoreceptor tyrosine-based activation motifs or ITAMs.

Examples of ITAM containing primary intracellular signaling domains that are of particular use in the invention include those of CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and DAP12. In one embodiment, a CAR of the invention comprises an intracellular signaling domain, e.g., a primary signaling domain of CD3-zeta.

In one embodiment, the encoded primary signaling domain comprises a functional signaling domain of CD3 zeta. The encoded CD3 zeta primary signaling domain can comprise an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of an amino acid sequence of SEQ ID NO: 6648 or SEQ ID NO: 6650, or a sequence with 95-99% identity to an amino acid sequence of SEQ ID NO: 6648 or SEQ ID NO: 6650. In some embodiments, the encoded primary signaling domain comprises a sequence of SEQ ID NO: 6648 or SEQ ID NO: 6650. In other embodiments, the nucleic acid sequence encoding the primary signaling domain comprises a sequence of SEQ ID NO: 6649 or SEQ ID NO: 6651, or a sequence with 95-99% identity thereof.

Costimulatory Signaling Domains

In some embodiments, the encoded intracellular signaling domain comprises a costimulatory signaling domain. For example, the intracellular signaling domain can comprise a primary signaling domain and a

costimulatory signaling domain. In some embodiments, the encoded costimulatory signaling domain comprises a functional signaling domain of a protein chosen from one or more of CD27, CD28, 4-1BB (CD137), OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, CDS, ICAM-1, GITR, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), CD160, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, NKp44, NKp30, NKp46, or NKG2D.

In certain embodiments, the encoded costimulatory signaling domain comprises an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of an amino acid sequence of SEQ ID NO: 6646 or SEQ ID NO: 6636, or a sequence with 95-99% identity to an amino acid sequence of SEQ ID NO: 6646 or SEQ ID NO: 6636. In one embodiment, the encoded costimulatory signaling domain comprises a sequence of SEQ ID NO: 6646 or SEQ ID NO: 6636. In other embodiments, the nucleic acid sequence encoding the costimulatory signaling domain comprises a sequence of SEQ ID NO: 6647 or SEQ ID NO: 6637, or a sequence with 95-99% identity thereof.

In other embodiments, the encoded intracellular domain comprises the sequence of SEQ ID NO: 6646 or SEQ ID NO: 6636, and the sequence of SEQ ID NO: 6648 or SEQ ID NO: 6650, wherein the sequences comprising the intracellular signaling domain are expressed in the same frame and as a single polypeptide chain.

In certain embodiments, the nucleic acid sequence encoding the intracellular signaling domain comprises a sequence of SEQ ID NO: 6647 or SEQ ID NO: 6637, or a sequence with 95-99% identity thereof, and a sequence of SEQ ID NO: 6649 or SEQ ID NO: 6651, or a sequence with 95-99% identity thereof.

In some embodiments, the nucleic acid molecule further encodes a leader sequence. In one embodiment, the leader sequence comprises the sequence of SEQ ID NO: 6640.

In one aspect, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of CD28. In one aspect, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of 4-1BB. In one aspect, the

signaling domain of 4-1BB is a signaling domain of SEQ ID NO: 6646. In one aspect, the signaling domain of CD3-zeta is a signaling domain of SEQ ID NO: 6648.

In one aspect, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of CD27. In one aspect, the signaling domain of CD27 comprises an amino acid sequence of QRRKYRSNKGESPVEPAEPCRYSCPREEEGSTIPIQEDYRKPEPACSP (SEQ ID NO: 6636). In one aspect, the signalling domain of CD27 is encoded by a nucleic acid sequence of AGGAGTAAGAGGAGCAGGCTCCTGCACAGTGACTACATGAACATGACTCCCCGCCGCCCCG GGCCCACCCGCAAGCATTACCAGCCCTATGCCCCACCACGCGACTTCGCAGCCTATCGCTCC (SEQ ID NO: 6637).

Vectors

In another aspect, the invention pertains to a vector comprising a nucleic acid sequence encoding a CAR described herein. In one embodiment, the vector is chosen from a DNA vector, an RNA vector, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector. In one embodiment, the vector is a lentivirus vector. These vectors or portions thereof may, among other things, be used to create template nucleic acids, as described herein for use with the CRISPR systems as described herein. Alternatively, the vectors may be used to deliver nucleic acid directly to the cell, e.g., the immune effector cell, e.g., the T cell, e.g., the allogeneic T cell, independent of the CRISPR system.

The present invention also provides vectors in which a DNA of the present invention is inserted. Vectors derived from retroviruses such as the lentivirus are suitable tools to achieve long-term gene transfer since they allow long-term, stable integration of a transgene and its propagation in daughter cells. Lentiviral vectors have the added advantage over vectors derived from onco-retroviruses such as murine leukemia viruses in that they can transduce non-proliferating cells, such as hepatocytes. They also have the added advantage of low immunogenicity. A retroviral vector may also be, e.g., a gammaretroviral vector. A gammaretroviral vector may include, e.g., a promoter, a packaging signal (ψ), a primer binding site (PBS), one or more (e.g., two) long terminal repeats (LTR), and a transgene of interest, e.g., a gene encoding a CAR. A gammaretroviral vector may lack viral structural gens such as gag, pol, and env. Exemplary gammaretroviral vectors include Murine Leukemia Virus (MLV), Spleen-Focus Forming Virus (SFFV), and Myeloproliferative Sarcoma Virus (MPSV), and vectors derived therefrom. Other gammaretroviral vectors are described, e.g., in Tobias Maetzig et al., "Gammaretroviral Vectors: Biology, Technology and Application" Viruses. 2011 Jun; 3(6): 677–713.

In another embodiment, the vector comprising the nucleic acid encoding the desired CAR of the invention is an adenoviral vector (A5/35). In another embodiment, the expression of nucleic acids encoding CARs can be accomplished using of transposons such as sleeping beauty, crisper, CAS9, and zinc finger

nucleases. See below June et al. 2009*Nature Reviews Immunology* 9.10: 704-716, is incorporated herein by reference.

The nucleic acid can be cloned into a number of types of vectors. For example, the nucleic acid can be cloned into a vector including, but not limited to a plasmid, a phagemid, a phage derivative, an animal virus, and a cosmid. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors, and sequencing vectors.

Disclosed herein are methods for producing an in vitro transcribed RNA CAR. The present invention also includes a CAR encoding RNA construct that can be directly transfected into a cell. A method for generating mRNA for use in transfection can involve in vitro transcription (IVT) of a template with specially designed primers, followed by polyA addition, to produce a construct containing 3' and 5' untranslated sequence ("UTR"), a 5' cap and/or Internal Ribosome Entry Site (IRES), the nucleic acid to be expressed, and a polyA tail, typically 50-2000 bases in length (SEQ ID NO: 6638). RNA so produced can efficiently transfect different kinds of cells. In one aspect, the template includes sequences for the CAR.

Non-viral delivery methods

In some aspects, non-viral methods can be used to deliver a nucleic acid encoding a CAR described herein into a cell or tissue or a subject.

In some embodiments, the non-viral method includes the use of a transposon (also called a transposable element). In some embodiments, a transposon is a piece of DNA that can insert itself at a location in a genome, for example, a piece of DNA that is capable of self-replicating and inserting its copy into a genome, or a piece of DNA that can be spliced out of a longer nucleic acid and inserted into another place in a genome. For example, a transposon comprises a DNA sequence made up of inverted repeats flanking genes for transposition.

In some embodiments, cells, e.g., T or NK cells, are generated that express a CAR described herein by using a combination of gene insertion using the SBTS and genetic editing using a nuclease (e.g., Zinc finger nucleases (ZFNs), Transcription Activator-Like Effector Nucleases (TALENs), the CRISPR/Cas system, or engineered meganuclease re-engineered homing endonucleases).

In some embodiments, cells of the invention, e.g., T or NK cells, e.g., allogeneic T cells, e.g., described herein, (e.g., that express a CAR described herein) are generated by contacting the cells with (a) a composition comprising one or more gRNA molecules, e.g., as described herein, and one or more Cas molecules, e.g., a Cas9 molecule, e.g., as described herein, and (b) nucleic acid comprising sequence encoding a CAR, e.g., described herein (such as a template nucleic acid molecule as described herein).

Without being bound by theory, said composition of (a), above, will induce a break at or near the genomic DNA targeted by the targeting domain of the gRNA molecule(s), and the nucleic acid of (b) will incorporate, e.g., partially or wholly, into the genome at or near said break, such that upon integration, the encoded CAR molecule is expressed. In embodiments, expression of the CAR will be controlled by promoters or other regulatory elements endogenous to the genome (e.g., the promoter controlling expression from the gene in which the nucleic acid of (b) was inserted). In other embodiments, the nucleic acid of (b) further comprises a promoter and/or other regulatory elements, e.g., as described herein, e.g., an EF1-alpha promoter, operably linked to the sequence encoding the CAR, such that upon integration, expression of the CAR is controlled by that promoter and/or other regulatory elements. Additional features of the invention relating to use of CRISPR/Cas9 systems, e.g., as described herein, to direct incorporation of nucleic acid sequence encoding a CAR, e.g., as described herein, are described elsewhere in this application, e.g., in the section relating to gene insertion and homologous recombination. In embodiments, the composition of a) above is a composition comprising RNPs comprising the one or more gRNA molecules. In embodiments, RNPs comprising gRNAs targeting unique target sequences are introduced into the cell simultaneously, e.g., as a mixture of RNPs comprising the one or more gRNAs. In embodiments, RNPs comprising gRNAs targeting unique target sequences are introduced into the cell sequentially.

In some embodiments, use of a non-viral method of delivery permits reprogramming of cells, e.g., T or NK cells, and direct infusion of the cells into a subject. Advantages of non-viral vectors include but are not limited to the ease and relatively low cost of producing sufficient amounts required to meet a patient population, stability during storage, and lack of immunogenicity.

Inhibitory domains

In an embodiment, the vector comprises a nucleic acid sequence that encodes a CAR, e.g., a CAR described herein, and a nucleic acid sequence that encodes an inhibitory molecule comprising: an inhKIR cytoplasmic domain; a transmembrane domain, e.g., a KIR transmembrane domain; and an inhibitor cytoplasmic domain, e.g., an ITIM domain, e.g., an inhKIR ITIM domain. In an embodiment the inhibitory molecule is a naturally occurring inhKIR, or a sequence sharing at least 50, 60, 70, 80, 85, 90, 95, or 99% homology with, or that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, or 20 residues from, a naturally occurring inhKIR.

In an embodiment, the nucleic acid sequence that encodes an inhibitory molecule comprises: a SLAM family cytoplasmic domain; a transmembrane domain, e.g., a SLAM family transmembrane domain; and an inhibitor cytoplasmic domain, e.g., a SLAM family domain, e.g., an SLAM family ITIM domain. In an embodiment the inhibitory molecule is a naturally occurring SLAM family member, or a sequence

sharing at least 50, 60, 70, 80, 85, 90, 95, or 99% homology with, or that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, or 20 residues from, a naturally occurring SLAM family member.

In one embodiment, the vector is an *in vitro* transcribed vector, e.g., a vector that transcribes RNA of a nucleic acid molecule described herein. In one embodiment, the nucleic acid sequence in the vector further comprises a poly(A) tail, e.g., a poly A tail. In one embodiment, the nucleic acid sequence in the vector further comprises a 3'UTR, e.g., a 3' UTR described herein, e.g., comprising at least one repeat of a 3'UTR derived from human beta-globulin. In one embodiment, the nucleic acid sequence in the vector further comprises promoter, e.g., a T2A promoter.

Promoters

In one embodiment, the vector further comprises a promoter. In some embodiments, the promoter is chosen from an EF-1 promoter, a CMV IE gene promoter, an EF-1α promoter, an ubiquitin C promoter, or a phosphoglycerate kinase (PGK) promoter. In one embodiment, the promoter is an EF-1 promoter. In one embodiment, the EF-1 promoter comprises a sequence of SEQ ID NO: 6639.

Host cells for CAR expression

As noted above, in some aspects the invention pertains to a cell, e.g., an immune effector cell, (e.g., a population of cells, e.g., a population of immune effector cells) comprising a nucleic acid molecule, a CAR polypeptide molecule, or a vector as described herein.

In certain aspects of the present disclosure, immune effector cells, e.g., T cells, can be obtained from a unit of blood collected from a subject using any number of techniques known to the skilled artisan, such as Ficoll™ separation. In one preferred aspect, cells from the circulating blood of an individual are obtained by apheresis. The apheresis product typically contains lymphocytes, including T cells, monocytes, granulocytes, B cells, other nucleated white blood cells, red blood cells, and platelets. In one aspect, the cells collected by apheresis may be washed to remove the plasma fraction and, optionally, to place the cells in an appropriate buffer or media for subsequent processing steps. In one embodiment, the cells are washed with phosphate buffered saline (PBS). In an alternative embodiment, the wash solution lacks calcium and may lack magnesium or may lack many if not all divalent cations.

Initial activation steps in the absence of calcium can lead to magnified activation. As those of ordinary skill in the art would readily appreciate a washing step may be accomplished by methods known to those in the art, such as by using a semi-automated "flow-through" centrifuge (for example, the Cobe 2991 cell processor, the Baxter CytoMate, or the Haemonetics Cell Saver 5) according to the manufacturer's instructions. After washing, the cells may be resuspended in a variety of biocompatible buffers, such as, for example, Ca-free, Mg-free PBS, PlasmaLyte A, or other saline solution with or without buffer.

Alternatively, the undesirable components of the apheresis sample may be removed and the cells directly resuspended in culture media.

It is recognized that the methods of the application can utilize culture media conditions comprising 5% or less, for example 2%, human AB serum, and employ known culture media conditions and compositions, for example those described in Smith *et al.*, "Ex vivo expansion of human T cells for adoptive immunotherapy using the novel Xeno-free CTS Immune Cell Serum Replacement" *Clinical & Translational Immunology* (2015) 4, e31; doi:10.1038/cti.2014.31.

In one aspect, T cells are isolated from peripheral blood lymphocytes by lysing the red blood cells and depleting the monocytes, for example, by centrifugation through a PERCOLL™ gradient or by counterflow centrifugal elutriation.

The methods described herein can include, e.g., selection of a specific subpopulation of immune effector cells, e.g., T cells, that are a T regulatory cell-depleted population, CD25+ depleted cells, using, e.g., a negative selection technique, e.g., described herein. Preferably, the population of T regulatory depleted cells contains less than 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells.

In one embodiment, T regulatory cells, e.g., CD25+ T cells, are removed from the population using an anti-CD25 antibody, or fragment thereof, or a CD25-binding ligand, IL-2. In one embodiment, the anti-CD25 antibody, or fragment thereof, or CD25-binding ligand is conjugated to a substrate, e.g., a bead, or is otherwise coated on a substrate, e.g., a bead. In one embodiment, the anti-CD25 antibody, or fragment thereof, is conjugated to a substrate as described herein.

In one embodiment, the T regulatory cells, e.g., CD25+ T cells, are removed from the population using CD25 depletion reagent from Miltenyi™. In one embodiment, the ratio of cells to CD25 depletion reagent is 1e7 cells to 20 uL, or 1e7 cells to15 uL, or 1e7 cells to 10 uL, or 1e7 cells to 5 uL, or 1e7 cells to 2.5 uL, or 1e7 cells to 1.25 uL. In one embodiment, e.g., for T regulatory cells, e.g., CD25+ depletion, greater than 500 million cells/ml is used. In a further aspect, a concentration of cells of 600, 700, 800, or 900 million cells/ml is used.

In one embodiment, the population of immune effector cells to be depleted includes about 6 x 10^9 CD25+ T cells. In other aspects, the population of immune effector cells to be depleted include about 1 x 10^9 to 1x 10^{10} CD25+ T cell, and any integer value in between. In one embodiment, the resulting population T regulatory depleted cells has 2 x 10^9 T regulatory cells, e.g., CD25+ cells, or less (e.g., 1 x 10^9, 5 x 10^8, 1 x 10^8, 5 x 10^7, 1 x 10^7, or less CD25+ cells).

In one embodiment, the T regulatory cells, e.g., CD25+ cells, are removed from the population using the CliniMAC system with a depletion tubing set, such as, e.g., tubing 162-01. In one embodiment, the CliniMAC system is run on a depletion setting such as, e.g., DEPLETION2.1.

Without wishing to be bound by a particular theory, decreasing the level of negative regulators of immune cells (e.g., decreasing the number of unwanted immune cells, e.g., T_{REG} cells), in a subject prior to apheresis or during manufacturing of a CAR-expressing cell product can reduce the risk of subject relapse. For example, methods of depleting T_{REG} cells are known in the art. Methods of decreasing T_{REG} cells include, but are not limited to, cyclophosphamide, anti-GITR antibody (an anti-GITR antibody described herein), CD25-depletion, and combinations thereof.

In some embodiments, the manufacturing methods comprise reducing the number of (e.g., depleting) T_{REG} cells prior to manufacturing of the CAR-expressing cell. For example, manufacturing methods comprise contacting the sample, e.g., the apheresis sample, with an anti-GITR antibody and/or an anti-CD25 antibody (or fragment thereof, or a CD25-binding ligand), e.g., to deplete T_{REG} cells prior to manufacturing of the CAR-expressing cell (e.g., T cell, NK cell) product.

In an embodiment, a subject is pre-treated with one or more therapies that reduce T_{REG} cells prior to collection of cells for CAR-expressing cell product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment. In an embodiment, methods of decreasing T_{REG} cells include, but are not limited to, administration to the subject of one or more of cyclophosphamide, anti-GITR antibody, CD25-depletion, or a combination thereof. Administration of one or more of cyclophosphamide, anti-GITR antibody, CD25-depletion, or a combination thereof, can occur before, during or after an infusion of the CAR-expressing cell product.

In an embodiment, a subject is pre-treated with cyclophosphamide prior to collection of cells for CAR-expressing cell product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment. In an embodiment, a subject is pre-treated with an anti-GITR antibody prior to collection of cells for CAR-expressing cell product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment.

In one embodiment, the population of cells to be removed are neither the regulatory T cells or tumor cells, but cells that otherwise negatively affect the expansion and/or function of CART cells, e.g. cells expressing CD14, CD11b, CD33, CD15, or other markers expressed by potentially immune suppressive cells. In one embodiment, such cells are envisioned to be removed concurrently with regulatory T cells and/or tumor cells, or following said depletion, or in another order.

The methods described herein can include more than one selection step, e.g., more than one depletion step. Enrichment of a T cell population by negative selection can be accomplished, e.g., with a combination of antibodies directed to surface markers unique to the negatively selected cells. One method is cell sorting and/or selection via negative magnetic immunoadherence or flow cytometry that uses a cocktail of monoclonal antibodies directed to cell surface markers present on the cells negatively selected. For example, to enrich for CD4+ cells by negative selection, a monoclonal antibody cocktail can include antibodies to CD14, CD20, CD11b, CD16, HLA-DR, and CD8.

The methods described herein can further include removing cells from the population which express a tumor antigen, e.g., a tumor antigen that does not comprise CD25, e.g., CD19, CD30, CD38, CD123, CD20, CD14 or CD11b, to thereby provide a population of T regulatory depleted, e.g., CD25+ depleted, and tumor antigen depleted cells that are suitable for expression of a CAR, e.g., a CAR described herein. In one embodiment, tumor antigen expressing cells are removed simultaneously with the T regulatory, e.g., CD25+ cells. For example, an anti-CD25 antibody, or fragment thereof, and an anti-tumor antigen antibody, or fragment thereof, can be attached to the same substrate, e.g., bead, which can be used to remove the cells or an anti-CD25 antibody, or fragment thereof, or the anti-tumor antigen antibody, or fragment thereof, can be attached to separate beads, a mixture of which can be used to remove the cells. In other embodiments, the removal of T regulatory cells, e.g., CD25+ cells, and the removal of the tumor antigen expressing cells is sequential, and can occur, e.g., in either order.

Also provided are methods that include removing cells from the population which express a check point inhibitor, e.g., a check point inhibitor described herein, e.g., one or more of PD1+ cells, LAG3+ cells, and TIM3+ cells, to thereby provide a population of T regulatory depleted, e.g., CD25+ depleted cells, and check point inhibitor depleted cells, e.g., PD1+, LAG3+ and/or TIM3+ depleted cells. Exemplary check point inhibitors include B7-H1, B7-1, CD160, P1H, 2B4, PD1, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, TIGIT, CTLA-4, BTLA and LAIR1. In one embodiment, check point inhibitor expressing cells are removed simultaneously with the T regulatory, e.g., CD25+ cells. For example, an anti-CD25 antibody, or fragment thereof, and an anti-check point inhibitor antibody, or fragment thereof, can be attached to the same bead which can be used to remove the cells, or an anti-CD25 antibody, or fragment thereof, and the anti-check point inhibitor antibody, or fragment there, can be attached to separate beads, a mixture of which can be used to remove the cells. In other embodiments, the removal of T regulatory cells, e.g., CD25+ cells, and the removal of the check point inhibitor expressing cells is sequential, and can occur, e.g., in either order.

Methods described herein can include a positive selection step. For example, T cells can isolated by incubation with anti-CD3/anti-CD28 (e.g., 3x28)-conjugated beads, such as DYNABEADS® M-450

CD3/CD28 T, for a time period sufficient for positive selection of the desired T cells. In one embodiment, the time period is about 30 minutes. In a further embodiment, the time period ranges from 30 minutes to 36 hours or longer and all integer values there between. In a further embodiment, the time period is at least 1, 2, 3, 4, 5, or 6 hours. In yet another embodiment, the time period is 10 to 24 hours, e.g., 24 hours. Longer incubation times may be used to isolate T cells in any situation where there are few T cells as compared to other cell types, such in isolating tumor infiltrating lymphocytes (TIL) from tumor tissue or from immunocompromised individuals. Further, use of longer incubation times can increase the efficiency of capture of CD8+ T cells. Thus, by simply shortening or lengthening the time T cells are allowed to bind to the CD3/CD28 beads and/or by increasing or decreasing the ratio of beads to T cells (as described further herein), subpopulations of T cells can be preferentially selected for or against at culture initiation or at other time points during the process. Additionally, by increasing or decreasing the ratio of anti-CD3 and/or anti-CD28 antibodies on the beads or other surface, subpopulations of T cells can be preferentially selected for or against at culture initiation or at other desired time points.

In one embodiment, a T cell population can be selected that expresses one or more of IFN-γ, TNFα, IL-17A, IL-2, IL-3, IL-4, GM-CSF, IL-10, IL-13, granzyme B, and perforin, or other appropriate molecules, e.g., other cytokines. Methods for screening for cell expression can be determined, e.g., by the methods described in PCT Publication No.: WO 2013/126712.

For isolation of a desired population of cells by positive or negative selection, the concentration of cells and surface (e.g., particles such as beads) can be varied. In certain aspects, it may be desirable to significantly decrease the volume in which beads and cells are mixed together (e.g., increase the concentration of cells), to ensure maximum contact of cells and beads. For example, in one aspect, a concentration of 10 billion cells/ml, 9 billion/ml, 8 billion/ml, 7 billion/ml, 6 billion/ml, or 5 billion/ml is used. In one aspect, a concentration of 1 billion cells/ml is used. In yet one aspect, a concentration of cells from 75, 80, 85, 90, 95, or 100 million cells/ml is used. In further aspects, concentrations of 125 or 150 million cells/ml can be used.

Using high concentrations can result in increased cell yield, cell activation, and cell expansion. Further, use of high cell concentrations allows more efficient capture of cells that may weakly express target antigens of interest, such as CD28-negative T cells, or from samples where there are many tumor cells present (e.g., leukemic blood, tumor tissue, etc.). Such populations of cells may have therapeutic value and would be desirable to obtain. For example, using high concentration of cells allows more efficient selection of CD8+ T cells that normally have weaker CD28 expression.

In a related aspect, it may be desirable to use lower concentrations of cells. By significantly diluting the mixture of T cells and surface (e.g., particles such as beads), interactions between the particles and cells is

minimized. This selects for cells that express high amounts of desired antigens to be bound to the particles. For example, CD4+ T cells express higher levels of CD28 and are more efficiently captured than CD8+ T cells in dilute concentrations. In one aspect, the concentration of cells used is 5 x 10^6/ml. In other aspects, the concentration used can be from about 1 x 10^5/ml to 1 x 10^6/ml, and any integer value in between.

In other aspects, the cells may be incubated on a rotator for varying lengths of time at varying speeds at either 2-10°C or at room temperature.

T cells for stimulation can also be frozen after a washing step. Wishing not to be bound by theory, the freeze and subsequent thaw step provides a more uniform product by removing granulocytes and to some extent monocytes in the cell population. After the washing step that removes plasma and platelets, the cells may be suspended in a freezing solution. While many freezing solutions and parameters are known in the art and will be useful in this context, one method involves using PBS containing 20% DMSO and 8% human serum albumin, or culture media containing 10% Dextran 40 and 5% Dextrose, 20% Human Serum Albumin and 7.5% DMSO, or 31.25% Plasmalyte-A, 31.25% Dextrose 5%, 0.45% NaCl, 10% Dextran 40 and 5% Dextrose, 20% Human Serum Albumin, and 7.5% DMSO or other suitable cell freezing media containing for example, Hespan and PlasmaLyte A, the cells then are frozen to -80°C at a rate of 1° per minute and stored in the vapor phase of a liquid nitrogen storage tank. Other methods of controlled freezing may be used as well as uncontrolled freezing immediately at -20° C or in liquid nitrogen.

In certain aspects, cryopreserved cells are thawed and washed as described herein and allowed to rest for one hour at room temperature prior to activation using the methods of the present invention.

Also contemplated in the context of the invention is the collection of blood samples or apheresis product from a subject at a time period prior to when the expanded cells as described herein might be needed. As such, the source of the cells to be expanded can be collected at any time point necessary, and desired cells, such as T cells, isolated and frozen for later use in immune effector cell therapy for any number of diseases or conditions that would benefit from immune effector cell therapy, such as those described herein. In one aspect a blood sample or an apheresis is taken from a generally healthy subject. In certain aspects, a blood sample or an apheresis is taken from a generally healthy subject who is at risk of developing a disease, but who has not yet developed a disease, and the cells of interest are isolated and frozen for later use. In certain aspects, the T cells may be expanded, frozen, and used at a later time. In certain aspects, samples are collected from a patient shortly after diagnosis of a particular disease as described herein but prior to any treatments. In a further aspect, the cells are isolated from a blood sample or an apheresis from a subject prior to any number of relevant treatment modalities, including but not

limited to treatment with agents such as natalizumab, efalizumab, antiviral agents, chemotherapy, radiation, immunosuppressive agents, such as cyclosporin, azathioprine, methotrexate, mycophenolate, and FK506, antibodies, or other immunoablative agents such as CAMPATH, anti-CD3 antibodies, cytoxan, fludarabine, cyclosporin, FK506, rapamycin, mycophenolic acid, steroids, FR901228, and irradiation.

In a further aspect of the present invention, T cells are obtained from a patient directly following treatment that leaves the subject with functional T cells. In this regard, it has been observed that following certain cancer treatments, in particular treatments with drugs that damage the immune system, shortly after treatment during the period when patients would normally be recovering from the treatment, the quality of T cells obtained may be optimal or improved for their ability to expand ex vivo. Likewise, following ex vivo manipulation using the methods described herein, these cells may be in a preferred state for enhanced engraftment and in vivo expansion. Thus, it is contemplated within the context of the present invention to collect blood cells, including T cells, dendritic cells, or other cells of the hematopoietic lineage, during this recovery phase. Further, in certain aspects, mobilization (for example, mobilization with GM-CSF) and conditioning regimens can be used to create a condition in a subject wherein repopulation, recirculation, regeneration, and/or expansion of particular cell types is favored, especially during a defined window of time following therapy. Illustrative cell types include T cells, B cells, dendritic cells, and other cells of the immune system.

In one embodiment, the immune effector cells expressing a CAR molecule, e.g., a CAR molecule described herein, are obtained from a subject that has received a low, immune enhancing dose of an mTOR inhibitor. In an embodiment, the population of immune effector cells, e.g., T cells, to be engineered to express a CAR, are harvested after a sufficient time, or after sufficient dosing of the low, immune enhancing, dose of an mTOR inhibitor, such that the level of PD1 negative immune effector cells, e.g., T cells, or the ratio of PD1 negative immune effector cells, e.g., T cells/ PD1 positive immune effector cells, e.g., T cells, in the subject or harvested from the subject has been, at least transiently, increased.

In other embodiments, population of immune effector cells, e.g., T cells, which have, or will be engineered to express a CAR, can be treated ex vivo by contact with an amount of an mTOR inhibitor that increases the number of PD1 negative immune effector cells, e.g., T cells or increases the ratio of PD1 negative immune effector cells, e.g., T cells/ PD1 positive immune effector cells, e.g., T cells.

In one embodiment, a T cell population is diaglycerol kinase (DGK)-deficient. DGK-deficient cells include cells that do not express DGK RNA or protein, or have reduced or inhibited DGK activity. DGK-deficient cells can be generated by genetic approaches, e.g., administering RNA-interfering agents, e.g.,

siRNA, shRNA, miRNA, to reduce or prevent DGK expression. Alternatively, DGK-deficient cells can be generated by treatment with DGK inhibitors described herein.

In one embodiment, a T cell population is Ikaros-deficient. Ikaros-deficient cells include cells that do not express Ikaros RNA or protein, or have reduced or inhibited Ikaros activity, Ikaros-deficient cells can be generated by genetic approaches, e.g., administering RNA-interfering agents, e.g., siRNA, shRNA, miRNA, to reduce or prevent Ikaros expression. Alternatively, Ikaros-deficient cells can be generated by treatment with Ikaros inhibitors, e.g., lenalidomide.

In embodiments, a T cell population is DGK-deficient and Ikaros-deficient, e.g., does not express DGK and Ikaros, or has reduced or inhibited DGK and Ikaros activity. Such DGK and Ikaros-deficient cells can be generated by any of the methods described herein.

In an embodiment, the NK cells are obtained from the subject. In another embodiment, the NK cells are an NK cell line, e.g., NK-92 cell line (Conkwest).

In some aspects, the cells of the invention (e.g., the immune effector cells of the invention, e.g., the CAR-expressing cells of the invention) are induced pluripotent stem cells ("iPSCs") or embryonic stem cells (ESCs), or are T cells generated from (e.g., differentiated from) said iPSC and/or ESC. iPSCs can be generated, for example, by methods known in the art, from peripheral blood T lymphocytes, e.g., peripheral blood T lymphocytes isolated from a healthy volunteer. As well, such cells may be differentiated into T cells by methods known in the art. See e.g., Themeli M. et al., *Nat. Biotechnol.*, 31, pp. 928-933 (2013); doi:10.1038/nbt.2678; WO2014/165707, the contents of each of which are incorporated herein by reference in their entirety.

Additional Expressed Agents

In another embodiment, a CAR-expressing immune effector cell described herein can further express another agent, e.g., an agent which enhances the activity of a CAR-expressing cell. For example, in one embodiment, the agent can be an agent which inhibits an inhibitory molecule. Examples of inhibitory molecules include PD-1, PD-L1, CTLA-4, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and TGF beta, e.g., as described herein. In one embodiment, the agent that inhibits an inhibitory molecule comprises a first polypeptide, e.g., an inhibitory molecule, associated with a second polypeptide that provides a positive signal to the cell, e.g., an intracellular signaling domain described herein. In one embodiment, the agent comprises a first polypeptide, e.g., of an inhibitory molecule such as PD-1, PD-L1, CTLA-4, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 or TGF beta, or a fragment of any of these, and a second polypeptide which is an intracellular signaling

domain described herein (e.g., comprising a costimulatory domain (e.g., 41BB, CD27 or CD28, e.g., as described herein) and/or a primary signaling domain (e.g., a CD3 zeta signaling domain described herein). In one embodiment, the agent comprises a first polypeptide of PD-1 or a fragment thereof, and a second polypeptide of an intracellular signaling domain described herein (e.g., a CD28, CD27, OX40 or 4-IBB signaling domain described herein and/or a CD3 zeta signaling domain described herein). In embodimentss, the agent comprises a first polypeptide of an extracellular domain of an inhibitory molecule and a second polypeptide of an intracellular signaling domain of a costimulatory molecule described herein or primary signaling molecule described herein. Such molecules in which an inhibitory molecule (e.g., a domain of an inhibitory molecule) is associated with a molecule that provides a positive signal (e.g., a domain of a costimulatory molecule or primary signaling molecule) are further described in, for example, WO2013/019615.

In one embodiment, the CAR-expressing immune effector cell described herein can further comprise a second CAR, e.g., a second CAR that includes a different antigen binding domain, e.g., to the same target (e.g., a target described above) or a different target. In one embodiment, the second CAR includes an antigen binding domain to a target expressed on the same cancer cell type as the target of the first CAR. In one embodiment, the CAR-expressing immune effector cell comprises a first CAR that targets a first antigen and includes an intracellular signaling domain having a costimulatory signaling domain but not a primary signaling domain, and a second CAR that targets a second, different, antigen and includes an intracellular signaling domain having a primary signaling domain but not a costimulatory signaling domain.

While not wishing to be bound by theory, placement of a costimulatory signaling domain, e.g., 4-1BB, CD28, CD27 or OX-40, onto the first CAR, and the primary signaling domain, e.g., CD3 zeta, on the second CAR can limit the CAR activity to cells where both targets are expressed. In one embodiment, the CAR expressing immune effector cell comprises a first CAR that includes an antigen binding domain that targets, e.g., a target described above, a transmembrane domain and a costimulatory domain and a second CAR that targets an antigen other than antigen targeted by the first CAR (e.g., an antigen expressed on the same cancer cell type as the first target) and includes an antigen binding domain, a transmembrane domain and a primary signaling domain. In another embodiment, the CAR expressing immune effector cell comprises a first CAR that includes an antigen binding domain that targets, e.g., a target described above, a transmembrane domain and a primary signaling domain and a second CAR that targets an antigen other than antigen targeted by the first CAR (e.g., an antigen expressed on the same cancer cell type as the first target) and includes an antigen binding domain to the antigen, a transmembrane domain and a costimulatory signaling domain.

In one embodiment, the CAR-expressing immune effector cell comprises a CAR described herein, e.g., a CAR to a target described above, and an inhibitory CAR. In one embodiment, the inhibitory CAR comprises an antigen binding domain that binds an antigen found on normal cells but not cancer cells, e.g., normal cells that also express the target. In one embodiment, the inhibitory CAR comprises the antigen binding domain, a transmembrane domain and an intracellular domain of an inhibitory molecule. For example, the intracellular domain of the inhibitory CAR can be an intracellular domain of PD1, PD-L1, CTLA-4, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 or TGF beta.

In one embodiment, an immune effector cell (e.g., T cell, NK cell) comprises a first CAR comprising an antigen binding domain that binds to a tumor antigen as described herein, and a second CAR comprising a PD1 extracellular domain or a fragment thereof.

In one embodiment, the cell further comprises an inhibitory molecule as described above.

In one embodiment, the second CAR in the cell is an inhibitory CAR, wherein the inhibitory CAR comprises an antigen binding domain, a transmembrane domain, and an intracellular domain of an inhibitory molecule. The inhibitory molecule can be chosen from one or more of: PD1, PD-L1, CTLA-4, TIM-3, LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, TGF beta, CEACAM-1, CEACAM-3, and CEACAM-5. In one embodiment, the second CAR molecule comprises the extracellular domain of PD1 or a fragment thereof.

In embodiments, the second CAR molecule in the cell further comprises an intracellular signaling domain comprising a primary signaling domain and/or an intracellular signaling domain.

In other embodiments, the intracellular signaling domain in the cell comprises a primary signaling domain comprising the functional domain of CD3 zeta and a costimulatory signaling domain comprising the functional domain of 4-1BB.

In one embodiment, the second CAR molecule in the cell comprises the amino acid sequence of SEQ ID NO: 6654.

In certain embodiments, the antigen binding domain of the first CAR molecule comprises a scFv and the antigen binding domain of the second CAR molecule does not comprise a scFv. For example, the antigen binding domain of the first CAR molecule comprises a scFv and the antigen binding domain of the second CAR molecule comprises a camelid VHH domain.

In other aspects and embodiments, a cell of the invention, e.g., a cell engineered to express a CAR, is also engineered to express a safety molecule, such as a molecule (or set of molecules) which mediates the

depleting of the cells, e.g., CAR T cells, when appropriate (e.g., after the T cells have accomplished the anti-tumor function, or if the T cells are causing life-threatening side effects). In one exemplary aspect, the safety molecule a molecule that does not affect the function of the cell, but which can be targeted by another agent, e.g., an antibody or ADC molecule targeting said molecule. One exemplary embodiment of such a molecule is a truncated receptor, e.g., a receptor comprising the extracellular domain and transmembrane domain of a receptor, but lacking all or a substantial portion of the intracellular domain of the receptor. An example is a truncated EGFR receptor, e.g., as described in WO2011/056894. Without being bound by theory, targeting said truncated EGFR receptor with an anti-EGFR antibody, e.g., cetuximab, will depelete cells expressing the truncated EGFR receptor. A second example is a iCasp9 switch polypeptide, e.g., a polypeptide having a dimerization domain, an optional linker, and a caspase domain oriented such that, when expressed in the presence of a dimerization compound in a mammalian host cell, the iCasp9 switch polypeptide homo-dimerizes, resulting in apoptosis of the host cell. In embodiments, the dimerization domain is a FKBP-based dimerization domain, e.g., the sequence harbors a mutation (F37V) which provides a complementary fitting cavity for AP1903 and AP1903-structurally related ligands (such as AP20187), which molecules may act as a dimerization compound. Such iCasp9 switch polypeptides (and associated dimerization compounds) are described in, for example, WO1997/031899, US2011/286980, WO2014/164348, WO2013/040371, US2013/071414, WO2014/255360, and *N Engl J Med.* 2011 Nov 3;365(18):1673–83. A third example of such a molecule is a molecule targeted by an anti-CD20 antibody, wherein, for example, administering an anti-CD20 antibody (e.g., rituximab) allows said cells to be depleted. Examples of molecules targetd by an anti-CD20 antibody include CD20, and truncated versions thereof (e.g., molecules comprising an extracellular domain recognizable by an anti-CD20 antibody, a transmembrane domain, and lacking at least a portion of an intracellular domain).

In other aspects and embodiments, the cell of the invention, e.g., a cell engineered to express a CAR, is also engineered to express an NK inhibitory molecule. As used herein, the term "NK inhibitory molecule" refers to a molecule which inhibits a function, e.g., a cytolytic function, of NK cells. Without being bound by theory, it is believed that a cell, e.g., a cell of the invention, which has reduced or eliminated expression of one or more MHC class I molecules (e.g., which have reduced or eliminated expression of B2M, NLRC5 and/or CIITA, e.g., by introduction of a CRISPR system targeting B2M, NLRC5 and/or CIITA as described herein into said cell) may be recognized by NK cells as non-self, and targeted for cytolysis. Thus, expression of one or more NK inhibitory molecules on said cell protects it from NK cell destruction. In one aspect, the NK inhibitory molecule is a ligand for an NK inhibitory receptor. Non-limiting examples of NK inhibitory receptors include NK cell surface receptors which

have or which associate with an immunoreceptor tyrosine-based inhibitory motif (ITIM). Non-liminting examples of such receptors include 2B4 (also known as CD244); a member of the NK-cell-receptor protein 1(NKR-P1) family (e.g., NKR-P1A, NKR-P1B, NKR-P1C, NKR-P1D, NKR-P1E and NKR-P1F, e.g., NKR-P1B and NKR-P1D); a member of the carcinoembryonic-antigen-related cell-adhesion molecule (CEACAM) family (e.g., CEACAM1); Sialicacid-binding immunoglobulin-like lectin (SIGLEC) family members (e.g., SIGLEC7 and SIGLEC9); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Glycoprotein 49 B1 (gp49B1) or human homolog thereof; CD81; and a member of the signal-regulatory protein (SIRP) family. In embodiments, the NK inhibitory molecule is a non-MHC class I molecule. Non-limiting examples of NK inhibitory molecules include ligands for the aforementioned receptors, e.g., CD48, a member of the C-type lectin-related family (e.g., CLR-B (also known as OCIL), CLR-F and CLR-G (also known as OCILrP2)), CEACAM1, a polypeptide displaying sialyic acid, and alpha V beta 3 integrin. In embodiments, the NK inhibitory molecule is a fragment of a naturally occurring molecule, e.g., comprises the extracellular domain and transmembrane domain of the NK inhibitory molecule, but lacks the all or a portion of the intracellular domain (e.g., lacks an intracellular ITIM or inhibitory domain). In other embodiments, the NK inhibitory molecule is an HLA-G molecule. HLA-G has been shown to arrest or reduce the function of the immune system, e.g., NK cells. Carosella et al., *Advances in Immunol.*, vol. 127, pp. 33-144, 2015; Torikai H. et al., *Blood.*, vol. 122(8), pp. 1341-1349, 2013. Without being bound by theory, the presence of HLA-G on the surface of a CAR-expressing cell, e.g., an allogeneic CAR-expressing cell, e.g., as described herein, e.g., a CAR-expressing cell that has reduced or eliminated expression of TCR, (B2M or NLRC5) and/or CIITA, e.g., as described herein, may protect the cell from NK cell attack. In embodiments, the NK inhibitory molecule is an isoform of HLA-G that does not require B2M, e.g., HLA-G2, HLA-G3, HLA-G4. Such embodiments are preferred with the cell of the invention, e.g., as described herein comprises an agent or system (e.g., a CRISPR/Cas system, e.g., as described herein) which inhibits the function and/or expression of B2M. Alternatively, in other embodiments in which the cell of the invention, e.g., as described herein, comprises (or at any time comprised) an agent or system (e.g., a CRISPR/Cas system, e.g., as described herein) which inhibits the function and/or expression of B2M (i.e., a cell in which the function and/or expression of B2M has been reduced or eliminated, e.g., as described herein), the NK inhibitory molecule may be an HLA-G molecule which under natural conditions forms a complex with B2M, provided that the NK inhibitory molecule comprises a fusion with a B2M molecule. Such fusions, and methods for their creation, are known in the art. See, e.g., Favier B, HoWangYin K-Y, Wu J, Caumartin J, Daouya M, et al. (2011) Tolerogenic Function of Dimeric Forms of HLA-G Recombinant Proteins: A Comparative Study In Vivo. *PLoS ONE* 6(7): e21011. doi:10.1371/journal.pone.0021011. In such embodiments, to the extent the gene encoding the HLA-G:B2M fusion molecule comprises a B2M-

encoding sequence which comprises a target sequence of a B2M targeting gRNA molecule, the sequence of said nucleic acid may be altered to reduce or eliminate binding of the gRNA to the HLA-G:B2M fusion-encoding nucleic acid so that expression and/or function of the HLA-G:B2M fusion is not reduced or eliminated. In embodiments, the HLA-G:B2M fusion may further comprise a transmembrane domain or sequence suitable for attachement of a membrane anchor molecule (such as a GPI anchor). An exemplary HLA-G:B2M fusion molecule (e.g., an HLA-G1:B2M fusion molecule) is provided below ((G4S)3 linker (SEQ ID NO: 6594) is highlighted in grey). The linker may be present or absent, and may alternatively comprise any peptidic linker, e.g., as described herein). This particular construct has the format B2M-linker ((G4S)3)-HLA-G:

MSRSVALAVLALLSLSGLEAIQRTPKIQVYSRHPAENGKSNFLNCYVSGFHPSDIEVDLLKNGERIEKVE
HSDLSFSKDWSFYLLYYTEFTPTEKDEYACRVNHVTLSQPKIVKWDRDMGGGGSGGGGSGGGGSGSHSMR
YFSAAVSRPGRGEPRFIAMGYVDDTQFVRFDSDSACPRMEPRAPWVEQEGPEYWEEETRNTKAHAQTDRM
NLQTLRGYYNQSEASSHTLQWMIGCDLGSDGRLLRGYEQYAYDGKDYLALNEDLRSWTAADTAAQISKRK
CEAANVAEQRRAYLEGTCVEWLHRYLENGKEMLQRADPPKTHVTHHPVFDYEATLRCWALGFYPAEIILT
WQRDGEDQTQDVELVETRPAGDGTFQKWAAVVVPSGEEQRYTCHVQHEGLPEPLMLRWKQSSLPTIPIMG
IVAGLVVLAAVVTGAAVAAVLWRKKSSD

SEQ ID NO: 10674

An exemplary codon-optimized nucleic acid sequence encoding the above HLA-G:B2M fusion is provided below:

GCC ACC ATG AGC AGA TCT GTG GCC CTG GCT GTG CTG GCC CTG CTG TCT CTG
TCT GGC CTG GAA GCC ATC CAG CGG ACC CCC AAG ATC CAG GTG TAC AGC AGA
CAC CCC GCC GAA AAC GGC AAG AGC AAC TTC CTG AAC TGC TAC GTG TCC GGC
TTC CAC CCC AGC GAC ATC GAG GTG GAC CTG CTG AAG AAC GGC GAG CGG ATC
GAA AAG GTG GAA CAT AGC GAC CTG AGC TTC AGC AAG GAC TGG TCC TTC TAC
CTG CTG TAC TAC ACC GAG TTC ACC CCC ACC GAA AAG GAC GAG TAC GCC TGC
AGA GTG AAC CAC GTG ACC CTG AGC CAG CCC AAG ATC GTG AAG TGG GAC CGG
GAT ATG GGC GGA GGC GGA TCC GGC GGC GGA GGA TCA GGG GGG GGA GGG TCC
GGA TCC CAC AGC ATG CGG TAC TTC TCT GCC GCC GTG TCC AGA CCT GGA AGA
GGC GAG CCC CGG TTT ATC GCC ATG GGC TAC GTG GAC GAC ACC CAG TTC GTC
AGA TTC GAC AGC GAC AGC GCC TGC CCC CGG ATG GAA CCT AGA GCA CCT TGG
GTG GAA CAG GAA GGC CCC GAG TAC TGG GAG GAA GAG ACA CGG AAC ACC AAG
GCC CAC GCC CAG ACC GAC AGA ATG AAC CTG CAG ACC CTG CGG GGC TAC TAC
AAC CAG AGC GAG GCC AGC AGC CAC ACC CTG CAG TGG ATG ATC GGC TGC GAT
CTG GGC AGC GAC GGC AGA CTG CTG AGA GGT TAC GAA CAG TAC GCC TAC GAC
GGC AAG GAC TAC CTG GCC CTG AAC GAG GAC CTG CGG TCT TGG ACA GCC GCC
GAT ACA GCC GCC CAG ATC AGC AAG AGA AAG TGC GAG GCC GCC AAC GTG GCC
GAG CAG AGA AGG GCT TAC CTG GAA GGC ACC TGT GTG GAA TGG CTG CAT AGA
TAC CTG GAA AAC GGC AAA GAG ATG CTG CAG CGG GCC GAC CCC CCT AAG ACA
CAC GTG ACA CAC CAC CCC GTG TTC GAC TAC GAG GCC ACC CTG AGA TGT TGG
GCC CTG GGC TTC TAT CCT GCC GAG ATC ATC CTG ACC TGG CAG AGG GAT GGC

GAG GAC CAG ACC CAG GAC GTG GAA CTG GTG GAA ACC AGA CCT GCC GGC GAC
GGC ACC TTC CAG AAA TGG GCT GCT GTG GTG GTG CCC AGC GGC GAA GAA CAG
AGA TAC ACC TGT CAC GTG CAG CAC GAG GGC CTG CCC GAA CCC CTG ATG CTG
AGA TGG AAG CAG AGC AGC CTG CCC ACC ATC CCC ATC ATG GGA ATC GTG GCC
GGA CTG GTG GTG CTG GCC GCT GTC GTG ACA GGC GCT GCA GTG GCC GCC GTG
CTG TGG CGG AAG AAG TCC AGC GAC TAA

SEQ ID NO: 10675

Another exemplary HLA-G molecule, which may be combined with a B2M sequence, or used without, is provided below (optional leader sequence is highlighted in grey):

MVVMAPRTLFLLLSGALTLTETWAGSHSMRYFSAAVSRPSRGEPRFIAMGYVDDTQFVRFDSDSACPRME
PRAPWVEREGPEYWEEETRNTKAHAQTDRMNLQTLRGYYNQSEASSHTLQWMIGCDLGSDGRLLRGYEQY
AYDGKDYLALNEDLRSWTAADTAAQISKRKCEAANVAEQRRAYLEGTCVEWLHRYLENGKEMLQRADPPK
THVTHHPVFDYEATLRCWALGFYPAEIILTWQRDGEDQTQDVELVETKPAGDGTFQKWAAVVVPSGEEQR
YTCHVQHEGLPEPLMLRWKQSSLPTIPIMGIVAGLVVLAAVVTGAAVAAVLWRKKSSD

SEQ ID NO: 10676

In other embodiments where the NK inhibitory molecule requires B2M, and it is desirable to reduce or eliminate experession of one or more HLA Class I molecules, a CRISPR/Cas system (e.g., as described herein) may be used which comprises a gRNA comprising a targeting domain which is complementary to a target sequence of NLRC5 (human NLRC5: Entrez 84166; UniProt Q86WI3) or its regulatory elements, e.g., a gRNA which comprises a targeting domain listed in Table 1 to NLRC5 (or a fragment of such targeting domain, e.g., the 3' 20 nucleotides of such targeting domain, listed in Table 1 to NLRC5; e.g., a gRNA comprising a targeting domain comprising of any one of SEQ ID NO: 8622 to SEQ ID NO: 10089 or fragment (e.g., 3' 20 nucleotide fragment) thereof). Without being bound by theory, it is believed that reduced or eliminated expression and/or function of NLRC5 will reduce or eliminate expression and/or function of one or more MHC Class I molecules, even in the presence of B2M. See e.g., Downs, I., Vijayan, S., Sidiq, T. and Kobayashi, K. S. (2016), CITA/NLRC5: A critical transcriptional regulator of MHC class I gene expression. *BioFactors*, 42: 349–357. doi:10.1002/biof.1285.

In other embodiements, the NK inhibitory molecule is a membrane-bound isoform of HLA-G, e.g., HLA-G1, HLA-G2, HLA-G3 and/or HLA-G4. In other embodiments, the NK inhibitory molecule is a soluble isoform of HLA-G, e.g., sHLA-G1 (shed), HLA-G5, HLA-G6, and/or HLA-G7. In embodiments, the NK inhibitory molecule is selected from one or more of HLA-G2, HLA-G3 and HLA-G4. In an embodiment, the NK inhibitory molecule is HLA-G2.

In other embodiments, the NK inhibitory molecule is an HLA-E molecule. HLA-E has been shown to arrest or reduce the function of NK cells against HLA Class I-negative cells. Torikai H. et al., *Blood.*,

vol. 122(8), pp. 1341-1349, 2013. Without being bound by theory, the presence of HLA-E on the surface of a CAR-expressing cell, e.g., an allogeneic CAR-expressing cell, e.g., as described herein, e.g., a CAR-expressing cell that has reduced or eliminated expression of TCR, (B2M or NLRC5) and/or CIITA, e.g., as described herein, may protect the cell from NK cell attack. In an embodiment, the NK inhibitory molecule is an HLA-G molecule and an HLA-E molecule.

In embodiments where the cell of the invention, e.g., the CAR expressing cell of the invention, e.g., as described herein, is engineered to express an NK inhibitory molecule, the cell may be further engineered to reduce or eliminate expression and/or function of one or more ligands or binding partners of said NK inhibitory molecule (herein referred to as "target of an NK inhibitory molecule"). Without being bound by theory, it is believed that reduction or elimination of expression and/or function, e.g., surface expression, of a target of an NK inhibitory molecule will reduce or avoid inhibition of the cell of interest, e.g., the CAR expressing cell of the invention, e.g., as described herein, by the expression of the NK inhibitory molecule, thereby improving the function of the cell of the invention, e.g., the CAR expressing cell of the invention, e.g., as described herein. In other embodiments, the inhibitory effects of the NK inhibitory molecule may be reduced or eliminated in the cell of interest, e.g., the CAR expressing cell of the invention, e.g., as described herein, by expressing a dominant negative mutant or fragment of the target of an NK inhibitory molecule, e.g., a target of an NK inhibitory molecule which has a modified or eliminated (partially or wholly) intracellular inhibitory domain (e.g., one or more ITIM domains), such that the inhibitory signal is not propagated upon binding of the NK inhibitory molecule. In embodiments where the NK inhibitory molecule is an HLA-G molecule, e.g., as described herein, the target of an NK inhibitory molecule is LILRB1 (e.g., human LILRB1: Entrez: 10859; UniProt Q8NHL6). In embodiments, the reduction or elimination of expression and/or function of the target of an NK inhibitory molecule, e.g., LILRB1, is accomplished by introducing a nucleic acid inhibitor of the target of an NK inhibitory molecule (e.g., an shRNA or siRNA molecule specific for LILRB1). In other embodiments, the reduction or elimination of expression and/or function of the target of an NK inhibitory molecule, e.g., LILRB1, is accomplished by introducing a gene editing system, e.g. a CRISPR/Cas gene editing system, e.g., as described herein, which recognizes a target sequence in the gene or its regulatory elements of the target of an NK inhibitory molecule (e.g., recognizes a target sequence in the LILRB1 gene or its regulatory elements), such that expression and/or function of the target of an NK inhibitory molecule, e.g., LILRB1, is reduced or eliminated. In embodiments, where the target of an NK inhibitory molecule is LILRB1, the gene editing system is a CRISPR/Cas system, e.g., as described herein, comprising a gRNA molecule comprising a targeting domain listed in Table 6d (or, as described herein, comprising a fragment, e.g., a 20 nucleotide fragment, e.g., the 3' 20 nucleotides, of a targeting domain listed in Table 6d).

In embodiments and aspects, the invention relates to a cell, e.g., an immune effector cell, (or population of said cells) comprising nucleic acid encoding an NK inhibitory molecule, e.g., such that the NK inhibitory molecule is expressed in said cell, e.g., comprises nucleic acid encoding an NK inhibitory molecule operably linked to a promoter operable in the cell. In embodiments, the nucleic acid molecule encoding an NK inhibitory molecule comprises additional sequence encoding a CAR. In embodiments, the nucleic acid sequence encoding an NK inhibitory molecule and the nucleic acid sequence encoding a CAR are operably linked to separate promoters, as described herein. In other embodiments, an NK inhibitory molecule the nucleic acid sequence encoding an NK inhibitory molecule and the nucleic acid sequence encoding a CAR are expressed from a single promoter, optionally with a sequence encoding a cleavable peptide (e.g., a 2A peptide) disposed between the sequences encoding the two molecules.

The cell of the invention, e.g., the cells engineered to express a CAR, may be engineered to express more than one of the additional molecules described above. In embodiments, the cell is engineered to express a CAR, e.g., as described herein, an iCasp9 switch polypeptide and an NK inhibitory molecule.

In embodiments and aspects, a cell of the invention, e.g., an immune effector cell (or population of said cells), e.g., a CAR-expressing cell as described herein, has reduced or eliminated expression of the protein comprising the target antigen of the CAR molecule (e.g., a target antigen described herein). Such reduced or eliminated expression of the protein comprising the target antigen of the CAR molecule may be affected, by for example, introducing a mutation (e.g., an indel) within the gene sequence encoding said protein comprising the target antigen (or its regulatory elements) using a gene editing system, e.g., a CRISPR gene editing system (e.g., comprising a gRNA molecule complmentary to a target sequence within said gene), e.g., described herein. Without being bound by theory, reduced or eliminated expression of the protein comprising the target antigen of the CAR molecule may protect said CAR-expressing cells from self-recognition and/or attack. In embodiments, the reduced or eliminated expression of said protein comprising the target antigen of the CAR molecule is relative to the expression of said protein comprising the target antigen of the CAR molecule in a resting cell, e.g., resting T cell. In other embodiments, the reduced or eliminated expression of said protein comprising the target antigen of the CAR molecule is relative to the expression of said protein comprising the target antigen of the CAR molecule in an activated cell, e.g., an activated T cell, e.g., a T cell activated by CD3 and/or CD28 stimulation, or by activation through signaling of the CAR molecule.

Split CAR

In some embodiments, the CAR-expressing cell uses a split CAR. The split CAR approach is described in more detail in publications WO2014/055442 and WO2014/055657. Briefly, a split CAR system comprises a cell expressing a first CAR having a first antigen binding domain and a costimulatory domain

(e.g., 41BB), and the cell also expresses a second CAR having a second antigen binding domain and an intracellular signaling domain (e.g., CD3 zeta). When the cell encounters the first antigen, the costimulatory domain is activated, and the cell proliferates. When the cell encounters the second antigen, the intracellular signaling domain is activated and cell-killing activity begins. Thus, the CAR-expressing cell is only fully activated in the presence of both antigens.

Multiple CAR expression

In one aspect, the CAR-expressing cell described herein can further comprise a second CAR, e.g., a second CAR that includes a different antigen binding domain, e.g., to the same target or a different target (e.g., a target other than a cancer associated antigen described herein or a different cancer associated antigen described herein). In one embodiment, the second CAR includes an antigen binding domain to a target expressed the same cancer cell type as the cancer associated antigen. In one embodiment, the CAR-expressing cell comprises a first CAR that targets a first antigen and includes an intracellular signaling domain having a costimulatory signaling domain but not a primary signaling domain, and a second CAR that targets a second, different, antigen and includes an intracellular signaling domain having a primary signaling domain but not a costimulatory signaling domain. While not wishing to be bound by theory, placement of a costimulatory signaling domain, e.g., 4-1BB, CD28, CD27 or OX-40, onto the first CAR, and the primary signaling domain, e.g.,CD3 zeta, on the second CAR can limit the CAR activity to cells where both targets are expressed. In one embodiment, the CAR expressing cell comprises a first cancer associated antigen CAR that includes an antigen binding domain that binds a target antigen described herein, a transmembrane domain and a costimulatory domain and a second CAR that targets a different target antigen (e.g., an antigen expressed on that same cancer cell type as the first target antigen) and includes an antigen binding domain, a transmembrane domain and a primary signaling domain. In another embodiment, the CAR expressing cell comprises a first CAR that includes an antigen binding domain that binds a target antigen described herein, a transmembrane domain and a primary signaling domain and a second CAR that targets an antigen other than the first target antigen (e.g., an antigen expressed on the same cancer cell type as the first target antigen) and includes an antigen binding domain to the antigen, a transmembrane domain and a costimulatory signaling domain.

In some embodiments, the claimed invention comprises a first and second CAR, wherein the antigen binding domain of one of said first CAR said second CAR does not comprise a variable light domain and a variable heavy domain. In some embodiments, the antigen binding domain of one of said first CAR said second CAR is an scFv, and the other is not an scFv. In some embodiments, the antigen binding domain of one of said first CAR said second CAR comprises a single VH domain, e.g., a camelid, shark, or lamprey single VH domain, or a single VH domain derived from a human or mouse sequence. In some

embodiments, the antigen binding domain of one of said first CAR said second CAR comprises a nanobody. In some embodiments, the antigen binding domain of one of said first CAR said second CAR comprises a camelid VHH domain.

Telomerase expression

While not wishing to be bound by any particular theory, in some embodiments, a therapeutic T cell has short term persistence in a patient, due to shortened telomeres in the T cell; accordingly, transfection with a telomerase gene can lengthen the telomeres of the T cell and improve persistence of the T cell in the patient. See Carl June, "Adoptive T cell therapy for cancer in the clinic", Journal of Clinical Investigation, 117:1466-1476 (2007). Thus, in an embodiment, an immune effector cell, e.g., a T cell, ectopically expresses a telomerase subunit, e.g., the catalytic subunit of telomerase, e.g., TERT, e.g., hTERT. In some aspects, this disclosure provides a method of producing a CAR-expressing cell, comprising contacting a cell with a nucleic acid encoding a telomerase subunit, e.g., the catalytic subunit of telomerase, e.g., TERT, e.g., hTERT. The cell may be contacted with the nucleic acid before, simultaneous with, or after being contacted with a construct encoding a CAR.

In embodiments in which a cell is engineered to express more than one molecule, sequence encoding each of said molecules (e.g., sequence encoding a CAR and sequence encoding an NK inhibitory molecule) can be disposed on the same nucleic acid molecule, e.g., the same plasmid or vector, e.g., viral vector, e.g., lentiviral vector. In an embodiment, (i) sequence encoding a CAR, as described herien, and (ii) sequence encoding an NK inhibitory molecule, as described herien, can be present on the same nucleic acid, e.g., vector. Production of the corresponding proteins can be achieved, e.g., by the use of separate promoters, or by the use of a bicistronic transcription product (which can result in the production of two proteins by cleavage of a single translation product or by the translation of two separate protein products). In an embodiment, a sequence encoding a cleavable peptide, e.g., a P2A, T2A or F2A sequence, is disposed between (i) and (ii). In an embodiment, a sequence encoding an IRES, e.g., an EMCV or EV71 IRES, is disposed between (i) and (ii). In these embodiments, (i) and (ii) are transcribed as a single RNA. In other aspects, each molecule may be expressed from a different promoter. In an embodiment, a first promoter is operably linked to (i) and a second promoter is operably linked to (ii), such that (i) and (ii) are transcribed as separate mRNAs.

Alternatively, the sequence encoding the more than one molecules can be disposed on the different nucleic acid molecules, e.g., different plasmids or vectors, e.g., viral vector, e.g., lentiviral vector. E.g., the (i) sequence encoding a CAR as described herein can be present on a first nucleic acid, e.g., a first vector, and the (ii) sequence encoding a NK inhibitory molecule can be present on the second nucleic acid, e.g., the second vector.

Table 7. Exemplary sequences of various components of CAR (aa – amino acids, na – nucleic acids that encodes the corresponding protein)

SEQ ID NO	description	Sequence	Corresp. To huCD19
6639	EF-1 promoter	CGTGAGGCTCCGGTGCCCGTCAGTGGGCAGAGCGCACA TCGCCCACAGTCCCCGAGAAGTTGGGGGGAGGGGTCGG CAATTGAACCGGTGCCTAGAGAAGGTGGCGCGGGGTAA ACTGGGAAAGTGATGTCGTGTACTGGCTCCGCCTTTTTC CCGAGGGTGGGGGAGAACCGTATATAAGTGCAGTAGTC GCCGTGAACGTTCTTTTTCGCAACGGGTTTGCCGCCAGA ACACAGGTAAGTGCCGTGTGTGGTTCCCGCGGGCCTGG CCTCTTTACGGGTTATGGCCCTTGCGTGCCTTGAATTAC TTCCACCTGGCTGCAGTACGTGATTCTTGATCCCGAGCT TCGGGTTGGAAGTGGGTGGGAGAGTTCGAGGCCTTGCG CTTAAGGAGCCCCTTCGCCTCGTGCTTGAGTTGAGGCCT GGCCTGGGCGCTGGGGCCGCCGCGTGCGAATCTGGTGG CACCTTCGCGCCTGTCTCGCTGCTTTCGATAAGTCTCTA GCCATTTAAAATTTTTGATGACCTGCTGCGACGCTTTTT TTCTGGCAAGATAGTCTTGTAAATGCGGGCCAAGATCT GCACACTGGTATTTCGGTTTTTGGGGCCGCGGGCGGCG ACGGGGCCCGTGCGTCCCAGCGCACATGTTCGGCGAGG CGGGGCCTGCGAGCGCGGCCACCGAGAATCGGACGGG GGTAGTCTCAAGCTGGCCGGCCTGCTCTGGTGCCTGGC CTCGCGCCGCCGTGTATCGCCCCGCCCTGGGCGGCAAG GCTGGCCCGGTCGGCACCAGTTGCGTGAGCGGAAAGAT GGCCGCTTCCCGGCCCTGCTGCAGGGAGCTCAAAATGG AGGACGCGGCGCTCGGGAGAGCGGGCGGGTGAGTCAC CCACACAAAGGAAAAGGGCCTTTCCGTCCTCAGCCGTC GCTTCATGTGACTCCACGGAGTACCGGGCGCCGTCCAG GCACCTCGATTAGTTCTCGAGCTTTTGGAGTACGTCGTC TTTAGGTTGGGGGGAGGGGTTTTATGCGATGGAGTTTC CCCACACTGAGTGGGTGGAGACTGAAGTTAGGCCAGCT TGGCACTTGATGTAATTCTCCTTGGAATTTGCCCTTTTT GAGTTTGGATCTTGGTTCATTCTCAAGCCTCAGACAGTG GTTCAAAGTTTTTTTCTTCCATTTCAGGTGTCGTGA	100
6640	Leader (aa)	MALPVTALLLPLALLLHAARP	13
6641	Leader (na)	ATGGCCCTGCCTGTGACAGCCCTGCTGCTGCCTCTGGCT CTGCTGCTGCATGCCGCTAGACCC	54
10802	Leader (na)	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCT CTTCTGCTCCACGCCGCTCGGCCC	
6642	CD 8 hinge (aa)	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLD FACD	14
6643	CD8 hinge (na)	ACCACGACGCCAGCGCCGCGACCACCAACACCGGCGCC CACCATCGCGTCGCAGCCCCTGTCCCTGCGCCCAGAGG CGTGCCGGCCAGCGGCGGGGGGCGCAGTGCACACGAG GGGGCTGGACTTCGCCTGTGAT	55
6630	Ig4 hinge (aa)	ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNS	102

		TYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISK AKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIA VEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKSLSLSLGKM	
6631	Ig4 hinge (na)	GAGAGCAAGTACGGCCCTCCCTGCCCCCCTTGCCCTGC CCCCGAGTTCCTGGGCGGACCCAGCGTGTTCCTGTTCCC CCCCAAGCCCAAGGACACCCTGATGATCAGCCGGACCC CCGAGGTGACCTGTGTGGTGGTGGACGTGTCCCAGGAG GACCCCGAGGTCCAGTTCAACTGGTACGTGGACGGCGT GGAGGTGCACAACGCCAAGACCAAGCCCCGGGAGGAG CAGTTCAATAGCACCTACCGGGTGGTGTCCGTGCTGAC CGTGCTGCACCAGGACTGGCTGAACGGCAAGGAATACA AGTGTAAGGTGTCCAACAAGGGCCTGCCCAGCAGCATC GAGAAAACCATCAGCAAGGCCAAGGGCCAGCCTCGGG AGCCCCAGGTGTACACCCTGCCCCCTAGCCAAGAGGAG ATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAA GGGCTTCTACCCCAGCGACATCGCCGTGGAGTGGGAGA GCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC CCTGTGCTGGACAGCGACGGCAGCTTCTTCCTGTACAG CCGGCTGACCGTGGACAAGAGCCGGTGGCAGGAGGGC AACGTCTTTAGCTGCTCCGTGATGCACGAGGCCCTGCA CAACCACTACACCCAGAAGAGCCTGAGCCTGTCCCTGG GCAAGATG	103
6632	IgD hinge (aa)	RWPESPKAQASSVPTAQPQAEGSLAKATTAPATTRNTGR GGEEKKKEKEKEEQEERETKTPECPSHTQPLGVYLLTPAV QDLWLRDKATFTCFVVGSDLKDAHLTWEVAGKVPTGGV EEGLLERHSNGSQSQHSRLTLPRSLWNAGTSVTCTLNHPS LPPQRLMALREPAAQAPVKLSLNLLASSDPPEAASWLLCE VSGFSPPNILLMWLEDQREVNTSGFAPARPPPQPGSTTFW AWSVLRVPAPPSPQPATYTCVVSHEDSRTLLNASRSLEVS YVTDH	47
6633	IgD hinge (na)	AGGTGGCCCGAAAGTCCCAAGGCCCAGGCATCTAGTGT TCCTACTGCACAGCCCCAGGCAGAAGGCAGCCTAGCCA AAGCTACTACTGCACCTGCCACTACGCGCAATACTGGC CGTGGCGGGGAGGAGAAGAAAAAGGAGAAAGAGAAA GAAGAACAGGAAGAGAGGGAGACCAAGACCCCTGAAT GTCCATCCCATACCCAGCCGCTGGGCGTCTATCTCTTGA CTCCCGCAGTACAGGACTTGTGGCTTAGAGATAAGGCC ACCTTTACATGTTTCGTCGTGGGCTCTGACCTGAAGGAT GCCCATTTGACTTGGGAGGTTGCCGGAAAGGTACCCAC AGGGGGGGTTGAGGAAGGGTTGCTGGAGCGCCATTCCA ATGGCTCTCAGAGCCAGCACTCAAGACTCACCCTTCCG AGATCCCTGTGGAACGCCGGGACCTCTGTCACATGTAC TCTAAATCATCCTAGCCTGCCCCCACAGCGTCTGATGGC CCTTAGAGAGCCAGCCGCCCAGGCACCAGTTAAGCTTA GCCTGAATCTGCTCGCCAGTAGTGATCCCCCAGAGGCC GCCAGCTGGCTCTTATGCGAAGTGTCCGGCTTTAGCCCG CCCAACATCTTGCTCATGTGGCTGGAGGACCAGCGAGA AGTGAACACCAGCGGCTTCGCTCCAGCCCGGCCCCCAC CCCAGCCGGGTTCTACCACATTCTGGGCCTGGAGTGTCT TAAGGGTCCCAGCACCACCTAGCCCCCAGCCAGCCACA	48

		TACACCTGTGTTGTGTCCCATGAAGATAGCAGGACCCT GCTAAATGCTTCTAGGAGTCTGGAGGTTTCCTACGTGAC TGACCATT	
6634	GS hinge/linker (aa)	GGGGSGGGGS	49
6635	GS hinge/linker (na)	GGTGGCGGAGGTTCTGGAGGTGGAGGTTCC	50
6644	CD8TM (aa)	IYIWAPLAGTCGVLLLSLVITLYC	15
6645	CD8 TM (na)	ATCTACATCTGGGCGCCCTTGGCCGGGACTTGTGGGGT CCTTCTCCTGTCACTGGTTATCACCCTTTACTGC	56
10803	CD8 TM (na)	ATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTC CTGCTGCTTTCACTCGTGATCACTCTTTACTGT	
6646	4-1BB intracellular domain (aa)	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGC EL	16
6647	4-1BB intracellular domain (na)	AAACGGGGCAGAAAGAAACTCCTGTATATATTCAAACA ACCATTTATGAGACCAGTACAAACTACTCAAGAGGAAG ATGGCTGTAGCTGCCGATTTCCAGAAGAAGAAGAAGGA GGATGTGAACTG	60
10804	4-1BB intracellular domain (na)	AAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCA ACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGG ACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGC GGCTGCGAACTG	
6636	CD27 (aa)	QRRKYRSNKGESPVEPAEPCRYSCPREEEGSTIPIQEDYRK PEPACSP	51
6637	CD27 (na)	AGGAGTAAGAGGAGCAGGCTCCTGCACAGTGACTACAT GAACATGACTCCCCGCCGCCCCGGGCCCACCCGCAAGC ATTACCAGCCCTATGCCCCACCACGCGACTTCGCAGCCT ATCGCTCC	52
6648	CD3-zeta (aa)	RVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDKRR GRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMK GERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR	17
6649	CD3-zeta (na)	AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTA CAAGCAGGGCCAGAACCAGCTCTATAACGAGCTCAATC TAGGACGAAGAGAGGAGTACGATGTTTTGGACAAGAG ACGTGGCCGGGACCCTGAGATGGGGGGAAAGCCGAGA AGGAAGAACCCTCAGGAAGGCCTGTACAATGAACTGCA GAAAGATAAGATGGCGGAGGCCTACAGTGAGATTGGG ATGAAAGGCGAGCGCCGGAGGGGCAAGGGGCACGATG GCCTTTACCAGGGTCTCAGTACAGCCACCAAGGACACC TACGACGCCCTTCACATGCAGGCCCTGCCCCCTCGC	101
10805	CD3-zeta (na)	CGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTA CAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATC TTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGCG GAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGC AGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCA AAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGT ATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGACG	

		GACTGTACCAGGGACTCAGCACCGCCACCAAGGACACC TATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG	
6650	CD3-zeta (aa)	RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRR GRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMK GERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR	43
6651	CD3-zeta (na)	AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTA CCAGCAGGGCCAG AACCAGCTCTATAACGAGCTCAATCTAGGACGAAGAGA GGAGTACGATGTTT TGGACAAGAGACGTGGCCGGGACCCTGAGATGGGGGG AAAGCCGAGAAGGA AGAACCCTCAGGAAGGCCTGTACAATGAACTGCAGAAA GATAAGATGGCGG AGGCCTACAGTGAGATTGGGATGAAAGGCGAGCGCCG GAGGGGCAAGGGGC ACGATGGCCTTTACCAGGGTCTCAGTACAGCCACCAAG GACACCTACGACGC CCTTCACATGCAGGCCCTGCCCCCTCGC	44
6629	linker	GGGGS	18
6635	linker	GGTGGCGGAGGTTCTGGAGGTGGAGGTTCC	50
6652	PD-1 extracellular domain (aa)	Pgwfldspdrpwnpptfspallvvtegdnatftcsfsntsesfvlnwyrmspsnqtdkla afpedrsqpgqdcrfrvtqlpngrdfhmsvvrarrndsgtylcgaislapkaqikeslrael rvterraevptahpspsprpagqfqtlv	
6653	PD-1 extracellular domain (na)	Cccggatggtttctggactctccggatcgcccgtggaatcccccaaccttctcaccggcact cttggttgtgactgagggcgataatgcgaccttcacgtgctcgttctccaacacctccgaatca ttcgtgctgaactggtaccgcatgagcccgtcaaaccagaccgacaagctcgccgcgtttcc ggaagatcggtcgcaaccgggacaggattgtcggttccgcgtgactcaactgccgaatgg cagagacttccacatgagcgtggtccgcgctaggcgaaacgactccgggacctacctgtgc ggagccatctcgctggcgcctaaggcccaaatcaaagagagcttgagggccgaactgaga gtgaccgagcgcagagctgaggtgccaactgcacatccatccccatcgcctcggcctgcg gggcagtttcagaccctggtc	
6654	PD-1 CAR (aa) with signal	Malpvtalllplalllhaarppgwfldspdrpwnpptfspallvvtegdnatftcsfsntses fvlnwyrmspsnqtdklaafpedrsqpgqdcrfrvtqlpngrdfhmsvvrarrndsgtyl cgaislapkaqikeslraelrvterraevptahpspsprpagqfqtlvtttpaprpptpaptia sqplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyif kqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapaykqgqnqlynelnlgrr eeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeayseigmkgerrrgkg hdglyqglstatkdtydalhmqalppr	
6655	PD-1 CAR (na)	Atggccctccctgtcactgccctgcttctcccctcgcactcctgctccacgccgctagacc acccggatggtttctggactctccggatcgcccgtggaatcccccaaccttctcaccggcact cttggttgtgactgagggcgataatgcgaccttcacgtgctcgttctccaacacctccgaatca ttcgtgctgaactggtaccgcatgagcccgtcaaaccagaccgacaagctcgccgcgtttcc ggaagatcggtcgcaaccgggacaggattgtcggttccgcgtgactcaactgccgaatgg cagagacttccacatgagcgtggtccgcgctaggcgaaacgactccgggacctacctgtgc ggagccatctcgctggcgcctaaggcccaaatcaaagagagcttgagggccgaactgaga gtgaccgagcgcagagctgaggtgccaactgcacatccatccccatcgcctcggcctgcg gggcagtttcagaccctggtcacgaccactccggcgccgcgcccaccgactccggcccca actatcgcgagccagcccctgtcgctgaggccggaagcatgccgccctgccgccggaggt gctgtgcatacccggggattggacttcgcatgcgacatctacatttgggctcctctcgccgga acttgtggcgtgctccttctgtccctggtcatcaccctgtactgcaagcggggtcggaaaaag	

		cttctgtacattttcaagcagcccttcatgaggcccgtgcaaaccacccaggaggaggacgg ttgctcctgccggttccccgaagaggaagaaggaggttgcgagctgcgcgtgaagttctcc cggagcgccgacgcccccgcctataagcagggccagaaccagctgtacaacgaactgaa cctgggacggcgggaagagtacgatgtgctggacaagcggcgcggccgggaccccgaa atgggcgggaagcctagaagaaagaaccctcaggaaggcctgtataacgagctgcagaa ggacaagatggccgaggcctactccgaaattgggatgaagggagagcggcggaggggca aaggggcacgacggcctgtaccaaggactgtccaccgccaccaaggacacatacgatgc cctgcacatgcaggcccttcccccctcgc	
6592	linker	(Gly-Gly-Gly-Ser)n, where n = 1-10	105
6593	linker	(Gly4 Ser)4	106
6594	linker	(Gly4 Ser)3	107
6595	linker	(Gly3Ser)	108
6656	PD1 CAR (aa)	Pgwfldspdrpwnpptfspallvvtegdnatftcsfsntsesfvlnwyrmspsnqtdkla afpedrsqpgqdcrfrvtqlpngrdfhmsvvrarrndsgtylcgaislapkaqikeslrael rvterraevptahpspsprpagqfqtlvtttpaprpptpaptiasqplslrpeacrpaaggav htrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcs crfpeeeeggcelrvkfsrsadapaykqgqnqlynelnlgrreeydvldkrrgrdpemg gkprrknpqeglynelqkdkmaeayseigmkgerrrgkghdglyqglstatkdtydal hmqalppr	

VI. Cells

In another aspect, the invention provides cells which comprise, or which at any time comprised, a gRNA molecule, e.g., one or more gRNA molecules, as described herein, or a CRISPR system as described herein. In an embodiment, the cell has been altered, e.g., the target sequence targeted by the gRNA molecule has been altered, e.g., to create an indel, by introduciton of a gRNA molecule as described herein (or nucleic acid encoding said gRNA molecule), or a CRISPR system (or nucleic acid encoding one or more components of said CRISPR system) as described herein, e.g., altered by a method described herein. In an embodiment, the alteration results in reduced or no expression of the functional (e.g., wild type) gene product of the gene comprising the target site.

In one aspect, the cell is an animal cell. In embodiments, the cell is a mammalian, primate, or human cell. In embodiments, the cell is a human cell. In embodiments, the cell is an immune effector cell (e.g., a population of immune effector cells), for example a T cell or NK cell. In embodiments, the T cell (e.g., population of T cells) is or comprises a CD4+ T cell, a CD8+ T cell, or a combination thereof. In embodiments, the cell is autologous. In embodiments, the cell is allogeneic.

In a preferred embodiment the cell (e.g., the population of cells) has been, or will be, engineered to express a chimeric antigen receptor (CAR), e.g., a CAR as described in Section V. In embodiments, the cell is engineered to express a BCMA CAR, e.g., as described herein. In embodiments, the CAR-engineered cell is allogeneic. In embodiments, the CAR-engineered cell is autologous.

In another aspect, the invention provides cells, such as those described above, which include, has at any time included, or will include a second gRNA molecule as described herein, e.g., a second gRNA molecule with a targeting domain different from that of the first gRNA moleucle. In embodiments, the two gRNA molecules are complementary to target sites within the same gene, for example, are complementary to two target sites within the gene for the same allogeneic T cell target, e.g., comprise two target sites within the TRAC gene. Such cells may comprise a large, e.g., 20-60, 20-70, 20-80, 20-90, 20-100, or greater than 1000, greater than 2000, greater than 3000, greater than 4000, greater than 5000, greater than 6000 base pair excision of DNA located between the target sites of the two gRNA moleucles, as described herein in Section VIII. Alternatively, the two gRNAs targeting target sequences of the same gene may not lead to an excision, but may instead, for example, create an indel at or near each of the targeted sites. In other embodiments, the two or more gRNA molecules are complementary to target sites withitn two different genes whose gene products associate to form a molecular complex. An example of such an embodiment is a first gRNA molecule targeting TRAC, and a second gRNA molecule targeting TRBC1 (wherein both the TCR alpha constant chain and the TCR beta constant chain 1 are components of the TCR on the cell surface). Without being bound by theory, introducing CRISPR systems which target two or more target sequences of the same gene, or which target two or more genes of the same molecular complex (e.g., in the case of targeting TRAC and TRBC1) may lead to further reduced or eliminated expresion of the target gene product, relative to introducing a CRISPR system which targets only a single target sequence of the target gene.

It will be understood that in any of the aspects and embodiments of the invention in which two or more target sites of different genes (or different molecular complexes, e.g., when targeting TCR, and B2M) are targeted, that for any or all of the different gene (or molecular complex) targets, two or more gRNAs may be empolyed with respect to one or more of said different genes or different molecular complexes. For example, in embodiments and aspects in which expression of TCR and expression of B2M is reduced or eliminated, the reduced or eliminated expression of TCR may be accomplished by, for example, one gRNA targeting TRAC, by more than one gRNA molecule targeting TRAC, or by one gRNA molecule targeting TRAC and a second gRNA targeting a different component of the TCR, e.g., TRBC1; while at the same time, or alternatively, targeting of B2M may be accomplished by, for example, one gRNA molecule targeting B2M or by two or more gRNA molecules targeting B2M.

In other embodiments, the two or more, e.g. two, gRNA molecules are complementary to target sites within different genes. Such cells may comprise alterations, e.g., indels, at or near each target site such that expression of the functional gene product of more than one gene is reduced or eliminated. As

discussed above, in such embodiments, more than one gRNA moleucle taregeted to each of the different genes may be employed.

In embodiments, the cell comprises, has comprised or will comprise a first gRNA molecule comprising a targeting domain complementary with a target sequence of an allogeneic T-cell target (e.g., a targeting domain described in Tables 1, 3, 4 or 5), and a second gRNA molecule comprising a targeting domain complementary with a target sequence of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule (e.g., comprises a targeting domain described in Table 2 or Table 6). In embodiments, the inhibitory molecule or downstream effector of signaling through an inhibitory molecule is CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, or PTPN11.

In embodiments, the cell comprises, has comprised or will comprise a first gRNA molecule comprising a targeting domain complementary with a target sequence of TRAC, TRBC1, TRBC2, CD247, CD3D, CD3E, or CD3G, and a second gRNA molecule comprising a targeting domain complementary with a target sequence of B2M, NLRC5, HLA-A, HLA-B or HLA-C.

In embodiments, a cell of the invention comprises, has comprised or will comprise a first gRNA molecule comprising a targeting domain complementary with a target sequence of TRAC, TRBC1, TRBC2, CD247, CD3D, CD3E, or CD3G; a second gRNA molecule comprising a targeting domain complementary with a target sequence of B2M, NLRC5, HLA-A, HLA-B or HLA-C; and a third gRNA molecule comprising a targeting domain complementary with a target sequence of CIITA. Without being bound by theory, it is believed that reducing or eliminating expression of a MHC class I molecule, e.g., by a method described herein employing a gRNA to B2M or a gRNA to NLRC5, may cause the modified cell to upregulate expression of one or more MHC class II molecules. In such circumstances, in order to create, for example, an allogeneic cell (e.g., an allogeneic T cell, e.g., a CAR-expressing allogeneic T cell described herein) able to avoid a host versus graft disease response, it may be beneficial to reduce or eliminate expression of one or more MHC class II molecules (in addition to the one or more MHC class I molecules), for example, by a method described herein employing a gRNA to CIITA. In one embodiment, the cell, e.g., a CAR-expressing cell, e.g., as described herein, comprises, has comprised or will comprise, a first gRNA to TRAC, e.g., as described herein, a second gRNA to B2M, e.g., as described herein, and a third gRNA to CIITA, e.g., as described herein. In one embodiment, the cell, e.g., a CAR-expressing cell, e.g., as described herein, comprises, has comprised or will comprise, a first gRNA

to TRAC, e.g., as described herein, a second gRNA to NLRC5, e.g., as described herein, and a third gRNA to CIITA, e.g., as described herein.

In embodiments, the invention provides a cell, e.g., a CAR-expressing cell, e.g., as described herein, that comprises one or more modifications (e.g., nucleotide insertions or deletions) to an endogenous gene encoding a component of the TCR, e.g., TRAC or TRBC (e.g., TRBC1 or TRBC2); one or more modifications (e.g., nucleotide insertions or deletions) to an endogenous B2M gene; and/or one or more modifications (e.g., nucleotide insertions or deletions) to an endogenous CIITA gene. In embodiments, said modifications reduce or eliminate expression of said gene. In embodiments, the invention provides a cell, e.g., a CAR-expressing cell, e.g., as described herein, that is TCR- (e.g., has a level of expression of TCR greater than 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, or 99% lower than that of an unmodified cell of the same type, as detected by FACS, e.g., FACS using an anti-CD3 antibody), B2M- (e.g., has a level of expression of B2M and/or one or more MHC class I proteins greater than 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, or 99% lower than that of an unmodified cell of the same type, as detected by FACS, e.g., FACS using an anti-B2M antibody) and/or CIITA- (e.g., has a level of expression of CIITA and/or a MHC class II protein greater than 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, or 99% lower than that of an unmodified cell of the same type, as detected by FACS, e.g., FACS using an anti-CIITA antibody). In an embodiment, the cell is engineered to express a CAR molecule, e.g., as described herein. In embodiments, the CAR is a CD19 CAR, e.g., as described herein. In other embodiments, the CAR is a BCMA CAR, e.g., as described herein. In other embodiments, the CAR is a CD123 CAR, e.g., as described herein.

In embodiments, the invention provides a cell, e.g., a CAR-expressing cell, e.g., as described herein, that comprises one or more modifications (e.g., nucleotide insertions or deletions) to an endogenous gene encoding a component of the TCR, e.g., TRAC or TRBC (e.g., TRBC1 or TRBC2); one or more modifications (e.g., nucleotide insertions or deletions) to an endogenous NLRC5 gene; and/or one or more modifications (e.g., nucleotide insertions or deletions) to an endogenous CIITA gene. In embodiments, said modifications reduce or eliminate expression of said gene. In embodiments, the invention provides a cell, e.g., a CAR-expressing cell, e.g., as described herein, that is TCR- (e.g., has a level of expression of TCR greater than 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, or 99% lower than that of an unmodified cell of the same type, as detected by FACS, e.g., FACS using an anti-CD3 antibody), NLRC5- (e.g., has a level of expression of NLRC5 and/or one or more MHC class I proteins greater than 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, or 99% lower than that of an unmodified cell of the same type, as detected by FACS, e.g., FACS using an anti-NLRC5 antibody) and/or CIITA- (e.g., has a level of expression of CIITA and/or a MHC class II protein greater than 50%, 60%, 70%,

80%, 90%, 95%, 96%, 97%, 98%, or 99% lower than that of an unmodified cell of the same type, as detected by FACS, e.g., FACS using an anti-CIITA antibody). In an embodiment, the cell is engineered to express a CAR molecule, e.g., as described herein. In embodiments, the CAR is a CD19 CAR, e.g., as described herein. In other embodiments, the CAR is a BCMA CAR, e.g., as described herein. In other embodiments, the CAR is a CD123 CAR, e.g., as described herein.

In embodiments, the cell comprises, has comprised or will comprise a first gRNA molecule comprising a targeting domain complementary with a target sequence of TRAC, TRBC1, TRBC2, CD247, CD3D, CD3E, or CD3G, and a second gRNA molecule comprises a targeting domain complementary with a target sequence of NR3C1, DCK, CD52 or FKBP1A.

In embodiments, the cell comprises, has comprised or will comprise a first gRNA molecule and a second gRNA molecule, wherein: (1) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527; (2) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345; (3) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698; (4) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068; (5) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941; (6) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491; (7) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324; (8) the

first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583; (9) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527; (10) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345; (11) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698; (12) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068; (13) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941; (14) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491; (15) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324; (16) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583; (17) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527; (18) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO:

5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345; (19) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698; (20) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: NO: 5644 to SEQ ID NO: NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068; (21) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941; (22) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491; (23) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324; (24) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583; (25) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527; (26) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345; (27) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698; (28) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068; (29) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the

second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941; (30) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491; (31) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324; (32) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583; (33) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527; (34) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345; (35) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698; (36) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068; (37) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941; (38) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491; (39) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324; (40) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583; (41) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected

from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527; (42) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345; (43) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698; (44) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068; (45) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941; (46) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491; (47) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324; (48) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583; (49) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527; (50) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345; (51) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698; (52) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068; (53) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID

NO: 2069 to SEQ ID NO: 2941; (54) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491; (55) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324; (55) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583; (56) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270; (57) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541; (58) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032; (59) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815; (60) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277; (61) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270; (62) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541; (63) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group

consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032; (64) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815; (65) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277; (66) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270; (67) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541; (68) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032; (69) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815; (70) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277; (71) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270; (72) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541; (73) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032; (74) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain

selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815; (75) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277; (76) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270; (77) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541; (78) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032; (79) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815; (80) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277; (81) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270; (82) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541; (83) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032; (85) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815; (86) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277; (87) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a

targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270; (88) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541; (89) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032; (90) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815; or (91) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277.

In an embodiment, the cell comprises, has comprised or will comprise a first gRNA molecule comprising a targeting domain comprising, e.g., consisting of, SEQ ID NO: 5569 or 5586, and a second gRNA molecule comprising a targeting domain comprising, e.g., consisting of, SEQ ID NO: 5775. Said cell preferably comprises an alteration to both TRAC and PDCD1, such that expression of functional TCR and expression of functional PD-1 is reduced or eliminated. In an embodiment, the cell is an immune effector cell, e.g., a T cell or NK cell. In an embodiment, the cell is allogeneic. In an embodiment, the cell is autologous. In an embodiment, the cell is or will be further engineered to express a CAR as described herein.

In embodiments of the invention, a cell of the invention comprises, has comprised or will comprise a first gRNA molecule comprising a targeting domain complementary to a target sequence of a component of the T cell receptor (e.g., TRAC); a second gRNA molecule comprising a targeting domain complementary to a target sequence of B2M; and a third gRNA molecule comprising a targeting domain complementary to a target sequence of CIITA. Said cell preferably comprises a modification at or near the target sequence of said first gRNA, said second gRNA, and said third gRNA molecules, such that expression of functional TCR, expression of functional B2M and expression of functional CIITA is reduced or eliminated. In an embodiment, the cell is an immune effector cell, e.g., a T cell or NK cell. In an embodiment, the cell is allogeneic. In an embodiment, the cell is autologous. In an embodiment, the cell is or will be further engineered to express a CAR as described herein.

In an aspect, a cell of the invention comprises (e.g., a population of cells of the invention comprises one or more cells which comprise):

(a) Nucleic acid sequence encoding a CAR, e.g., as described herein;
(b) Nucleic acid sequence encoding an NK inhibitory molecule, e.g., as described herein, e.g., nucleic acid encoding an HLA-G or HLA-G:B2M fusion as described herein;
(c) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC), e.g., comprising a targeting domain listed in Table 1, Table 4 or Table 5;
(d) An indel at or near a sequence of the gene encoding B2M or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to B2M, e.g., comprising a targeting domain listed in Table 1 or Table 3;
(e) Optionally, an indel at or near a sequence of the gene encoding CIITA or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to CIITA, e.g., comprising a targeting domain listed in Table 1 or Table 6c; and
(f) Optionally, an indel at or near a sequence of the gene encoding LILRB1 or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to LILRB1, e.g., comprising a targeting domain listed in Table 6d;

Wherein the cell (or population of cells comprises one or more cells which) expresses the CAR and the NK inhibitory molecule, and exhibits reduced or eliminated expression and/or function of one or more of: i) a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC), ii) B2M, iii) CIITA, and/or iv) LILRB1. In embodiments the indels are

In an aspect, a cell of the invention comprises (e.g., a population of cells of the invention comprises one or more cells which comprise):

(a) Nucleic acid sequence encoding a CAR, e.g., as described herein;
(b) Nucleic acid sequence encoding an NK inhibitory molecule, e.g., as described herein, e.g., nucleic acid encoding an HLA-G as described herein;
(c) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC), e.g., comprising a targeting domain listed in Table 1, Table 4 or Table 5;

(d) An indel at or near a sequence of the gene encoding NLRC5 or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to NLRC5, e.g., comprising a targeting domain listed in Table 1;

(e) Optionally, an indel at or near a sequence of the gene encoding CIITA or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to CIITA, e.g., comprising a targeting domain listed in Table 1 or Table 6c; and

(f) Optionally, an indel at or near a sequence of the gene encoding LILRB1 or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to LILRB1, e.g., comprising a targeting domain listed in Table 6d;

Wherein the cell (or population of cells comprises one or more cells which) expresses the CAR and the NK inhibitory molecule, and exhibits reduced or eliminated expression and/or function of one or more of: i) a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC), ii) B2M, iii) NLRC5, and/or iv) LILRB1.

In an aspect, a cell of the invention comprises (e.g., a population of cells of the invention comprises one or more cells which comprise):

(a) Nucleic acid sequence encoding a CAR, e.g., as described herein;

(b) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC), e.g., comprising a targeting domain listed in Table 1, Table 4 or Table 5; and

(c) An indel at or near a sequence of the gene encoding FKBP1A or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to FKBP1A, e.g., comprising a targeting domain listed in Table 1 or Table 6b;

Wherein the cell (or population of cells comprises one or more cells which) expresses the CAR, and exhibits reduced or eliminated expression and/or function of one or more of: i) a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC), and/or ii) FKBP12. Such cells (or population of cells comprising said cells) are particularly useful, for example, in methods of treatment which comprise administering an immunosuppressant (e.g., cyclosporine, rapamycin or rapalog, or mTor inhibitor, e.g., RAD001).

In an aspect, a cell of the invention comprises (e.g., a population of cells of the invention comprises one or more cells which comprise):

(a) Nucleic acid sequence encoding a CAR, e.g., as described herein;

(b) Nucleic acid sequence encoding a rapamycin-resistant mTor, e.g., as described herein, e.g., nucleic acid sequence encoding an mTor comprising a S2035 mutation, e.g., an S2035I mutation; and;

(c) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC), e.g., comprising a targeting domain listed in Table 1, Table 4 or Table 5;

Wherein the cell (or population of cells comprises one or more cells which) expresses the CAR and the rapamycin-resistant mTor, and exhibits reduced or eliminated expression and/or function of a component of a TCR (e.g., TRAC, TRBC1 or TRBC2, e.g. TRAC). Such cells (or population of cells comprising said cells) are particularly useful, for example, in methods of treatment which comprise administering an immunosuppressant (e.g., cyclosporine, rapamycin or rapalog, or mTor inhibitor, e.g., RAD001).

In any of the aforementioned embodiments and aspects the cell comprises one or more CRISPR systems, e.g., as described herein, comprising the gRNA molecule(s) indicated. In embodiments, the cell comprises one or more ribonuclear protein (RNP) complexes each comprising a Cas9 molecule, e.g., as described herein, and a gRNA molecule comprising the indicated targeting domain, e.g., as described herein. In embodiments, including in any of the methods described herein, where gRNAs to more than one target sequence are employed, the gRNAs (and CRISPR systems comprising said gRNAs) may be introduced into the cell simultaneously. In other embodiments, including in any of the methods described herein, where gRNAs to more than one target sequence are employed, the gRNAs (and CRISPR systems comprising said gRNAs) may be introduced into the cell sequentially.

In an aspect involving any of the aforementioned embodiments or aspects, the population of cells comprises at least 20%, e.g., at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, or at least 99%, of cells which include an indel at or near each of the target sequences targeted by each of the gRNA molecules. Said population may be obtained, for example, by utilizing high efficiency gRNA molecules (e.g., gRNA molecules which cause an indel in >85% of said cells which are exposed to said gRNA molecule), or by enriching the population for the desired cell, e.g., by selecting for the desired cell population, e.g., by affinity chromatography or cell sorting.

VII. Template Nucleic Acids (For Introduction of Nucleic Acids)

The term "template nucleic acid" or "donor template" as used herein refers to a nucleic acid to be inserted at or near a target sequence that has been modified, e.g., cleaved, by a CRISPR system of the present invention. In an embodiment, nucleic acid sequence at or near the target sequence is modified to have some or all of the sequence of the template nucleic acid, typically at or near cleavage site(s). In an embodiment, the template nucleic acid is single stranded. In an alternate embodiment, the template nucleic acid is double stranded. In an embodiment, the template nucleic acid is DNA, e.g., double stranded DNA. In an alternate embodiment, the template nucleic acid is single stranded DNA.

In embodiments, the template nucleic acid comprises sequence encoding a chimeric antigen receptor (CAR), e.g., a CAR as described above in section V.

In an embodiment, the template nucleic acid alters the structure of the target position by participating in a homology directed repair event. In an embodiment, the template nucleic acid alters the sequence of the target position. In an embodiment, the template nucleic acid results in the incorporation of a modified, or non-naturally occurring base into the target nucleic acid.

Mutations in a gene or pathway described herein may be corrected using one of the approaches discussed herein. In an embodiment, a mutation in a gene or pathway described herein is corrected by homology directed repair (HDR) using a template nucleic acid. In an embodiment, a mutation in a gene or pathway described herein is corrected by homologous recombination (HR) using a template nucleic acid. In an embodiment, a mutation in a gene or pathway described herein is corrected by Non-Homologous End Joining (NHEJ) repair using a template nucleic acid. In other embodiments, nucleic acid encoding molecules of interest may be inserted at or near a site modified by a CRISPR system of the present invention. In an embodiment, the nucleic acid inserted encodes a chimeric antigen receptor as described herein. In embodiments, the template nucleic acid comprises regulatory elements, e.g., one or more promotors and/or enhancers, operably linked to the nucleic acid sequence encoding a molecule of interest, e.g., a chimeric antigen receptor, e.g., as described herein.

HDR Repair and Template Nucleic Acids

As described herein, nuclease-induced homology directed repair (HDR) can be used to alter a target sequence and correct (e.g., repair or edit) a mutation in the genome. While not wishing to be bound by theory, it is believed that alteration of the target sequence occurs by homology-directed repair (HDR) with a donor template or template nucleic acid. For example, the donor template or the template nucleic acid provides for alteration of the target sequence. It is contemplated that a plasmid donor can be used as a template for homologous recombination. It is further contemplated that a single stranded donor template can be used as a template for alteration of the target sequence by alternate methods of homology directed

repair (e.g., single strand annealing) between the target sequence and the donor template. Donor template-effected alteration of a target sequence depends on cleavage by a Cas9 molecule. Cleavage by Cas9 can comprise a double strand break or two single strand breaks.

In an embodiment, a mutation can be corrected by either a single double-strand break or two single strand breaks. In an embodiment, a mutation can be corrected by (1) a single double- strand break, (2) two single strand breaks, (3) two double stranded breaks with a break occurring on each side of the target sequence, (4) one double stranded breaks and two single strand breaks with the double strand break and two single strand breaks occurring on each side of the target sequence or (5) four single stranded breaks with a pair of single stranded breaks occurring on each side of the target sequence.

Double strand break mediated correction

In an embodiment, double strand cleavage is effected by a Cas9 molecule having cleavage activity associated with an HNH-like domain and cleavage activity associated with a RuvC-like domain, e.g., an N-terminal RuvC-like domain, e.g., a wild type Cas9. Such embodiments require only a single gRNA.

Single strand break mediated correction

In other embodiments, two single strand breaks, or nicks, are effected by a Cas9 molecule having nickase activity, e.g., cleavage activity associated with an HNH-like domain or cleavage activity associated with an N-terminal RuvC-like domain. Such embodiments require two gRNAs, one for placement of each single strand break. In an embodiment, the Cas9 molecule having nickase activity cleaves the strand to which the gRNA hybridizes, but not the strand that is complementary to the strand to which the gRNA hybridizes. In an embodiment, the Cas9 molecule having nickase activity does not cleave the strand to which the gRNA hybridizes, but rather cleaves the strand that is complementary to the strand to which the gRNA hybridizes.

In an embodiment, the nickase has HNH activity, e.g., a Cas9 molecule having the RuvC activity inactivated, e.g., a Cas9 molecule having a mutation at D10, e.g., the D10A mutation. D10A inactivates RuvC; therefore, the Cas9 nickase has (only) HN H activity and will cut on the strand to which the gRNA hybridizes (e.g., the complementary strand, which does not have the NGG PAM on it). In other embodiments, a Cas9 molecule having an H840, e.g., an H840A, mutation can be used as a nickase. H840A inactivates HNH; therefore, the Cas9 nickase has (only) RuvC activity and cuts on the non-complementary strand (e.g., the strand that has the NGG PAM and whose sequence is identical to the gRNA).

In an embodiment, in which a nickase and two gRNAs are used to position two single strand nicks, one nick is on the + strand and one nick is on the - strand of the target nucleic acid. The PAMs are outwardly facing. The gRNAs can be selected such that the gRNAs are separated by, from about 0-50, 0- 100, or 0-200 nucleotides. In an embodiment, there is no overlap between the target sequence that is complementary to the targeting domains of the two gRNAs. In an embodiment, the gRNAs do not overlap and are separated by as much as 50, 100, or 200 nucleotides. In an embodiment, the use of two gRNAs can increase specificity, e.g., by decreasing off-target binding (Ran el cil., CELL 2013).

In an embodiment, a single nick can be used to induce HDR. It is contemplated herein that a single nick can be used to increase the ratio of HDR, HR or NHEJ at a given cleavage site.

Placement of the double strand break or a single strand break relative to target position

The double strand break or single strand break in one of the strands should be sufficiently close to target position such that correction occurs. In an embodiment, the distance is not more than 50, 100, 200, 300, 350 or 400 nucleotides. While not wishing to be bound by theory, it is believed that the break should be sufficiently close to target position such that the break is within the region that is subject to exonuclease-mediated removal during end resection. If the distance between the target position and a break is too great, the mutation may not be included in the end resection and, therefore, may not be corrected, as donor sequence may only be used to correct sequence within the end resection region.

In an embodiment, in which a gRNA (unimolecular (or chimeric) or modular gRNA) and Cas9 nuclease induce a double strand break for the purpose of inducing HDR- or HR-mediated correction, the cleavage site is between 0-200 bp (e.g., 0 to 175, 0 to 150, 0 to 125, 0 to 100, 0 to 75, 0 to 50, 0 to 25, 25 to 200, 25 to 175, 25 to 150, 25 to 125, 25 to 100, 25 to 75, 25 to 50, 50 to 200, 50 to 175, 50 to 150, 50 to 125, 50 to 100, 50 to 75, 75 to 200, 75 to 175, 75 to 150, 75 to 1 25, 75 to 100 bp) away from the target position. In an embodiment, the cleavage site is between 0- 100 bp (e.g., 0 to 75, 0 to 50, 0 to 25, 25 to 100, 25 to 75, 25 to 50, 50 to 100, 50 to 75 or 75 to 100 bp) away from the target position.

In an embodiment, in which two gRNAs (independently, unimolecular (or chimeric) or modular gRNA) complexing with Cas9 nickases induce two single strand breaks for the purpose of inducing HDR-mediated correction, the closer nick is between 0-200 bp (e.g., 0 to 175, 0 to 150, 0 to 125, 0 to 100, 0 to 75, 0 to 50, 0 to 25, 25 to 200, 25 to 175, 25 to 150, 25 to 125, 25 to 100, 25 to 75, 25 to 50, 50 to 200, 50 to 175, 50 to 150, 50 to 125, 50 to 100, 50 to 75, 75 to 200, 75 to 175, 75 to 150, 75 to 125, 75 to 100 bp) away from the target position and the two nicks will ideally be within 25-55 bp of each other (e.g., 25 to 50, 25 to 45, 25 to 40, 25 to 35, 25 to 30, 30 to 55, 30 to 50, 30 to 45, 30 to 40, 30 to 35, 35 to 55, 35 to 50, 35 to 45, 35 to 40, 40 to 55, 40 to 50, 40 to 45 bp) and no more than 100 bp away from each other

(e.g., no more than 90, 80, 70, 60, 50, 40, 30, 20, 10 or 5 bp away from each other). In an embodiment, the cleavage site is between 0- 100 bp (e.g., 0 to 75, 0 to 50, 0 to 25, 25 to 100, 25 to 75, 25 to 50, 50 to 100, 50 to 75 or 75 to 100 bp) away from the target position.

In one embodiment, two gRNAs, e.g., independently, unimolecular (or chimeric) or modular gRNA, are configured to position a double-strand break on both sides of a target position. In an alternate embodiment, three gRNAs, e.g., independently, unimolecular (or chimeric) or modular gRNA, are configured to position a double strand break (i.e., one gRNA complexes with a Cas9 nuclease) and two single strand breaks or paired single stranded breaks (i.e., two gRNAs complex with Cas9 nickases) on either side of the target position (e.g., the first gRNA is used to target upstream (i.e., 5') of the target positionand the second gRNA is used to target downstream (i.e., 3') of the target position). In another embodiment, four gRNAs, e.g., independently, unimolecular (or chimeric) or modular gRNA, are configured to generate two pairs of single stranded breaks (i.e., two pairs of two gRNAs complex with Cas9 nickases) on either side of the target position (e.g., the first gRNA is used to target upstream (i.e., 5') of the target position and the second gRNA is used to target downstream (i.e., 3') of the target position). The double strand break(s) or the closer of the two single strand nicks in a pair will . ideally be within 0-500 bp of the target position (e.g., no more than 450, 400, 350, 300, 250, 200, 150, l00, 50 or 25 bp from the target position). When nickases are used, the two nicks in a pair are within 25-55 bp of each other (e.g., between 25 to 50, 25 to 45, 25 to 40, 25 to 35, 25 to 30, 50 to 55, 45 to 55, 40 to 55, 35 to 55, 30 to 55, 30 to 50, 35. to 50, 40 to 50 , 45 to 50, 35 to 45, or 40 to 45 bp) and no more than 100 bp away from each other (e.g., no more than 90, 80, 70, 60, 50, 40, 30, 20 or 10 bp).

In one embodiment, two gRNAs, e.g., independently, unimolecular (or chimeric) or modular gRNA, are configured to position a double-strand break on both sides of a target position. In an alternate embodiment, three gRNAs, e.g., independently, unimolecular (or chimeric) or modular gRNA, are configured to position a double strand break (i.e., one gRNA complexes with a Cas9 nuclease) and two single strand breaks or paired single stranded breaks (i.e., two gRNAs complex with Cas9 nickases) on two target sequences (e.g., the first gRNA is used to target an upstream (i.e., 5') target sequence and the second gRNA is used to target a downstream (i.e., 3') target sequence of an insertion site. In another embodiment, four gRNAs, e.g., independently, unimolecular (or chimeric) or modular gRNA, are configured to generate two pairs of single stranded breaks (i.e., two pairs of two gRNAs complex with Cas9 nickases) on either side of an insertion site (e.g., the first gRNA is used to target an upstream (i.e., 5') target sequence described herein, and the second gRNA is used to target a downstream (i.e., 3') target sequence described herein). The double strand break(s) or the closer of the two single strand nicks in a pair will ideally be within 0-500 bp of the target position (e.g., no more than 450, 400, 350, 300, 250, 200,

150, 100, 50 or 25 bp from the target position). When nickases are used, the two nicks in a pair are within 25-55 bp of each other (e.g., between 25 to 50, 25 to 45, 25 to 40, 25 to 35, 25 to 30, 50 to 55, 45 to 55, 40 to 55, 35 to 55, 30 to 55, 30 to 50, 35 to 50, 40 to 50 , 45 to 50, 35 to 45, or 40 to 45 bp) and no more than 100 bp away from each other (e.g., no more than 90, 80, 70, 60, 50, 40, 30, 20 or 10 bp).

Length of the homology arms

The homology arm should extend at least as far as the region in which end resection may occur, e.g., in order to allow the resected single stranded overhang to find a complementary region within the donor template. The overall length could be limited by parameters such as plasmid size or viral packaging limits. In an embodiment, a homology arm does not extend into repeated elements, e.g., ALU repeats, LINE repeats. A template may have two homology arms of the same or different lengths.

Exemplary homology arm lengths include at least 25, 50, 100, 250, 500, 750 or 1000 nucleotides.

Target position, as used herein, refers to a site on a target nucleic acid (e.g., the chromosome) that is modified by a Cas9 molecule-dependent process. For example, the target position can be a modified Cas9 molecule cleavage of the target nucleic acid and template nucleic acid directed modification, e.g., correction, of the target position. In an embodiment, a target position can be a site between two nucleotides, e.g., adjacent nucleotides, on the target nucleic acid into which one or more nucleotides is added. The target position may comprise one or more nucleotides that are altered, e.g., corrected, by a template nucleic acid. In an embodiment, the target position is within a target sequence (e.g., the sequence to which the gRN A binds). In an embodiment, a target position is upstream or downstream of a target sequence (e.g., the sequence to which the gRNA binds).

Typically, the template sequence undergoes a breakage mediated or catalyzed recombination with the target sequence. In an embodiment, the template nucleic acid includes sequence that corresponds to a site on the target sequence that is cleaved by a Cas9 mediated cleavage event. In an embodiment, the template nucleic acid includes sequence that corresponds to both, a first site on the target sequence that is cleaved in a first Cas9 mediated event, and a second site on the target sequence that is cleaved in a second Cas9 mediated event.

In an embodiment, the template nucleic acid can include sequence which results in an alteration in the coding sequence of a translated sequence, e.g., one which results in the substitution of one amino acid for another in a protein product, e.g., transforming a mutant allele into a wild type allele, transforming a wild type allele into a mutant allele, and/or introducing a stop codon, insertion of an amino acid residue, deletion of an amino acid residue, or a nonsense mutation.

In other embodiments, the template nucleic acid can include sequence which results in an alteration in a non-coding sequence, e.g., an alteration in an exon or in a 5' or 3' non-translated or non-transcribed region. Such alterations include an alteration in a control element, e.g., a promoter, enhancer, and an alteration in a cis-acting or trans-acting control element.

The template nucleic acid can include sequence which, when integrated, results in:

decreasing the activity of a positive control element;

increasing the activity of a positive control element;

decreasing the activity of a negative control element;

increasing the activityof a negative control element;

decreasing the expression of a gene;

increasing the expression of a gene;

increasing resistance to a disorder or disease;

increasing resistance to viral entry;

correcting a mutation or altering an unwanted amino acid residue

conferring, increasing, abolishing or decreasing a biological property of a gene product, e.g., increasing the enzymatic activity of an enzyme, or increasing the ability of a gene product to interact with another molecule.

The template nucleic acid can include sequence which results in:

a change in sequence of 1 , 2, 3, 4, 5, 6, 7, 8, 9, 10, 1 1 , 12 or more nucleotides of the target sequence.

In an embodiment, the template nucleic acid is 20+/- 10, 30+/- 10, 40+/- 10, 50+/- 10, 60+/- 10, 70+/- 10, 80+/- 10, 90+/- 10, 100+/- 10, 1 10+/- 10, 120+/- 10, 130+/- 10, 140+/- 10, 150+/- 10, 160+/- 10, 170+/- 10, 1 80+/- 10, 190+/- 10, 200+/- 10, 210+/-10, 220+/- 10, 200-300, 300-400, 400-500, 500-600, 600-700, 700-800, 800-900, 900-1000, 1000-2000, 2000-3000 or more than 3000 nucleotides in length.

A template nucleic acid comprises the following components:

[5' homology arm]-[insertion sequence]-[3' homology arm].

The homology arms provide for recombination into the chromosome, which can replace the undesired element, e.g., a mutation or signature, with the replacement sequence. In an embodiment, the homology arms flank the most distal cleavage sites.

In an embodiment, the 3' end of the 5' homology arm is the position next to the 5' end of the replacement sequence. In an embodiment, the 5' homology arm can extend at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 120, 150, 180, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1500, or 2000 nucleotides 5' from the 5' end of the replacement sequence.

In an embodiment, the 5' end of the 3' homology arm is the position next to the 3' end of the replacement sequence. In an embodiment, the 3' homology arm can extend at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 120, 150, 180, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1500, or 2000 nucleotides 3' from the 3' end of the replacement sequence.

It is contemplated herein that one or both homology arms may be shortened to avoid including certain sequence repeat elements, e.g., Alu repeats, LINE elements. For example, a 5' homology arm may be shortened to avoid a sequence repeat element. In other embodiments, a 3' homology arm may be shortened to avoid a sequence repeat element. In some embodiments, both the 5' and the 3' homology arms may be shortened to avoid including certain sequence repeat elements.

It is contemplated herein that template nucleic acids for correcting a mutation may designed for use as a single-stranded oligonucleotide (ssODN). When using a ssODN, 5' and 3' homology arms may range up to about 200 base pairs (bp) in length, e.g., at least 25, 50, 75, 100, 125, 150, 175, or 200 bp in length. Longer homology arms are also contemplated for ssODNs as improvements in oligonucleotide synthesis continue to be made.

In one aspect, the insertion sequence comprises nucleic acid sequence that encodes a chimeric antigen receptor, e.g., as described herein. In one embodiment the insertion sequence further comprises a promotor operably linked to the nucleic acid sequence encoding a chimeric antigen receptor, e.g., an EF-1 alpha promoter. In one aspect, the insertion sequence comprises a vector encoding a chimeric antigen receptor, e.g., as described herein, or a portion thereof.

NHEJ Approaches for Gene Targeting

As described herein, nuclease-induced non-homologous end-joining (NHEJ) can be used to target gene-specific knockouts. Nuclease-induced NHEJ can also be used to remove (e.g., delete) sequence in a gene of interest.

While not wishing to be bound by theory, it is believed that, in an embodiment, the genomic alterations associated with the methods described herein rely on nuclease-induced NHEJ and the error-prone nature of the NHEJ repair pathway. NHEJ repairs a double-strand break in the DNA by joining together the two ends; however, generally, the original sequence is restored only if two compatible ends, exactly as they were formed by the double-strand break, are perfectly ligated. The DNA ends of the double-strand break are frequently the subject of enzymatic processing, resulting in the addition or removal of nucleotides, at one or both strands, prior to rejoining of the ends. This results in the presence of insertion and/or deletion (indel) mutations in the DNA sequence at the site of the NHEJ repair. Two-thirds of these mutations may alter the reading frame and, therefore, produce a non-functional protein. Additionally, mutations that maintain the reading frame, but which insert or delete a significant amount of sequence, can destroy functionality of the protein. This is locus dependent as mutations in critical functional domains are likely less tolerable than mutations in non-critical regions of the protein.

The indel mutations generated by NHEJ are unpredictable in nature; however, at a given break site certain indel sequences are favored and are over represented in the population. The lengths of deletions can vary widely; most commonly in the 1 -50 bp range, but they can easily reach greater than 100-200 bp. Insertions tend to be shorter and often include short duplications of the sequence immediately surrounding the break site. However, it is possible to obtain large insertions, and in these cases, the inserted sequence has often been traced to other regions of the genome or to plasmid DNA present in the cells.

Because NHEJ is a mutagenic process, it can also be used to delete small sequence motifs as long as the generation of a specific final sequence is not required. If a double-strand break is targeted near to a short target sequence, the deletion mutations caused by the NHEJ repair often span, and therefore remove, the unwanted nucleotides. For the deletion of larger DNA segments, introducing two double-strand breaks, one on each side of the sequence, can result in NHEJ between the ends with removal of the entire intervening sequence. Both of these approaches can be used to delete specific DNA sequences; however, the error-prone nature of NHEJ may still produce indel mutations at the site of repair.

Both double strand cleaving Cas9 molecules and single strand, or nickase, Cas9 molecules can be used in the methods and compositions described herein to generate NHEJ- mediated indels. NHEJ-mediated indels targeted to the gene, e.g., a coding region, e.g., an early coding region of a gene of interest can be used to knockout (i.e., eliminate expression of) a gene of interest. For example, early coding region of a gene of interest includes sequence immediately following a transcription start site, within a first exon of the coding sequence, or within 500 bp of the transcription start site (e.g., less than 500, 450, 400, 350, 300, 250, 200, 150, 100 or 50 bp).

Placement of double strand or single strand breaks relative to the target position

In an embodiment, in which a gRNA and Cas9 nuclease generate a double strand break for the purpose of inducing NHEJ-mediated indels, a gRNA, e.g., a unimolecular (or chimeric) or modular gRNA molecule, is configured to position one double-strand break in close proximity to a nucleotide of the target position. In an embodiment, the cleavage site is between 0-500 bp away from the target position (e.g., less than 500, 400, 300, 200, 100, 50, 40, 30, 25, 20, 15, 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 bp from the target position).

In an embodiment, in which two gRNAs complexing with Cas9 nickases induce two single strand breaks for the puipose of inducing NHEJ-mediated indels, two gRNAs, e.g., independently, unimolecular (or chimeric) or modular gRNA, are configured to position two single-strand breaks to provide for NHEJ repair a nucleotide of the target position. In an embodiment, the gRNAs are configured to position cuts at the same position, or within a few nucleotides of one another, on different strands, essentially mimicking a double strand break. In an embodiment, the closer nick is between 0-30 bp away from the target position (e.g., less than 30, 25, 20, 1 , 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 bp from the target position), and the two nicks are within 25-55 bp of each other (e.g., between 25 to 50, 25 to 45, 25 to 40, 25 to 35, 25 to 30, 50 to 55, 45 to 55, 40 to 55, 35 to 55, 30 to 55, 30 to 50, 35 to 50, 40 to 50 , 45 to 50, 35 to 45, or 40 to 45 bp) and no more than 100 bp away from each other (e.g., no more than 90, 80, 70, 60, 50, 40, 30, 20 or 10 bp). In an embodiment, the gRNAs are configured to place a single strand break on either side of a nucleotide of the target position.

Both double strand cleaving Cas9 molecules and single strand, or nickase, Cas9 molecules can be used in the methods and compositions described herein to generate breaks both sides of a target position. Double strand or paired single strand breaks may be generated on both sides of a target position to remove the nucleic acid sequence between the two cuts (e.g., the region between the two breaks is deleted). In one embodiment, two gRNAs, e.g., independently, unimolecular (or chimeric) or modular gRNA, are configured to position a double-strand break on both sides of a target position (e.g., the first gRNA is used to target upstream (i.e., 5') of the mutation in a gene or pathway described herein, and the second gRNA is used to target downstream (i.e., 3') of the mutation in a gene or pathway described herein). In an alternate embodiment, three gRNAs, e.g., independently, unimolecular (or chimeric) or modular gRNA, are configured to position a double strand break (i.e., one gRNA complexes with a Cas9 nuclease) and two single strand breaks or paired single stranded breaks (i.e., two gRNAs complex with Cas9 nickases) on either side of a target position (e.g., the fu st gRNA is used to target upstream (i.e., 5') of the mutation in a gene or pathway described herein, and the second gRNA is used to target downstream (i.e., 3') of the mutation in a gene or pathway described herein). In another embodiment, four gRNAs, e.g., independently, unimolecular (or chimeric) or modular gRNA, are configured to generate two pairs of

single stranded breaks (i.e., two pairs of two gRNAs complex with Cas9 nickases) on either side of the target position (e.g., the first gRNA is used to target upstream (i.e., 5') of the mutation in a gene or pathway described herein, and the second gRNA is used to target downstream (i.e., 3') of the mutation in a gene or pathway described herein). The double strand break(s) or the closer of the two single strand nicks in a pair will ideally be within 0-500 bp of the target position (e.g., no more than 450, 400, 350, 300, 250, 200, 150, 100, 50 or 25 bp from the target position). When nickases are used, the two nicks in a pair are within 25-55 bp of each other (e.g., between 25 to 50, 25 to 45, 25 to 40, 25 to 35, 25 to 30, 50 to 55, 45 to 55, 40 to 55, 35 to 55, 30 to 55, 30 to 50, 35 to 50, 40 to 50 , 45 to 50, 35 to 45, or 40 to 45 bp) and no more than 100 bp away from each other (e.g., no more than 90, 80, 70, 60, 50, 40, 30, 20 or 10 bp).

VIII. Systems Comprising More Than One gRNA Molecule

While not intending to be bound by theory, it has been surprisingly shown herein that the targeting of two target sequences (e.g., by two gRNA molecule/Cas9 molecule complexes which each induce a single- or double-strand break at or near their respective target sequences) located in close proximity on a continuous nucleic acid induces excision (e.g., deletion) of the nucleic acid sequence (or at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% of the nucleic acid sequence) located between the two target sequences. In some aspects, the present disclosure provides for the use of two or more gRNA molecules that comprise targeting domains targeting target sequences in close proximity on a continuous nucleic acid, e.g., a chromosome, e.g., a gene or gene locus, including its introns, exons and regulatory elements. The use may be, for example, by introduction of the two or more gRNA molecules, together with one or more Cas9 molecules (or nucleic acid encoding the two or more gRNA molecules and/or the one or more Cas9 molecules) into a cell.

In some aspects, the target sequences of the two or more gRNA molecules are located at least 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 2000, 3000, 4000, 5000, 6000, or 70000 nucleotides apart on a continuous nucleic acid, but not more than 10000 nucleotides apart on a continuous nucleic acid. In an embodiment, the target sequences are located about 4000 nucleotides apart. In an embodiment, the target sequences are located about 6000 nucleotides apart.

In some aspects, the plurality of gRNA molecules each target sequences within the same gene or gene locus. In another aspect, the plurality of gRNA molecules each target sequences within 2 or more different genes.

In some aspects, the invention provides compositions and cells comprising a plurality, for example, 2 or more, for example, 2, gRNA molecules of the invention, wherien the plurality of gRNA molecules target

sequences less than 10,000, less than 9,000, less than 8,000, less than 7,000, less than 6,000, less than 5,000, less than 4,000, less than 3,000, less than 2,000, less than 1,000, less than 900, less than 800, less than 700, less than 600, less than 500, less than 400, less than 300, less than 200, less than 100, less than 90, less than 80, less than 70, less than 60, less than 50, less than 40, or less than 30 nucleotides apart. In an embodiment, the target sequences are on the same strand of duplex nulceic acid. In an embodiment, the target sequences are on different strands of duplex nucleic acid.

In one embodiment, the invention provides a method for excising (e.g., deleting) nucleic acid disposed between two gRNA binding sites disposed less than 10,000, less than 9,000, less than 8,000, less than 7,000, less than 6,000, less than 5,000, less than 4,000, less than 3,000, less than 2,000, less than 1,000, less than 900, less than 800, less than 700, less than 600, less than 500, less than 400, less than 300, less than 200, less than 100, less than 90, less than 80, less than 70, less than 60, less than 50, less than 40, or less than 30 nucleotides apart on the same or different strands of duplex nucleic acid. In an embodiment, the method provides for deletion of more than 50%, more than 60%, more than 70%, more than 80%, more than 85%, more than 86%, more than 87%, more than 88%, more than 89%, more than 90%, more than 91%, more than 92%, more than 93%, more than 94%, more than 95%, more than 96%, more than 97%, more than 98%, more than 99%, or 100% of the nucleotides disposed between the PAM sites associated with each gRNA binding site. In embodiments, the deletion further comprises of one or more nucleotides within one or more of the PAM sites associated with each gRNA binding site. In embodiments, the deletion also comprises one or more nucleotides outside of the region between the PAM sites associated with each gRNA binding site.

In one aspect, the two or more gRNA molecules comprise targeting domains targeting target sequences flanking a gene regulatory element, e.g., a promotor binding site, an enhancer region, or a repressor region, such that excision of the intervening sequence (or a portion of the intervening sequence) causes up- or down-regulation of a gene of interest.

In an embodiment, the two or more gRNA molecules are selected from the gRNA molecules of Table 1. In aspects, the two or more gRNA molecules comprise targeting domains that are complementary with sequences in the same gene. In aspects, the two or more gRNA molecules comprise targeting domains that are complementary with sequences of different genes. In an embodiment, the two or more gRNA molecules are selected from the gRNA molecules of Table 2. In aspects, the two or more gRNA molecules comprise targeting domains that are complementary with sequences in the same gene. In aspects, the two or more gRNA molecules comprise targeting domains that are complementary with sequences of different genes. In an embodiment, the two or more gRNA molecules are selected from the gRNA molecules of Table 3. In an embodiment, the two or more gRNA molecules are selected from the

gRNA molecules of Table 4. In an embodiment, the two or more gRNA molecules are selected from the gRNA molecules of Table 5. In an embodiment, the two or more gRNA molecules are selected from the gRNA molecules of Table 6. In an embodiment, the first and second gRNA molecules are selected from Tables 1-6, and are selected from different tables, e.g., and comprise targeting domains that are complementary with sequences of different genes. In embodiments, such two or more gRNA molecules may additionally be combined with one or more additional gRNA molecules which are complementary to a target domain of a different gene, as described herein.

In aspects of the invention that utilize two or more, e.g., two, gRNA molecules, it may be particularly useful for a first gRNA molecule (or more than one gRNA moleucles) to comprise a targeting domain specific for a sequence of TRAC and a second gRNA molecule (or more than one gRNA moleucles) to comprise a targeting domain specific for a sequence of B2M. In such aspects, it is particularly preferred that the first gRNA molecule to TRAC comprises a targeting domain of any gRNA molecule of Figure 12, and the second gRNA molecule to B2M comprises a targeting domain of any gRNA molecule of Figure 14. In an aspect, the first gRNA molecule to TRAC includes a targeting domain comprising, e.g., consisting of, SEQ ID NO: 5569, SEQ ID NO: 5587, SEQ ID NO: 5592 or SEQ ID NO: 5586, and the second gRNA molecule to B2M includes a targeting domain comprising, e.g., consisting of, SEQ ID NO: 5496, SEQ ID NO: 5498, or SEQ ID NO: 5509. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ

ID NO: 5569 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising,

e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting

domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule

include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second

gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA

molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5493, respectively. In an

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e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting

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ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ

ID NO: 5619 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising,

e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5492, respectively. In any of the aforementioned combinations, the aspect or the embodiment of the invention may additionally include a third gRNA molecule (or more than one gRNA molecules) comprising a targeting domain specific for a sequence of CIITA, e.g. as described herein, e.g., as described herein in Table 6c.

In aspects of the invention that utilize two or more, e.g., two, gRNA molecules, it may be particularly useful for a first gRNA molecule to comprise a targeting domain specific for a sequence of TRBC (e.g., TRBC1 or TRBC2) and a second gRNA molecule to comprise a targeting domain specific for a sequence of B2M. In such aspects, it is particularly preferred that the first gRNA molecule to TRBC comprises a targeting domain of any gRNA molecule of Figure 13, and the second gRNA molecule to B2M comprises a targeting domain of any gRNA molecule of Figure 14. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting

domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5719 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule

include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5694 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second

gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5706 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA

molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5696 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5497, respectively. In an

aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5711 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5497,

respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5708 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and

SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5709 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ

ID NO: 5712 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5712 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising,

e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5703 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting

domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5707 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule

include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5687 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA molecule and the

second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5705 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5519, respectively. In an aspect, the first gRNA

molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5713 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5519, respectively. In an

aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5715 and SEQ ID NO: 5492, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5519,

respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5494, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5508, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5514, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5710 and SEQ ID NO: 5492, respectively. In any of the aforementioned combinations, the aspect or the embodiment of the invention may additionally include a third gRNA molecule (or more than one

gRNA molecules) comprising a targeting domain specific for a sequence of CIITA, e.g. as described herein, e.g., as described herein in Table 6c.

In aspects of the invention that utilize two or more, e.g., two, gRNA molecules, it may be particularly useful for a first gRNA molecule to comprise a targeting domain specific for a sequence of TRAC and a second gRNA molecule to comprise a targeting domain specific for a sequence of PDCD1. In such aspects, it is particularly preferred that the first gRNA molecule to TRAC comprises a targeting domain of any gRNA molecule of Figure 12, and the second gRNA molecule to PDCD1 comprises a targeting domain of any gRNA molecule of Figure 16. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5497, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5499, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5498, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5503, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5496, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5507, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5515, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5493, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5506, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5509, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5517, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5521, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5569 and SEQ ID NO: 5520, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ

ID NO: 5569 and SEQ ID NO: 5500, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5585 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising,

e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5592 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting

domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5601 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule

include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5589 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5600 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the

second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5594 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA

molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5571 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5731, respectively. In an

aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5593 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5727,

respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5574 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5598 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and

SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5586 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ

ID NO: 5599 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5599 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising,

e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5591 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting

domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5568 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5610 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule

include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5608 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second

gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5617 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA

molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5744, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5619 and SEQ ID NO: 5734, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5743, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5798, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5748, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5722, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5800, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5735, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5724, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5731, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5725, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5775, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5766, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5727, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5744, respectively. In an

aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5751, respectively. In an aspect, the first gRNA molecule and the second gRNA molecule include targeting domains comprising, e.g., consisting of, SEQ ID NO: 5620 and SEQ ID NO: 5734, respectively.

As described herein, it is contemplated to generate a cell (or population of cells), e.g., an immune effector cell, e.g., a CAR-expressing immune effector cell, e.g., as described herein, which has reduced or eliminated expression of TRAC, B2M and CIITA. While it is contemplated that gRNAs comprising any targeting domain disclosed herein to each of these targets may be used in combination, particularly preferred targeting domain sequences to be used, for example, in combination are provided in the Table 33 below. In embodiments, each of the gRNA molecules are provided in dual guide RNA format and include a crRNA comprising, e.g., consisting of, the sequence [targeting domain]-SEQ ID NO: 6607, and a tracr comprising, e.g., consisting of, the sequence of SEQ ID NO: 6660. In other embodiments, each of the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 6601. In other embodiments, each of the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 7811. In embodiments, one or more of the gRNA molecules, e.g., all of the gRNA molecules, additionally comprise one or more modifications described herein, e.g., comprise one or more, e.g., 3, 3' and/or 5' phosphorotioate bonds, and/or one or more, e.g., 3, 3' and/or 5' 2'-OMe modifications. In embodiments, each of the gRNA molecules is complexed with a Cas9 molecule (e.g., described herein) and delivered to the cell (or population of cells, e.g., as described herein) as RNP, e.g., by electroporation. In embodiments, the RNP comprising each gRNA molecule are mixed with the cells and introduced simultaneously, e.g., by a single electroporation step. In other embodiments, the RNP may be introduced sequentially. Where it is contemplated to reduce or eliminate expression of both B2M and CIITA in a cell (such as here), in embodiments the cells may be further engineered to express a NK inhibitory molecule, e.g., as described herein, e.g., an HLA-G:B2M fusion described herein.

Table 33: Examples of preferred targeting domains of first, second and third gRNA molecules that can be used in combination to reduce or eliminate expression of TRAC, B2M and CIITA in a cell (as described herein).

Combination Number	SEQ ID NO:s of targeting domains of first gRNA, second gRNA and third gRNA, respectively	Combination Number	SEQ ID NO:s of targeting domains of first gRNA, second gRNA and third gRNA, respectively
A1	SEQ ID NO: 5569 and SEQ ID NO: 7769 and SEQ ID NO: 5496	A37	SEQ ID NO: 5592 and SEQ ID NO: 7769 and SEQ ID NO: 5496

A2	SEQ ID NO: 5569 and SEQ ID NO: 7771 and SEQ ID NO: 5496	A38	SEQ ID NO: 5592 and SEQ ID NO: 7771 and SEQ ID NO: 5496
A3	SEQ ID NO: 5569 and SEQ ID NO: 7739 and SEQ ID NO: 5496	A39	SEQ ID NO: 5592 and SEQ ID NO: 7739 and SEQ ID NO: 5496
A4	SEQ ID NO: 5569 and SEQ ID NO: 7785 and SEQ ID NO: 5496	A40	SEQ ID NO: 5592 and SEQ ID NO: 7785 and SEQ ID NO: 5496
A5	SEQ ID NO: 5569 and SEQ ID NO: 7769 and SEQ ID NO: 5498	A41	SEQ ID NO: 5592 and SEQ ID NO: 7769 and SEQ ID NO: 5498
A6	SEQ ID NO: 5569 and SEQ ID NO: 7771 and SEQ ID NO: 5498	A42	SEQ ID NO: 5592 and SEQ ID NO: 7771 and SEQ ID NO: 5498
A7	SEQ ID NO: 5569 and SEQ ID NO: 7739 and SEQ ID NO: 5498	A43	SEQ ID NO: 5592 and SEQ ID NO: 7739 and SEQ ID NO: 5498
A8	SEQ ID NO: 5569 and SEQ ID NO: 7785 and SEQ ID NO: 5498	A44	SEQ ID NO: 5592 and SEQ ID NO: 7785 and SEQ ID NO: 5498
A9	SEQ ID NO: 5569 and SEQ ID NO: 7769 and SEQ ID NO: 5509	A45	SEQ ID NO: 5592 and SEQ ID NO: 7769 and SEQ ID NO: 5509
A10	SEQ ID NO: 5569 and SEQ ID NO: 7771 and SEQ ID NO: 5509	A46	SEQ ID NO: 5592 and SEQ ID NO: 7771 and SEQ ID NO: 5509
A11	SEQ ID NO: 5569 and SEQ ID NO: 7739 and SEQ ID NO: 5509	A47	SEQ ID NO: 5592 and SEQ ID NO: 7739 and SEQ ID NO: 5509
A12	SEQ ID NO: 5569 and SEQ ID NO: 7785 and SEQ ID NO: 5509	A48	SEQ ID NO: 5592 and SEQ ID NO: 7785 and SEQ ID NO: 5509
A13	SEQ ID NO: 5586 and SEQ ID NO: 7769 and SEQ ID NO: 5496	A49	SEQ ID NO: 5599 and SEQ ID NO: 7769 and SEQ ID NO: 5496
A14	SEQ ID NO: 5586 and SEQ ID NO: 7771 and SEQ ID NO: 5496	A50	SEQ ID NO: 5599 and SEQ ID NO: 7771 and SEQ ID NO: 5496
A15	SEQ ID NO: 5586 and SEQ ID NO: 7739 and SEQ ID NO: 5496	A51	SEQ ID NO: 5599 and SEQ ID NO: 7739 and SEQ ID NO: 5496
A16	SEQ ID NO: 5586 and SEQ ID NO: 7785 and SEQ ID NO: 5496	A52	SEQ ID NO: 5599 and SEQ ID NO: 7785 and SEQ ID NO: 5496
A17	SEQ ID NO: 5586 and SEQ ID NO: 7769 and SEQ ID NO: 5498	A53	SEQ ID NO: 5599 and SEQ ID NO: 7769 and SEQ ID NO: 5498
A18	SEQ ID NO: 5586 and SEQ ID NO: 7771 and SEQ ID NO: 5498	A54	SEQ ID NO: 5599 and SEQ ID NO: 7771 and SEQ ID NO: 5498
A19	SEQ ID NO: 5586 and SEQ ID NO: 7739 and SEQ ID NO: 5498	A55	SEQ ID NO: 5599 and SEQ ID NO: 7739 and SEQ ID NO: 5498
A20	SEQ ID NO: 5586 and SEQ ID NO: 7785 and SEQ ID NO: 5498	A56	SEQ ID NO: 5599 and SEQ ID NO: 7785 and SEQ ID NO: 5498
A21	SEQ ID NO: 5586 and SEQ ID NO: 7769 and SEQ ID NO: 5509	A57	SEQ ID NO: 5599 and SEQ ID NO: 7769 and SEQ ID NO: 5509
A22	SEQ ID NO: 5586 and SEQ ID NO: 7771 and SEQ ID NO: 5509	A58	SEQ ID NO: 5599 and SEQ ID NO: 7771 and SEQ ID NO: 5509

A23	SEQ ID NO: 5586 and SEQ ID NO: 7739 and SEQ ID NO: 5509	A59	SEQ ID NO: 5599 and SEQ ID NO: 7739 and SEQ ID NO: 5509
A24	SEQ ID NO: 5586 and SEQ ID NO: 7785 and SEQ ID NO: 5509	A60	SEQ ID NO: 5599 and SEQ ID NO: 7785 and SEQ ID NO: 5509
A25	SEQ ID NO: 5587 and SEQ ID NO: 7769 and SEQ ID NO: 5496	A61	SEQ ID NO: 5600 and SEQ ID NO: 7769 and SEQ ID NO: 5496
A26	SEQ ID NO: 5587 and SEQ ID NO: 7771 and SEQ ID NO: 5496	A62	SEQ ID NO: 5600 and SEQ ID NO: 7771 and SEQ ID NO: 5496
A27	SEQ ID NO: 5587 and SEQ ID NO: 7739 and SEQ ID NO: 5496	A63	SEQ ID NO: 5600 and SEQ ID NO: 7739 and SEQ ID NO: 5496
A28	SEQ ID NO: 5587 and SEQ ID NO: 7785 and SEQ ID NO: 5496	A64	SEQ ID NO: 5600 and SEQ ID NO: 7785 and SEQ ID NO: 5496
A29	SEQ ID NO: 5587 and SEQ ID NO: 7769 and SEQ ID NO: 5498	A65	SEQ ID NO: 5600 and SEQ ID NO: 7769 and SEQ ID NO: 5498
A30	SEQ ID NO: 5587 and SEQ ID NO: 7771 and SEQ ID NO: 5498	A66	SEQ ID NO: 5600 and SEQ ID NO: 7771 and SEQ ID NO: 5498
A31	SEQ ID NO: 5587 and SEQ ID NO: 7739 and SEQ ID NO: 5498	A67	SEQ ID NO: 5600 and SEQ ID NO: 7739 and SEQ ID NO: 5498
A32	SEQ ID NO: 5587 and SEQ ID NO: 7785 and SEQ ID NO: 5498	A68	SEQ ID NO: 5600 and SEQ ID NO: 7785 and SEQ ID NO: 5498
A33	SEQ ID NO: 5587 and SEQ ID NO: 7769 and SEQ ID NO: 5509	A69	SEQ ID NO: 5600 and SEQ ID NO: 7769 and SEQ ID NO: 5509
A34	SEQ ID NO: 5587 and SEQ ID NO: 7771 and SEQ ID NO: 5509	A70	SEQ ID NO: 5600 and SEQ ID NO: 7771 and SEQ ID NO: 5509
A35	SEQ ID NO: 5587 and SEQ ID NO: 7739 and SEQ ID NO: 5509	A71	SEQ ID NO: 5600 and SEQ ID NO: 7739 and SEQ ID NO: 5509
A36	SEQ ID NO: 5587 and SEQ ID NO: 7785 and SEQ ID NO: 5509	A72	SEQ ID NO: 5600 and SEQ ID NO: 7785 and SEQ ID NO: 5509

Particularly preferred combinations include combination A1 to A4, combination A5 to A8, combination A37 to A40, or combination A41 to A44.

As described herein, it is contemplated to generate a cell (or population of cells), e.g., an immune effector cell, e.g., a CAR-expressing immune effector cell, e.g., as described herein, which has reduced or eliminated expression of CD3E, B2M and CIITA. While it is contemplated that gRNAs comprising any targeting domain disclosed herein to each of these targets may be used in combination, particularly preferred targeting domain sequences to be used, for example, in combination are provided in the Table 34 below. In embodiments, each of the gRNA molecules are provided in dual guide RNA format and include a crRNA comprising, e.g., consisting of, the sequence [targeting domain]-SEQ ID NO: 6607, and a tracr comprising, e.g., consisting of, the sequence of SEQ ID NO: 6660. In other embodiments, each of

the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 6601. In other embodiments, each of the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 7811. In embodiments, one or more of the gRNA molecules, e.g., all of the gRNA molecules, additionally comprise one or more modifications described herein, e.g., comprise one or more, e.g., 3, 3' and/or 5' phosphorotioate bonds, and/or one or more, e.g., 3, 3' and/or 5' 2'-OMe modifications. In embodiments, each of the gRNA molecules is complexed with a Cas9 molecule (e.g., described herein) and delivered to the cell (or population of cells, e.g., as described herein) as RNP, e.g., by electroporation. In embodiments, the RNP comprising each gRNA molecule are mixed with the cells and introduced simultaneously, e.g., by a single electroporation step. In other embodiments, the RNP may be introduced sequentially. Where it is contemplated to reduce or eliminate expression of both B2M and CIITA in a cell (such as here), in embodiments the cells may be further engineered to express a NK inhibitory molecule, e.g., as described herein, e.g., an HLA-G:B2M fusion described herein.

Table 34: Examples of preferred targeting domains of first, second and third gRNA molecules that can be used in combination to reduce or eliminate expression of CD3E, B2M and CIITA in a cell (as described herein).

Combination Number	SEQ ID NO:s of targeting domains of first gRNA, second gRNA and third gRNA, respectively	Combination Number	SEQ ID NO:s of targeting domains of first gRNA, second gRNA and third gRNA, respectively
B1	SEQ ID NO: 10729 and SEQ ID NO: 7769 and SEQ ID NO: 5496	B49	SEQ ID NO: 10701 and SEQ ID NO: 7769 and SEQ ID NO: 5496
B2	SEQ ID NO: 10729 and SEQ ID NO: 7771 and SEQ ID NO: 5496	B50	SEQ ID NO: 10701 and SEQ ID NO: 7771 and SEQ ID NO: 5496
B3	SEQ ID NO: 10729 and SEQ ID NO: 7739 and SEQ ID NO: 5496	B51	SEQ ID NO: 10701 and SEQ ID NO: 7739 and SEQ ID NO: 5496
B4	SEQ ID NO: 10729 and SEQ ID NO: 7785 and SEQ ID NO: 5496	B52	SEQ ID NO: 10701 and SEQ ID NO: 7785 and SEQ ID NO: 5496
B5	SEQ ID NO: 10729 and SEQ ID NO: 7769 and SEQ ID NO: 5498	B53	SEQ ID NO: 10701 and SEQ ID NO: 7769 and SEQ ID NO: 5498
B6	SEQ ID NO: 10729 and SEQ ID NO: 7771 and SEQ ID NO: 5498	B54	SEQ ID NO: 10701 and SEQ ID NO: 7771 and SEQ ID NO: 5498
B7	SEQ ID NO: 10729 and SEQ ID NO: 7739 and SEQ ID NO: 5498	B55	SEQ ID NO: 10701 and SEQ ID NO: 7739 and SEQ ID NO: 5498
B8	SEQ ID NO: 10729 and SEQ ID NO: 7785 and SEQ ID NO: 5498	B56	SEQ ID NO: 10701 and SEQ ID NO: 7785 and SEQ ID NO: 5498
B9	SEQ ID NO: 10729 and SEQ ID NO: 7769 and SEQ ID NO: 5509	B57	SEQ ID NO: 10701 and SEQ ID NO: 7769 and SEQ ID NO: 5509

B10	SEQ ID NO: 10729 and SEQ ID NO: 7771 and SEQ ID NO: 5509	B58	SEQ ID NO: 10701 and SEQ ID NO: 7771 and SEQ ID NO: 5509
B11	SEQ ID NO: 10729 and SEQ ID NO: 7739 and SEQ ID NO: 5509	B59	SEQ ID NO: 10701 and SEQ ID NO: 7739 and SEQ ID NO: 5509
B12	SEQ ID NO: 10729 and SEQ ID NO: 7785 and SEQ ID NO: 5509	B60	SEQ ID NO: 10701 and SEQ ID NO: 7785 and SEQ ID NO: 5509
B13	SEQ ID NO: 10719 and SEQ ID NO: 7769 and SEQ ID NO: 5496	B61	SEQ ID NO: 10700 and SEQ ID NO: 7769 and SEQ ID NO: 5496
B14	SEQ ID NO: 10719 and SEQ ID NO: 7771 and SEQ ID NO: 5496	B62	SEQ ID NO: 10700 and SEQ ID NO: 7771 and SEQ ID NO: 5496
B15	SEQ ID NO: 10719 and SEQ ID NO: 7739 and SEQ ID NO: 5496	B63	SEQ ID NO: 10700 and SEQ ID NO: 7739 and SEQ ID NO: 5496
B16	SEQ ID NO: 10719 and SEQ ID NO: 7785 and SEQ ID NO: 5496	B64	SEQ ID NO: 10700 and SEQ ID NO: 7785 and SEQ ID NO: 5496
B17	SEQ ID NO: 10719 and SEQ ID NO: 7769 and SEQ ID NO: 5498	B65	SEQ ID NO: 10700 and SEQ ID NO: 7769 and SEQ ID NO: 5498
B18	SEQ ID NO: 10719 and SEQ ID NO: 7771 and SEQ ID NO: 5498	B66	SEQ ID NO: 10700 and SEQ ID NO: 7771 and SEQ ID NO: 5498
B19	SEQ ID NO: 10719 and SEQ ID NO: 7739 and SEQ ID NO: 5498	B67	SEQ ID NO: 10700 and SEQ ID NO: 7739 and SEQ ID NO: 5498
B20	SEQ ID NO: 10719 and SEQ ID NO: 7785 and SEQ ID NO: 5498	B68	SEQ ID NO: 10700 and SEQ ID NO: 7785 and SEQ ID NO: 5498
B21	SEQ ID NO: 10719 and SEQ ID NO: 7769 and SEQ ID NO: 5509	B69	SEQ ID NO: 10700 and SEQ ID NO: 7769 and SEQ ID NO: 5509
B22	SEQ ID NO: 10719 and SEQ ID NO: 7771 and SEQ ID NO: 5509	B70	SEQ ID NO: 10700 and SEQ ID NO: 7771 and SEQ ID NO: 5509
B23	SEQ ID NO: 10719 and SEQ ID NO: 7739 and SEQ ID NO: 5509	B71	SEQ ID NO: 10700 and SEQ ID NO: 7739 and SEQ ID NO: 5509
B24	SEQ ID NO: 10719 and SEQ ID NO: 7785 and SEQ ID NO: 5509	B72	SEQ ID NO: 10700 and SEQ ID NO: 7785 and SEQ ID NO: 5509
B25	SEQ ID NO: 10764 and SEQ ID NO: 7769 and SEQ ID NO: 5496	B73	SEQ ID NO: 10722 and SEQ ID NO: 7769 and SEQ ID NO: 5496
B26	SEQ ID NO: 10764 and SEQ ID NO: 7771 and SEQ ID NO: 5496	B74	SEQ ID NO: 10722 and SEQ ID NO: 7771 and SEQ ID NO: 5496
B27	SEQ ID NO: 10764 and SEQ ID NO: 7739 and SEQ ID NO: 5496	B75	SEQ ID NO: 10722 and SEQ ID NO: 7739 and SEQ ID NO: 5496
B28	SEQ ID NO: 10764 and SEQ ID NO: 7785 and SEQ ID NO: 5496	B76	SEQ ID NO: 10722 and SEQ ID NO: 7785 and SEQ ID NO: 5496
B29	SEQ ID NO: 10764 and SEQ ID NO: 7769 and SEQ ID NO: 5498	B77	SEQ ID NO: 10722 and SEQ ID NO: 7769 and SEQ ID NO: 5498
B30	SEQ ID NO: 10764 and SEQ ID NO: 7771 and SEQ ID NO: 5498	B78	SEQ ID NO: 10722 and SEQ ID NO: 7771 and SEQ ID NO: 5498

B31	SEQ ID NO: 10764 and SEQ ID NO: 7739 and SEQ ID NO: 5498	B79	SEQ ID NO: 10722 and SEQ ID NO: 7739 and SEQ ID NO: 5498
B32	SEQ ID NO: 10764 and SEQ ID NO: 7785 and SEQ ID NO: 5498	B80	SEQ ID NO: 10722 and SEQ ID NO: 7785 and SEQ ID NO: 5498
B33	SEQ ID NO: 10764 and SEQ ID NO: 7769 and SEQ ID NO: 5509	B81	SEQ ID NO: 10722 and SEQ ID NO: 7769 and SEQ ID NO: 5509
B34	SEQ ID NO: 10764 and SEQ ID NO: 7771 and SEQ ID NO: 5509	B82	SEQ ID NO: 10722 and SEQ ID NO: 7771 and SEQ ID NO: 5509
B35	SEQ ID NO: 10764 and SEQ ID NO: 7739 and SEQ ID NO: 5509	B83	SEQ ID NO: 10722 and SEQ ID NO: 7739 and SEQ ID NO: 5509
B36	SEQ ID NO: 10764 and SEQ ID NO: 7785 and SEQ ID NO: 5509	B84	SEQ ID NO: 10722 and SEQ ID NO: 7785 and SEQ ID NO: 5509
B37	SEQ ID NO: 10689 and SEQ ID NO: 7769 and SEQ ID NO: 5496		
B38	SEQ ID NO: 10689 and SEQ ID NO: 7771 and SEQ ID NO: 5496		
B39	SEQ ID NO: 10689 and SEQ ID NO: 7739 and SEQ ID NO: 5496		
B40	SEQ ID NO: 10689 and SEQ ID NO: 7785 and SEQ ID NO: 5496		
B41	SEQ ID NO: 10689 and SEQ ID NO: 7769 and SEQ ID NO: 5498		
B42	SEQ ID NO: 10689 and SEQ ID NO: 7771 and SEQ ID NO: 5498		
B43	SEQ ID NO: 10689 and SEQ ID NO: 7739 and SEQ ID NO: 5498		
B44	SEQ ID NO: 10689 and SEQ ID NO: 7785 and SEQ ID NO: 5498		
B45	SEQ ID NO: 10689 and SEQ ID NO: 7769 and SEQ ID NO: 5509		
B46	SEQ ID NO: 10689 and SEQ ID NO: 7771 and SEQ ID NO: 5509		
B47	SEQ ID NO: 10689 and SEQ ID NO: 7739 and SEQ ID NO: 5509		
B48	SEQ ID NO: 10689 and SEQ ID NO: 7785 and SEQ ID NO: 5509		

As described herein, it is contemplated to generate a cell (or population of cells), e.g., an immune effector cell, e.g., a CAR-expressing immune effector cell, e.g., as described herein, which has reduced or eliminated expression of TRBC, B2M and CIITA. While it is contemplated that gRNAs comprising any targeting domain disclosed herein to each of these targets may be used in combination, particularly

preferred targeting domain sequences to be used, for example, in combination are provided in the Table 38 below. In embodiments, each of the gRNA molecules are provided in dual guide RNA format and include a crRNA comprising, e.g., consisting of, the sequence [targeting domain]-SEQ ID NO: 6607, and a tracr comprising, e.g., consisting of, the sequence of SEQ ID NO: 6660. In other embodiments, each of the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 6601. In other embodiments, each of the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 7811. In embodiments, one or more of the gRNA molecules, e.g., all of the gRNA molecules, additionally comprise one or more modifications described herein, e.g., comprise one or more, e.g., 3, 3' and/or 5' phosphorotioate bonds, and/or one or more, e.g., 3, 3' and/or 5' 2'-OMe modifications. In embodiments, each of the gRNA molecules is complexed with a Cas9 molecule (e.g., described herein) and delivered to the cell (or population of cells, e.g., as described herein) as RNP, e.g., by electroporation. In embodiments, the RNP comprising each gRNA molecule are mixed with the cells and introduced simultaneously, e.g., by a single electroporation step. In other embodiments, the RNP may be introduced sequentially. Where it is contemplated to reduce or eliminate expression of both B2M and CIITA in a cell (such as here), in embodiments the cells may be further engineered to express a NK inhibitory molecule, e.g., as described herein, e.g., an HLA-G:B2M fusion described herein.

Table 38: Examples of preferred targeting domains of first, second and third gRNA molecules that can be used in combination to reduce or eliminate expression of TRBC, B2M and CIITA in a cell (as described herein).

Combination Number	**SEQ ID NO:s of targeting domains of first gRNA, second gRNA and third gRNA, respectively**	**Combination Number**	**SEQ ID NO:s of targeting domains of first gRNA, second gRNA and third gRNA, respectively**
F1	SEQ ID NO: 5719 and SEQ ID NO: 5496 and SEQ ID NO: 7769	F33	SEQ ID NO: 5706 and SEQ ID NO: 5499 and SEQ ID NO: 7769
F2	SEQ ID NO: 5719 and SEQ ID NO: 5496 and SEQ ID NO: 7771	F34	SEQ ID NO: 5706 and SEQ ID NO: 5499 and SEQ ID NO: 7771
F3	SEQ ID NO: 5719 and SEQ ID NO: 5496 and SEQ ID NO: 7739	F35	SEQ ID NO: 5706 and SEQ ID NO: 5499 and SEQ ID NO: 7739
F4	SEQ ID NO: 5719 and SEQ ID NO: 5496 and SEQ ID NO: 7785	F36	SEQ ID NO: 5706 and SEQ ID NO: 5499 and SEQ ID NO: 7785
F5	SEQ ID NO: 5719 and SEQ ID NO: 5498 and SEQ ID NO: 7769	F37	SEQ ID NO: 5696 and SEQ ID NO: 5496 and SEQ ID NO: 7769

F6	SEQ ID NO: 5719 and SEQ ID NO: 5498 and SEQ ID NO: 7771	F38	SEQ ID NO: 5696 and SEQ ID NO: 5496 and SEQ ID NO: 7771
F7	SEQ ID NO: 5719 and SEQ ID NO: 5498 and SEQ ID NO: 7739	F39	SEQ ID NO: 5696 and SEQ ID NO: 5496 and SEQ ID NO: 7739
F8	SEQ ID NO: 5719 and SEQ ID NO: 5498 and SEQ ID NO: 7785	F40	SEQ ID NO: 5696 and SEQ ID NO: 5496 and SEQ ID NO: 7785
F9	SEQ ID NO: 5719 and SEQ ID NO: 5499 and SEQ ID NO: 7769	F41	SEQ ID NO: 5696 and SEQ ID NO: 5498 and SEQ ID NO: 7769
F10	SEQ ID NO: 5719 and SEQ ID NO: 5499 and SEQ ID NO: 7771	F42	SEQ ID NO: 5696 and SEQ ID NO: 5498 and SEQ ID NO: 7771
F11	SEQ ID NO: 5719 and SEQ ID NO: 5499 and SEQ ID NO: 7739	F43	SEQ ID NO: 5696 and SEQ ID NO: 5498 and SEQ ID NO: 7739
F12	SEQ ID NO: 5719 and SEQ ID NO: 5499 and SEQ ID NO: 7785	F44	SEQ ID NO: 5696 and SEQ ID NO: 5498 and SEQ ID NO: 7785
F13	SEQ ID NO: 5694 and SEQ ID NO: 5496 and SEQ ID NO: 7769	F45	SEQ ID NO: 5696 and SEQ ID NO: 5499 and SEQ ID NO: 7769
F14	SEQ ID NO: 5694 and SEQ ID NO: 5496 and SEQ ID NO: 7771	F46	SEQ ID NO: 5696 and SEQ ID NO: 5499 and SEQ ID NO: 7771
F15	SEQ ID NO: 5694 and SEQ ID NO: 5496 and SEQ ID NO: 7739	F47	SEQ ID NO: 5696 and SEQ ID NO: 5499 and SEQ ID NO: 7739
F16	SEQ ID NO: 5694 and SEQ ID NO: 5496 and SEQ ID NO: 7785	F48	SEQ ID NO: 5696 and SEQ ID NO: 5499 and SEQ ID NO: 7785
F17	SEQ ID NO: 5694 and SEQ ID NO: 5498 and SEQ ID NO: 7769	F49	SEQ ID NO: 5711 and SEQ ID NO: 5496 and SEQ ID NO: 7769
F18	SEQ ID NO: 5694 and SEQ ID NO: 5498 and SEQ ID NO: 7771	F50	SEQ ID NO: 5711 and SEQ ID NO: 5496 and SEQ ID NO: 7771
F19	SEQ ID NO: 5694 and SEQ ID NO: 5498 and SEQ ID NO: 7739	F51	SEQ ID NO: 5711 and SEQ ID NO: 5496 and SEQ ID NO: 7739
F20	SEQ ID NO: 5694 and SEQ ID NO: 5498 and SEQ ID NO: 7785	F52	SEQ ID NO: 5711 and SEQ ID NO: 5496 and SEQ ID NO: 7785
F21	SEQ ID NO: 5694 and SEQ ID NO: 5499 and SEQ ID NO: 7769	F53	SEQ ID NO: 5711 and SEQ ID NO: 5498 and SEQ ID NO: 7769
F22	SEQ ID NO: 5694 and SEQ ID NO: 5499 and SEQ ID NO:	F54	SEQ ID NO: 5711 and SEQ ID NO: 5498 and SEQ ID NO: 7771

	7771		
F23	SEQ ID NO: 5694 and SEQ ID NO: 5499 and SEQ ID NO: 7739	F55	SEQ ID NO: 5711 and SEQ ID NO: 5498 and SEQ ID NO: 7739
F24	SEQ ID NO: 5694 and SEQ ID NO: 5499 and SEQ ID NO: 7785	F56	SEQ ID NO: 5711 and SEQ ID NO: 5498 and SEQ ID NO: 7785
F25	SEQ ID NO: 5706 and SEQ ID NO: 5496 and SEQ ID NO: 7769	F57	SEQ ID NO: 5711 and SEQ ID NO: 5499 and SEQ ID NO: 7769
F26	SEQ ID NO: 5706 and SEQ ID NO: 5496 and SEQ ID NO: 7771	F58	SEQ ID NO: 5711 and SEQ ID NO: 5499 and SEQ ID NO: 7771
F27	SEQ ID NO: 5706 and SEQ ID NO: 5496 and SEQ ID NO: 7739	F59	SEQ ID NO: 5711 and SEQ ID NO: 5499 and SEQ ID NO: 7739
F28	SEQ ID NO: 5706 and SEQ ID NO: 5496 and SEQ ID NO: 7785	F60	SEQ ID NO: 5711 and SEQ ID NO: 5499 and SEQ ID NO: 7785
F29	SEQ ID NO: 5706 and SEQ ID NO: 5498 and SEQ ID NO: 7769		
F30	SEQ ID NO: 5706 and SEQ ID NO: 5498 and SEQ ID NO: 7771		
F31	SEQ ID NO: 5706 and SEQ ID NO: 5498 and SEQ ID NO: 7739		
F32	SEQ ID NO: 5706 and SEQ ID NO: 5498 and SEQ ID NO: 7785		

Particularly preferred combinations include combination F1 to F4, combination F5 to F8, combination F13 to F16, or combination F17 to F20.

As described herein, it is contemplated to generate a cell (or population of cells), e.g., an immune effector cell, e.g., a CAR-expressing immune effector cell, e.g., as described herein, which has reduced or eliminated expression of CD3E and FKBP1A. While it is contemplated that gRNAs comprising any targeting domain disclosed herein to each of these targets may be used in combination, particularly preferred targeting domain sequences to be used, for example, in combination are provided in the Table 35 below. In embodiments, each of the gRNA molecules are provided in dual guide RNA format and include a crRNA comprising, e.g., consisting of, the sequence [targeting domain]-SEQ ID NO: 6607, and a tracr comprising, e.g., consisting of, the sequence of SEQ ID NO: 6660. In other embodiments, each of

the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 6601. In other embodiments, each of the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 7811. In embodiments, one or more of the gRNA molecules, e.g., all of the gRNA molecules, additionally comprise one or more modifications described herein, e.g., comprise one or more, e.g., 3, 3' and/or 5' phosphorotioate bonds, and/or one or more, e.g., 3, 3' and/or 5' 2'-OMe modifications. In embodiments, each of the gRNA molecules is complexed with a Cas9 molecule (e.g., described herein) and delivered to the cell (or population of cells) as RNP, e.g., by electroporation. In embodiments, the RNP comprising each gRNA molecule are mixed with the cells and introduced simultaneously, e.g., by a single electroporation step. In other embodiments, the RNP may be introduced sequentially.

Table 35: Examples of preferred targeting domains of first, second and (optionally) third gRNA molecules that can be used in combination to reduce or eliminate expression of CD3E and FKBP1A in a cell (as described herein).

Combination Number	SEQ ID NO:s of targeting domains of first gRNA, second gRNA and, optionally, third gRNA, respectively	Combination Number	SEQ ID NO:s of targeting domains of first gRNA, second gRNA and, optionally, third gRNA, respectively
C1	SEQ ID NO: 10729 and SEQ ID NO: 6693	C25	SEQ ID NO: 10701 and SEQ ID NO: 6693
C2	SEQ ID NO: 10729 and SEQ ID NO: 6705	C26	SEQ ID NO: 10701 and SEQ ID NO: 6705
C3	SEQ ID NO: 10729 and SEQ ID NO: 6694	C27	SEQ ID NO: 10701 and SEQ ID NO: 6694
C4	SEQ ID NO: 10729 and SEQ ID NO: 6708	C28	SEQ ID NO: 10701 and SEQ ID NO: 6708
C5	SEQ ID NO: 10729 and SEQ ID NO: 6699	C29	SEQ ID NO: 10701 and SEQ ID NO: 6699
C6	SEQ ID NO: 10729 and SEQ ID NO: 6705 and SEQ ID NO: 6694	C30	SEQ ID NO: 10701 and SEQ ID NO: 6705 and SEQ ID NO: 6694
C7	SEQ ID NO: 10719 and SEQ ID NO: 6693	C31	SEQ ID NO: 10700 and SEQ ID NO: 6693
C8	SEQ ID NO: 10719 and SEQ ID NO: 6705	C32	SEQ ID NO: 10700 and SEQ ID NO: 6705
C9	SEQ ID NO: 10719 and SEQ ID NO: 6694	C33	SEQ ID NO: 10700 and SEQ ID NO: 6694
C10	SEQ ID NO: 10719 and SEQ ID NO: 6708	C34	SEQ ID NO: 10700 and SEQ ID NO: 6708
C11	SEQ ID NO: 10719 and SEQ ID NO: 6699	C35	SEQ ID NO: 10700 and SEQ ID NO: 6699
C12	SEQ ID NO: 10719 and SEQ ID NO: 6705 and SEQ ID NO: 6694	C36	SEQ ID NO: 10700 and SEQ ID NO: 6705 and SEQ ID NO: 6694

C13	SEQ ID NO: 10764 and SEQ ID NO: 6693	C37	SEQ ID NO: 10722 and SEQ ID NO: 6693
C14	SEQ ID NO: 10764 and SEQ ID NO: 6705	C38	SEQ ID NO: 10722 and SEQ ID NO: 6705
C15	SEQ ID NO: 10764 and SEQ ID NO: 6694	C39	SEQ ID NO: 10722 and SEQ ID NO: 6694
C16	SEQ ID NO: 10764 and SEQ ID NO: 6708	C40	SEQ ID NO: 10722 and SEQ ID NO: 6708
C17	SEQ ID NO: 10764 and SEQ ID NO: 6699	C41	SEQ ID NO: 10722 and SEQ ID NO: 6699
C18	SEQ ID NO: 10764 and SEQ ID NO: 6705 and SEQ ID NO: 6694	C42	SEQ ID NO: 10722 and SEQ ID NO: 6705 and SEQ ID NO: 6694
C19	SEQ ID NO: 10689 and SEQ ID NO: 6693		
C20	SEQ ID NO: 10689 and SEQ ID NO: 6705		
C21	SEQ ID NO: 10689 and SEQ ID NO: 6694		
C22	SEQ ID NO: 10689 and SEQ ID NO: 6708		
C23	SEQ ID NO: 10689 and SEQ ID NO: 6699		
C24	SEQ ID NO: 10689 and SEQ ID NO: 6705 and SEQ ID NO: 6694		

As described herein, it is contemplated to generate a cell (or population of cells), e.g., an immune effector cell, e.g., a CAR-expressing immune effector cell, e.g., as described herein, which has reduced or eliminated expression of TRAC and FKBP1A. While it is contemplated that gRNAs comprising any targeting domain disclosed herein to each of these targets may be used in combination, particularly preferred targeting domain sequences to be used, for example, in combination are provided in the Table 36 below. In embodiments, each of the gRNA molecules are provided in dual guide RNA format and include a crRNA comprising, e.g., consisting of, the sequence [targeting domain]-SEQ ID NO: 6607, and a tracr comprising, e.g., consisting of, the sequence of SEQ ID NO: 6660. In other embodiments, each of the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 6601. In other embodiments, each of the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 7811. In embodiments, one or more of the gRNA molecules, e.g., all of the gRNA molecules, additionally comprise one or more modifications described herein, e.g., comprise one or more, e.g., 3, 3' and/or 5' phosphorotioate bonds, and/or one or more, e.g., 3, 3' and/or 5' 2'-OMe modifications. In embodiments, each of the gRNA molecules is complexed with a Cas9 molecule (e.g., described herein) and delivered to the cell (or population of cells, e.g., as described herein) as RNP, e.g.,

by electroporation. In embodiments, the RNP comprising each gRNA molecule are mixed with the cells and introduced simultaneously, e.g., by a single electroporation step. In other embodiments, the RNP may be introduced sequentially.

Table 36: Examples of preferred targeting domains of first, second and (optionally) third gRNA molecules that can be used in combination to reduce or eliminate expression of TRAC and FKBP1A in a cell (as described herein).

Combination Number	SEQ ID NO:s of targeting domains of first gRNA, second gRNA and, optionally, third gRNA, respectively	Combination Number	SEQ ID NO:s of targeting domains of first gRNA, second gRNA and, optionally, third gRNA, respectively
D1	SEQ ID NO: 5569 and SEQ ID NO: 6693	D19	SEQ ID NO: 5592 and SEQ ID NO: 6693
D2	SEQ ID NO: 5569 and SEQ ID NO: 6705	D20	SEQ ID NO: 5592 and SEQ ID NO: 6705
D3	SEQ ID NO: 5569 and SEQ ID NO: 6694	D21	SEQ ID NO: 5592 and SEQ ID NO: 6694
D4	SEQ ID NO: 5569 and SEQ ID NO: 6708	D22	SEQ ID NO: 5592 and SEQ ID NO: 6708
D5	SEQ ID NO: 5569 and SEQ ID NO: 6699	D23	SEQ ID NO: 5592 and SEQ ID NO: 6699
D6	SEQ ID NO: 5569 and SEQ ID NO: 6705 and SEQ ID NO: 6694	D24	SEQ ID NO: 5592 and SEQ ID NO: 6705 and SEQ ID NO: 6694
D7	SEQ ID NO: 5586 and SEQ ID NO: 6693	D25	SEQ ID NO: 5599 and SEQ ID NO: 6693
D8	SEQ ID NO: 5586 and SEQ ID NO: 6705	D26	SEQ ID NO: 5599 and SEQ ID NO: 6705
D9	SEQ ID NO: 5586 and SEQ ID NO: 6694	D27	SEQ ID NO: 5599 and SEQ ID NO: 6694
D10	SEQ ID NO: 5586 and SEQ ID NO: 6708	D28	SEQ ID NO: 5599 and SEQ ID NO: 6708
D11	SEQ ID NO: 5586 and SEQ ID NO: 6699	D29	SEQ ID NO: 5599 and SEQ ID NO: 6699
D12	SEQ ID NO: 5586 and SEQ ID NO: 6705 and SEQ ID NO: 6694	D30	SEQ ID NO: 5599 and SEQ ID NO: 6705 and SEQ ID NO: 6694
D13	SEQ ID NO: 5587 and SEQ ID NO: 6693	D31	SEQ ID NO: 5600 and SEQ ID NO: 6693
D14	SEQ ID NO: 5587 and SEQ ID NO: 6705	D32	SEQ ID NO: 5600 and SEQ ID NO: 6705
D15	SEQ ID NO: 5587 and SEQ ID NO: 6694	D33	SEQ ID NO: 5600 and SEQ ID NO: 6694

D16	SEQ ID NO: 5587 and SEQ ID NO: 6708	D34	SEQ ID NO: 5600 and SEQ ID NO: 6708
D17	SEQ ID NO: 5587 and SEQ ID NO: 6699	D35	SEQ ID NO: 5600 and SEQ ID NO: 6699
D18	SEQ ID NO: 5587 and SEQ ID NO: 6705 and SEQ ID NO: 6694	D36	SEQ ID NO: 5600 and SEQ ID NO: 6705 and SEQ ID NO: 6694

Particularly preferred combinations include combination D2, combination D4, combination D20, or combination D22.

As described herein, it is contemplated to generate a cell (or population of cells), e.g., an immune effector cell, e.g., a CAR-expressing immune effector cell, e.g., as described herein, which has reduced or eliminated expression of TRBC and FKBP1A. While it is contemplated that gRNAs comprising any targeting domain disclosed herein to each of these targets may be used in combination, particularly preferred targeting domain sequences to be used, for example, in combination are provided in the Table 37 below. In embodiments, each of the gRNA molecules are provided in dual guide RNA format and include a crRNA comprising, e.g., consisting of, the sequence [targeting domain]-SEQ ID NO: 6607, and a tracr comprising, e.g., consisting of, the sequence of SEQ ID NO: 6660. In other embodiments, each of the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 6601. In other embodiments, each of the gRNA moleucles are provided in single guide RNA format comprising, e.g., consisting of, the sequence: [targeting domain]-SEQ ID NO: 7811. In embodiments, one or more of the gRNA molecules, e.g., all of the gRNA molecules, additionally comprise one or more modifications described herein, e.g., comprise one or more, e.g., 3, 3' and/or 5' phosphorotioate bonds, and/or one or more, e.g., 3, 3' and/or 5' 2'-OMe modifications. In embodiments, each of the gRNA molecules is complexed with a Cas9 molecule (e.g., described herein) and delivered to the cell (or population of cells) as RNP, e.g., by electroporation. In embodiments, the RNP comprising each gRNA molecule are mixed with the cells and introduced simultaneously, e.g., by a single electroporation step. In other embodiments, the RNP may be introduced sequentially.

Table 37: Examples of preferred targeting domains of first, second and (optionally) third gRNA molecules that can be used in combination to reduce or eliminate expression of TRBC and FKBP1A in a cell (as described herein).

Combination Number	**SEQ ID NO:s of targeting domains of first gRNA, second gRNA and, optionally, third gRNA, respectively**	**Combination Number**	**SEQ ID NO:s of targeting domains of first gRNA, second gRNA and, optionally, third gRNA, respectively**

E1	SEQ ID NO: 5719 and SEQ ID NO: 6693	E19	SEQ ID NO: 5696 and SEQ ID NO: 6693
E2	SEQ ID NO: 5719 and SEQ ID NO: 6705	E20	SEQ ID NO: 5696 and SEQ ID NO: 6705
E3	SEQ ID NO: 5719 and SEQ ID NO: 6694	E21	SEQ ID NO: 5696 and SEQ ID NO: 6694
E4	SEQ ID NO: 5719 and SEQ ID NO: 6708	E22	SEQ ID NO: 5696 and SEQ ID NO: 6708
E5	SEQ ID NO: 5719 and SEQ ID NO: 6699	E23	SEQ ID NO: 5696 and SEQ ID NO: 6699
E6	SEQ ID NO: 5719 and SEQ ID NO: 6705 and SEQ ID NO: 6694	E24	SEQ ID NO: 5696 and SEQ ID NO: 6705 and SEQ ID NO: 6694
E7	SEQ ID NO: 5694 and SEQ ID NO: 6693	E25	SEQ ID NO: 5711 and SEQ ID NO: 6693
E8	SEQ ID NO: 5694 and SEQ ID NO: 6705	E26	SEQ ID NO: 5711 and SEQ ID NO: 6705
E9	SEQ ID NO: 5694 and SEQ ID NO: 6694	E27	SEQ ID NO: 5711 and SEQ ID NO: 6694
E10	SEQ ID NO: 5694 and SEQ ID NO: 6708	E28	SEQ ID NO: 5711 and SEQ ID NO: 6708
E11	SEQ ID NO: 5694 and SEQ ID NO: 6699	E29	SEQ ID NO: 5711 and SEQ ID NO: 6699
E12	SEQ ID NO: 5694 and SEQ ID NO: 6705 and SEQ ID NO: 6694	E30	SEQ ID NO: 5711 and SEQ ID NO: 6705 and SEQ ID NO: 6694
E13	SEQ ID NO: 5706 and SEQ ID NO: 6693		
E14	SEQ ID NO: 5706 and SEQ ID NO: 6705		
E15	SEQ ID NO: 5706 and SEQ ID NO: 6694		
E16	SEQ ID NO: 5706 and SEQ ID NO: 6708		
E17	SEQ ID NO: 5706 and SEQ ID NO: 6699		
E18	SEQ ID NO: 5706 and SEQ ID NO: 6705 and SEQ ID NO: 6694		

Particularly preferred combinations include combination E2, combination E4, combination E8, or combination E10.

While not intending to be bound by theory, it has also been surprisingly shown herein that the targeting of two or more target sequences located within different genes may induce mutations (e.g., insertions or deletions or one or more nucleic acid residues) at each of the targeted sites, thereby reducing or

eliminating expression of two or more proteins within the cell. Combinations of gRNAs targeting two or more different genes of interest are described herein.

As described herein, when utilizing more than one gRNA molecule (or CRISPR system comprising more than one gRNA molecule, e.g., a CRISPR system comprising a first gRNA moleucle and a CRISPR system comprising a second gRNA molecule, e.g., wherien each gRNA molecule is complexed with a Cas molecule, e.g., a Cas9 molecule, e.g., as described herein), the more than one gRNA molecules may be introduced into a cell simultaneously, e.g., in a single introduction step, e.g., a single electroporation step. Alternatively, the more than one gRNA molecules (or CRISPR systems comprising said gRNA molecules) can be introduced into a cell in more than one steps, e.g., more than one electroporations. If multiple introduction steps are utilized, the steps may be separated by a period of hours, days, or weeks, e.g., by a period of 1 hour, 2 hours, 5 hours, 10 hours, 15 hours, 20 hours, 24 hours, 2 days, 3, days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, or more.

IX. Properties of the gRNA

It has further been surprisingly shown herein that gRNA molecules and CRISPR systems comprising said gRNA molecules produce similar or identical indel patterns in different cell types, across different methods of delivery and using different crRNA/tracr components. Without being bound by theory, it is believed that some indel patterns may be more advantageous than others. For example, indels which predominantly include insertions and/or deletions wich result in a "frameshift mutation" (e.g., 1- or 2-base pair insertion or deletions, or any insertion or deletion where n/3 is not a whole number (where n=the number of nucleotides in the insertion or deletion)) may be beneficial in reducing or eliminating expression of a functional protein. Likewise, indels which predominantly include "large deletions" (deletions of more than 10, 11, 12, 13, 14, 15, 20, 25, or 30 nucleotides) may also be beneficial in, for example, removing critical regulatory sequences such as promoter binding sites, which may similarly have an impoved effect on expression of functional protein. While the indel patterns induced by a given gRNA/CRISPR system have surprisingly been found to be consistently reproduced across cell types, as described herein, not any single indel structure will inevtiably be produced in a given cell upon introduction of a gRNA/CRISPR system.

The invention thus provides for gRNA molecules which create a beneficial indel pattern or structure, for example, which have indel patterns or structures predominantly composed of frameshif mutation(s) and/or large deletions. Such gRNA molecules may be selected by assessing the indel pattern or structure created by a candidate gRNA molecule in a test cell (for example, a HEK293 cell or in the cell of interest, e.g., a T cell) by NGS, as described herein. As shown in the Examples, gRNA molecules have been

discovered, which, when introduced into the desired cell population, result in a population of cells comprising a significant fraction of the cells having a frameshift mutation in the targeted gene. In some cases, the rate of frameshift mutation is as high as 75%, 80%, 85%, 90% or more. The invention thus provides for populations of cells which comprise at least about 40% of cells (e.g., at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, or at least about 99%) having a frameshift mutation, e.g., as described herein, at or near the target site of a gRNA moleucle described herein. The invention also provides for populations of cells which comprise at least about 50% of cells (e.g., at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, or at least about 99%) having a frameshift mutation, e.g., as described herein, at or near the target site of a gRNA moleucle described herein.

The invention thus provides methods of selecting gRNA molecules for use in the therapeutic methods of the invention comprising: 1) providing a plurality of gRNA molecules to a target of interest, 2) assessing the indel pattern or structure created by use of said gRNA molecules, 3) selecting a gRNA molecule that forms an indel pattern or structure composed predominantly of frameshift mutations, large deletions or a combination thereof, and 4) using said selected gRNA in a methods of the invention.

The invention further provides methods of altering cells, and altered cells, wherien a particular indel pattern is constently produced with a given gRNA/CRISPR system in that cell type. The indel patterns, including the top 5 most frequently occuring indels observed with the gRNA/CRISPR systems described herein are disclosed, for example, in the Examples. As shown in the examples, populations of cells are generated, wherien a signficant fraction of the cells comprises one of the top 5 indels (for example, populations of cells wherein one of the top 5 indels is present in more than 30%, more than 40%, more than 50%, more than 60% or more of the cells of the population. Thus, the invention provides cells, e.g., immune effector cells, e.g., CAR-expressing immune effector cells (as described herein), which comprise an indel of any one of the top 5 indels observed with a given gRNA/CRISPR system. Further, the invention provides populations of cells, e.g., immune effector cells, e.g., CAR-expressing immune effector cells (as described herein), which when assessed by, for example, NGS, comprise a high percentage of cells comprising one of the top 5 indels described herein for a given gRNA/CRISPR system. When used in connection with indel pattern analysis, a "high percentage" refers to at least about 50% (e.g., at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, or at least about 99%) of the cells of the population comprising one of the top 5 indels described herein for a given

gRNA/CRISPR system. In other embodiments, the population of cells comprises at least about 25% (e.g., from about 25% to about 60%, e.g., from about 25% to about 50%, e.g., from about 25% to about 40%, e.g., from about 25% to about 35%) of cells which have one of the top 5 indels described herein for a given gRNA/CRISPR system. In embodiments, the top 5 indels for a given gRNA/CRISPR system which targets TRAC are provided in Figure 34A, Figure 34B and Figure 49. In embodiments, the top 5 indels for a given gRNA/CRISPR system which targets B2M are provided in Figure 36 and Figure 48. In embodiments, the top 5 indels for a given gRNA/CRISPR system which targets CIITA are provided in Figure 38, Figure 41, Figure 44, and Figure 50. In embodiments, the top 5 indels for a given gRNA/CRISPR system which targets FKBP1A are provided in Figure 53.

It has also been discovered that certain gRNA molecules do not create indels at off-target sequences within the genome of the target cell type, or produce indels at off target sites at very low frequencies (e.g., <5% of cells within a population) relative to the frequency of indel creation at the target site. Thus, the invention provides for gRNA molecules and CRISPR systems which do not exhibit off-target indel formation in the target cell type, or which produce a frequency of off-target indel formation of <5%. In embodiments, the invention provides gRNA molecules and CRISPR systems which do not exhibit any off target indel formation in the target cell type. Thus, the invention further provides a cell, e.g., a population of cells, e.g., immune effector cells, e.g., CAR-expressing immune effector cells, e.g., as described herein, which comprise an indel at or near a target site of a gRNA molecule described herein (e.g., a frameshift indel, or any one of the top 5 indels produced by a given gRNA/CRISPR system, e.g., as described herein), but does not comprise an indel at any off-target site of the gRNA molecule. In other embodiments, the invention further provides a a population of cells, e.g., immune effector cells, e.g., CAR-expressing immune effector cells, e.g., as described herein, which comprises > 50% of cells which have an indel at or near a target site of a gRNA molecule described herein (e.g., a frameshift indel, or any one of the top 5 indels produced by a given gRNA/CRISPR system, e.g., as described herein), but which comprises less than 5%, e.g., less than 4%, less than 3%, less than 2% or less than 1%, of cells comprising an indel at any off-target site of the gRNA molecule.

X. Delivery/Constructs

The components, e.g., a Cas9 molecule or gRNA molecule, or both, can be delivered, formulated, or administered in a variety of forms. As a non-limiting example, the gRNA molecule and Cas9 molecule can be formulated (in one or more compositions), directly delivered or administered to a cell in which a genome editing event is desired. Alternatively, nucleic acid encoding one or more components, e.g., a Cas9 molecule or gRNA molecule, or both, can be formulated (in one or more compositions), delivered or administered. In one aspect, the gRNA molecule is provided as DNA encoding the gRNA molecule and

the Cas9 molecule is provided as DNA encoding the Cas9 molecule. In one embodiment, the gRNA molecule and Cas9 molecule are encoded on separate nucleic acid molecules. In one embodiment, the gRNA molecule and Cas9 molecule are encoded on the same nucleic acid molecule. In one aspect, the gRNA molecule is provided as RNA and the Cas9 molecule is provided as DNA encoding the Cas9 molecule. In one embodiment, the gRNA molecule is provided with one or more modifications, e.g., as described herein. In one aspect, the gRNA molecule is provided as RNA and the Cas9 molecule is provided as mRNA encoding the Cas9 molecule. In one aspect, the gRNA molecule is provided as RNA and the Cas9 molecule is provided as a protein. In one embodiment, the gRNA and Cas9 molecule are provided as a ribonuclear protein complex (RNP). In one aspect, the gRNA molecule is provided as DNA encoding the gRNA molecule and the Cas9 molecule is provided as a protein.

Delivery may be accomplished by, for example, electroporation (e.g., as known in the art) or other method that renders the cell membrane permeable to nucleic acid and/or polypeptide molecules. Additional techniques for rendering the membrane permeable are known in the art and include, for example, cell squeezing (e.g., as described in WO2015/023982 and WO2013/059343, the contents of which are hereby incorporated by reference in their entirety), nanoneedles (e.g., as described in Chiappini et al., Nat. Mat., 14; 532-39, or US2014/0295558, the contents of which are hereby incorporated by reference in their entirety) and nanostraws (e.g., as described in Xie, ACS Nano, 7(5); 4351-58, the contents of which are hereby incorporated by reference in their entirety).

When a component is delivered encoded in DNA the DNA will typically include a control region, e.g., comprising a promoter, to effect expression. Useful promoters for Cas9 molecule sequences include CMV, EF- lalpha, MSCV, PGK, CAG control promoters. Useful promoters for gRNAs include H1, EF-1a and U6 promoters. Promoters with similar or dissimilar strengths can be selected to tune the expression of components. Sequences encoding a Cas9 molecule can comprise a nuclear localization signal (NLS), e.g., an SV40 NLS. In an embodiment, a promoter for a Cas9 molecule or a gRNA molecule can be, independently, inducible, tissue specific, or cell specific.

DNA-based Delivery of a Cas9 molecule and or a gRNA molecule

DNA encoding Cas9 molecules and/or gRNA molecules, can be administered to subjects or delivered into cells by art-known methods or as described herein. For example, Cas9-encoding and/or gRNA-encoding DNA can be delivered, e.g., by vectors (e.g., viral or non-viral vectors), non-vector based methods (e.g., using naked DNA or DNA complexes), or a combination thereof.

In some embodiments, the Cas9- and/or gRNA-encoding DNA is delivered by a vector (e.g., viral vector/virus, plasmid, minicircle or nanoplasmid).

A vector can comprise a sequence that encodes a Cas9 molecule and/or a gRNA molecule. A vector can also comprise a sequence encoding a signal peptide (e.g., for nuclear localization, nucleolar localization, mitochondrial localization), fused, e.g., to a Cas9 molecule sequence. For example, a vector can comprise one or more nuclear localization sequence (e.g., from SV40) fused to the sequence encoding the Cas9 molecule.

One or more regulatory/control elements, e.g., a promoter, an enhancer, an intron, a polyadenylation signal, a Kozak consensus sequence, internal ribosome entry sites (IRES), a 2A sequence, and a splice acceptor or donor can be included in the vectors. In some embodiments, the promoter is recognized by RNA polymerase II (e.g., a CMV promoter). In other embodiments, the promoter is recognized by RNA polymerase III (e.g., a U6 promoter). In some embodiments, the promoter is a regulated promoter (e.g., inducible promoter). In other embodiments, the promoter is a constitutive promoter. In some embodiments, the promoter is a tissue specific promoter. In some embodiments, the promoter is a viral promoter. In other embodiments, the promoter is a non-viral promoter.

In some embodiments, the vector or delivery vehicle is a minicircle. In some embodiments, the vector or delivery vehicle is a nanoplasmid.

In some embodiments, the vector or delivery vehicle is a viral vector (e.g., for generation of recombinant viruses). In some embodiments, the virus is a DNA virus (e.g., dsDNA or ssDNA virus). In other embodiments, the virus is an RNA virus (e.g., an ssRNA virus).

Exemplary viral vectors/viruses include, e.g., retroviruses, lentiviruses, adenovirus, adeno- associated virus (AAV), vaccinia viruses, poxviruses, and herpes simplex viruses. Viral vector technology is well known in the art and is described, for example, in Sambrook et al., 2012, MOLECULAR CLONING: A LABORATORY MANUAL, volumes 1 -4, Cold Spring Harbor Press, NY), and in other virology and molecular biology manuals.

In some embodiments, the virus infects dividing cells. In other embodiments, the virus infects non-dividing cells. In some embodiments, the virus infects both dividing and non-dividing cells. In some embodiments, the virus can integrate into the host genome. In some embodiments, the virus is engineered to have reduced immunity, e.g., in human. In some embodiments, the virus is replication-competent. In other embodiments, the virus is replication- defective, e.g., having one or more coding regions for the genes necessary for additional rounds of virion replication and/or packaging replaced with other genes or deleted. In some embodiments, the virus causes transient expression of the Cas9 molecule and/or the gRNA molecule. In other embodiments, the viurs causes long-lasting, e.g., at least 1 week, 2 weeks, 1 month, 2 months, 3 months, 6 months, 9 months, 1 year, 2 years, or permanent expression, of the Cas9

molecule and/or the gRNA molecule. The packaging capacity of the viruses may vary, e.g., from at least about 4 kb to at least about 30 kb, e.g., at least about 5 kb, 10 kb, 15 kb, 20 kb, 25 kb, 30 kb, 35 kb, 40 kb, 45 kb, or 50 kb.

In some embodiments, the Cas9- and/or gRNA-encoding DNA is delivered by a recombinant retrovirus. In some embodiments, the retrovirus (e.g., Moloney murine leukemia vims) comprises a reverse transcriptase, e.g., that allows integration into the host genome. In some embodiments, the retrovirus is replication-competent. In other embodiments, the retrovirus is replication-defective, e.g., having one of more coding regions for the genes necessary for additional rounds of virion replication and packaging replaced with other genes, or deleted.

In some embodiments, the Cas9- and/or gRNA-encoding DNA is delivered by a recombinant lentivirus. For example, the lentivirus is replication-defective, e.g., does not comprise one or more genes required for viral replication.

In some embodiments, the Cas9- and/or gRNA-encoding DNA is delivered by a recombinant adenovirus. In some embodiments, the adenovirus is engineered to have reduced immunity in human.

In some embodiments, the Cas9- and/or gRNA-encoding DNA is delivered by a recombinant AAV. In some embodiments, the AAV can incorporate its genome into that of a host cell, e.g., a target cell as described herein. In some embodiments, the AAV is a self- complementary adeno-associated virus (scAAV), e.g., a scAAV that packages both strands which anneal together to form double stranded DNA. AAV serotypes that may be used in the disclosed methods include, e.g., AAV 1 , AAV2, modified AAV2 (e.g., modifications at Y444F, Y500F, Y730F and/or S662V), AAV3, modified AAV3 (e.g., modifications at Y705F, Y73 1 F and/or. T492V), AAV4, AAV5, AAV6, modified AAV6 (e.g., modifications at S663V and/or T492V), AAV8. AAV 8.2, AAV9, AAV rh 10, and pseudotyped AAV, such as AAV2/8, AAV2/5 and AAV2/6 can also be used in the disclosed methods.

In some embodiments, the Cas9- and/or gRNA-encoding DNA is delivered by a hybrid virus, e.g., a hybrid of one or more of the viruses described herein.

A Packaging cell is used to form a virus particle that is capable of infecting a host or target cell. Such a cell includes a 293 cell, which can package adenovirus, and a ψ2 cell or a PA317 cell, which can package retrovirus. A viral vector used in gene therapy is usually generated by a producer cell line that packages a nucleic acid vector into a viral particle. The vector typically contains the minimal viral sequences required for packaging and subsequent integration into a host or target cell (if applicable), with other viral sequences being replaced by an expression cassette encoding the protein to be expressed. For example, an AAV vector used in gene therapy typically only possesses inverted terminal repeat (ITR) sequences from

the AAV genome which are required for packaging and gene expression in the host or target cell. The missing viral functions are supplied in trans by the packaging cell line. Henceforth, the viral DNA is packaged in a cell line, which contains a helper plasmid encoding the other AAV genes, namely rep and cap, but lacking ITR sequences. The cell line is also infected with adenovirus as a helper. The helper virus promotes replication of the AAV vector and expression of AAV genes from the helper plasmid. The helper plasmid is not packaged in significant amounts due to a lack of ITR sequences. Contamination with adenovirus can be reduced by, e.g., heat treatment to which adenovirus is more sensitive than AAV.

In an embodiment, the viral vector has the ability of cell type and/or tissue type recognition. For example, the viral vector can be pseudotyped with a different/alternative viral envelope glycoprotein; engineered with a cell type-specific receptor (e.g., genetic modification of the viral envelope glycoproteins to incorporate targeting ligands such as a peptide ligand, a single chain antibodie, a growth factor); and/or engineered to have a molecular bridge with dual specificities with one end recognizing a viral glycoprotein and the other end recognizing a moiety of the target cell surface (e.g., ligand-receptor, monoclonal antibody, avidin-biotin and chemical conjugation).

In an embodiment, the viral vector achieves cell type specific expression. For example, a tissue-specific promoter can be constructed to restrict expression of the transgene (Cas 9 and gRNA) in only the target cell. The specificity of the vector can also be mediated by microRNA- dependent control of transgene expression. In an embodiment, the viral vector has increased efficiency of fusion of the viral vector and a target cell membrane. For example, a fusion protein such as fusion-competent hemagglutin (HA) can be incorporated to increase viral uptake into cells. In an embodiment, the viral vector has the ability of nuclear localization. For example, aviruse that requires the breakdown of the cell wall (during cell division) and therefore will not infect a non-diving cell can be altered to incorporate a nuclear localization peptide in the matrix protein of the virus thereby enabling the transduction of non-proliferating cells.

In some embodiments, the Cas9- and/or gRNA-encoding DNA is delivered by a non- vector based method (e.g., using naked DNA or DNA complexes). For example, the DNA can be delivered, e.g., by organically modified silica or silicate (Ormosil), electroporation, gene gun, sonoporation, magnetofection, lipid-mediated transfection, dendrimers, inorganic nanoparticles, calcium phosphates, or a combination thereof.

In some embodiments, the Cas9- and/or gRNA-encoding DNA is delivered by a combination of a vector and a non-vector based method. For example, a virosome comprises a liposome combined with an inactivated virus (e.g., HIV or influenza virus), which can result in more efficient gene transfer, e.g., in a respiratory epithelial cell than either a viral or a liposomal method alone.

In an embodiment, the delivery vehicle is a non-viral vector. In an embodiment, the non- viral vector is an inorganic nanoparticle (e.g., attached to the payload to the surface of the nanoparticle). Exemplary inorganic nanoparticles include, e.g., magnetic nanoparticles (e.g., Fe lvln0_2), or silica. The outer surface of the nanoparticle can be conjugated with a positively charged polymer (e.g., polyethylenimine, polylysine, polyserine) which allows for attachment (e.g., conjugation or entrapment) of payload. In an embodiment, the non-viral vector is an organic nanoparticle (e.g., entrapment of the payload inside the nanoparticle). Exemplary organic nanoparticles include, e.g., SNALP liposomes that contain cationic lipids together with neutral helper lipids which are coated with polyethylene glycol (PEG) and protamine and nucleic acid complex coated with lipid coating.

Exemplary lipids and/or polymers for for transfer of CRISPR systems or nucleic acid, e.g., vectors, encoding CRISPR systems or components thereof include, for example, those described in WO2011/076807, WO2014/136086, WO2005/060697, WO2014/140211, WO2012/031046, WO2013/103467, WO2013/006825, WO2012/006378, WO2015/095340, and WO2015/095346, the contents of each of the foregoing are hereby incorported by reference in their entirety. In an embodiment, the vehicle has targeting modifications to increase target cell update of nanoparticles and liposomes, e.g., cell specific antigens, monoclonal antibodies, single chain antibodies, aptamers, polymers, sugars, and cell penetrating peptides. In an embodiment, the vehicle uses fusogenic and endosome-destabilizing peptides/polymers. In an embodiment, the vehicle undergoes acid-triggered conformational changes (e.g., to accelerate endosomal escape of the cargo). In an embodiment, a stimuli-cleavable polymer is used, e.g., for release in a cellular compartment. For example, disulfide-based cationic polymers that are cleaved in the reducing cellular environment can be used.

In an embodiment, the delivery vehicle is a biological non-viral delivery vehicle. In an embodiment, the vehicle is an attenuated bacterium (e.g., naturally or artificially engineered to be invasive but attenuated to prevent pathogenesis and expressing the transgene (e.g., Listeria monocytogenes, certain Salmonella strains, Bifidobacterium longum, and modified Escherichia coli), bacteria having nutritional and tissue-specific tropism to target specific tissues, bacteria having modified surface proteins to alter target tissue specificity). In an embodiment, the vehicle is a genetically modified bacteriophage (e.g., engineered phages having large packaging capacity, less immunogenic, containing mammalian plasmid maintenance sequences and having incorporated targeting ligands). In an embodiment, the vehicle is a mammalian virus-like particle. For example, modified viral particles can be generated (e.g., by purification of the "empty" particles followed by ex vivo assembly of the virus with the desired cargo). The vehicle can also be engineered to incorporate targeting ligands to alter target tissue specificity. In an embodiment, the vehicle is a biological liposome. For example, the biological liposome is a phospholipid-based particle

derived from human cells (e.g., erythrocyte ghosts, which are red blood cells broken down into spherical structures derived from the subject (e.g., tissue targeting can be achieved by attachment of various tissue or cell-specific ligands), or secretory exosomes - subject (i.e., patient) derived membrane-bound nanovescicle (30 - 100 nm) of endocytic origin (e.g., can be produced from various cell types and can therefore be taken up by cells without the need of for targeting ligands).

In an embodiment, one or more nucleic acid molecules (e.g., DNA molecules) other than the components of a Cas system, e.g., the Cas9 molecule component and/or the gRNA molecule component described herein, are delivered. In an embodiment, the nucleic acid molecule is delivered at the same time as one or more of the components of the Cas system are delivered. In an embodiment, the nucleic acid molecule is delivered before or after (e.g., less than about 30 minutes, 1 hour, 2 hours, 3 hours, 6 hours, 9 hours, 12 hours, 1 day, 2 days, 3 days, 1 week, 2 weeks, or 4 weeks) one or more of the components of the Cas9 system are delivered. In an embodiment, the nucleic acid molecule is delivered by a different means than one or more of the components of the Cas9 system, e.g., the Cas9 molecule component and/or the gRNA molecule component, are delivered. The nucleic acid molecule can be delivered by any of the delivery methods described herein. For example, the nucleic acid molecule can be delivered by a viral vector, e.g., an integration-deficient lentivirus, and the Cas9 molecule component and/or the gRNA molecule component can be delivered by electroporation, e.g., such that the toxicity caused by nucleic acids (e.g., DNAs) can be reduced. In an embodiment, the nucleic acid molecule encodes a therapeutic protein, e.g., a protein described herein. In an embodiment, the nucleic acid molecule encodes an RNA molecule, e.g., an RNA molecule described herein. Delivery of RNA encoding a Cas9 molecule

RNA encoding Cas9 molecules (e.g., active Cas9 molecules, inactive Cas9 molecules or inactive Cas9 fusion proteins) and/or gRNA molecules, can be delivered into cells, e.g., target cells described herein, by art-known methods or as described herein. For example, Cas9-encoding and/or gRNA-encoding RNA can be delivered, e.g., by microinjection, electroporation, lipid-mediated transfection, peptide-mediated delivery, or a combination thereof.

Delivery of Cas9 molecule as protein

Cas9 molecules (e.g., active Cas9 molecules, inactive Cas9 molecules or inactive Cas9 fusion proteins) can be delivered into cells by art-known methods or as described herein. For example, Cas9 protein molecules can be delivered, e.g., by microinjection, electroporation, lipid-mediated transfection, peptide-mediated delivery, cell squeezing or abrasion (e.g., by nanoneedles) or a combination thereof. Delivery can be accompanied by DNA encoding a gRNA or by a gRNA.

In an embodiment the Cas9 molecule, e.g., as described herein, is delivered as a protein and the gRNA molecule is delivered at one or more RNAs (e.g., as a dgRNA or sgRNA, as described herein). In embodiments, the Cas9 protein is complexed with the gRNA molecule prior to delivery to a cell, e.g., as described herein, as a ribonuclear protein complex ("RNP"). In embodiments, the RNP can be delivered into cells, e.g., described herein, by any art-known method, e.g., electroporation. As described herein, and without being bound by theory, it can be preferrable to use a gRNA moleucle and Cas9 molecule which result in high % editing at the target sequence (e.g., >85%, >90%, >95%, >98%, or >99%) in the target cell, e.g., described herein, even when the concentration of RNP delivered to the cell is reduced. Again, without being bound by theory, delivering a reduced or low concentration of RNP comprising a gRNA moleucle that produces a high % editing at the target sequence in the target cell (including at the low RNP concentration), can be beneficial because it may reduce the frequency and number of off-target editing events. In one aspect, where a low or reduced concentration of RNP is to be used, the following procedure can be used to generate the RNP:

1. Provide the Cas9 molecule and the tracr in solution at a high concentration (e.g., a concentration higher than the final RNP concentration to be delivered to the cell), and allow the two components to equilibrate;
2. Provide the crRNA molecule, and allow the components to equilibrate (thereby forming a high-concentration solution of the RNP);
3. Dilute the RNP solution to the desired concentration;
4. Deliver said RNP at said desired concentration to the target cells, e.g., by electroporation.

The above procedure may be modified for use with sgRNA molecules by omitting step 2, above, and in step 1, providing the Cas9 molecule and the sgRNA molecule in solution at high concentraiton, and allowing the components to equilibrate. In embodiments, the Cas9 moleucle and each gRNA component are provided in solution at a 1:2 ratio (Cas9:gRNA), e.g., a 1:2 molar ratio of Cas9:gRNA molecule. Where dgRNA molecules are used, the ratio, e.g., molar rato, is 1:2:2 (Cas9:tracr:crRNA). In embodiments, the RNP is formed at a concentration of 20uM or higher, e.g., a concentration from about 20uM to about 50 uM. In embodiments, the RNP is formed at a concentration of 10 uM or higher, e.g., a concentration from about 10 uM to about 30 uM. In embodiments, the RNP is diluted to a final concentration of 10uM or less (e.g., a concentration from about 0.01 uM to about 10uM) in a solution comprising the target cell (e.g., described herein) for delivery to said target cell. In embodiments, the RNP is diluted to a final concentration of 3uM or less (e.g., a concentration from about 0.01 uM to about 3uM) in a solution comprising the target cell (e.g., described herein) for delivery to said target cell. In embodiments, the RNP is diluted to a final concentration of 1uM or less (e.g., a concentration from about

0.01 uM to about 1uM) in a solution comprising the target cell (e.g., described herein) for delivery to said target cell. In embodiments, the RNP is diluted to a final concentration of 0.3uM or less (e.g., a concentration from about 0.01 uM to about 0.3uM) in a solution comprising the target cell (e.g., described herein) for delivery to said target cell. In embodiments, the RNP is provided at a final concentration of about 3uM in a solution comprising the target cell (e.g., described herein) for delivery to said target cell. In embodiments, the RNP is provided at a final concentration of about 1uM in a solution comprising the target cell (e.g., described herein) for delivery to said target cell. In embodiments, the RNP is provided at a final concentration of about 0.3uM in a solution comprising the target cell (e.g., described herein) for delivery to said target cell. In embodiments, the RNP is provided at a final concentration of about 0.1uM in a solution comprising the target cell (e.g., described herein) for delivery to said target cell. In embodiments, the RNP is provided at a final concentration of about 0.05uM in a solution comprising the target cell (e.g., described herein) for delivery to said target cell. In embodiments, the RNP is provided at a final concentration of about 0.03uM in a solution comprising the target cell (e.g., described herein) for delivery to said target cell. In embodiments, the RNP is provided at a final concentration of about 0.01uM in a solution comprising the target cell (e.g., described herein) for delivery to said target cell.

Bi-Modal or Differential Delivery of Components

Separate delivery of the components of a Cas system, e.g., the Cas9 molecule component and the gRNA molecule component, and more particularly, delivery of the components by differing modes, can enhance performance, e.g., by improving tissue specificity and safety.

In an embodiment, the Cas9 molecule and the gRNA molecule are delivered by different modes, or as sometimes referred to herein as differential modes. Different or differential modes, as used herein, refer modes of delivery that confer different pharmacodynamic or pharmacokinetic properties on the subject component molecule, e.g., a Cas9 molecule, gRNA molecule, or template nucleic acid. For example, the modes of delivery can result in different tissue distribution, different half-life, or different temporal distribution, e.g., in a selected compartment, tissue, or organ.

Some modes of delivery, e.g., delivery by a nucleic acid vector that persists in a cell, or in progeny of a cell, e.g., by autonomous replication or insertion into cellular nucleic acid, result- in more persistent expression of and presence of a component.

XI. Methods of Treatment

The Cas systems, e.g., one or more gRNA molecules and one or more Cas molecules (e.g., Cas9 molecules), described herein are useful for the treatment of disease in a mammal, e.g., in a human. The terms “treat,” “treated,” “treating,” and “treatment,” include the administration of cas systems, e.g., one or

more gRNA molecules and one or more Cas9 molecules, to cells to prevent or delay the onset of the symptoms, complications, or biochemical indicia of a disease, alleviating the symptoms or arresting or inhibiting further development of the disease, condition, or disorder. Treatment may be prophylactic (to prevent or delay the onset of the disease, or to prevent the manifestation of clinical or subclinical symptoms thereof) or therapeutic suppression or alleviation of symptoms after the manifestation of the disease. Treatment can be measured by the therapeutic measures described hererin. The methods of "treatment" of the present invention also include administration of cells altered by the introduction of a cas system (e.g., one or more gRNA molecules and one or more Cas molecules) into said cells to a subject in order to cure, reduce the severity of, or ameliorate one or more symptoms of a disease or condition, in order to prolong the health or survival of a subject beyond that expected in the absence of such treatment. For example, "treatment" includes the alleviation of a disease symptom in a subject by at least 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more.

Methods of treatment/Combination therapies

In another aspect, the present invention provides a method comprising administering a cell of the invention, e.g., a cell which comprises or which at any time comprised a gRNA molecule as described herein, to a subject. In embodiments, the cell has been altered by the introduction of the gRNA molecule such that the gene comprising sequence complementary to the gRNA molecule targeting domain is altered, such that expression of functional product of that gene is reduced or eliminated relative to an unmodified cell. In embodiments, the cell is further engineered to express a CAR, e.g., as described herein. In embodiments, the cell is an immune effector cell, e.g., an NK cell or T cell. In embodiments, the cell is allogeneic. In embodiments, the cell is autologous.

In another aspect, the present invention provides a method comprising administering a gRNA molecule, e.g., a gRNA molecule described herein, or a cell comprising or which at any time comprised a gRNA molecule, e.g., a gRNA molecule described herein, to a subject in need thereof. In one embodiment, the subject has a disorder described herein, e.g., the subject has cancer, e.g., the subject has a cancer which expresses a target antigen described herein. In one embodiment, the subject is a human.

In another aspect, the invention pertains to a method of treating a subject having a disease associated with expression of a cancer associated antigen as described herein comprising administering to the subject an effective amount of a a gRNA molecule, e.g., a gRNA molecule described herein, or a cell comprising or which at any time comprised a gRNA molecule, e.g., a gRNA molecule described herein.

In yet another aspect, the invention features a method of treating a subject having a disease associated with expression of a tumor antigen (e.g., an antigen described herein), comprising administering to the

subject an effective amount of a cell, e.g., an immune effector cell (*e.g.*, a population of immune effector cells) comprising or which at any time comprised a gRNA molecule, e.g., a gRNA molecule described herein, further comprising a CAR molecule, wherein the CAR molecule comprises an antigen binding domain, a transmembrane domain, and an intracellular domain, said intracellular domain comprises a costimulatory domain and/or a primary signaling domain, wherein said antigen binding domain binds to the tumor antigen associated with the disease, e.g. a tumor antigen as described herein.

In a related aspect, the invention features a method of treating a subject having a disease associated with expression of a tumor antigen. The method comprises administering to the subject an effective amount of a gRNA molecule, e.g., a gRNA molecule described herein, or a cell comprising or which at any time comprised a gRNA molecule, e.g., a gRNA molecule described herein, in combination with an agent that increases the efficacy of the cell, wherein:

the agent that increases the efficacy of the immune cell is chosen from one or more of:

a protein phosphatase inhibitor;
a kinase inhibitor;
a cytokine;
an inhibitor of an immune inhibitory molecule; or
an agent that decreases the level or activity of a T_{REG} cell.

In another aspect, the invention features a composition comprising an immune effector cell (*e.g.*, a population of immune effector cells) comprising or which at any time comprised a gRNA molecule, e.g., a gRNA molecule described herein, for use in the treatment of a subject having a disease associated with expression of a tumor antigen, e.g., a disorder as described herein.

In certain embodiments of any of the aforesaid methods or uses, the cell comprising or which at any time comprised a gRNA described herein, has been altered such that the expression of the functional gene product of the gene comprising the target sequence complementary to the gRNA targeting domain has been reduced or abolished. In an embodiment, expression of the functional gene product of the gene comprising the target sequence complementary to the gRNA targeting domain has been abolished. In embodiments, the cell further expresses a CAR, e.g., as described herein. In embodiments the cell is allogeneic. In embodiments, the cell is autologous.

In certain embodiments of any of the aforesaid methods or uses, the disease associated with a tumor antigen, e.g., a tumor antigen described herein, is selected from a proliferative disease such as a cancer or malignancy or a precancerous condition such as a myelodysplasia, a myelodysplastic syndrome or a

preleukemia, or is a non-cancer related indication associated with expression of a tumor antigen described herein. In one embodiment, the disease is a cancer described herein, e.g., a cancer described herein as being associated with a target described herein. In one embodiment, the disease is a hematologic cancer. In one embodiment, the hematologic cancer is leukemia. In one embodiment, the cancer is selected from the group consisting of one or more acute leukemias including but not limited to B-cell acute lymphoid leukemia ("BALL"), T-cell acute lymphoid leukemia ("TALL"), acute lymphoid leukemia (ALL); one or more chronic leukemias including but not limited to chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL); additional hematologic cancers or hematologic conditions including, but not limited to B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin lymphoma, Hodgkin lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and "preleukemia" which are a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells, and to disease associated with expression of a tumor antigen described herein include, but not limited to, atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases expressing a tumor antigen as described herein; and any combination thereof. In another embodiment, the disease associated with a tumor antigen described herein is a solid tumor.

In certain embodiments, the methods or uses are carried out in combination with an agent that increases the efficacy of the immune effector cell, e.g., an agent as described herein.

In any of the aforesaid methods or uses, the disease associated with expression of the tumor antigen is selected from the group consisting of a proliferative disease, a precancerous condition, a cancer, and a non-cancer related indication associated with expression of the tumor antigen.

The cancer can be a hematologic cancer, e.g., a cancer chosen from one or more of chronic lymphocytic leukemia (CLL), acute leukemias, acute lymphoid leukemia (ALL), B-cell acute lymphoid leukemia (B-ALL), T-cell acute lymphoid leukemia (T-ALL), chronic myelogenous leukemia (CML), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, or pre-leukemia.

The cancer can also be chosen from colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers, combinations of said cancers, and metastatic lesions of said cancers.

In certain embodiments of the methods or uses described herein, the cell is administered in combination with an agent that increases the efficacy of the immune effector cell, e.g., one or more of a protein phosphatase inhibitor, a kinase inhibitor, a cytokine, an inhibitor of an immune inhibitory molecule; or an agent that decreases the level or activity of a T_{REG} cell.

In certain embodiments of the methods or uses described herein, the protein phosphatase inhibitor is a SHP-1 inhibitor and/or an SHP-2 inhibitor.

In other embodiments of the methods or uses described herein, kinase inhibitor is chosen from one or more of a CDK4 inhibitor, a CDK4/6 inhibitor (e.g., palbociclib), a BTK inhibitor (e.g., ibrutinib or RN-486), an mTOR inhibitor (e.g., rapamycin or everolimus (RAD001)), an MNK inhibitor, or a dual P13K/mTOR inhibitor. In one embodiment, the BTK inhibitor does not reduce or inhibit the kinase activity of interleukin-2-inducible kinase (ITK).

In other embodiments of the methods or uses described herein, the agent that decreases the level or activity of the T_{REG} cells is chosen from cyclophosphamide, anti-GITR antibody, CD25-depletion, or a combination thereof.

In other embodiments, the agent that inhibits the inhibitory molecule comprises a first polypeptide comprising an inhibitory molecule or a fragment thereof and a second polypeptide that provides a positive signal to the cell, and wherein the first and second polypeptides are expressed on the CAR-containing immune cells, wherein (i) the first polypeptide comprises PD1, PD-L1, CTLA-4, TIM-3, LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, TGF beta, CEACAM-1, CEACAM-3, and CEACAM-5 or a

fragment thereof; and/or (ii) the second polypeptide comprises an intracellular signaling domain comprising a primary signaling domain and/or a costimulatory signaling domain. In one embodiment, the primary signaling domain comprises a functional domain of CD3 zeta; and/or the costimulatory signaling domain comprises a functional domain of a protein selected from 41BB, CD27 and CD28.

In other embodiments, cytokine is chosen from IL-7; IL-15; a composition comprising a interleukin-15 (IL-15) polypeptide, a interleukin-15 receptor alpha (IL-15Ra) polypeptide, or a combination of both a IL-15 polypeptide and a IL-15Ra polypeptide e.g., hetIL-15; IL-18; IL-21, or a combination thereof. Exemplary hetIL-15 are heterodimeric non-covalent complexes of IL-15 and IL-15Ra (Admune Therapeutics, LLC). Such hetIL-15 is described in, e.g., U.S. 8,124,084, U.S. 2012/0177598, U.S. 2009/0082299, U.S. 2012/0141413, and U.S. 2011/0081311, incorporated herein by referen. hetIL-15 is described in, e.g., U.S. 8,124,084, U.S. 2012/0177598, U.S. 2009/0082299, U.S. 2012/0141413, and U.S. 2011/0081311, incorporated herein by reference. Other exemplary embodiments of hetIL-15 are covalent complexes between an IL-15 polypeptide and an IL-15R (e.g., IL-15Ra) polypeptide.

In other embodiments, the cell and a second, e.g., any of the combination therapies disclosed herein (e.g., the agent that that increases the efficacy of the cell) are administered substantially simultaneously or sequentially.

In other embodiments, the cell is administered in combination with a molecule that targets GITR and/or modulates GITR function. In certain embodiments, the molecule targeting GITR and/or modulating GITR function is administered prior to the CAR-expressing cell or population of cells, or prior to apheresis.

In one embodiment, lymphocyte infusion, for example allogeneic lymphocyte infusion, is used in the treatment of the cancer, wherein the lymphocyte infusion comprises at least one cell, e.g., CAR-expressing cell, of the present invention. In one embodiment, autologous lymphocyte infusion is used in the treatment of the cancer, wherein the autologous lymphocyte infusion comprises at least one cell, e.g., CAR-expressing cell described herein.

In one embodiment, the cell is a T cell and the T cell is diaglycerol kinase (DGK) deficient. In one embodiment, the cell is a T cell and the T cell is Ikaros deficient. In one embodiment, the cell is a T cell and the T cell is both DGK and Ikaros deficient.

In one embodiment, the method includes administering a cell of the invention, as described herein, in combination with an agent which enhances the activity of the cell, wherein the agent is a cytokine, e.g., IL-7; IL-15; a composition comprising a interleukin-15 (IL-15) polypeptide, a interleukin-15 receptor alpha (IL-15Ra) polypeptide, or a combination of both a IL-15 polypeptide and a IL-15Ra polypeptide

e.g., hetIL-15; IL-18; IL-21; or a combination thereof. The cytokine can be delivered in combination with, e.g., simultaneously or shortly after, administration of the cell. Alternatively, the cytokine can be delivered after a prolonged period of time after administration of the cell, e.g., after assessment of the subject's response to the cell. In one embodiment the cytokine is administered to the subject simultaneously (e.g., administered on the same day) with or shortly after administration (e.g., administered 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, or 7 days after administration) of the cell or population of cells of any of claims 61-80. In other embodiments, the cytokine is administered to the subject after a prolonged period of time (e.g., e.g., at least 2 weeks, 3 weeks, 4 weeks, 6 weeks, 8 weeks, 10 weeks, or more) after administration of the cell or population of cells of any of claims 61-80, or after assessment of the subject's response to the cell.

In other embodiments, the cells of the invention that are further engineered to express a CAR are administered in combination with an agent that ameliorates one or more side effects associated with administration of a cell expressing a CAR molecule. Side effects associated with the CAR-expressing cell can be chosen from cytokine release syndrome (CRS) or hemophagocytic lymphohistiocytosis (HLH).

In embodiments of any of the aforeseaid methods or uses, the cells expressing the CAR molecule are administered in combination with an agent that treats the disease associated with expression of the tumor antigen, e.g., any of the second or third therapies disclosed herein. Additional exemplary combinations include one or more of the following.

In another embodiment, the cell, e.g., as described herein, can be administered in combination with another agent, e.g., a kinase inhibitor and/or checkpoint inhibitor described herein. In an embodiment, a cell of the invention can further express another agent, e.g., an agent which enhances the activity of the cell.

For example, in one embodiment, the agent that enhances the activity of the cell can be an agent which inhibits an inhibitory molecule.

In one embodiment, the agent that inhibits the inhibitory molecule is an inhibitory nucleic acid is a dsRNA, a siRNA, or a shRNA.

In another embodiment, the agent which inhibits an inhibitory molecule, e.g., is a molecule described herein, e.g., an agent that comprises a first polypeptide, e.g., an inhibitory molecule, associated with a second polypeptide that provides a positive signal to the cell, e.g., an intracellular signaling domain described herein. In one embodiment, the agent comprises a first polypeptide, e.g., of an inhibitory molecule, or a fragment thereof (e.g., at least a portion of the extracellular domain of any of these), and a

second polypeptide which is an intracellular signaling domain described herein (e.g., comprising a costimulatory domain (e.g., 41BB, CD27 or CD28, e.g., as described herein) and/or a primary signaling domain (e.g., a CD3 zeta signaling domain described herein). In one embodiment, the agent comprises a first polypeptide of PD1 or a fragment thereof (e.g., at least a portion of the extracellular domain of PD1), and a second polypeptide of an intracellular signaling domain described herein (e.g., a CD28 signaling domain described herein and/or a CD3 zeta signaling domain described herein).

In one embodiment, the cell of the present invention, e.g., T cell or NK cell, is administered to a subject that has received a previous stem cell transplantation, e.g., autologous stem cell transplantation.

In one embodiment, the cell of the present invention, e.g., T cell or NK cells, is administered to a subject that has received a previous dose of melphalan.

In one embodiment, the cell of the invention, is administered in combination with an agent that increases the efficacy of the cell, e.g., an agent described herein.

In one embodiment, the cells of the invention, are administered in combination with a low, immune enhancing dose of an mTOR inhibitor. While not wishing to be bound by theory, it is believed that treatment with a low, immune enhancing, dose (e.g., a dose that is insufficient to completely suppress the immune system but sufficient to improve immune function) is accompanied by a decrease in PD-1 positive T cells or an increase in PD-1 negative cells. PD-1 positive T cells, but not PD-1 negative T cells, can be exhausted by engagement with cells which express a PD-1 ligand, e.g., PD-L1 or PD-L2. In an embodiment this approach can be used to optimize the performance of the cells described herein in the subject. While not wishing to be bound by theory, it is believed that, in an embodiment, the performance of endogenous, non-modified immune effector cells, e.g., T cells or NK cells, is improved. While not wishing to be bound by theory, it is believed that, in an embodiment, the performance of a CAR- expressing cell is improved. In other embodiments, cells, e.g., T cells or NK cells, which comprise or will be engineered to comprise a gRNA molecule of the invention, can be treated ex vivo by contact with an amount of an mTOR inhibitor that increases the number of PD1 negative immune effector cells, e.g., T cells or increases the ratio of PD1 negative immune effector cells, e.g., T cells/ PD1 positive immune effector cells, e.g., T cells.

In an embodiment, administration of a low, immune enhancing, dose of an mTOR inhibitor, e.g., an allosteric inhibitor, e.g., RAD001, or a catalytic inhibitor, is initiated prior to administration of an CAR expressing cell described herein, e.g., T cells or NK cells. In an embodiment, the cells are administered after a sufficient time, or sufficient dosing, of an mTOR inhibitor, such that the level of PD1 negative immune effector cells, e.g., T cells or NK cells, or the ratio of PD1 negative immune effector cells, e.g., T cells/ PD1 positive immune effector cells, e.g., T cells, has been, at least transiently, increased.

In an embodiment, the cell, e.g., T cell or NK cell, to be engineered to comprise a gRNA of the invention, is harvested after a sufficient time, or after sufficient dosing of the low, immune enhancing, dose of an mTOR inhibitor, such that the level of PD1 negative immune effector cells, e.g., T cells, or the ratio of PD1 negative immune effector cells, e.g., T cells/ PD1 positive immune effector cells, e.g., T cells, in the subject or harvested from the subject has been, at least transiently, increased.

In one embodiment, the cell of the invention, is administered in combination with an agent that ameliorates one or more side effect associated with administration of a cell, e.g., an agent described herein.

In one embodiment, the cell is administered in combination with an agent that treats the disease associated with a cancer associated antigen as described herein, e.g., an agent described herein.

In one embodiment, the cell is administered at a dose and/or dosing schedule described herein.

In one embodiment, the subject (e.g., human) receives an initial administration of cells of the invention, and one or more subsequent administrations of cells of the invention, wherein the one or more subsequent administrations are administered less than 15 days, e.g., 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, or 2 days after the previous administration. In one embodiment, more than one administration of cells of the invention are administered to the subject (e.g., human) per week, e.g., 2, 3, or 4 administrations of cells comprising a CAR molecule are administered per week. In one embodiment, the subject (e.g., human subject) receives more than one administration of cells of the invention per week (e.g., 2, 3 or 4 administrations per week) (also referred to herein as a cycle), followed by a week of no administration of cells of the invention, and then one or more additional administration of cells of the invention (e.g., more than one administration of the cells of the invention per week) is administered to the subject. In another embodiment, the subject (e.g., human subject) receives more than one cycle of cells of the invention, and the time between each cycle is less than 10, 9, 8, 7, 6, 5, 4, or 3 days. In one embodiment, the cells of the invention are administered every other day for 3 administrations per week. In one embodiment, the cells of the invention are administered for at least two, three, four, five, six, seven, eight or more weeks.

In one embodiment, the cells of the invention, are administered as a first line treatment for the disease, e.g., the cancer, e.g., the cancer described herein. In another embodiment, the cells of the invention, are administered as a second, third, fourth line treatment for the disease, e.g., the cancer, e.g., the cancer described herein.

In one embodiment, a population of cells described herein is administered.

In another aspect, the invention pertains to the isolated nucleic acid molecule encoding a gRNA of the invention, the gRNA molecule of the invention, and the cell comprising or which at any time comprised a

gRNA of the invention for use as a medicament. In embodiments, the cell comprising or which at any time comprised a gRNA of the invention is or will be altered such that expression of the functional product of the gene comprising sequence complimentary to the gRNA targeting domain is reduced or abolished.

In another aspect, the invention pertains to the isolated nucleic acid molecule encoding a gRNA of the invention, the gRNA molecule of the invention, and the cell comprising or which at any time comprised a gRNA of the invention for use in the treatment of a disease expressing a cancer associated antigen as described herein. In embodiments, the cell comprising or which at any time comprised a gRNA of the invention is or will be altered such that expression of the functional product of the gene comprising sequence complimentary to the gRNA targeting domain is reduced or abolished.

In another aspect, the invention pertains to the isolated nucleic acid molecule encoding a gRNA of the invention, the gRNA molecule of the invention, and the cell comprising or which at any time comprised a gRNA of the invention for use as a medicament in combination with a cytokine, e.g., IL-7; IL-15; a composition comprising a interleukin-15 (IL-15) polypeptide, a interleukin-15 receptor alpha (IL-15Ra) polypeptide, or a combination of both a IL-15 polypeptide and a IL-15Ra polypeptide e.g., hetIL-15; IL-18; and/or IL-21; and/or combinations thereof as described herein. In another aspect, the invention pertains to a cytokine described herein for use as a medicament in combination with a cell described herein. In embodiments, the cell comprising or which at any time comprised a gRNA of the invention is or will be altered such that expression of the functional product of the gene comprising sequence complimentary to the gRNA targeting domain is reduced or abolished.

In another aspect, the invention pertains to the isolated nucleic acid molecule encoding a gRNA of the invention, the gRNA molecule of the invention, and the cell comprising or which at any time comprised a gRNA of the invention for use as a medicament in combination with a kinase inhibitor and/or a checkpoint inhibitor as described herein. In another aspect, the invention pertains to a kinase inhibitor and/or a checkpoint inhibitor described herein for use as a medicament in combination with a cell comprising or which at any time comprised a gRNA of the invention.

In another aspect, the invention features a composition comprising a cell of the invention for use in the treatment of a subject having a disease associated with expression of a tumor-supporting antigen, e.g., a disorder as described herein.

In any of the aforesaid methods or uses, the disease associated with expression of the tumor-supporting antigen is selected from the group consisting of a proliferative disease, a precancerous condition, a cancer,

and a non-cancer related indication associated with expression of the tumor-supporting antigen. In an embodiment, the disease associated with a tumor-supporting antigen described herein is a solid tumor.

In one embodiment of the methods or uses described herein, the cell of the invention is administered in combination with another agent. In one embodiment, the agent can be a kinase inhibitor, e.g., a CDK4/6 inhibitor, a BTK inhibitor, an mTOR inhibitor, a MNK inhibitor, or a dual PI3K/mTOR inhibitor, and combinations thereof. In one embodiment, the kinase inhibitor is a CDK4 inhibitor, e.g., a CDK4 inhibitor described herein, e.g., a CD4/6 inhibitor, such as, e.g., 6-Acetyl-8-cyclopentyl-5-methyl-2-(5-piperazin-1-yl-pyridin-2-ylamino)-8*H*-pyrido[2,3-*d*]pyrimidin-7-one, hydrochloride (also referred to as palbociclib or PD0332991). In one embodiment, the kinase inhibitor is a BTK inhibitor, e.g., a BTK inhibitor described herein, such as, e.g., ibrutinib. In one embodiment, the kinase inhibitor is an mTOR inhibitor, e.g., an mTOR inhibitor described herein, such as, e.g., rapamycin, a rapamycin analog, OSI-027. The mTOR inhibitor can be, e.g., an mTORC1 inhibitor and/or an mTORC2 inhibitor, e.g., an mTORC1 inhibitor and/or mTORC2 inhibitor described herein. In one embodiment, the kinase inhibitor is a MNK inhibitor, e.g., a MNK inhibitor described herein, such as, e.g., 4-amino-5-(4-fluoroanilino)-pyrazolo [3,4-*d*] pyrimidine. The MNK inhibitor can be, e.g., a MNK1a, MNK1b, MNK2a and/or MNK2b inhibitor. The dual PI3K/mTOR inhibitor can be, e.g., PF-04695102.

In one embodiment of the methods or uses described herein, the kinase inhibitor is a CDK4 inhibitor selected from aloisine A; flavopiridol or HMR-1275, 2-(2-chlorophenyl)-5,7-dihydroxy-8-[(3S,4R)-3-hydroxy-1-methyl-4-piperidinyl]-4-chromenone; crizotinib (PF-02341066; 2-(2-Chlorophenyl)-5,7-dihydroxy-8-[(2*R*,3*S*)-2-(hydroxymethyl)-1-methyl-3-pyrrolidinyl]- 4*H*-1-benzopyran-4-one, hydrochloride (P276-00); 1-methyl-5-[[2-[5-(trifluoromethyl)-1*H*-imidazol-2-yl]-4-pyridinyl]oxy]-*N*-[4-(trifluoromethyl)phenyl]-1*H*-benzimidazol-2-amine (RAF265); indisulam (E7070); roscovitine (CYC202); palbociclib (PD0332991); dinaciclib (SCH727965); N-[5-[[(5-*tert*-butyloxazol-2-yl)methyl]thio]thiazol-2-yl]piperidine-4-carboxamide (BMS 387032); 4-[[9-chloro-7-(2,6-difluorophenyl)-5*H*-pyrimido[5,4-*d*][2]benzazepin-2-yl]amino]-benzoic acid (MLN8054); 5-[3-(4,6-difluoro-1H-benzimidazol-2-yl)-1H-indazol-5-yl]-N-ethyl-4-methyl-3-pyridinemethanamine (AG-024322); 4-(2,6-dichlorobenzoylamino)-1H-pyrazole-3-carboxylic acid N-(piperidin-4-yl)amide (AT7519); 4-[2-methyl-1-(1-methylethyl)-1*H*-imidazol-5-yl]-*N*-[4-(methylsulfonyl)phenyl]- 2-pyrimidinamine (AZD5438); and XL281 (BMS908662).

In one embodiment of the methods or uses described herein, the kinase inhibitor is a CDK4 inhibitor, e.g., palbociclib (PD0332991), and the palbociclib is administered at a dose of about 50 mg, 60 mg, 70 mg, 75 mg, 80 mg, 90 mg, 100 mg, 105 mg, 110 mg, 115 mg, 120 mg, 125 mg, 130 mg, 135 mg (e.g., 75 mg, 100 mg or 125 mg) daily for a period of time, e.g., daily for 14-21 days of a 28 day cycle, or daily for 7-

12 days of a 21 day cycle. In one embodiment, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more cycles of palbociclib are administered.

In one embodiment of the methods or uses described herein, the kinase inhibitor is a BTK inhibitor selected from ibrutinib (PCI-32765); GDC-0834; RN-486; CGI-560; CGI-1764; HM-71224; CC-292; ONO-4059; CNX-774; and LFM-A13. In one embodiment, the BTK inhibitor does not reduce or inhibit the kinase activity of interleukin-2-inducible kinase (ITK), and is selected from GDC-0834; RN-486; CGI-560; CGI-1764; HM-71224; CC-292; ONO-4059; CNX-774; and LFM-A13.

In one embodiment of the methods or uses described herein, the kinase inhibitor is a BTK inhibitor, e.g., ibrutinib (PCI-32765), and the ibrutinib is administered at a dose of about 250 mg, 300 mg, 350 mg, 400 mg, 420 mg, 440 mg, 460 mg, 480 mg, 500 mg, 520 mg, 540 mg, 560 mg, 580 mg, 600 mg (e.g., 250 mg, 420 mg or 560 mg) daily for a period of time, e.g., daily for 21 day cycle, or daily for 28 day cycle. In one embodiment, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more cycles of ibrutinib are administered.

In one embodiment of the methods or uses described herein, the kinase inhibitor is a BTK inhibitor that does not inhibit the kinase activity of ITK, e.g., RN-486, and RN-486 is administered at a dose of about 100 mg, 110 mg, 120 mg, 130 mg, 140 mg, 150 mg, 160 mg, 170 mg, 180 mg, 190 mg, 200 mg, 210 mg, 220 mg, 230 mg, 240 mg, 250 mg (e.g., 150 mg, 200 mg or 250 mg) daily for a period of time, e.g., daily a 28 day cycle. In one embodiment, 1, 2, 3, 4, 5, 6, 7, or more cycles of RN-486 are administered.

In one embodiment of the methods or uses described herein, the kinase inhibitor is an mTOR inhibitor selected from temsirolimus; ridaforolimus (1*R*,2*R*,4*S*)-4-[(2*R*)-2 [(1*R*,9*S*,12*S*,15*R*,16*E*,18*R*,19*R*,21*R*, 23*S*,24*E*,26*E*,28*Z*,30*S*,32*S*,35*R*)-1,18-dihydroxy-19,30-dimethoxy-15,17,21,23, 29,35-hexamethyl-2,3,10,14,20-pentaoxo-11,36-dioxa-4-azatricyclo[30.3.1.$0^{4,9}$] hexatriaconta-16,24,26,28-tetraen-12-yl]propyl]-2-methoxycyclohexyl dimethylphosphinate, also known as AP23573 and MK8669; everolimus (RAD001); rapamycin (AY22989); simapimod; (5-{2,4-bis[(3*S*)-3-methylmorpholin-4-yl]pyrido[2,3-*d*]pyrimidin-7-yl}-2-methoxyphenyl)methanol (AZD8055); 2-amino-8-[*trans*-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PF04691502); and N^2-[1,4-dioxo-4-[[4-(4-oxo-8-phenyl-4*H*-1-benzopyran-2-yl)morpholinium-4-yl]methoxy]butyl]-L-arginylglycyl-L-α-aspartylL-serine- (SEQ ID NO: 6659), inner salt (SF1126); and XL765.

In one embodiment of the methods or uses described herein, the kinase inhibitor is an mTOR inhibitor, e.g., rapamycin, and the rapamycin is administered at a dose of about 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg (e.g., 6 mg) daily for a period of time, e.g., daily for 21 day cycle, or daily for 28 day cycle. In one embodiment, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more cycles of rapamycin are

administered. In one embodiment, the kinase inhibitor is an mTOR inhibitor, e.g., everolimus and the everolimus is administered at a dose of about 2 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg, 11 mg, 12 mg, 13 mg, 14 mg, 15 mg (e.g., 10 mg) daily for a period of time, e.g., daily for 28 day cycle. In one embodiment, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more cycles of everolimus are administered.

In one embodiment of the methods or uses described herein, the kinase inhibitor is an MNK inhibitor selected from CGP052088; 4-amino-3-(p-fluorophenylamino)-pyrazolo [3,4-*d*] pyrimidine (CGP57380); cercosporamide; ETC-1780445-2; and 4-amino-5-(4-fluoroanilino)-pyrazolo [3,4-*d*] pyrimidine.

In one embodiment of the methods or uses described herein, the kinase inhibitor is a dual phosphatidylinositol 3-kinase (PI3K) and mTOR inhibitor selected from 2-Amino-8-[*trans*-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PF-04691502); *N*-[4-[[4-(Dimethylamino)-1-piperidinyl]carbonyl]phenyl]-*N*'-[4-(4,6-di-4-morpholinyl-1,3,5-triazin-2-yl)phenyl]urea (PF-05212384, PKI-587); 2-Methyl-2-{4-[3-methyl-2-oxo-8-(quinolin-3-yl)-2,3-dihydro-1*H*-imidazo[4,5-c]quinolin-1-yl]phenyl}propanenitrile (BEZ-235); apitolisib (GDC-0980, RG7422); 2,4-Difluoro-N-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide (GSK2126458); 8-(6-methoxypyridin-3-yl)-3-methyl-1-(4-(piperazin-1-yl)-3-(trifluoromethyl)phenyl)-1H-imidazo[4,5-c]quinolin-2(3H)-one Maleic acid (NVP-BGT226); 3-[4-(4-Morpholinylpyrido[3',2':4,5]furo[3,2-d]pyrimidin-2-yl]phenol (PI-103); 5-(9-isopropyl-8-methyl-2-morpholino-9H-purin-6-yl)pyrimidin-2-amine (VS-5584, SB2343); and N-[2-[(3,5-Dimethoxyphenyl)amino]quinoxalin-3-yl]-4-[(4-methyl-3-methoxyphenyl)carbonyl]aminophenylsulfonamide (XL765).

In one embodiment of the methods or uses described herein, a CAR expressing immune effector cell described herein is administered to a subject in combination with a protein tyrosine phosphatase inhibitor, e.g., a protein tyrosine phosphatase inhibitor described herein. In one embodiment, the protein tyrosine phosphatase inhibitor is an SHP-1 inhibitor, e.g., an SHP-1 inhibitor described herein, such as, e.g., sodium stibogluconate. In one embodiment, the protein tyrosine phosphatase inhibitor is an SHP-2 inhibitor.

In one embodiment of the methods or uses described herein, the cell of the invention is administered in combination with another agent, and the agent is a cytokine. The cytokine can be, e.g., IL-7; IL-15; a composition comprising a interleukin-15 (IL-15) polypeptide, a interleukin-15 receptor alpha (IL-15Ra) polypeptide, or a combination of both a IL-15 polypeptide and a IL-15Ra polypeptide e.g., hetIL-15; IL-18; IL-21; or a combination thereof. In another embodiment, the cell of the invention is administered in combination with a checkpoint inhibitor, e.g., a checkpoint inhibitor described herein. For example, in

one embodiment, the check point inhibitor inhibits an inhibitory molecule selected from PD-1, PD-L1, CTLA-4, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and TGF beta.

In one aspect, the invention provides a method of treating a subject, e.g., a subject having a condition described herein, with an allogeneic cell, for example an allogeneic immune effector cell, for example an allogeneic CAR-expressing T cell, comprising or which at any time comprised a gRNA molecule of the invention. In embodiments, the cell has been altered such that expression of the functional gene product of a gene comprising a target sequence complementary to the gRNA targeting domain has been reduced or eliminated.

In one aspect, the invention provides a method of treatment comprising:

(a) providing a population of cells from an allogeneic donor;

(b) introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a first gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule);

(c) optionally, selecting those cells in which expression of the gene product (e.g., functional gene product) of the gene comprising the target sequence complementary to the targeting domain of the first gRNA has been reduced or eliminated;

(d) transducing the cells with nucleic acid encoding a CAR as described herein; and

(e) administering the cells to a patient in need thereof, e.g., a patient who has a disease associated with expression of an antigen recognized by the CAR.

In embodiments, the first gRNA molecule comprises a targeting domain complementary to an allogeneic T cell target, e.g., a component of the TCR, for example, a first gRNA molecule comprising a targeting domain complementary to a target sequence in a gene selected from CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, and TRBC2. In embodiments, the first gRNA to CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, or TRBC2 is a first gRNA comprising a targeting domain listed in Table 1, Table 4 or Table 5. In embodiments, step (c) comprises selected those cells which are negative for TCR expression. In embodiments, the method further comprises administering to the patient an agent which selectively inhibits or depletes NK cells, for example and antibody or antigen binding fragment to an antigen specific to NK cells, e.g., which is not expressed on T cells.

In embodiments, the method further comprises introducing into the cells a second gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule), e.g., introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a second gRNA molecule of the invention

(or nucleic acid encoding said gRNA molecule). In embodiments, the second gRNA molecule comprises a targeting domain complementary to an allogeneic T cell target, e.g., a second gRNA molecule comprising a targeting domain complementary to a target sequence in a gene selected from B2M, HLA-A, HLA-B and HLA-C. In embodiments, the second gRNA to B2M, HLA-A, HLA-B or HLA-C is a second gRNA comprising a targeting domain of Table 1, or Table 3. In embodiments, step (c) optionally includes, selecting those cells in which expression of the gene product (e.g., functional gene product) of the gene comprising the target sequence complementary to the targeting domain of the first gRNA and in which expression of the gene product (e.g., functional gene product) of the gene comprising the target sequence complementary to the targeting domain of the second gRNA has been reduced or eliminated. In embodiments, step (c) comprises selected those cells which are negative for TCR expression and/or negative for B2M or HLA expression. In embodiments, the method further comprises administering to the patient an agent which selectively inhibits or depletes NK cells, for example and antibody or antigen binding fragment to an antigen specific to NK cells, e.g., which is not expressed on T cells.

In embodiments, the method further comprises introducing into the cells a third gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule), e.g., introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a second gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule). In embodiments, the third gRNA molecule comprises a targeting domain complementary to a target sequence in a gene of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule, e.g., a third gRNA molecule comprising a targeting domain complementary to a target sequence in a gene selected from CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, and PTPN11. In embodiments, the third gRNA comprises a targeting domain to CD274, HAVCR2, LAG3, PDCD1 or PTPN11 selected from the targeting domains of Table 2, or Table 6. In embodiments, step (c) optionally includes, selecting those cells in which expression of the gene product (e.g., functional gene product) of the gene comprising the target sequence complementary to the targeting domain of the first gRNA, in which expression of the gene product (e.g., functional gene product) of the gene comprising the target sequence complementary to the targeting domain of the second gRNA, and/or in which expression of the gene product (e.g., functional gene product) of the gene comprising the target sequence complementary to the targeting domain of the third gRNA has been reduced or eliminated. In embodiments, step (c) comprises selecting those cells which are negative for TCR expression, negative for B2M or HLA expression, and/or negative for expression of a targeted inhibitory molecule or downstream effector of signaling through an inhibitory molecule. In embodiments, the method further comprises administering

to the patient an agent which selectively inhibits or depletes NK cells, for example and antibody or antigen binding fragment to an antigen specific to NK cells, e.g., which is not expressed on T cells. In other embodiments, the third gRNA comprises a targeting domain complementary to a target sequence in a gene selected from CIITA, RFXANK, RFX5, RFXAP, e.g., as described herein. In embodiments, the third gRNA comprises a targeting domain complementary to a target sequence in a CIITA gene, e.g., as described herein, e.g., in Table 6c.

In any of the aforementioned aspects and embodiments the CAR is a CAR as described herein. In any of the aforementioned aspects and embodiments, the CAR is a BCMA CAR, e.g., a BCMA CAR described herein, e.g., comprises or is engineered to express a CAR comprising SEQ ID NO:8559. In aspects, the nucleic acid encoding the CAR is introduced into the cell by viral vector, e.g., lentiviral vector, transduction. In other aspects, the nucleic acid encoding the CAR is introduced as DNA that is incorporated in the host cell genome at or near a site modified by one of theCRISPR systems introduced into said cells.

In one aspect, the invention provides a method of treatment comprising:

(a) providing a population of cells, e.g, immune effector cells, e.g., T cell or NK cells, e.g., as described herein, (e.g., a population of said cells from an allogeneic donor);

(b) introducing into the population of cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a first gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, TRBC2, e.g., a target sequence in TRAC, TRBC1 or TRBC2, e.g., a target sequence in TRAC, e.g., as described herein;

(c) introducing into the population of cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a second gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in B2M, e.g., as described herein;

(d) optionally, selecting those cells in which expression of functional TCR has been reduced or eliminated;

(e) transducing the population of cells with nucleic acid encoding a CAR, e.g., as described herein, e.g., a BCMA CAR as described herein; and

(f) administering the population of cells to a patient in need thereof, e.g., a patient who has a disease associated with expression of an antigen recognized by the CAR.

In one embodiment, the method further comprises the step of (g) introducing into said population of cells into the population of cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a third gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in CIITA, RFXANK, RFX5 or RFXAP, e.g., complementary to a target sequence in CIITA, e.g., as described herein.

In one aspect, the invention provides a method of treatment comprising:

(a) providing a population of cells, e.g, immune effector cells, e.g., T cell or NK cells, e.g., as described herein, (e.g., a population of said cells from an allogeneic donor);

(b) introducing into the population of cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a first gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, TRBC2, e.g., a target sequence in TRAC, TRBC1 or TRBC2, e.g., a target sequence in TRAC, e.g., as described herein;

(c) introducing into the population of cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a second gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in NLRC5, e.g., as described herein;

(d) optionally, selecting those cells in which expression of functional TCR has been reduced or eliminated;

(e) transducing the population of cells with nucleic acid encoding a CAR, e.g., as described herein, e.g., a BCMA CAR as described herein; and

(f) administering the population of cells to a patient in need thereof, e.g., a patient who has a disease associated with expression of an antigen recognized by the CAR.

In one embodiment, the method further comprises the step of (g) introducing into said population of cells into the population of cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a third gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in CIITA, RFXANK, RFX5 or RFXAP, e.g., complementary to a target sequence in CIITA, e.g., as described herein.

In one aspect, the invention provides a method of treatment comprising:

(a) providing a population of cells, for example immune effector cells (e.g., NK or T cells), from an allogeneic or autologous donor;

(b) introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a first gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule);

(c) optionally, selecting those cells in which expression of the gene product (e.g., functional gene product) of the gene comprising the target sequence complementary to the targeting domain of the first gRNA has been reduced or eliminated;

(d) transducing the cells with nucleic acid encoding a CAR as described herein; and

(e) administering the cells to a patient in need thereof, e.g., a patient who has a disease associated with expression of an antigen recognized by the CAR.

In embodiments, the first gRNA molecule comprises a targeting domain complementary to a target sequence in a gene of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule, e.g., a first gRNA molecule comprising a targeting domain complementary to a target sequence in a gene selected from CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, and PTPN11. In embodiments, the first gRNA comprises a targeting domain to CD274, HAVCR2, LAG3, PDCD1 or PTPN11 selected from the targeting domains of Table 2 or Table 6. In embodiments, step (c) optionally includes selecting those cells in which expression of the gene product (e.g., functional gene product) of the gene comprising the target sequence complementary to the targeting domain of the first gRNA has been reduced or eliminated.

In embodiments, the method further comprises introducing into the cells at least a second gRNA molecule (e.g., 2 or more gRNA molecules) of the invention (or nucleic acid encoding said gRNA molecule(s)). In embodiments, each additional gRNA molecule(s), e.g., the second gRNA molecule, comprises a targeting domain complementary to a target sequence in a gene of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule, e.g., to a target sequence in a gene selected from CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, and PTPN11. In embodiments, the third gRNA comprises a targeting domain to CD274, HAVCR2, LAG3, PDCD1 or PTPN11 selected from the targeting domains of Table 2 or Table 6. In embodiments, each additional gRNA molecule comprises a targeting domain complementary to a sequence in the gene of a different inhibitory molecule or downstream effector of signaling through an inhibitory molecule In embodiments, step (c) optionally includes, selecting those

cells in which expression of the gene product (e.g., functional gene product) of the gene comprising the target sequence complementary to the targeting domain of the first gRNA, in which expression of the gene product (e.g., functional gene product) of the gene comprising the target sequence complementary to the targeting domain of the second gRNA, and/or in which expression of the gene product (e.g., functional gene product) of the gene comprising the target sequence complementary to the targeting domain of the third or more gRNA (if present) has been reduced or eliminated.

In one aspect, the invention provides a method of treating a subject, e.g., a subject having a condition described herein, with an allogeneic cell, for example an allogeneic immune effector cell, for example an allogeneic CAR-expressing T cell, comprising or which at any time comprised a gRNA molecule targeting a component of the TCR and a gRNA molecule targeting a target of an immunosuppressant. In embodiments, the cell has been altered such that expression of a functional TCR and expression of a functional target of an immunosuppressant has been reduced or eliminated.

In one aspect, the invention provides a method of treatment comprising:

(a) providing a population of cells from an allogeneic donor;

(b) introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a first gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, TRBC2;

(c) introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a second gRNA molecule of the invention (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in DCK, CD52, FKBP1A or NR3C1;

(d) optionally, selecting those cells in which expression of functional TCR, expression of functional target of an immunosuppressant, or expression of functional TCR and functional target of an immunosuppressant has been reduced or eliminated;

(e) transducing the cells with nucleic acid encoding a CAR as described herein; and

(f) administering the cells to a patient in need thereof, e.g., a patient who has a disease associated with expression of an antigen recognized by the CAR; and

(g) administering to the patient an immunosuppressant that binds to the target of an immunosuppressant targeted by the gRNA of (c).

In embodiments, the first gRNA to CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, or TRBC2 is a first gRNA comprising a targeting domain listed in Table 1, Table 4 or Table 5. In embodiments, the second

gRNA to DCK, CD52, FKBP1A or NR3C1 is a second gRNA molecule comprising a targeting domain listed in Table 1. In embodiments, the first gRNA targets TRAC, TRBC1 or TRBC2. In embodiments, the second gRNA targets DCK, and the immunosuppressant of (g) is a nucleoside analog-based drug such as cytarabine (cytosine arabinoside) or gemcitabine. In an embodiment, the second gRNA targets NR3C1 (the gene encoding for glucocorticoid receptor (GR)), and the immunosuppressant is a corticosteroid such as dexamethasone. In an embodiment, the second gRNA targets CD52, and the immunosuppressant is an anti-CD52 antibody or antigen-binding fragment thereof such as alemtuzumab (CAMPATH®). In an embodiment, the second gRNA targets FKBP1A, and the immunosuppressant is FK506 (or FKBP12-binding fragment or analog thereof), cyclosporine, rapamycin or rapalog, or mTor inhibitor such as RAD001.

In any of the embodiments and aspects of the invention, including in any of the aforementioned aspects and embodiments, the population of cells may be enriched, for example, during manufacturing, for a particular subset or subpopulation, e.g., for T-cells, e.g., for stem-cell memory-like T cells.

In another aspect, a method of treating a subject, e.g., reducing or ameliorating, a hyperproliferative condition or disorder (e.g., a cancer), e.g., solid tumor, a soft tissue tumor, or a metastatic lesion, in a subject is provided. As used herein, the term "cancer" is meant to include all types of cancerous growths or oncogenic processes, metastatic tissues or malignantly transformed cells, tissues, or organs, irrespective of histopathologic type or stage of invasiveness. Examples of solid tumors include malignancies, e.g., sarcomas, adenocarcinomas, and carcinomas, of the various organ systems, such as those affecting liver, lung, breast, lymphoid, gastrointestinal (e.g., colon), genitourinary tract (e.g., renal, urothelial cells), prostate and pharynx. Adenocarcinomas include malignancies such as most colon cancers, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine and cancer of the esophagus. In one embodiment, the cancer is a melanoma, e.g., an advanced stage melanoma. Metastatic lesions of the aforementioned cancers can also be treated or prevented using the methods and compositions of the invention. Examples of other cancers that can be treated include bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin Disease, non-Hodgkin lymphoma, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic

lymphocytic leukemia, solid tumors of childhood, lymphocytic lymphoma, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers including those induced by asbestos, and combinations of said cancers. Treatment of metastatic cancers, e.g., metastatic cancers that express PD-L1 (Iwai et al. (2005) Int. Immunol. 17:133-144) can be effected using the antibody molecules described herein.

Exemplary cancers whose growth can be inhibited include cancers typically responsive to immunotherapy. Non-limiting examples of cancers for treatment include melanoma (e.g., metastatic malignant melanoma), renal cancer (e.g. clear cell carcinoma), prostate cancer (e.g. hormone refractory prostate adenocarcinoma), breast cancer, colon cancer and lung cancer (e.g. non-small cell lung cancer). Additionally, refractory or recurrent malignancies can be treated using the molecules described herein.

In one aspect, the invention pertains to a method of treating cancer in a subject. In one aspect, the cancer associated with expression of a cancer associate antigen as described herein is a hematological cancer. In one aspect, the hematological cancer is a leukemia or a lymphoma. In one aspect, a cancer associated with expression of a cancer associate antigen as described herein includes cancers and malignancies including, but not limited to, e.g., one or more acute leukemias including but not limited to, e.g., B-cell acute Lymphoid Leukemia ("BALL"), T-cell acute Lymphoid Leukemia ("TALL"), acute lymphoid leukemia (ALL); one or more chronic leukemias including but not limited to, e.g., chronic myelogenous leukemia (CML), Chronic Lymphoid Leukemia (CLL). Additional cancers or hematologic conditions associated with expression of a cancer associate antigen as described herein include, but are not limited to, e.g., B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, Follicular lymphoma, Hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and "preleukemia" which are a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells, and the like. Further a disease associated with a cancer associate antigen as described herein expression include, but not limited to, e.g., atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases associated with expression of a cancer associate antigen as described herein.

In some embodiments, a cancer that can be treated is multiple myeloma. Generally, myeloma cells are thought to be negative for a cancer associate antigen as described herein expression by flow cytometry.

Thus, in some embodiments, a cell further engineered to express a CAR as described herein, e.g., a CD19 CAR or BCMA CAR as described herein, may be used to target myeloma cells. In some embodiments, cars of the present invention therapy can be used in combination with one or more additional therapies, e.g., lenalidomide treatment.

In various aspects, the immune effector cells (e.g., T cells, NK cells) of the invention administered to the patient, or their progeny, persist in the patient for at least four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve months, thirteen months, fourteen month, fifteen months, sixteen months, seventeen months, eighteen months, nineteen months, twenty months, twenty-one months, twenty-two months, twenty-three months, two years, three years, four years, or five years after administration of the T cell or NK cell to the patient.

The invention also includes a type of cellular therapy where immune effector cells (e.g., T cells, NK cells) are further modified, e.g., by in vitro transcribed RNA, to transiently express a chimeric antigen receptor (CAR) and the CAR T cell or NK cell is infused to a recipient in need thereof. The infused cell is able to kill tumor cells in the recipient. Thus, in various aspects, the immune effector cells (e.g., T cells, NK cells) administered to the patient, is present for less than one month, e.g., three weeks, two weeks, one week, after administration of the T cell or NK cell to the patient.

Without wishing to be bound by any particular theory, the anti-tumor immunity response elicited by the CAR-modified immune effector cells (e.g., T cells, NK cells) may be an active or a passive immune response, or alternatively may be due to a direct vs indirect immune response. In one aspect, the CAR transduced immune effector cells (e.g., T cells, NK cells) exhibit specific proinflammatory cytokine secretion and potent cytolytic activity in response to human cancer cells expressing the a cancer associate antigen as described herein, resist soluble a cancer associate antigen as described herein inhibition, mediate bystander killing and mediate regression of an established human tumor. For example, antigen-less tumor cells within a heterogeneous field of a cancer associate antigen as described herein-expressing tumor may be susceptible to indirect destruction by a cancer associate antigen as described herein-redirected immune effector cells (e.g., T cells, NK cells) that has previously reacted against adjacent antigen-positive cancer cells.

Ex vivo procedures are well known in the art and are discussed more fully below. Briefly, cells are isolated from a mammal (e.g., a human) and genetically modified (i.e., transduced or transfected in vitro) with a gRNA molecule of the invention, and optionally, a vector expressing a CAR disclosed herein. The modified cell can be administered to a mammalian recipient to provide a therapeutic benefit. The mammalian recipient may be a human and the cell can be autologous with respect to the recipient. Alternatively, the cells can be allogeneic with respect to the recipient.

The procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference, can be applied to the cells of the present invention. Other suitable methods are known in the art, therefore the present invention is not limited to any particular method of ex vivo expansion of the cells. Briefly, ex vivo culture and expansion of immune effector cells (e.g., T cells, NK cells) comprises: (1) collecting CD34+ hematopoietic stem and progenitor cells from a mammal from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-L, IL-1, IL-3 and c-kit ligand, can be used for culturing and expansion of the cells.

Procedures for ex vivo expansion of immune effector cells, e.g., T cells, are described, for example, in WO2015/142675, the contents of which are hereby incorporated by reference in their entirety. Such procedures may be useful when used in conjunction with the methods described herein.

In addition to using a cell-based vaccine in terms of ex vivo immunization, the present invention also provides compositions and methods for in vivo immunization to elicit an immune response directed against an antigen in a patient.

Generally, the cells activated and expanded as described herein may be utilized in the treatment and prevention of diseases that arise in individuals who are immunocompromised. In particular, the CAR-modified immune effector cells (e.g., T cells, NK cells) of the invention are used in the treatment of diseases, disorders and conditions associated with expression of a cancer associate antigen as described herein. In certain aspects, the cells of the invention are used in the treatment of patients at risk for developing diseases, disorders and conditions associated with expression of a cancer associate antigen as described herein. Thus, the present invention provides methods for the treatment or prevention of diseases, disorders and conditions associated with expression of a cancer associate antigen as described herein comprising administering to a subject in need thereof, a therapeutically effective amount of the CAR-modified immune effector cells (e.g., T cells, NK cells) of the invention.

In one aspect the cells of the invention, including the cells further engineered to express a CAR, may be used to treat a proliferative disease such as a cancer or malignancy or is a precancerous condition such as a myelodysplasia, a myelodysplastic syndrome or a preleukemia. Further a disease associated with a cancer associate antigen as described herein expression include, but not limited to, e.g., atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases expressing a cancer associated antigen as described herein. Non-cancer related indications associated with expression of a cancer associate antigen as described herein include, but are not limited to, e.g., autoimmune disease, (e.g., lupus), inflammatory disorders (allergy and asthma) and transplantation.

The cells (e.g., T cells, NK cells) of the present invention may be administered either alone, or as a pharmaceutical composition in combination with diluents and/or with other components such as IL-2 or other cytokines or cell populations.

Hematologic Cancer

Hematological cancer conditions are the types of cancer such as leukemia, lymphoma, and malignant lymphoproliferative conditions that affect blood, bone marrow and the lymphatic system.

Leukemia can be classified as acute leukemia and chronic leukemia. Acute leukemia can be further classified as acute myelogenous leukemia (AML) and acute lymphoid leukemia (ALL). Chronic leukemia includes chronic myelogenous leukemia (CML) and chronic lymphoid leukemia (CLL). Other related conditions include myelodysplastic syndromes (MDS, formerly known as "preleukemia") which are a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells and risk of transformation to AML.

Lymphoma is a group of blood cell tumors that develop from lymphocytes. Exemplary lymphomas include non-Hodgkin lymphoma and Hodgkin lymphoma.

The present invention also provides methods for inhibiting the proliferation or reducing a cancer associated antigen as described herein-expressing cell population, the methods comprising contacting a population of cells comprising a cancer associated antigen as described herein-expressing cell with a cell of the invention (e.g., an NK cell or T cell) further engineered to express a CAR that binds to the a cancer associated antigen as described herein-expressing cell. In a specific aspect, the present invention provides methods for inhibiting the proliferation or reducing the population of cancer cells expressing a cancer associated antigen as described herein, the methods comprising contacting a cancer associate antigen as described herein-expressing cancer cell population with a T cell or NK cell of the invention further engineered to express a CAR that binds to a cancer associated antigen as described herein-expressing cell. In one aspect, the present invention provides methods for inhibiting the proliferation or reducing the population of cancer cells expressing a cancer associated antigen as described herein, the methods comprising contacting a cancer associated antigen as described herein-expressing cancer cell population with a T cell or NK cell of the invention further engineered to express a CAR that binds to a cancer associated antigen as described herein-expressing cell. In certain aspects, T cell or NK cell of the invention reduces the quantity, number, amount or percentage of cells and/or cancer cells by at least 25%, at least 30%, at least 40%, at least 50%, at least 65%, at least 75%, at least 85%, at least 95%, or at least 99% in a subject with or animal model for myeloid leukemia or another cancer associated with a cancer

associated antigen as described herein-expressing cells relative to a negative control. In one aspect, the subject is a human.

The present invention also provides methods for preventing, treating and/or managing a disease associated with a cancer associated antigen as described herein-expressing cells (e.g., a hematologic cancer or atypical cancer expessing a cancer associated antigen as described herein), the methods comprising administering to a subject in need a T cell or NK cell of the invention, including those further engineered to express a CAR that binds to a cancer associated antigen as described herein-expressing cell. In one aspect, the subject is a human. Non-limiting examples of disorders associated with a cancer associated antigen as described herein-expressing cells include autoimmune disorders (such as lupus), inflammatory disorders (such as allergies and asthma) and cancers (such as hematological cancers or atypical cancers expessing a cancer associated antigen as described herein).

The present invention also provides methods for preventing, treating and/or managing a disease associated with a cancer associated antigen as described herein-expressing cells, the methods comprising administering to a subject in need a T cell or NK cell of the invention, including those further engineered to express a CAR that binds to a cancer associated antigen as described herein-expressing cell. In one aspect, the subject is a human.

The present invention provides methods for preventing relapse of cancer associated with a cancer associated antigen as described herein-expressing cells, the methods comprising administering to a subject in need thereof aT cell or NK cell of the invention, including those further engineered to express a CAR that binds to a cancer associated antigen as described herein-expressing cell. In one aspect, the methods comprise administering cell in combination with an effective amount of another therapy.

Pharmaceutical compositions and treatments

Pharmaceutical compositions of the present invention may comprise a cell, e.g., a plurality of cells, as described herein, in combination with one or more pharmaceutically or physiologically acceptable carriers, diluents or excipients. Such compositions may comprise buffers such as neutral buffered saline, phosphate buffered saline and the like; carbohydrates such as glucose, mannose, sucrose or dextrans, mannitol; proteins; polypeptides or amino acids such as glycine; antioxidants; chelating agents such as EDTA or glutathione; adjuvants (e.g., aluminum hydroxide); and preservatives. Compositions of the present invention are in one aspect formulated for intravenous administration.

Pharmaceutical compositions of the present invention may be administered in a manner appropriate to the disease to be treated (or prevented). The quantity and frequency of administration will be determined by

such factors as the condition of the patient, and the type and severity of the patient's disease, although appropriate dosages may be determined by clinical trials.

In one embodiment, the pharmaceutical composition is substantially free of, e.g., there are no detectable levels of a contaminant, e.g., selected from the group consisting of endotoxin, mycoplasma, replication competent lentivirus (RCL), p24, VSV-G nucleic acid, HIV gag, residual anti-CD3/anti-CD28 coated beads, mouse antibodies, pooled human serum, bovine serum albumin, bovine serum, culture media components, vector packaging cell or plasmid components, a bacterium and a fungus. In one embodiment, the bacterium is at least one selected from the group consisting of Alcaligenes faecalis, Candida albicans, Escherichia coli, Haemophilus influenza, Neisseria meningitides, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pneumonia, and Streptococcus pyogenes group A.

When "an immunologically effective amount," "an anti-tumor effective amount," "a tumor-inhibiting effective amount," or "therapeutic amount" is indicated, the precise amount of the compositions of the present invention to be administered can be determined by a physician with consideration of individual differences in age, weight, tumor size, extent of infection or metastasis, and condition of the patient (subject). It can generally be stated that a pharmaceutical composition comprising the immune effector cells (e.g., T cells, NK cells) described herein may be administered at a dosage of 10^4 to 10^9 cells/kg body weight, in some instances 10^5 to 10^6 cells/kg body weight, including all integer values within those ranges. T cell compositions may also be administered multiple times at these dosages. The cells can be administered by using infusion techniques that are commonly known in immunotherapy (see, e.g., Rosenberg et al., New Eng. J. of Med. 319:1676, 1988).

In certain aspects, it may be desired to administer activated immune effector cells (e.g., T cells, NK cells) to a subject and then subsequently redraw blood (or have an apheresis performed), activate immune effector cells (e.g., T cells, NK cells) therefrom according to the present invention, and reinfuse the patient with these activated and expanded immune effector cells (e.g., T cells, NK cells). This process can be carried out multiple times every few weeks. In certain aspects, immune effector cells (e.g., T cells, NK cells) can be activated from blood draws of from 10cc to 400cc. In certain aspects, immune effector cells (e.g., T cells, NK cells) are activated from blood draws of 20cc, 30cc, 40cc, 50cc, 60cc, 70cc, 80cc, 90cc, or 100cc.

The administration of the subject compositions may be carried out in any convenient manner, including by aerosol inhalation, injection, ingestion, transfusion, implantation or transplantation. The compositions described herein may be administered to a patient trans arterially, subcutaneously, intradermally, intratumorally, intranodally, intramedullary, intramuscularly, by intravenous (i.v.) injection, or intraperitoneally. In one aspect, the T cell compositions of the present invention are administered to a

patient by intradermal or subcutaneous injection. In one aspect, the T cell compositions of the present invention are administered by i.v. injection. The compositions of immune effector cells (e.g., T cells, NK cells) may be injected directly into a tumor, lymph node, or site of infection.

In a particular exemplary aspect, subjects may undergo leukapheresis, wherein leukocytes are collected, enriched, or depleted ex vivo to select and/or isolate the cells of interest, e.g., T cells. These T cell isolates may be expanded by methods known in the art and treated as described herein thereby creating a T cell of the invention. Subjects in need thereof may subsequently undergo standard treatment with high dose chemotherapy followed by peripheral blood stem cell transplantation. In certain aspects, following or concurrent with the transplant, subjects receive an infusion of the expanded T cells of the present invention. In an additional aspect, expanded cells are administered before or following surgery.

The dosage of the above treatments to be administered to a patient will vary with the precise nature of the condition being treated and the recipient of the treatment. The scaling of dosages for human administration can be performed according to art-accepted practices. The dose for CAMPATH, for example, will generally be in the range 1 to about 100 mg for an adult patient, usually administered daily for a period between 1 and 30 days. The preferred daily dose is 1 to 10 mg per day although in some instances larger doses of up to 40 mg per day may be used (described in U.S. Patent No. 6,120,766).

In one aspect, CAR-expressing cells of the present inventions are generated using lentiviral viral vectors, such as lentivirus. Cells, e.g., CARTs, generated that way will have stable CAR expression.

In one aspect, CAR-expressing cells, e.g., CARTs, are generated using a viral vector such as a gammaretroviral vector, e.g., a gammaretroviral vector described herein. CARTs generated using these vectors can have stable CAR expression.

In one aspect, CARTs transiently express CAR vectors for 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 days after transduction. Transient expression of CARs can be effected by RNA CAR vector delivery. In one aspect, the CAR RNA is transduced into the T cell by electroporation.

A potential issue that can arise in patients being treated using transiently expressing CAR immune effector cells (e.g., T cells, NK cells) (particularly with murine scFv bearing CARTs) is anaphylaxis after multiple treatments.

Without being bound by this theory, it is believed that such an anaphylactic response might be caused by a patient developing humoral anti-CAR response, i.e., anti-CAR antibodies having an anti-IgE isotype. It is thought that a patient's antibody producing cells undergo a class switch from IgG isotype (that does not cause anaphylaxis) to IgE isotype when there is a ten to fourteen day break in exposure to antigen.

If a patient is at high risk of generating an anti-CAR antibody response during the course of transient CAR therapy (such as those generated by RNA transductions), CART infusion breaks should not last more than ten to fourteen days.

Methods of making modified CAR-expressing cells

In another aspect, the invention pertains to a method of making a cell (e.g., an immune effector cell or population thereof) comprising introducing into (e.g., transducing) a cell, e.g., a T cell or a NK cell described herein, with a vector of comprising a nucleic acid encoding a CAR, e.g., a CAR described herein; or a nucleic acid encoding a CAR molecule e.g., a CAR described herein.

The cell in the methods is an immune effector cell (e.g., aT cell or a NK cell, or a combination thereof). In some embodiments, the cell in the methods is diaglycerol kinase (DGK) and/or Ikaros deficient.

In some embodiments, the introducing the nucleic acid molecule encoding a CAR comprises transducing a vector comprising the nucleic acid molecule encoding a CAR, or transfecting the nucleic acid molecule encoding a CAR, wherein the nucleic acid molecule is an in vitro transcribed RNA.

In some embodiments, the method further comprises:

providing a population of immune effector cells (e.g., T cells or NK cells); and
removing T regulatory cells from the population, thereby providing a population of T regulatory-depleted cells;
wherein steps a) and b) are performed prior to introducing the nucleic acid encoding the CAR and/or CRISPR system to the population.

In embodiments of the methods, the T regulatory cells comprise CD25+ T cells, and are removed from the cell population using an anti-CD25 antibody, or fragment thereof. The anti-CD25 antibody, or fragment thereof, can be conjugated to a substrate, e.g., a bead.
In other embodiments, the population of T regulatory-depleted cells provided from step (b) contains less than 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells.

In yet other embodiments, the method further comprises removing cells from the population which express a tumor antigen that does not comprise CD25 to provide a population of T regulatory-depleted and tumor antigen depleted cells prior to introducing the nucleic acid encoding a CAR to the population. The tumor antigen can be selected from CD19, CD30, CD38, CD123, CD20, CD14 or CD11b, or a combination thereof.

In other embodiments, the method further comprises removing cells from the population which express a checkpoint inhibitor, to provide a population of T regulatory-depleted and inhibitory molecule depleted cells prior to introducing the nucleic acid encoding a CAR or CRISPR system to the population. The

checkpoint inhibitor can be chosen from PD-1, LAG-3, TIM3, B7-H1, CD160, P1H, 2B4, CEACAM (e.g., CEACAM-1, CEACAM-3, and/or CEACAM-5), TIGIT, CTLA-4, BTLA, and LAIR1.

Further embodiments disclosed herein encompass providing a population of immune effector cells. The population of immune effector cells provided can be selected based upon the expression of one or more of CD3, CD28, CD4, CD8, CD45RA, and/or CD45RO. In certain embodiments, the population of immune effector cells provided are CD3+ and/or CD28+.

In certain embodiments of the method, the method further comprises expanding the population of cells after the nucleic acid molecule encoding a CAR has been introduced.

In embodiments, the population of cells is expanded for a period of 8 days or less.

In certain embodiments, the population of cells is expanded in culture for 5 days, and the resulting cells are more potent than the same cells expanded in culture for 9 days under the same culture conditions.

In other embodiments, the population of cells is expanded in culture for 5 days show at least a one, two, three or four fold increase in cell doublings upon antigen stimulation as compared to the same cells expanded in culture for 9 days under the same culture conditions.

In yet other embodiments, the population of cells is expanded in culture for 5 days, and the resulting cells exhibit higher proinflammatory IFN-γ and/or GM-CSF levels, as compared to the same cells expanded in culture for 9 days under the same culture conditions.

In other embodiments, the population of cells is expanded by culturing the cells in the presence of an agent that stimulates a CD3/TCR complex associated signal and/or a ligand that stimulates a costimulatory molecule on the surface of the cells. The agent can be a bead conjugated with anti-CD3 antibody, or a fragment thereof, and/or anti-CD28 antibody, or a fragment thereof.

In other embodiments, the population of cells is expanded in an appropriate media that includes one or more interleukin that result in at least a 200-fold, 250-fold, 300-fold, or 350-fold increase in cells over a 14 day expansion period, as measured by flow cytometry.

In other embodiments, the population of cells is expanded in the presence IL-15 and/or IL-7.

In certain embodiments, the method further includes cryopresercing he population of the cells after the appropriate expansion period.

In yet other embodiments, the method of making discosed herein further comprises contacting the population of immune effector cells with a nucleic acid encoding a telomerase subunit, e.g., hTERT. The the nucleic acid encoding the telomerase subunit can be DNA.

The present invention also provides a method of generating a population of RNA-engineered cells, e.g., cells described herein, e.g., immune effector cells (e.g., T cells, NK cells), transiently expressing exogenous RNA. The method comprises introducing an *in vitro* transcribed RNA or synthetic RNA into a cell, where the RNA comprises a nucleic acid encoding a CAR molecule described herein.

In another aspect, the invention pertains to a method of providing an anti-tumor immunity in a subject comprising administering to the subject an effective amount of a cell comprising a CAR molecule, e.g., a cell expressing a CAR molecule described herein. In one embodiment, the cell is an autologous T cell or NK cell. In one embodiment, the cell is an allogeneic T cell or NK cell. In one embodiment, the subject is a human.

In one aspect, the invention includes a population of autologous cells that are transfected or transduced with a vector comprising a nucleic acid molecule encoding a CAR molecule, e.g., as described herein. In one embodiment, the vector is a retroviral vector. In one embodiment, the vector is a self-inactivating lentiviral vector as described elsewhere herein. In one embodiment, the vector is delivered (e.g., by transfecting or electroporating) to a cell, e.g., a T cell or a NK cell, wherein the vector comprises a nucleic acid molecule encoding a CAR of the present invention as described herein, which is transcribed as an mRNA molecule, and the CARs of the present invention is translated from the RNA molecule and expressed on the surface of the cell.

In another aspect, the present invention provides a population of CAR-expressing cells, e.g., CAR-expressing immune effector cells (e.g., T cells or NK cells). In some embodiments, the population of CAR-expressing cells comprises a mixture of cells expressing different CARs. For example, in one embodiment, the population of CAR-expressing immune effector cells (e.g., T cells or NK cells) can include a first cell expressing a CAR having an antigen binding domain that binds to a first tumor antigen as described herein, and a second cell expressing a CAR having a different antigen binding domain that binds to a second tumor antigen as described herein. As another example, the population of CAR-expressing cells can include a first cell expressing a CAR that includes an antigen binding domain that binds to a tumor antigen as described herein, and a second cell expressing a CAR that includes an antigen binding domain to a target other than a tumor antigen as described herein. In one embodiment, the population of CAR-expressing cells includes, e.g., a first cell expressing a CAR that includes a primary intracellular signaling domain, and a second cell expressing a CAR that includes a secondary signaling domain, e.g., a costimulatory signaling domain.

In another aspect, the present invention provides a population of cells wherein at least one cell in the population expresses a CAR having an antigen binding domain that binds to a tumor antigen as described herein, and a second cell expressing another agent, e.g., an agent which enhances the activity of a CAR-

expressing cell. For example, in one embodiment, the agent can be an agent which inhibits an inhibitory molecule. Examples of inhibitory molecules include PD-1, PD-L1, CTLA-4, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and TGF beta. In one embodiment, the agent which inhibits an inhibitory molecule, e.g., is a molecule described herein, e.g., an agent that comprises a first polypeptide, e.g., an inhibitory molecule, associated with a second polypeptide that provides a positive signal to the cell, e.g., an intracellular signaling domain described herein. In one embodiment, the agent comprises a first polypeptide, e.g., of an inhibitory molecule such as PD-1, LAG-3, CTLA-4, CD160, BTLA, LAIR1, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), 2B4 and TIGIT, or a fragment of any of these, and a second polypeptide which is an intracellular signaling domain described herein (e.g., comprising a costimulatory domain (e.g., 41BB, CD27 or CD28, e.g., as described herein) and/or a primary signaling domain (e.g., a CD3 zeta signaling domain described herein). In one embodiment, the agent comprises a first polypeptide of PD-1 or a fragment thereof, and a second polypeptide of an intracellular signaling domain described herein (e.g., a CD28, CD27, OX40 or 4-IBB signaling domain described herein and/or a CD3 zeta signaling domain described herein).

In one embodiment, the nucleic acid molecule encoding a CAR of the present invention molecule, e.g., as described herein, is expressed as an mRNA molecule. In one embodiment, the genetically modified CAR of the present invention-expressing cells, e.g., immune effector cells (e.g., T cells, NK cells), can be generated by transfecting or electroporating an RNA molecule encoding the desired CARs (e.g., without a vector sequence) into the cell. In one embodiment, a CAR of the present invention molecule is translated from the RNA molecule once it is incorporated and expressed on the surface of the recombinant cell.

A method for generating mRNA for use in transfection involves *in vitro* transcription (IVT) of a template with specially designed primers, followed by polyA addition, to produce a construct containing 3' and 5' untranslated sequence ("UTR") (e.g., a 3' and/or 5' UTR described herein), a 5' cap (e.g., a 5' cap described herein) and/or Internal Ribosome Entry Site (IRES) (e.g., an IRES described herein), the nucleic acid to be expressed, and a polyA tail, typically 50-2000 bases in length (SEQ ID NO: 6638). RNA so produced can efficiently transfect different kinds of cells. In one embodiment, the template includes sequences for the CAR. In an embodiment, an RNA CAR vector is transduced into a cell, e.g., a T cell or a NK cell, by electroporation.

XII. Methods of Manufacture

The disclosure provides methods of manufacturing cells, e.g., T cells, e.g., allogeneic T cells, e.g., CAR-engineered cells modified, or to be modified, with the gRNA molecules described herein.

Introduction of CRISPR systems

The invention comprises cells, e.g immune effector cells, e.g., allogeneic or autologous cells, which comprise, or at one time comprised, one or more gRNA molecules as described herein. The CRISPR systems described herein may be introduced into the cells by any of the methods described herein. The cells may further be engineered to express a CAR as described herein.

In one aspect, the disclosure provides a method for making a cell comprising:

a) introducing a gRNA molecule, or nucleic acid encoding said gRNA molecule, as described herein into said cell;

b) introducing a Cas9 molecule as described herein, or nucleic acid encoding said Cas9 molecule, into said cell;

c) introducing nucleic acid encoding a CAR into said cell; and

d) expanding and activating the cells.

In embodiments, the introduction of a) and b) occur before steps c) and d). In embodiments, the introduciton of c) occurs before the introduciton of a) and b). In embodiments, the introduciton of c) and the expanding and activating of d) occurs before the introduciton of a) and b). In embodiments, the method further comprises e) selecting the cells which are CAR-expressing. In embodiments, the method further comprieses f) selecting the cells which have no or reduced expression of the gene targeted by the gRNA molecule of step a). For example, if the gRNA molecule comprises a targeting domain complementary to a target sequence in the TRAC gene (e.g., comprises a targeting domain comprising any one of SEQ ID NO: 5816 to SEQ ID NO: 5965 or SEQ ID NO: 5528 to SEQ ID NO: 5623), after the introduction of a) and b), cells which lack TCR expression (e.g., as detectible by, for example, an anti-CD3 antibody) may be sorted for further application in the methods of manufacture as described herein, or for further application in the therapeutic methods described herein. Such sorting may be done by methods known in the art such as cell sorting or mechanical separation (e.g., separation by magnetic bead-bound anti-CD3 antibody to remove those cells still expressing CD3/TCR).

Expansion and Activation of Cells

Immune effector cells such as T cells may be activated and expanded generally using methods as described, for example, in U.S. Patents 6,352,694; 6,534,055; 6,905,680; 6,692,964; 5,858,358; 6,887,466; 6,905,681; 7,144,575; 7,067,318; 7,172,869; 7,232,566; 7,175,843; 5,883,223; 6,905,874; 6,797,514; 6,867,041; and U.S. Patent Application Publication No. 20060121005, each of which is incorporated by reference in its entirety.

Generally, a population of immune effector cells e.g., T regulatory cell depleted cells, may be expanded by contact with a surface having attached thereto an agent that stimulates a CD3/TCR complex associated signal and a ligand that stimulates a costimulatory molecule on the surface of the T cells. In particular, T cell populations may be stimulated as described herein, such as by contact with an anti-CD3 antibody, or antigen-binding fragment thereof, or an anti-CD2 antibody immobilized on a surface, or by contact with a protein kinase C activator (e.g., bryostatin) in conjunction with a calcium ionophore. For co-stimulation of an accessory molecule on the surface of the T cells, a ligand that binds the accessory molecule is used. For example, a population of T cells can be contacted with an anti-CD3 antibody and an anti-CD28 antibody, under conditions appropriate for stimulating proliferation of the T cells. To stimulate proliferation of either CD4+ T cells or CD8+ T cells, an anti-CD3 antibody and an anti-CD28 antibody can be used. Examples of an anti-CD28 antibody include 9.3, B-T3, XR-CD28 (Diaclone, Besançon, France) can be used as can other methods commonly known in the art (Berg et al., Transplant Proc. 30(8):3975-3977, 1998; Haanen et al., J. Exp. Med. 190(9):13191328, 1999; Garland et al., J. Immunol Meth. 227(1-2):53-63, 1999).

In embodiments in which the cells have reduced or absent levels of expression or levels of a component of the TCR, activation may be achieved through means other than interatction with CD3. In cells which further express a CAR, activation may be achieved by contacting said cells with the antigen bound by the antigen-binding domain of the CAR, or a fragment thereof capable of binding the CAR. Such antigen or fragment thereof may be present on, for example, an antibody scaffold, a cell (e.g., an antigen presenting cell, e.g., a cell which naturally expresses said antigen or one which has been artificially engineered to express said antigen on its cell surface), or a solid support such as a bead or membrane.

In certain aspects, the primary stimulatory signal and the costimulatory signal for the T cell may be provided by different protocols. For example, the agents providing each signal may be in solution or coupled to a surface. When coupled to a surface, the agents may be coupled to the same surface (i.e., in "cis" formation) or to separate surfaces (i.e., in "trans" formation). Alternatively, one agent may be coupled to a surface and the other agent in solution. In one aspect, the agent providing the costimulatory signal is bound to a cell surface and the agent providing the primary activation signal is in solution or coupled to a surface. In certain aspects, both agents can be in solution. In one aspect, the agents may be in soluble form, and then cross-linked to a surface, such as a cell expressing Fc receptors or an antibody or other binding agent which will bind to the agents. In this regard, see for example, U.S. Patent Application Publication Nos. 20040101519 and 20060034810 for artificial antigen presenting cells (aAPCs) that are contemplated for use in activating and expanding T cells in the present invention.

In one aspect, the two agents are immobilized on beads, either on the same bead, i.e., "cis," or to separate beads, i.e., "trans." By way of example, the agent providing the primary activation signal is an anti-CD3 antibody or an antigen-binding fragment thereof and the agent providing the costimulatory signal is an anti-CD28 antibody or antigen-binding fragment thereof; and both agents are co-immobilized to the same bead in equivalent molecular amounts. In one aspect, a 1:1 ratio of each antibody bound to the beads for CD4+ T cell expansion and T cell growth is used. In certain aspects of the present invention, a ratio of anti CD3:CD28 antibodies bound to the beads is used such that an increase in T cell expansion is observed as compared to the expansion observed using a ratio of 1:1. In one particular aspect an increase of from about 1 to about 3 fold is observed as compared to the expansion observed using a ratio of 1:1. In one aspect, the ratio of CD3:CD28 antibody bound to the beads ranges from 100:1 to 1:100 and all integer values there between. In one aspect, more anti-CD28 antibody is bound to the particles than anti-CD3 antibody, i.e., the ratio of CD3:CD28 is less than one. In certain aspects, the ratio of anti CD28 antibody to anti CD3 antibody bound to the beads is greater than 2:1. In one particular aspect, a 1:100 CD3:CD28 ratio of antibody bound to beads is used. In one aspect, a 1:75 CD3:CD28 ratio of antibody bound to beads is used. In a further aspect, a 1:50 CD3:CD28 ratio of antibody bound to beads is used. In one aspect, a 1:30 CD3:CD28 ratio of antibody bound to beads is used. In one preferred aspect, a 1:10 CD3:CD28 ratio of antibody bound to beads is used. In one aspect, a 1:3 CD3:CD28 ratio of antibody bound to the beads is used. In yet one aspect, a 3:1 CD3:CD28 ratio of antibody bound to the beads is used.

Ratios of particles to cells from 1:500 to 500:1 and any integer values in between may be used to stimulate T cells or other target cells. As those of ordinary skill in the art can readily appreciate, the ratio of particles to cells may depend on particle size relative to the target cell. For example, small sized beads could only bind a few cells, while larger beads could bind many. In certain aspects the ratio of cells to particles ranges from 1:100 to 100:1 and any integer values in-between and in further aspects the ratio comprises 1:9 to 9:1 and any integer values in between, can also be used to stimulate T cells. The ratio of anti-CD3- and anti-CD28-coupled particles to T cells that result in T cell stimulation can vary as noted above, however certain preferred values include 1:100, 1:50, 1:40, 1:30, 1:20, 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, and 15:1 with one preferred ratio being at least 1:1 particles per T cell. In one aspect, a ratio of particles to cells of 1:1 or less is used. In one particular aspect, a preferred particle: cell ratio is 1:5. In further aspects, the ratio of particles to cells can be varied depending on the day of stimulation. For example, in one aspect, the ratio of particles to cells is from 1:1 to 10:1 on the first day and additional particles are added to the cells every day or every other day thereafter for up to 10 days, at final ratios of from 1:1 to 1:10 (based on cell counts on the day of addition). In one particular aspect, the ratio of particles to cells is 1:1 on the first day of stimulation and

adjusted to 1:5 on the third and fifth days of stimulation. In one aspect, particles are added on a daily or every other day basis to a final ratio of 1:1 on the first day, and 1:5 on the third and fifth days of stimulation. In one aspect, the ratio of particles to cells is 2:1 on the first day of stimulation and adjusted to 1:10 on the third and fifth days of stimulation. In one aspect, particles are added on a daily or every other day basis to a final ratio of 1:1 on the first day, and 1:10 on the third and fifth days of stimulation. One of skill in the art will appreciate that a variety of other ratios may be suitable for use in the present invention. In particular, ratios will vary depending on particle size and on cell size and type. In one aspect, the most typical ratios for use are in the neighborhood of 1:1, 2:1 and 3:1 on the first day.

In further aspects, the cells, such as T cells, are combined with agent-coated beads, the beads and the cells are subsequently separated, and then the cells are cultured. In an alternative aspect, prior to culture, the agent-coated beads and cells are not separated but are cultured together. In a further aspect, the beads and cells are first concentrated by application of a force, such as a magnetic force, resulting in increased ligation of cell surface markers, thereby inducing cell stimulation.

By way of example, cell surface proteins may be ligated by allowing paramagnetic beads to which anti-CD3 and anti-CD28 are attached (3x28 beads) to contact the T cells. In one aspect the cells (for example, 10^4 to 10^9 T cells) and beads (for example, DYNABEADS® M-450 CD3/CD28 T paramagnetic beads at a ratio of 1:1) are combined in a buffer, for example PBS (without divalent cations such as, calcium and magnesium). Again, those of ordinary skill in the art can readily appreciate any cell concentration may be used. For example, the target cell may be very rare in the sample and comprise only 0.01% of the sample or the entire sample (i.e., 100%) may comprise the target cell of interest. Accordingly, any cell number is within the context of the present invention. In certain aspects, it may be desirable to significantly decrease the volume in which particles and cells are mixed together (i.e., increase the concentration of cells), to ensure maximum contact of cells and particles. For example, in one aspect, a concentration of about 10 billion cells/ml, 9 billion/ml, 8 billion/ml, 7 billion/ml, 6 billion/ml, 5 billion/ml, or 2 billion cells/ml is used. In one aspect, greater than 100 million cells/ml is used. In a further aspect, a concentration of cells of 10, 15, 20, 25, 30, 35, 40, 45, or 50 million cells/ml is used. In yet one aspect, a concentration of cells from 75, 80, 85, 90, 95, or 100 million cells/ml is used. In further aspects, concentrations of 125 or 150 million cells/ml can be used. Using high concentrations can result in increased cell yield, cell activation, and cell expansion. Further, use of high cell concentrations allows more efficient capture of cells that may weakly express target antigens of interest, such as CD28-negative T cells. Such populations of cells may have therapeutic value and would be desirable to obtain in certain aspects. For example, using high concentration of cells allows more efficient selection of CD8+ T cells that normally have weaker CD28 expression.

In one embodiment, cells of the invention, e.g., cells comprising or which at any time comprised or will comprise a gRNA molecule as described herein, e.g., said cells transduced with a nucleic acid encoding a CAR, e.g., a CAR described herein, are expanded, e.g., by a method described herein. In one embodiment, the cells are expanded in culture for a period of several hours (e.g., about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 18, 21 hours) to about 14 days (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 days). In one embodiment, the cells are expanded for a period of 4 to 9 days. In one embodiment, the cells are expanded for a period of 8 days or less, e.g., 7, 6 or 5 days. In one embodiment, the cells are expanded in culture for 5 days, and the resulting cells are more potent than the same cells expanded in culture for 9 days under the same culture conditions. Potency can be defined, e.g., by various T cell functions, e.g. proliferation, target cell killing, cytokine production, activation, migration, or combinations thereof. In one embodiment, the cells are expanded for 5 days show at least a one, two, three or four fold increase in cells doublings upon antigen stimulation as compared to the same cells expanded in culture for 9 days under the same culture conditions. In one embodiment, the cells are expanded in culture for 5 days, and the resulting cells exhibit higher proinflammatory cytokine production, e.g., IFN-γ and/or GM-CSF levels, as compared to the same cells expanded in culture for 9 days under the same culture conditions. In one embodiment, the cells expanded for 5 days show at least a one, two, three, four, five, ten fold or more increase in pg/ml of proinflammatory cytokine production, e.g., IFN-γ and/or GM-CSF levels, as compared to the same cells expanded in culture for 9 days under the same culture conditions.

Several cycles of stimulation may also be desired such that culture time of T cells can be 60 days or more. Conditions appropriate for T cell culture include an appropriate media (e.g., Minimal Essential Media or RPMI Media 1640 or, X-vivo 15, (Lonza)) that may contain factors necessary for proliferation and viability, including serum (e.g., fetal bovine or human serum), interleukin-2 (IL-2), insulin, IFN-γ, IL-4, IL-7, GM-CSF, IL-10, IL-12, IL-15, TGFβ, and TNF-α or any other additives for the growth of cells known to the skilled artisan. Other additives for the growth of cells include, but are not limited to, surfactant, plasmanate, and reducing agents such as N-acetyl-cysteine and 2-mercaptoethanol. Media can include RPMI 1640, AIM-V, DMEM, MEM, α-MEM, F-12, X-Vivo 15, and X-Vivo 20, Optimizer, with added amino acids, sodium pyruvate, and vitamins, either serum-free or supplemented with an appropriate amount of serum (or plasma) or a defined set of hormones, and/or an amount of cytokine(s) sufficient for the growth and expansion of T cells. Antibiotics, e.g., penicillin and streptomycin, are included only in experimental cultures, not in cultures of cells that are to be infused into a subject. The target cells are maintained under conditions necessary to support growth, for example, an appropriate temperature (e.g., 37° C) and atmosphere (e.g., air plus 5% CO_2).

In one embodiment, the cells are expanded in an appropriate media (e.g., media described herein) that includes one or more interleukin that result in at least a 200-fold (e.g., 200-fold, 250-fold, 300-fold, 350-fold) increase in cells over a 14 day expansion period, e.g., as measured by a method described herein such as flow cytometry. In one embodiment, the cells are expanded in the presence of IL-15 and/or IL-7 (e.g., IL-15 and IL-7).

In embodiments, methods described herein, manufacturing methods for cells of the invention, e.g., cells comprising or which at any time comprised or will comprise a gRNA molecule as described herein, e.g., said cells expressing a CAR, comprise removing T regulatory cells, e.g., CD25+ T cells, from a cell population, e.g., using an anti-CD25 antibody, or fragment thereof, or a CD25-binding ligand, IL-2. Methods of removing T regulatory cells, e.g., CD25+ T cells, from a cell population are described herein. In embodiments, the methods, e.g., manufacturing methods, further comprise contacting a cell population (e.g., a cell population in which T regulatory cells, such as CD25+ T cells, have been depleted; or a cell population that has previously contacted an anti-CD25 antibody, fragment thereof, or CD25-binding ligand) with IL-15 and/or IL-7. For example, the cell population (e.g., that has previously contacted an anti-CD25 antibody, fragment thereof, or CD25-binding ligand) is expanded in the presence of IL-15 and/or IL-7.

In some embodiments the cells of the invention, e.g., cells comprising or which at any time comprised or will comprise a gRNA molecule as described herein, e.g., said cells expressing a CAR as described herein, are contacted with a composition comprising a interleukin-15 (IL-15) polypeptide, a interleukin-15 receptor alpha (IL-15Ra) polypeptide, or a combination of both a IL-15 polypeptide and a IL-15Ra polypeptide e.g., hetIL-15, during the manufacturing of the CAR-expressing cell, e.g., ex vivo. In embodiments, a cell described herein is contacted with a composition comprising a IL-15 polypeptide during the manufacturing of the cell, e.g., ex vivo. In embodiments, a cell described herein is contacted with a composition comprising a combination of both a IL-15 polypeptide and a IL-15 Ra polypeptide during the manufacturing of the CAR-expressing cell, e.g., ex vivo. In embodiments, a cell described herein is contacted with a composition comprising hetIL-15 during the manufacturing of the CAR-expressing cell, e.g., ex vivo.

In one embodiment the the cells of the invention, e.g., cells comprising or which at any time comprised or will comprise a gRNA molecule as described herein, e.g., said cells expressing a CAR as described herein, is contacted with a composition comprising hetIL-15 during ex vivo expansion. In an embodiment, the cell described herein is contacted with a composition comprising an IL-15 polypeptide during ex vivo expansion. In an embodiment, the CAR-expressing cell described herein is contacted with a composition comprising both an IL-15 polypeptide and an IL-15Ra polypeptide during ex vivo

expansion. In one embodiment the contacting results in the survival and proliferation of a lymphocyte subpopulation, e.g., CD8+ T cells.

T cells that have been exposed to varied stimulation times may exhibit different characteristics. For example, typical blood or apheresed peripheral blood mononuclear cell products have a helper T cell population (TH, CD4+) that is greater than the cytotoxic or suppressor T cell population (TC, CD8+). Ex vivo expansion of T cells by stimulating CD3 and CD28 receptors produces a population of T cells that prior to about days 8-9 consists predominately of TH cells, while after about days 8-9, the population of T cells comprises an increasingly greater population of TC cells. Accordingly, depending on the purpose of treatment, infusing a subject with a T cell population comprising predominately of TH cells may be advantageous. Similarly, if an antigen-specific subset of TC cells has been isolated it may be beneficial to expand this subset to a greater degree.

Further, in addition to CD4 and CD8 markers, other phenotypic markers vary significantly, but in large part, reproducibly during the course of the cell expansion process. Thus, such reproducibility enables the ability to tailor an activated T cell product for specific purposes.

Once a cell of the invention has been engineered to express a CAR described herein is constructed, various assays can be used to evaluate the activity of the molecule, such as but not limited to, the ability to expand T cells following antigen stimulation, sustain T cell expansion in the absence of re-stimulation, and anti-cancer activities in appropriate in vitro and animal models. Assays to evaluate the effects of a cars of the present invention are described in further detail below

Western blot analysis of CAR expression in primary T cells can be used to detect the presence of monomers and dimers. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Very briefly, T cells (1:1 mixture of $CD4^+$ and $CD8^+$ T cells) expressing the CARs are expanded *in vitro* for more than 10 days followed by lysis and SDS-PAGE under reducing conditions. CARs containing the full length TCR-ζ cytoplasmic domain and the endogenous TCR-ζ chain are detected by western blotting using an antibody to the TCR-ζ chain. The same T cell subsets are used for SDS-PAGE analysis under non-reducing conditions to permit evaluation of covalent dimer formation.

In vitro expansion of CAR^+ T cells following antigen stimulation can be measured by flow cytometry. For example, a mixture of $CD4^+$ and $CD8^+$ T cells are stimulated with αCD3/αCD28 aAPCs followed by transduction with lentiviral vectors expressing GFP under the control of the promoters to be analyzed. Exemplary promoters include the CMV IE gene, EF-1α, ubiquitin C, or phosphoglycerokinase (PGK) promoters. GFP fluorescence is evaluated on day 6 of culture in the $CD4^+$ and/or $CD8^+$ T cell subsets by flow cytometry. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Alternatively, a

mixture of $CD4^+$ and $CD8^+$ T cells are stimulated with αCD3/αCD28 coated magnetic beads on day 0, and transduced with CAR on day 1 using a bicistronic lentiviral vector expressing CAR along with eGFP using a 2A ribosomal skipping sequence. Cultures are re-stimulated with either a cancer associated antigen as described herein$^+$ K562 cells (K562 expressing a cancer associated antigen as described herein), wild-type K562 cells (K562 wild type) or K562 cells expressing hCD32 and 4-1BBL in the presence of antiCD3 and anti-CD28 antibody (K562-BBL-3/28) following washing. Exogenous IL-2 is added to the cultures every other day at 100 IU/ml. GFP^+ T cells are enumerated by flow cytometry using bead-based counting. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009).

Sustained CAR^+ T cell expansion in the absence of re-stimulation can also be measured. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Briefly, mean T cell volume (fl) is measured on day 8 of culture using a Coulter Multisizer III particle counter, a Nexcelom Cellometer Vision or Millipore Scepter, following stimulation with αCD3/αCD28 coated magnetic beads on day 0, and transduction with the indicated CAR on day 1.

Animal models can also be used to measure a CART activity. For example, xenograft model using human a cancer associated antigen described herein-specific CAR^+ T cells to treat a primary human pre-B ALL in immunodeficient mice can be used. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Very briefly, after establishment of ALL, mice are randomized as to treatment groups. Different numbers of a cancer associated antigen -specific CARengineered T cells are coinjected at a 1:1 ratio into NOD-SCID-$\gamma^{-/-}$ mice bearing B-ALL. The number of copies of a cancer associated antigen -specific CAR vector in spleen DNA from mice is evaluated at various times following T cell injection. Animals are assessed for leukemia at weekly intervals. Peripheral blood a cancer associate antigen as described herein$^+$ B-ALL blast cell counts are measured in mice that are injected with a cancer associated antigen described herein-ζ CAR^+ T cells or mock-transduced T cells. Survival curves for the groups are compared using the log-rank test. In addition, absolute peripheral blood $CD4^+$ and $CD8^+$ T cell counts 4 weeks following T cell injection in NOD-SCID-$\gamma^{-/-}$ mice can also be analyzed. Mice are injected with leukemic cells and 3 weeks later are injected with T cells engineered to express CAR by a bicistronic lentiviral vector that encodes the CAR linked to eGFP. T cells are normalized to 45–50% input GFP^+ T cells by mixing with mock-transduced cells prior to injection, and confirmed by flow cytometry. Animals are assessed for leukemia at 1-week intervals. Survival curves for the CAR^+ T cell groups are compared using the log-rank test.

Dose dependent CAR treatment response can be evaluated. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). For example, peripheral blood is obtained 35–70 days after establishing leukemia in mice injected on day 21 with CAR T cells, an equivalent number of mock-transduced T cells,

or no T cells. Mice from each group are randomly bled for determination of peripheral blood a cancer associate antigen as described herein^{+} ALL blast counts and then killed on days 35 and 49. The remaining animals are evaluated on days 57 and 70.

Assessment of cell proliferation and cytokine production has been previously described, *e.g.*, at Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Briefly, assessment of CAR-mediated proliferation is performed in microtiter plates by mixing washed T cells with K562 cells expressing a cancer associated antigen described herein (K19) or CD32 and CD137 (KT32-BBL) for a final T-cell:K562 ratio of 2:1. K562 cells are irradiated with gamma-radiation prior to use. Anti-CD3 (clone OKT3) and anti- CD28 (clone 9.3) monoclonal antibodies are added to cultures with KT32-BBL cells to serve as a positive control for stimulating T-cell proliferation since these signals support long-term CD8^{+} T cell expansion *ex vivo*. T cells are enumerated in cultures using CountBright™ fluorescent beads (Invitrogen, Carlsbad, CA) and flow cytometry as described by the manufacturer. CAR^{+} T cells are identified by GFP expression using T cells that are engineered with eGFP-2A linked CAR-expressing lentiviral vectors. For CAR+ T cells not expressing GFP, the CAR+ T cells are detected with biotinylated recombinant a cancer associate antigen as described herein protein and a secondary avidin-PE conjugate. CD4+ and CD8^{+} expression on T cells are also simultaneously detected with specific monoclonal antibodies (BD Biosciences). Cytokine measurements are performed on supernatants collected 24 hours following re-stimulation using the human TH1/TH2 cytokine cytometric bead array kit (BD Biosciences, San Diego, CA) according the manufacturer's instructions. Fluorescence is assessed using a FACScalibur flow cytometer, and data is analyzed according to the manufacturer's instructions.

Cytotoxicity can be assessed by a standard 51Cr-release assay. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Briefly, target cells (K562 lines and primary pro-B-ALL cells) are loaded with 51Cr (as NaCrO4, New England Nuclear, Boston, MA) at 37°C for 2 hours with frequent agitation, washed twice in complete RPMI and plated into microtiter plates. Effector T cells are mixed with target cells in the wells in complete RPMI at varying ratios of effector cell:target cell (E:T). Additional wells containing media only (spontaneous release, SR) or a 1% solution of triton-X 100 detergent (total release, TR) are also prepared. After 4 hours of incubation at 37°C, supernatant from each well is harvested. Released 51Cr is then measured using a gamma particle counter (Packard Instrument Co., Waltham, MA). Each condition is performed in at least triplicate, and the percentage of lysis is calculated using the formula: % Lysis = (ER− SR) / (TR – SR), where ER represents the average 51Cr released for each experimental condition.

Imaging technologies can be used to evaluate specific trafficking and proliferation of CARs in tumor-bearing animal models. Such assays have been described, for example, in Barrett *et al.*, Human Gene

Therapy 22:1575-1586 (2011). Briefly, NOD/SCID/$\gamma c^{-/-}$ (NSG) mice are injected IV with Nalm-6 cells followed 7 days later with T cells 4 hour after electroporation with the CAR constructs. The T cells are stably transfected with a lentiviral construct to express firefly luciferase, and mice are imaged for bioluminescence. Alternatively, therapeutic efficacy and specificity of a single injection of CAR^+ T cells in Nalm-6 xenograft model can be measured as the following: NSG mice are injected with Nalm-6 transduced to stably express firefly luciferase, followed by a single tail-vein injection of T cells electroporated with cars of the present invention 7 days later. Animals are imaged at various time points post injection. For example, photon-density heat maps of firefly luciferasepositive leukemia in representative mice at day 5 (2 days before treatment) and day 8 (24 hr post CAR^+ PBLs) can be generated.

Other assays, including those described in the Example section herein as well as those that are known in the art can also be used to evaluate the cells and cells expressing CARs described herein.

Delivery Timing

In an embodiment, one or more nucleic acid molecules (e.g., DNA molecules) other than the components of a Cas system, e.g., the Cas9 molecule component and/or the gRNA molecule component described herein, are delivered. In an embodiment, the nucleic acid molecule is delivered at the same time as one or more of the compoments of the Cas system are delivered. In an embodiment, the nucleic acid molecule is delivered before or after (e.g., less than about 30 minutes, 1 hour, 2 hours, 3 hours, 6 hours, 9 hours, 12 hours, 1 day, 2 days, 3 days, 1 week, 2 weeks, or 4 weeks) one or more of the components of the Cas system are delivered. In an

embodiment, the nucleic acid molecule is delivered by a different means than one or more of the components of the Cas system, e.g., the Cas9 molecule component and/or the gRNA molecule compoment, are delivered. The nucleic acid molecule can be delivered by any of the delivery methods described herein. For example, the nucleic acid molecule can be delivered by a viral vector, e.g., an integration-deficient lentivirus, and the Cas9 molecule component and/or the gRNA molecule component can be delivered by electroporation, e.g., such that the toxicity caused by nucleic acids (e.g., DNAs) can be reduced. In an embodiment, the nucleic acid molecule encodes a therapeutic protein, e.g., a protein described herein. In an embodiment, the nucleic acid molecule encodes an RNA molecule, e.g, an RNA molecule described herein.

Bi-modal or Differential Delivery of Components

Separate delivery of the components of a Cas system, e.g., the Cas9 molecule component and the gRNA molecule component, and more particularly, delivery of the components by differing modes, can enhance

performance, e.g., by improving tissue specificity and safety. In an embodiment, the Cas9 molecule and the gRNA molecule are delivered by different modes, or as sometimes referred to herein as differential modes. Different or differential modes, as used herein, refer modes of delivery, that confer different pharmacodynamic or pharmacokinetic properties on the subject component molecule, e.g., a Cas9 molecule, gRNA molecule, template nucleic acid, or payload. E.g., the modes of delivery can result in different tissue distribution, different half-life, or different temporal distribution, e.g., in a selected compartment, tissue, or organ.

Some modes of delivery, e.g., delivery by a nucleic acid vector that persists in a cell, or in progeny of a cell, e.g., by autonomous replication or insertion into cellular nucleic acid, result in more persistent expression of and presence of a component. Examples include viral, e.g., adeno associated virus or lentivirus, delivery.

By way of example, the components, e.g., a Cas9 molecule and a gRNA molecule, can be delivered by modes that differ in terms of resulting half life or persistent of the delivered component the body, or in a particular compartment, tissue or organ. In an embodiment, a gRNA molecule can be delivered by such modes. The Cas9 molecule component can be delivered by a mode which results in less persistence or less exposure of its to the body or a particular compartment or tissue or organ.

More generally, in an embodiment, a first mode of delivery is used to deliver a first component and a second mode of delivery is used to deliver a second component. The first mode of delivery confers a first pharmacodynamic or pharmacokinetic property. The first pharmacodynamic property can be, e.g., distribution, persistence, or exposure, of the component, or of a nucleic acid that encodes the component, in the body, a compartment, tissue or organ. The second mode of delivery confers a second pharmacodynamic or pharmacokinetic property. The second pharmacodynamic property can be, e.g., distribution, persistence, or exposure, of the component, or of a nucleic acid that encodes the component, in the body, a compartment, tissue or organ.

In an embodiment, the first pharmacodynamic or pharmacokinetic property, e.g., distribution, persistence or exposure, is more limited than the second pharmacodynamic or pharmacokinetic property.

In an embodiment, the first mode of delivery is selected to optimize, e.g., minimize, a pharmacodynamic or pharmacokinetic property, e.g., distribution, persistence or exposure.

In an embodiment, the second mode of delivery is selected to optimize, e.g., maximize, a pharmacodynamic or pharmcokinetic property, e.g., distribution, persistence or exposure.

In an embodiment, the first mode of delivery comprises the use of a relatively persistent element, e.g., a nucleic acid, e.g., a plasmid or viral vector, e.g., an AAV or lentivirus. As such vectors are relatively persistent product transcribed from them would be relatively persistent.

In an embodiment, the second mode of delivery comprises a relatively transient element, e.g., an RNA or protein.

In an embodiment, the first component comprises gRNA, and the delivery mode is relatively persistent, e.g., the gRNA is transcribed from a plasmid or viral vector, e.g., an AAV or lentivirus. Transcription of these genes would be of little physiological consequence because the genes do not encode for a protein product, and the gR As are incapable of acting in isolation. The second component, a Cas9 molecule, is delivered in a transient manner, for example as mRNA or as protein, ensuring that the full Cas9 molecule/gRNA molecule complex is only present and active for a short period of time.

Furthermore, the components can be delivered in different molecular form or with different delivery vectors that complement one another to enhance safety and tissue specificity.

Use of differential delivery modes can enhance performance,' safety and efficacy. For example, the likelihood of an eventual off-target modification can be reduced. Delivery of immunogenic components, e.g., Cas9 molecules, by less persistent modes can reduce immunogenicity, as peptides from the bacterially-derived Cas enzyme are displayed on the surface of the cell by MHC molecules. A two-part deliveiy system can alleviate these drawbacks.

Differential delivery modes can be used to deliver components to different, but overlapping target regions. The formation active complex is minimized outside the overlap of the target regions. Thus, in an embodiment, a first component, e.g., a gRNA molecule is delivered by a first delivery mode that results in a first spatial, e.g., tissue, distribution. A second component, e.g., a Cas9 molecule is delivered by a second delivery mode that results in a second spatial, e.g., tissue, distribution. In an embodiment, the first mode comprises a first element selected from a liposome, nanoparticle, e.g., polymeric nanoparticle, and a nucleic acid, e.g., viral vector. The second mode comprises a second element selected from the group. In an embodiment, the first mode of delivery comprises a first targeting element, e.g., a cell specific receptor or an antibody, and the second mode of delivery does not include that element. In an embodiment, the second mode of delivery comprises a second targeting element, e.g., a second cell specific receptor or second antibody.

When the Cas9 molecule is delivered in a virus delivery vector, a liposome, or polymeric nanoparticle, there is the potential for delivery to and therapeutic activity in multiple tissues, when it may be desirable to only target a single tissue. A two-part delivery system can resolve this challenge and enhance tissue

specificity. If the gRNA molecule and the Cas9 molecule are packaged in separated delivery vehicles with distinct but overlapping tissue tropism, the fully functional complex is only be formed in the tissue that is targeted by both vectors.

In one aspect, the delivery is accomplished ex vivo.

XIII. Modified Nucleosides, Nucleotides, and Nucleic Acids

Modified nucleosides and modified nucleotides can be present in nucleic acids, e.g., particularly gRNA, but also other forms of RNA, e.g., mRNA, RNAi, or siRNA. As described herein "nucleoside" is defined as a compound containing a five-carbon sugar molecule (a pentose or ribose) or derivative thereof, and an organic base, purine or pyrimidine, or a derivative thereof. As described herein, "nucleotide" is defined as a nucleoside further comprising a phosphate group.

Modified nucleosides and nucleotides can include one or more of:

(i) alteration, e.g., replacement, of one or both of the non-linking phosphate oxygens and/or of one or more of the linking phosphate oxygens in the phosphodiester backbone linkage;

(ii) alteration, e.g., replacement, of a constituent of the ribose sugar, e.g., of the 2' hydroxyl on the ribose sugar;

(iii) wholesale replacement of the phosphate moiety with "dephospho" linkers;

(iv) modification or replacement of a naturally occurring nucleobase, including with a non-canonical nucleobase;

(v) replacement or modification of the ribose-phosphate backbone;

(vi) modification of the 3' end or 5' end of the oligonucleotide, e.g., removal, modification or replacement of a terminal phosphate group or conjugation of a moiety, cap or linker; and

(vii) modification or replacement of the sugar.

The modifications listed above can be combined to provide modified nucleosides and nucleotides that can have two, three, four, or more modifications. For example, a modified nucleoside or nucleotide can have a modified sugar and a modified nucleobase. In an embodiment, every base of a gRNA is modified, e.g., all bases have a modified phosphate group, e.g., all are phosphorothioate groups. In an embodiment, all, or substantially all, of the phosphate groups of a unimolecular or modular gRNA molecule are replaced with phosphorothioate groups.

In an embodiment, modified nucleotides, e.g., nucleotides having modifications as described herein, can be incorporated into a nucleic acid, e.g., a "modified nucleic acid." In some embodiments, the modified nucleic acids comprise one, two, three or more modified nucleotides. In some embodiments, at least 5% (e.g., at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, or about 100%) of the positions in a modified nucleic acid are a modified nucleotides.

Unmodified nucleic acids can be prone to degradation by, e.g., cellular nucleases. For example, nucleases can hydrolyze nucleic acid phosphodiester bonds. Accordingly, in one aspect the modified nucleic acids described herein can contain one or more modified nucleosides or nucleotides, e.g., to introduce stability toward nucleases.

In some embodiments, the modified nucleosides, modified nucleotides, and modified nucleic acids described herein can exhibit a reduced innate immune response when introduced into a population of cells, both in vivo and ex vivo. The term "innate immune response" includes a cellular response to exogenous nucleic acids, including single stranded nucleic acids, generally of viral or bacterial origin, which involves the induction of cytokine expression and release, particularly the interferons, and cell death. In some embodiments, the modified nucleosides, modified nucleotides, and modified nucleic acids described herein can disrupt binding of a major groove interacting partner with the nucleic acid. In some embodiments, the modified nucleosides, modified nucleotides, and modified nucleic acids described herein can exhibit a reduced innate immune response when introduced into a population of cells, both in vivo and ex vivo, and also disrupt binding of a major groove interacting partner with the nucleic acid.

Definitions of Chemical Groups

As used herein, "alkyl" is meant to refer to a saturated hydrocarbon group which is straight-chained or branched. Example alkyl groups include methyl (Me), ethyl (Et), propyl (e.g. , n-propyl and isopropyl), butyl (e.g. , n-butyl, isobutyl, t-butyl), pentyl (e.g. , n-pentyl, isopentyl, neopentyl), and the like. An alkyl group can contain from 1 to about 20, from 2 to about 20, from 1 to about 12, from 1 to about 8, from 1 to about 6, from 1 to about 4, or from 1 to about 3 carbon atoms.

As used herein, "aryl" refers to monocyclic or polycyclic (e.g. , having 2, 3 or 4 fused rings) aromatic hydrocarbons such as, for example, phenyl, naphthyl, anthracenyl,

phenanthrenyl, indanyl, indenyl, and the like. In some embodiments, aryl groups have from 6 to about 20 carbon atoms.

As used herein, "alkenyl" refers to an aliphatic group containing at least one double bond. As used herein, "alkynyl" refers to a straight or branched hydrocarbon chain containing 2- 12 carbon atoms and characterized in having one or more triple bonds. Examples of alkynyl groups include, but are not limited to, ethynyl, propargyl, and 3-hexynyl.

As used herein, "arylalkyl" or "aralkyl" refers to an alkyl moiety in which an alkyl hydrogen atom is replaced by an aryl group. Aralkyl includes groups in which more than one hydrogen atom has been replaced by an aryl group. Examples of "arylalkyl" or "aralkyl" include benzyl, 2-phenylethyl, 3-phenylpropyl, 9-fluorenyl, benzhydryl, and trityl groups.

As used herein, "cycloalkyl" refers to a cyclic, bicyclic, tricyclic, or polycyclic non- aromatic hydrocarbon groups having 3 to 12 carbons. Examples of cycloalkyl moieties include, but are not limited to, cyclopropyl, cyclopentyl, and cyclohexyl.

As used herein, "heterocyclyl" refers to a monovalent radical of a heterocyclic ring system. Representative heterocyclyls include, without limitation, tetrahydrofuranyl, tetrahydrothienyl, pyrrolidinyl, pyrrolidonyl, piperidinyl, pyrrolinyl, piperazinyl, dioxanyl, dioxolanyl, diazepinyl, oxazepinyl, thiazepinyl, and morpholinyl.

As used herein, "heteroaryl" refers to a monovalent radical of a heteroaromatic ring system. Examples of heteroaryl moieties include, but are not limited to, imidazolyl, oxazolyl, thiazolyl, triazolyl, pyrrolyl, furanyl, indolyl, thiophenyl pyrazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolizinyl, purinyl, naphthyridinyl, quinolyl, and pteridinyl.

Phosphate Backbone Modifications

The Phosphate Group

In some embodiments, the phosphate group of a modified nucleotide can be modified by replacing one or more of the oxygens with a different substituent. Further, the modified nucleotide, e.g., modified nucleotide present in a modified nucleic acid, can include the wholesale replacement of an unmodified phosphate moiety with a modified phosphate as described herein. In some embodiments, the modification of the phosphate backbone can include alterations that result in either an uncharged linker or a charged linker with unsymmetrical charge distribution.

Examples of modified phosphate groups include, phosphorothioate, phosphoroselenates, borano phosphates, borano phosphate esters, hydrogen phosphonates, phosphoroamidates, alkyl or aryl phosphonates and phosphotriesters. In some embodiments, one of the non-bridging phosphate oxygen atoms in the phosphate backbone moiety can be replaced by any of the following groups: sulfur (S),

selenium (Se), BR_3 (wherein R can be, e.g., hydrogen, alkyl, or aryl), C (e.g., an alkyl group, an aryl group, and the like), H, NR_2 (wherein R can be, e.g., hydrogen, alkyl, or aryl), or OR (wherein R can be, e.g., alkyl or aryl). The phosphorous atom in an unmodified phosphate group is achiral. However, replacement of one of the non-bridging oxygens with one of the above atoms or groups of atoms can render the phosphorous atom chiral; that is to say that a phosphorous atom in a phosphate group modified in this way is a stereogenic center. The stereogenic phosphorous atom can possess either the "R" configuration (herein Rp) or the "S" configuration (herein Sp).

Phosphorodithioates have both non-bridging oxygens replaced by sulfur. The phosphorus center in the phosphorodithioates is achiral which precludes the formation of oligoribonucleotide diastereomers. In some embodiments, modifications to one or both non-bridging oxygens can also include the replacement of the non-bridging oxygens with a group independently selected from S, Se, B, C, H, N, and OR (R can be, e.g., alkyl or aryl).

The phosphate linker can also be modified by replacement of a bridging oxygen, (i.e., the oxygen that links the phosphate to the nucleoside), with nitrogen (bridged phosphoroamidates), sulfur (bridged phosphorothioates) and carbon (bridged methylenephosphonates). The replacement can occur at either linking oxygen or at both of the linking oxygens.

Replacement of the Phosphate Group

The phosphate group can be replaced by non-phosphorus containing connectors. In some embodiments, the charge phosphate group can be replaced by a neutral moiety.

Examples of moieties which can replace the phosphate group can include, without limitation, e.g., methyl phosphonate, hydroxylamino, siloxane, carbonate, carboxymethyl, carbamate, amide, thioether, ethylene oxide linker, sulfonate, sulfonamide, thioformacetal, formacetal, oxime, methyleneimino, methylenemethylimino, methylenehydrazo, methylenedimethylhydrazo and methyleneoxymethylimino.

Replacement of the Ribophosphate Backbone

Scaffolds that can mimic nucleic acids can also be constructed wherein the phosphate linker and ribose sugar are replaced by nuclease resistant nucleoside or nucleotide surrogates. In some embodiments, the nucleobases can be tethered by a surrogate backbone. Examples can include, without limitation, the morpholino, cyclobutyl, pyrrolidine and peptide nucleic acid (PNA) nucleoside surrogates.

Sugar Modifications

The modified nucleosides and modified nucleotides can include one or more modifications to the sugar group. For example, the 2' hydroxyl group (OH) can be modified or replaced with a number of different "oxy" or "deoxy" substituents. In some embodiments, modifications to the 2' hydroxyl group can enhance the stability of the nucleic acid since the hydroxyl can no longer be deprotonated to form a 2'-alkoxide ion. The 2'-alkoxide can catalyze degradation by intramolecular nucleophilic attack on the linker phosphorus atom.

Examples of "oxy"-2' hydroxyl group modifications can include alkoxy or aryloxy (OR, wherein "R" can be, e.g., alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or a sugar); polyethyleneglycols (PEG), $0(CH_2CH_20)_nCH2CH_2OR$ wherein R can be, e.g., H or optionally substituted alkyl, and n can be an integer from 0 to 20 (e.g., from 0 to 4, from 0 to 8, from 0 to 10, from 0 to 16, from 1 to 4, from 1 to 8, from 1 to 10, from 1 to 16, from 1 to 20, from 2 to 4, from 2 to 8, from 2 to 10, from 2 to 16, from 2 to 20, from 4 to 8, from 4 to 10, from 4 to 16, and from 4 to 20). In some embodiments, the "oxy"-2' hydroxyl group modification can include "locked" nucleic acids (LNA) in which the 2' hydroxyl can be connected, e.g., by a $Ci-_6$ alkylene or Cj-6 heteroalkylene bridge, to the 4' carbon of the same ribose sugar, where exemplary bridges can include methylene, propylene, ether, or amino bridges; O-amino (wherein amino can be, e.g., NH_2; alkylamino, dialkylamino, heterocyclyl, arylamino, diarylamino, heteroarylamino, or diheteroarylamino, ethylenediamine, or polyamino) and aminoalkoxy, $0(CH_2)_n$-amino, (wherein amino can be, e.g., NH_2; alkylamino, dialkylamino, heterocyclyl, arylamino, diarylamino, heteroarylamino, or diheteroarylamino, ethylenediamine, or polyamino). In some embodiments, the "oxy"-2' hydroxyl group modification can include the methoxyethyl group (MOE), ($OCH_2CH_2OCH_3$, e.g., a PEG derivative).

"Deoxy" modifications can include hydrogen (i.e. deoxyribose sugars, e.g., at the overhang portions of partially ds RNA); halo (e.g., bromo, chloro, fluoro, or iodo); amino (wherein amino can be, e.g., NH_2; alkylamino, dialkylamino, heterocyclyl, arylamino, diarylamino, heteroarylamino, diheteroarylamino, or amino acid); $NH(CH_2CH_2NH)_nCH2CH_2$- amino (wherein amino can be, e.g., as described herein), -NHC(0)R (wherein R can be, e.g., alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or sugar), cyano; mercapto; alkyl-thio-alkyl; thioalkoxy; and alkyl, cycloalkyl, aryl, alkenyl and alkynyl, which may be optionally substituted with e.g., an amino as described herein.

The sugar group can also contain one or more carbons that possess the opposite stereochemical configuration than that of the corresponding carbon in ribose. Thus, a modified nucleic acid can include nucleotides containing e.g., arabinose, as the sugar. The nucleotide "monomer" can have an alpha linkage at the Γ position on the sugar, e.g., alpha-nucleosides. The modified nucleic acids can also include "abasic" sugars, which lack a nucleobase at C- . These abasic sugars can also be further modified at one

or more of the constituent sugar atoms. The modified nucleic acids can also include one or more sugars that are in the L form, e.g. L- nucleosides.

Generally, RNA includes the sugar group ribose, which is a 5-membered ring having an oxygen. Exemplary modified nucleosides and modified nucleotides can include, without limitation, replacement of the oxygen in ribose (e.g., with sulfur (S), selenium (Se), or alkylene, such as, e.g., methylene or ethylene); addition of a double bond (e.g., to replace ribose with cyclopentenyl or cyclohexenyl); ring contraction of ribose (e.g., to form a 4-membered ring of cyclobutane or oxetane); ring expansion of ribose (e.g., to form a 6- or 7-membered ring having an additional carbon or heteroatom, such as for example, anhydrohexitol, altritol, mannitol, cyclohexanyl, cyclohexenyl, and morpholino that also has a phosphoramidate backbone). In some embodiments, the modified nucleotides can include multicyclic forms (e.g., tricyclo; and "unlocked" forms, such as glycol nucleic acid (GNA) (e.g., R-GNA or S-GNA, where ribose is replaced by glycol units attached to phosphodiester bonds), threose nucleic acid (TNA, where ribose is replaced with a-L-threofuranosyl-(3'-→2')).

Modifications on the Nucleobase

The modified nucleosides and modified nucleotides described herein, which can be incorporated into a modified nucleic acid, can include a modified nucleobase. Examples of nucleobases include, but are not limited to, adenine (A), guanine (G), cytosine (C), and uracil (U). These nucleobases can be modified or wholly replaced to provide modified nucleosides and modified nucleotides that can be incorporated into modified nucleic acids. The nucleobase of the nucleotide can be independently selected from a purine, a pyrimidine, a purine or pyrimidine analog. In some embodiments, the nucleobase can include, for example, naturally-occurring and synthetic derivatives of a base.

Uracil

In some embodiments, the modified nucleobase is a modified uracil. Exemplary nucleobases and nucleosides having a modified uracil include without limitation pseudouridine (ψ), pyridin-4-one ribonucleoside, 5-aza-uridine, 6-aza-uridine, 2-thio-5-aza-uridine, 2-thio- uridine (s2U), 4-thio-uridine (s4U), 4-thio-pseudouridine, 2-thio-pseudouridine, 5-hydroxy- u,ridine (ho^{5}U), 5-aminoallyl-uridine, 5-halo-uridine (e.g., 5-iodo-uridine or 5-bromo-uridine), 3- methyl-uridine (m^{3}U), 5-methoxy-uridine (mo^{5}U), uridine 5-oxyacetic acid (cmo^{5}U), uridine 5- oxyacetic acid methyl ester (mcmo^U), 5-carboxymethyl-uridine (cm^{5}U), 1 -carboxymethyl- pseudouridine, 5-carboxyhydroxymethyl-uridine (chm^{5}U), 5-carboxyhydroxymethyl-uridine methyl ester (mchm^{5}U), 5-methoxycarbonylmethyl-uridine (mcm^{5}U), 5- methoxycarbonylmethyl-2-thio-uridine (mcm^{5}s2U), 5-aminomethyl-2-thio-uridine (nm^{5}s2U), 5- methylaminomethyl-uridine (mnm^{5}U), 5-methylaminomethyl-2-thio-uridine (mnm^{5}s2U), 5-

methylaminomethyl-2-seleno-uridine (mnm^{5}se^{2}U), 5-carbamoylmethyl-uridine (ncm^{5}U), 5-carboxymethylaminomethyl-uridine (cmnm^{5}U), 5-carboxymethylaminomethyl-2-thio-uridine (cmnm \s2U), 5-propynyl-uridine, 1 -propynyl-pseudouridine, 5-taurinomethyl-uridine (xcm^{5}U), 1 -taurinomethyl-pseudouridine, 5-taurinomethyl-2-thio-uridine(Trn^{5}s2U), l-taurinomethyl-4- thio-pseudouridine, 5-methyl-uridine (m^{5}U, i.e., having the nucleobase deoxythymine), 1- methyl-pseudouridine (ιτι'ψ). 5-methyl-2-thio-uridine (m^{5}s2U), l-methyl-4-thio-pseudouridine (m' s \|/), 4-thio- l-methyl-pseudouridine, 3-methyl-pseudouridine (m'V), 2-thio- l -methyl- pseudouridine, 1 -methyl- 1 -deaza-pseudouridine, 2-thio- 1 -methyl- 1 -deaza-pseudouridine, dihydroundine (D), dihydropseudoundine, 5,6-dihydrouridine, 5-methyl-dihydrouridine (m^{5}D), 2- thio-dihydrouridine, 2-thio-dihydropseudouridine, 2-methoxy-uridine, 2-methoxy-4-thio- uridine, 4-methoxy-pseudouridine, 4-methoxy-2-thio-pseudouridine, N l -methyl-pseudouridine, 3- (3-amino-3-carboxypropyl)uridine (acp^{3}U), l-methyl-3-(3-amino-3- carboxypropy pseudouridine 5-(isopentenylaminomethyl)uridine (inm^{5}U), 5-(isopentenylaminomethy])-2-thio-uridine (inm^{5}s2U), a-thio-uridine, 2'-0-methyl-uridine (Urn), 5,2'-0-dimethyl-uridine (m^{5}Um), 2'-0-methyl-pseudouridine (ψπι), 2-thio-2'-0-methyl-uridine (s2Um), 5-methoxycarbonylmethyl-2'-0-methyl-uridine (mcm ^{5}Um), 5-carbamoylmethyl-2'-0- methyl-uridine (ncm ^{5}Um), 5-carboxymethylaminomethyl-2'-0-methyl-uridine (cmnm ^{5}Um), 3,2'-0-dimethyl-uridine (m^{3}Um), 5-(isopentenylaminomethyl)-2'-0-methyl-uridine (inm ^{5}Um), l -thio-uridine, deoxythymidine, 2'-F-ara-uridine, 2'-F-uridine, 2'-OH-ara-uridine, 5-(2- carbomethoxyvinyl) uridine, 5-[3-(l-E-propenylamino)uridine, pyrazolo[3,4-d]pyrimidines, xanthine, and hypoxanthine.

Cytosine

In some embodiments, the modified nucleobase is a modified cytosine. Exemplary nucleobases and nucleosides having a modified cytosine include without limitation 5-aza- cytidine, 6-aza-cytidine, pseudoisocytidine, 3-methyl-cytidine (m^{3}C), N4-acetyl-cytidine (act), 5- formyl-cytidine (f^{5}C), N4-methyl-cytidine (m^{4}C), 5-methyl-cytidine (m^{5}C), 5-halo-cytidine (e.g., 5-iodo-cytidine), 5-hydroxymethyl-cytidine (hm^{5}C), 1-methyl-pseudoisocytidine, pyrrolo- cytidine, pyrrolo-pseudoisocytidine, 2-thio-cytidine (s2C), 2-thio-5-methyl-cytidine, 4-thio- pseudoisocytidine, 4-thio- 1 -methyl-pseudoisocytidine, 4-thio-l -methyl- 1-deaza- pseudoisocytidine, 1-methyl- l-deaza-pseudoisocytidine, zebularine, 5-aza-zebularine, 5-methyl- zebularine, 5-aza-2-thio-zebularine, 2-thio-zebularine, 2-methoxy-cytidine, 2-methoxy-5-methyl- cytidine, 4-methoxy-pseudoisocytidine, 4-methoxy- 1 -methyl-pseudoisocytidine, lysidine (k^{2}C), a-thio-cytidine, 2'-0-methyl-cytidine (Cm), 5,2'-0-dimethyl-cytidine (m^{5}Cm), N4-acetyl-2'-0- methyl-cytidine (ac^{4}Cm), N4,2'-0-dimethyl-cytidine (m^{4}Cm), 5-formyl-2'-0-methyl-cytidine (f ^{5}Cm), N4,N4,2'-0-trimethyl-cytidine (m$^4{}_2$Cm), 1 -thio-cytidine, 2'-F-ara-cytidine, 2'-F-cytidine, and 2'-OH-ara-cytidine.

Adenine

In some embodiments, the modified nucleobase is a modified adenine. Exemplary nucleobases and nucleosides having a modified adenine include without limitation 2-amino- purine, 2,6-diaminopurine, 2-amino-6-halo-purine (e.g., 2-amino-6-chloro-purine), 6-halo-purine (e.g., 6-chloi -purine), 2-amino-6-methyl-purine, 8-azido-adenosine, 7-deaza-adenine, 7-deaza- 8-aza-adenine, 7-deaza-2-amino-purine, 7-deaza-8-aza-2-amino-purine, 7-deaza-2,6- diaminopurine, 7-deaza-8-aza-2,6-diaminopurine, 1-methyl-adenosine (m'A), 2-methyl-adenine (m A), N6-methyl-adenosine (m^6A), 2-methylthio-N6-methyl-adenosine ($ms2m^6A$), N6- isopentenyl-adenosine (i^6A), 2-methylthio-N6-isopentenyl-adenosine (ms^2i^6A), N6-(cis- hydroxyisopentenyl)adenos'ine (io^6A), 2-methylthio-N6-(cis-hydroxyisopentenyl)adenosine ($ms2io^6A$), N6-glycinylcarbamoyl-adenosine (g^6A), N6-threonylcarbamoyl-adenosine (t^6A), N6- methyl-N6-threonylcarbamoyl-adenosine (m^6t^6A), 2-methylthio-N6-threonylcarbamoyl- adenosine (ms^2g^6A), N6,N6-dimethyl-adenosine ($m^6{}_2A$), N6-hydroxynorvalylcarbamoyl- adenosine (hn^6A), 2-methylthio-N6-hydroxynorvalylcarbamoyl-adenosine ($ms2hn^6A$), N6- acetyl-adenosine (ac^6A), 7-methyl-adenine, 2-methylthio-adenine, 2-methoxy-adenine, a-thio- adenosine, 2'-0-methyl-adenosine (Am), N^6,2'-0-dimethyl-adenosine (m^5Am), N^6-Methyl-2'- deoxyadenosine, N6,N6,2'-0-trimethyl-adenosine ($m^6{}_2Am$), 1 ,2'-0-dimethyl-adenosine (m' Am), 2'-0-ribosyladenosine (phosphate) (Ar(p)), 2-amino-N6-methyl-purine, 1 -thio-adenosine, 8- azido-adenosine, 2'-F-ara-adenosine, 2'-F-adenosine, 2'-OH-ara-adenosine, and N6-(19-amino- pentaoxanonadecyl)-adenosine.

Guanine

In some embodiments, the modified nucleobase is a modified guanine. Exemplary nucleobases and nucleosides having a modified guanine include without limitation inosine (I), 1 - methyl-inosine (m 'l), wyosine (imG), methylwyosine (mimG), 4-demethyl-wyo"sine (imG- 14), isowyosine (imG2), wybutosine (yW), peroxywybutosine (o_2yW), hydroxywybutosine (OHyW), undemriodified hydroxywybutosine (OHyW*), 7-deaza-guanosine, queuosine (Q), epoxyqueuosine (oQ), galactosyl-queuosine (galQ), mannosyl-queuosine (manQ), 7-cyano-7- deaza-guanosine ($preQ_0$), 7-aminomethyI-7-deaza-guanosine (preQi), archaeosine (G^+), 7-deaza- 8-aza-guanosine, 6-thio-guanosine, 6-thio-7-deaza-guanosine, 6-thio-7-deaza-8-aza-guanosine, 7-methyl-guanosine (m^7G), 6-thio-7-methyl-guanosine, 7-methyl-inosine, 6-methoxy-guanosine, 1 -methyl-guanosine (m'G), N2-methyl-guanosine (m^2G), N2,N2-dimethyl-guanosine ($m^2{}_2G$), N2,7-dimethyl-guanosine (m^2,7G), N2, N2,7-dimethyl-guanosine (m^2,2,7G), 8-oxo-guanosine, 7-methyl-8-oxo-guanosine, 1 -meth thio-guanosine, N2-methyl-6-thio-guanosine, N2,N2- dimethyl-6-thio-guanosine, a-thio-guanosine, 2'-0-methyl-guanosine (Gm), N2-methyl-2'-0-methyl-guanosine (m¾m), N2,N2-dimethyl-2'-0-methyl-guanosine ($m^2{}_2Gm$), 1 -methyl-2'-0- methyl-guanosine (m'Gm), N2,7-dimethyl-2'-0-methyl-guanosine (m^2,7Gm), 2'-0-methyl- inosine (Im), 1 ,2'-0-

dimethyl-inosine (m'lm), 0^6-phenyl-2'-deoxyinosine, 2'-0-ribosylguanosine (phosphate) (Gr(p)), 1 -thio-guanosine, 0^6-methy]-guanosine, 0^6-Methyl-2'-deoxyguanosine, 2'- F-ara-guanosine, and 2'-F-guanosine.

Modified gRNAs

In some embodiments, the modified nucleic acids can be modified gRNAs. In some embodiments, gRNAs can be modified at the 3' end. In this embodiment, the gRNAs can be modified at the 3' terminal U ribose. For example, the two terminal hydroxyl groups of the U ribose can be oxidized to aldehyde groups and a concomitant opening of the ribose ring to afford a modified nucleoside, wherein U can be an unmodified or modified uridine.

In another embodiment, the 3' terminal U can be modified with a 2' 3' cyclic phosphate, wherein U can be an unmodified or modified uridine. In some embodiments, the gRNA molecules may contain 3' nucleotides which can be stabilized against degradation, e.g., by incorporating one or more of the modified nucleotides described herein. In this embodiment, e.g., uridines can be replaced with modified uridines, e.g., 5-(2-amino)propyl uridine, and 5-bromo uridine, or with any of the modified uridines described herein; adenosines and guanosines can be replaced with modified adenosines and guanosines, e.g., with modifications at the 8-position, e.g., 8-bromo guanosine, or with any of the modified adenosines or guanosines described herein. In some embodiments, deaza nucleotides, e.g., 7- deaza-adenosine, can be incoiporated into the gRNA. In some embodiments, O- and N-alkylated nucleotides, e.g., N6-methyl andenosine, can be incorporated into the gRNA. In some embodiments, sugar-modified ribonucleotides can be incorporated, e.g., wherein the 2' OH- group is replaced by a group selected from H, -OR, -R (wherein R can be, e.g., methyl, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or sugar), halo, -SH, -SR (wherein R can be, e.g., alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or sugar), amino (wherein amino can be, e.g., NH_2; alkylamino, dialkylamino, heterocyclyl, arylamino, diarylamino, heteroarylamino, diheteroarylamino, or amino acid); or cyano (-CN). In some embodiments, the phosphate backbone can be modified as described herein, e.g., with a phosphothioate group. In some embodiments, the nucleotides in the overhang region of the gRNA can each independently be a modified or unmodified nucleotide including, but not limited to 2'-sugar modified, such as, 2-F 2'-0-methyl, thymidine (T), 2'-O-methoxyethyl-5-methyluridine (Teo), 2'-O-methoxyethyladenosine (Aeo), 2'-O-methoxyethyl- 5-methylcytidine (m5Ceo), and any combinations thereof.

In an embodiment, a one or more or all of the nucleotides in single stranded overhang of an RNA molecule, e.g., a gRNA molecule, are deoxynucleotides.

Candidate Cas molecules, e.g., Cas9 molecules, candidate gRNA molecules, candidate Cas9 molecule/gRNA molecule complexes, and candidate CRISPR systems, can be evaluated by art-known

methods or as described herein. For example, exemplary methods for evaluating the endonuclease activity of Cas9 molecule are described, e.g., in Jinek el al., SCIENCE 2012; 337(6096):8 16-821.

EXAMPLES

Example 1: Assays

Guide Selection

Initial guide selection was performed *in silico* using a human reference genome and user defined genomic regions of interest (e.g., a gene, an exon of a gene, non-coding regulatory region, etc), for identifying PAMs in the regions of interest. For each identified PAM, analyses were performed and statistics reported. gRNA molecules were further selected and rank-ordered based on a number of criteria known in the art. gRNA molecules were then tested as described herein for cutting efficiency and indel formation as described herein.

Throughout the Examples, in the experiments below, either sgRNA molecules or dgRNA molecules were used. Unless indicated otherwise, experiments referring to a CRxxxxx identifier for the targeting domain employed a dgRNA format. Unless indicated otherwise, where dgRNA molecules were used, the gRNA includes the following:

crRNA: [targeting domain]-[SEQ ID NO: 6607]

tracr (trRNA): SEQ ID NO: 6660.

Unless indicated otherwise, in experiments employing a sgRNA molecule, the following sequence was used:

[targeting domain]-[SEQ ID NO: 6601]-UUUU

Transfection of HEK-293_Cas9GFP Cells for Primary Guide Screening

Transfection of Cas9GFP-expressing HEK293 cells (HEK-293_Cas9GFP) was used for primary screening of target specific crRNAs. In this example, target specific crRNAs were designed and selected for primary screening using defined criteria including *in silico* off-target detection, e.g., as described herein. Selected crRNAs were chemically synthesized and delivered in a 96 well format. HEK-293-Cas9GFP cells were transfected with target crRNAs comprising a flagpole region of SEQ ID NO: 6607 in a 1:1 ratio with stock trRNA of SEQ ID NO: 6660. The transfection was mediated using lipofection technology according to manufacturer's protocol (DharmaFECT Duo, GE LifeSciences; or RNAiMax,

LifeTechnologies). Transfected cells were lysed 24h following lipofection and editing (e.g., cleavage) was detected within lysates with the T7E1 assay and/or next generation sequencing (NGS; below).

T7E1 Assay

The T7E1 assay was used to detect mutation events in genomic DNA such as insertions, deletions and substitutions created through non-homologous end joining (NHEJ) following DNA cleavage by Cas9 (See Cho et al., Targeted genome engineering in human cells with the Cas9 RNA-guided endonuclease. *Nature Biotechnology.* 2013; **31**, 230–232).

Genomic DNA regions that have been targeted for cutting by CRISPR/Cas9 were amplified by PCR, denatured at 95°C for 10 minutes, and then re-annealed by ramping down from 95°C to 25°C at 0.5°C per second. If mutations were present within the amplified region, the DNA combined to form heteroduplexes. The re-annealed heteroduplexes were then digested with T7E1 (New England Biolabs) at 37°C for 1 hour. T7E1 endonuclease recognizes DNA mismatches, heteroduplexes and nicked double stranded DNA and generates a double stranded break at these sites. The resulting DNA fragments were analyzed using a Fragment Analyzer and quantified to determine cleavage efficiency.

Next-Generation Sequencing (NGS) and Analysis For On-Target Cleavage Efficiency and Indel Formation

To determine the efficiency of editing (e.g., cleaving) the target location in the genome, deep sequencing was utilized to identify the presence of insertions and deletions introduced by non-homologous end joining.

PCR primers were first designed around the target site, and the genomic area of interest PCR amplified. Additional PCR was performed according to manufacturer's protocols (Illumina) to add the necessary chemistry for sequencing. The amplicons were then sequenced on an Illumina MiSeq instrument. The reads were then aligned to the human reference genome (e.g., hg38) after eliminating those having low quality scores. From the resulting files containing the reads mapped to the reference genome (BAM files), reads which overlap the target region of interest were selected and the number of wild type reads versus the number of reads which contain an insertion or deletion was calculated. The editing percentage was then defined as the total number of reads with insertions or deletions over the total number of reads, including wild type. To determine the pattern of insertions and/or deletions that resulted from the edit, the aligned reads with indels were selected and the number of a reads with a given indel were summed. This information was then displayed as a list as well as visualized in the form on histograms which represent the frequency of each indel.

RNP generation

The addition of crRNA and trRNA (for a dgRNA), or chimeric gRNA (for sgRNA) to Cas9 protein results in the formation of the active Cas9 ribonucleoprotein complex (RNP), which mediates binding to the target region specified by the crRNA and specific cleavage of the targeted genomic DNA. This complex was formed by loading trRNA and crRNA into Cas9, which is believed to cause conformational changes to Cas9 allowing it to bind and cleave dsDNA.

The crRNA and trRNA were separately denatured at 95°C for 2 minutes, and allowed to come to room temperature. Cas9 protein (10mg/ml) was added to 5X CCE buffer (20mM HEPES, 100mM KCl, 5mM $MgCl_2$, 1mM DTT, 5% glycerol), to which trRNA and crRNAs were added (in separate reactions) and incubated at 37°C for 10 minutes, thereby forming the active RNP complex. The complex was delivered by electroportation and other methods into a wide variety of cells, including HEK-293 and CD3+ T cells.

Delivery of RNPs to T cells

CD3+ T cells are comprised of multiple T cell populations including CD4+ T helper cells and CD8+ cytotoxic T cells. These cells can be isolated from whole blood or from leukophoresis samples. T cells can be modified to specifically target cancerous cells and to be less immunogenic, by engineering patient T cells using Cas9-mediated editing. This example describes a basic method used to deliver Cas9 RNP, for example, Cas9 RNP targeting B2M, in T cells. Only the targeting crRNA in the RNP would need to be changed to adapt this protocol to a different T cell target (e.g., any of those provided herein).

T cells were first enriched from a leukopak using a commercially available kit (e.g., EasySep™ Human T Cell Isolation Kit, Stem Cell Technology). Enriched T cells were aliquoted and frozen down (at 10x106/vial) for future use. Vials were subsequently thawed as needed, and activated by addition of 3:1 ratio of CD3/CD28 beads (Dynabeads, Life Technologies) or using ImmunoCult Human CD3/CD28 T cell Activator (Stem Cell Technologies) in T cell media (RPMI 1640, FBS, L-glutamine, non-essential amino acids, sodium pyruvate, HEPES buffer, 2-mercaptoethanol and optionally IL2). RNPs were generated as described herein, and were added to ~50,000-100,000 CD3+ T cells resuspended in P3 buffer and nucleofected using the Amaxa nucleofection program EO-115. T cell media was added to cells immediately post-nucleofection and cultured for 24 h or more.

Example 2: Editing of B2M

Results of Editing using B2M-targeted gRNAs in HEK-293 cells stably expressing Cas9

NGS assay results for cutting efficiency of gRNAs targeting B2M are summarized in Table 9, and in Figure 1. These results demonstrate that multiple guide RNA molecules are able to mediate high efficiency editing of the B2M locus. The top gRNA molecules, as ranked by % editing in HEK cells (followed by % editing in CD34+ cells) are shown in Figure 14, together with the results of 1) % editing in CD34+ cells as measured by NGS, and 2) % loss of B2M as measured by flow cytometry in CD3+ T cells). As shown in Figure 14, three dgRNA molecules, e.g., dgRNA molecules that include the targeting domain of CR00442, CR00444 and CR00455 showed greater than 40% editing in CD3+ T cells as measured by flow cytometry.

Table 9: Editing of B2M by dgRNA-CRISPR systems in HEK-293 Cas9GFP as determined by NGS. gRNAs are ranked according to % editing in HEK cells.

		HEK (NGS) % Editing	
gRNA ID	target name	Mean	Std Dev
CR00465	B2M	89.7	1.7
CR00443	B2M	82.9	3.2
CR00445	B2M	80.9	8.4
CR00444	B2M	80.4	5.8
CR00449	B2M	79.3	5.1
CR00442	B2M	77.7	2.1
CR00453	B2M	74.3	3.6
CR00461	B2M	73.6	5.2
CR00439	B2M	71.8	12.5
CR00452	B2M	71.7	10.6
CR00455	B2M	70.4	11.1
CR00463	B2M	70.2	6.7
CR00467	B2M	69.6	12.5
CR00466	B2M	67.6	11.4
CR00446	B2M	64.4	6.0
CR00440	B2M	62.6	9.1
CR00472	B2M	57.5	4.0
CR00459	B2M	55.8	19.8
CR00468	B2M	54.8	11.9
CR00469	B2M	52.6	13.6
CR00450	B2M	51.6	4.5
CR00456	B2M	50.3	9.6
CR00454	B2M	49.2	16.8
CR00464	B2M	47.3	8.2
CR00460	B2M	45.1	9.8

CR00457	B2M	43.6	11.5
CR00451	B2M	39.8	8.0
CR00462	B2M	34.6	9.5
CR00470	B2M	31.3	7.0
CR00447	B2M	31.2	7.0
CR00458	B2M	20.6	9.0
CR00471	B2M	17.1	4.7
CR00473	B2M	15.6	2.1
CR000129	B2M	NA	NA
CR000131	B2M	NA	NA
CR00438	B2M	NA	NA

Flow cytometric analysis of B2M expression

A flow based assay was developed to monitor editing efficiency following RNP formulation and delivery. Beta-2-microglobin (B2M) is an essential component of the MHC class I (HLA-type 1) complex that is presented on the surface of all nucleated cells. MHC class I presents endogenous (e.g., self and non-self) peptides to the immune system. A series of crRNAs targeting B2M were tested using flow cytometry assay to detect B2M expression. From this initial screen, crRNAs were identified which showed consistent editing ranging between 5-25%.

Cells in suspension were labeled with APC conjugated anti-human B2M (BioLegend, cat#316312), PE conjugated anti-human HLA-A,B,C (BioLegend, cat#311405), and propidium iodide (0.5 mg/ml diluted to 1/1000). Appropriate controls were established (e.g., isotype-APC, isotype-PE, PE-anti-HLA separately, APC-anti-B2M separately). The samples were then run on a flow cytometer. In this example, loss of B2M expression as assessed by surface marker staining was indicative of Cas9-mediated editing (e.g., cleavage). Results are reported in Figure 14.

Example 3: Editing of TCR and/or PD-1 in T Cells, including in CAR-T cells

Table 10 lists gRNA targeting domains for editing of the genes for TCR alpha and for PD-1. gRNA molecules were generated as described below as sgRNAs comprising, from 5' to 3' the indicated targeting domain-SEQ ID NO: 6601-$(U)_7$.

Table 10: gRNA targeting domains to TCR alpha and PD-1

Id.	gRNA Targeting Domain	SEQ ID NO:
TRAC-1	UCUCUCAGCUGGUACACGGC	5568

(CR000960)		
TRAC-2 (CR000964)	GAGAAUCAAAAUCGGUGAAU	5572
TRAC-3 (CR000966)	AACAAAUGUGUCACAAAGUA	5574
TRAC-5 (CR000971)	AAAGUCAGAUUUGUUGCUCC	5579
TRAC-6 (CR000973)	CUGGGGAAGAAGGUGUCUUC	5581
TRAC-7 (CR000980)	CUCGACCAGCUUGACAUCAC	5588
TRAC-8 (CR000979)	AAGUUCCUGUGAUGUCAAGC	5587
TRAC-9 (CR000984)	UUCGGAACCCAAUCACUGAC	5592
TRAC-10 (CR000991)	GAUUAAACCCGGCCACUUUC	5599
PD1-1 (CR000837)	UGUAGCACCGCCCAGACGAC	5733
PD1-2 (3'- 20 nt of 5133_1_37)	UGCAGAUCCCACAGGCGCCC	6657
PD1-3 (CR000868)	UGACACGGAAGCGGCAGUCC	5764
PD1-4 (CR000853)	CACGAAGCUCUCCGAUGUGU	5749
PD1-5 (CR000881)	AGGUGCCGCUGUCAUUGCGC	5777
PD1-6	AGGGCCCGGCGCAAUGACAG	5775
PD1-7 (CR000859)	CAGCAACCAGACGGACAAGC	5755
PD1-8 (CR000850)	CCUGCUCGUGGUGACCGAAG	5746

Forward and reverse DNA oligonucleotides encoding gRNA molecules comprising the targeting domains listed above in Table 10 were cloned into a lentiviral vector downstream of a U6 promoter. Using standard procedures, briefly, the vector was digested with BBSI for 1 hour at 37C. The vector was purified using a PCR-purification kit (Qiagen). The gRNA forward and reverse DNA oligonucleotides were synthesized by IDT (Integrated DNA Technologies) with the addition of BBSI site overhangs (ACCG 5' of the forward oligo and AAAC 5' of the reverse strand). The oligos were annealed using IDT duplex buffer by heating up to 95C and letting cool down at room temperature. The annealed oligo was then ligated to the cut and purified vector using NEB quick ligation kit. The vector also contains nucleic acid encoding Cas9 and a mCherry reporter (mCherry is expressed using a T2A sequence downstream of CAS9) downstream of an EF1-alpha promoter. Lentivirus was packaged using a packaging system (Cellecta catalog number CPCP-K2A). The virus was concentrated 200x for all the CRISPR viral productions. In a 96 well flat bottom plate, 1E5 Jurkat cells were plated in 100ul RPMI 10%FBS media. 50ul of concentrated virus was added directly to each well. Then 24 hours post viral addition 100ul of media was added to the cells. Cells were cultured by passaging every 3 days by adding new media to maintain the cells at 0.5e6 cells/mL. Expression of the TCR was measured 7 days post viral transduction. The TCR was detected using anti-CD3 epsilon antibody clone OKT3 conjugated to APC from ebioscience (catalog number 17-0037-42). 1E5 cells were incubated with 2ul of antibody for 20 minutes, analyzed by flow cytometery (BD Fortessa). Data was analyzed using Flow Jo software. mCherry positive cells were gated first to detect CRISPR/Cas9 positive cells. This population was analyzed for TCR loss. The results are shown in Figure 2. These results demonstrate that TCR-alpha targeted gRNAs are able to cause loss of surface TCR expression in Jurkat cells.

Generation of TCR- primary T cells using TCR-alpha targeting gRNAs

The procedure noted above was followed for assessing editing and loss of TCR in primary T cells, with the following modifications. 1E5 primary T cells were activated on Day 0 using 3:1 dyna beads anti-CD3/CD28 in 10ul T cells media in a 96 well flat bottom plate. On Day1 50ul of lentivirus encoding gRNA and Cas9/mCherry (as described above) was added. T cells were cultured for 12 days by adding fresh media every 2 days to maintain a concentration of 5E5cells/ml. Loss of TCR was measured as described above at day 6 and day 12 after lentivirus introduction. The results are shown in Figure 3. These results demonstrate that TCR-alpha targeted gRNAs are able to cause loss of surface TCR expression in primary T cells.

Generation of PD1- primary T cells using PDCD1 targeting gRNAs

Editing of the PD-1 locus and loss of PD-1 expression was assessed as described above using lentiviral vectors encoding gRNA molecules to PD-1 listed in Table 10. Experiments were performed as described above for assessing TCR knockout in primary T cells, except that cells were restimulated with 3:1 dyna beads anti-CD3/CD28 in culture on Day5 to drive increased expression of PD-1, enabling better detection of the protein. The results are reported in Figure 4. These results demonstrate that gRNA molecules of the invention targeting PD-1 (PDCD1) lead to high efficiency loss of PD-1 expression in primary T cells.

Editing of PD-1 or TCR in primary T cells using RNP

Editing of TCR or PD-1 in primary T cells was tested using Cas9/gRNA Ribonucleoprotein (RNP) complexes. RNPs were generated by mixing 20ug of CAS9 (PNA bio) and 20ug of chemically synthesized sgRNA (TriLink biotech) comprising either the targeting domain of TRAC-8 or of PD1-6, and incubating for 15 minutes at room temperature. T cells were isolated from Leukopak PBMCs using Pan T cell Isolation kit (Miltenyi) then activated with 3:1 CD3/CD28 dyna beads (invtrogen). 48 hours post activation, 2E5 T cells (without bead removal) were centrifuged at 300g for 6 minutes and resuspended in 20ul of Optimem and the RNP complex was added and mixed. Then the cells were transferred into a 1mm electroporation cuvette (BTX) and pulsed using the BTX ECM 830 machine at 250V for 500us and 1 pulse. The cells were returned into their T cell media and cultured for 5 days before analyses. Figure 5 shows histograms of TCR or PD-1 expression as detected by flow cytometry after 7 days in culture. These results show that gRNAs targeting TCR alpha and PD-1 are effective at generating either TCR negative or PD1 negative T cells when introduced as RNP.

TCR negative CAR T cells

The ability of gRNA molecules targeting the TRAC locus to edit and lead to TCR negative phenotype in T cells engineered to express a chimeric antigen receptor (CAR) was determined. On Day 0 primary T cells were activated with 3:1 CD3/CD28 dyna beads at a concentration of 5E5 cells/ml in T cell media. On Day 1, T cells were engineered to express a CD19 CAR using lentiviral particles. T cells were engineered to express a CD19 CAR using lentiviral particles (lentivirus, as described in WO2012/079000) at MOI of 5-. On Day 2, T cells were electroporated with RNP comprising Cas9 protein and a gRNA molecule comprising the targeting domain of either TRAC-1 or TRAC-8. On Day 4 onwards, T cells were replenished with fresh media every 2 days to maintain a concentration of 5E5 cells/ml. On day 11 of T cell culture, the T cells were counted, and CD3 microbeads from Miltenyi biotech were added per manufacturer protocol. An LD magnetic column (Miltenyi) was used to perform the positive selection. As shown in Figure 6, T cell populations which were ~40-50% TCR negative could be enriched to create isolated populations of TCRnegative CART cells at greater than 98% purity.

Activity of TCR negative CART cells

The T cells were cultured under standard culture conditions with the following modifications. On day 2 T cells were electroporated with RNP comprising gRNA targeting TCR alpha (TRAC-1 or TRAC-8) as described in "Editing of PD-1 or TCR in primary T cells using RNP," above, or were transduced with lentivirus encoding said gRNA and Cas9/mCherry, as described in Generation of TCR- primary T cells using TCR-alpha targeting gRNAs," above. On day 11 a purification of TCR- cells was added described in "TCR- CAR T cells," above. Isolated TCR negative cells were co-cultured with luciferase-expressing CD19+ NALM6 (B-ALL cell) or CD19- K562 (CML cell) cells and the ability of the TCR- CART cells to specifically kill CD19+ cells was assessed. The results are shown in Figure 7 (% cell lysis), and demonstrate that TCR negative CD19 CART cells comprising TCR-targeting gRNAs (by either lentiviral or RNP transfection) are capable of specifically killing CD19+ cells.

Example 4: B2M excision using two gRNA molecules

To test the ability of two gRNA molecules which bind to the same gene to excise large section of the target gene, we exposed cells to two gRNA molecules. In each experiment, CR00442 was used, in addition to a second gRNA molecule predicted to bind to a target site located from about 10 to about 6000 base pairs away from the binding site of CR00442. Figure 8 shows the predicted excision product size based on the number of base pairs between the two gRNA molecule target sites. Experiments were performed as above, with crRNA molecules comprising the targeting domains of the indicated gRNA molecule (e.g., CR00442) and trRNA being transfected into HEK293 cells engineered to stably express Cas9. Cell lysates were collected at 24 hours and subjected to PCR. Figures 9-11 show the results of these experiments. As shown in Figure 9, CR00442 paired with CR00438, CR00439, CR00440, CR00445 or CR00446 showed DNA fragments corresponding to the expected excision product, ranging from 40-65 base pairs. Pairs of gRNA molecules expected to yield excision products less than 20 base pairs did not result in a detectable excision product as measured by PCR. As shown in Figures 10 and 11, when the expected excision product is about 4000 base pairs (Figure 10) or about 6000 base pairs (Figure 11), many of the guide pairs produced the expected excision with >10% editing. These results demonstrate the feasibility of excising large protions of DNA from a host gene or geneome through the use of two gRNA molecules, and offer an alternative approach to deactivate a gene or gene product.

Example 5: Editing of TRAC in HEK and primary human CD3+ cells

Editing of CRISPR systems containting dgRNA molecules comprising targeting domains to sequences of TRAC were tested for editing in HEK (gRNA delivered to cells stably expressing Cas9) and in primary CD3+ T cells (gRNA/Cas9 RNP delivered by electroporation) according to the methods described herein.

As well, surface expression of TCR after editing was assayed by flow cytometry. Briefly, edited CD3+ cells were stained with antibodies against CD3 (OKT3, eBioscience) and /or TCR-alpha/beta (IP26#, Biolegend) at day 3-5 post-electroporation. Expression of CD3 or TCR-alpha/beta in live cells (identified by propidium iodide exclusion) relative to the un-edited controls was used to determine frequency of RNP editing.

The results are reported in Table 11. All mean editing % are as measured by NGS and are based on at least 3 experiments. gRNA molecules are ranked by the % editing in HEK cells. Figure 12 shows the top gRNA molecules to TRAC as ranked according to the % editing in HEK cells, together with the flow cytometry data showing the % editing in primary human CD3+ T cells as measured by loss of surface expression of TCR.

The indels formed after editing in CD3+ T cells were also assayed. The % of edited cells containing a frameshift mutation is shown in Table 11 ("mean FS edit%). As the TRAC locus results in an expressed protein, it is possible that 3 bp deletions or insertions may not result in disruption and degradation of TRAC. In constrast, frameshift mutations (1-2bp in/dels) would cause the sequence subsequent to the edit to be out of frame and likely result in nonsense mediated degradation. Of note, there were often large differences in the editing % between the HEK and CD3+ T cells, namely the % editing in T cells was typically less than that observed in HEK cells. These differences were reproducible across multiple samples, including in Jurkat cells and different donor sources of primary T cells (not shown). Without being bound by theory, one explanation may be that the TCR locus undergoes rearrangement in T cells and Jurkat cells, but not in HEK cells. Indeed, NGS sequencing runs consistently failed or were of poor quality for the T cells or the Jurkat cells, regardless of donor, primers used or days post-editing that the cells were harvested for analysis (not shown). Thus, a more reliable measurement of % editing in primary T cells may be knockout at the protein level (e.g., loss of TCR by flow cytometry).

Table 11.

		CD3+ (NGS)				HEK (NGS)	
gRNA ID	Target	mean total % edit	SD	mean FS edit (%)	SD2	mean % edit	SD
CR000961	TRAC	3.4	0.9	3.1	0.7	87.9	2.8
CR000924	TRAC	37.4	6.1	30.9	5.5	87.3	2.9
CR000948	TRAC	20.3	4.5	18.4	6.1	84.5	5.6
CR000931	TRAC	37.7	11.4	34.9	9.3	83.6	7.6
CR000929	TRAC	40.3	6.3	36.1	4.8	81.6	0.7

CR000977	TRAC	44.2	4.5	35.7	4.4	80.6	4.8
CR000944	TRAC	4.3	4.5	4.3	4.6	77.6	8.5
CR000984	TRAC	52.1	4.6	42.1	4.2	77.0	5.3
CR000933	TRAC	30.6	12.5	25.2	8.3	74.8	8.6
CR000926	TRAC	22.5	9.2	19.9	6.9	73.0	4.5
CR000943	TRAC	18.1	13.9	14.5	11.3	72.4	9.2
CR000959	TRAC	2.4	0.4	2.1	0.2	71.9	4.1
CR000993	TRAC	24.1	5.7	17.8	3.9	71.0	5.3
CR000947	TRAC	7.2	3.3	6.5	2.8	70.7	9.5
CR000981	TRAC	37.6	10.0	25.1	3.5	70.0	11.6
CR000992	TRAC	33.7	12.0	29.1	12.0	69.2	12.4
CR001002	TRAC	21.8	3.7	19.7	4.8	69.1	5.2
CR001000	TRAC	26.2	9.5	22.7	7.6	68.9	7.4
CR000927	TRAC	23.8	4.5	22.6	4.1	68.7	7.2
CR000986	TRAC	36.4	5.1	14.8	3.0	68.6	14.9
CR000963	TRAC	32.5	7.1	25.3	6.3	68.4	5.4
CR000985	TRAC	17.7	5.4	16.3	4.4	68.1	10.0
CR000923	TRAC	37.3	6.5	32.7	4.6	67.4	3.3
CR000953	TRAC	17.7	2.1	14.4	1.1	66.0	12.8
CR000946	TRAC	9.8	2.9	9.2	2.3	65.9	10.1
CR000932	TRAC	9.9	3.3	7.9	4.1	65.7	7.8
CR001009	TRAC	27.3	9.4	22.8	7.8	65.3	10.6
CR000966	TRAC	22.0	2.9	21.0	2.6	65.2	2.7
CR001011	TRAC	13.2	1.2	10.8	1.8	64.8	13.5
CR001012	TRAC	31.5	14.2	22.9	12.0	64.5	1.4
CR000990	TRAC	36.1	7.0	25.3	5.9	63.7	8.9
CR000951	TRAC	6.7	3.0	6.0	3.5	63.5	16.5
CR001001	TRAC	14.4	0.2	10.9	0.4	61.8	8.0
CR000978	TRAC	24.7	5.1	20.8	4.4	60.7	2.3
CR000934	TRAC	4.4	3.0	4.1	2.6	60.6	4.6
CR000950	TRAC	7.5	0.8	5.4	0.4	60.4	9.2
CR000920	TRAC	12.8	1.9	10.5	0.4	60.2	12.9
CR000991	TRAC	51.2	8.1	45.4	6.9	60.1	6.4
CR000956	TRAC	2.2	0.5	1.9	0.0	59.9	10.5
CR000983	TRAC	26.6	2.0	18.2	0.7	59.8	1.8
CR000936	TRAC	NA	NA	NA	NA	59.7	12.9
CR000960	TRAC	1.2	0.1	1.2	0.2	59.4	6.5
CR001007	TRAC	22.0	4.4	19.0	3.2	58.4	13.9
CR000921	TRAC	12.7	2.0	11.3	1.1	58.3	9.1

CR000952	TRAC	5.8	1.7	5.6	1.8	57.9	7.9
CR000925	TRAC	19.1	4.3	12.3	5.1	56.9	6.1
CR001006	TRAC	13.6	4.3	10.4	3.2	56.8	14.3
CR000942	TRAC	9.8	6.4	9.8	6.3	56.8	1.6
CR000938	TRAC	13.9	0.3	12.5	2.2	55.0	7.1
CR000940	TRAC	22.1	4.7	14.4	4.1	55.0	10.4
CR000989	TRAC	28.2	12.5	18.2	7.6	54.5	1.1
CR000928	TRAC	18.1	1.8	14.6	0.4	54.2	22.1
CR000935	TRAC	NA	NA	NA	NA	54.2	8.2
CR001003	TRAC	13.6	4.6	10.1	4.3	53.5	9.5
CR001014	TRAC	27.3	6.8	24.3	5.9	52.7	4.3
CR000996	TRAC	11.1	0.7	8.6	0.2	52.3	7.3
CR000967	TRAC	31.1	6.3	27.3	3.8	51.9	2.7
CR000968	TRAC	26.1	4.1	24.1	4.2	51.6	10.5
CR000964	TRAC	27.0	7.9	23.5	8.9	51.2	8.9
CR000937	TRAC	15.8	3.4	10.8	2.0	50.9	6.6
CR001005	TRAC	13.9	2.4	13.0	2.4	50.5	12.9
CR001010	TRAC	21.2	4.4	18.6	3.2	48.3	7.0
CR000982	TRAC	28.5	8.9	23.2	7.3	48.1	9.5
CR001004	TRAC	6.7	2.8	6.4	2.5	47.2	15.3
CR000994	TRAC	21.5	2.7	10.8	0.6	46.9	3.4
CR000988	TRAC	22.3	4.7	17.4	3.5	41.9	5.4
CR000973	TRAC	16.2	1.0	12.4	1.1	39.7	16.1
CR000987	TRAC	20.6	1.8	18.2	2.2	39.6	4.0
CR000922	TRAC	6.4	4.5	5.0	3.4	37.8	7.6
CR001015	TRAC	21.8	0.2	20.4	0.0	35.9	17.5
CR000969	TRAC	24.8	6.0	20.9	4.4	34.0	4.9
CR000941	TRAC	9.6	4.5	7.6	4.1	33.4	3.9
CR000945	TRAC	2.3	1.1	2.2	1.1	32.3	7.2
CR000949	TRAC	2.5	2.0	2.5	1.9	30.2	6.2
CR001013	TRAC	19.6	11.5	17.6	10.0	29.7	5.3
CR000939	TRAC	13.5	3.1	12.1	2.2	27.7	5.2
CR000995	TRAC	1.9	1.8	2.5	1.2	23.2	6.3
CR000954	TRAC	2.7	0.4	2.6	0.3	22.3	6.7
CR000962	TRAC	10.4	1.3	8.6	1.2	21.3	5.0
CR000958	TRAC	1.0	0.3	1.0	0.3	20.4	4.4
CR000972	TRAC	6.9	2.5	6.4	2.3	16.2	4.9
CR001008	TRAC	5.1	1.1	4.5	0.9	13.6	1.7
CR000970	TRAC	10.9	2.3	9.3	2.8	13.4	4.7

CR000999	TRAC	12.0	2.4	11.4	2.1	13.1	17.9
CR000930	TRAC	9.9	0.6	7.1	3.2	12.2	1.6
CR000997	TRAC	6.7	0.8	6.4	0.8	11.6	4.7
CR000955	TRAC	2.7	0.7	2.7	0.7	10.0	1.5
CR000975	TRAC	3.8	2.0	3.1	1.4	8.0	0.8
CR000998	TRAC	2.4	0.6	2.2	0.8	4.3	1.3
CR000974	TRAC	1.9	0.5	1.8	0.6	3.3	0.8
CR000971	TRAC	3.0	1.0	2.4	0.5	3.1	0.6
CR000979	TRAC	2.2	1.0	2.2	1.0	3.0	0.4
CR000976	TRAC	1.8	0.6	1.7	0.6	2.8	0.1
CR000957	TRAC	1.3	0.0	1.3	0.0	1.6	0.4
CR000965	TRAC	1.0	0.1	1.0	0.1	1.4	0.1
CR000980	TRAC	33.0	5.0	26.1	3.7	N/A	N/A

Editing in primary human T cells with systems comprising gRNAs targeting TRAC were next tested in primary human CD3+ T cells from 3 different donors. As shown in Figure 15, % editing (as determined by loss of TCR by flow cytometry) was consistent across all donors. These data demonstrated that certain gRNA moleucles, in combination with Cas9, were capable of creating indels within the TCR-alpha sub-unit that result in loss of TCR expression on the surface of T cells. The editing efficiency is donor independent thus showing the broad applicability of this approach.

Example 6: Editing of TRBC1 and TRBC2 in HEK cells

Editing of CRISPR systems containting dgRNA molecules comprising targeting domains to sequences of TRBC1 and TRBC2 were tested for editing in HEK (gRNA delivered to cells stably expressing Cas9) and CD3+ T cells (gRNA and Cas9 delivered as RNP) according to the methods described herein. The results are reported in Table 12. All mean editing % are as measured by NGS and are based on at least 3 experiments. Figure 13 shows the top gRNA molecules to TRBC1 and TRBC2 as ranked according to the % editing in HEK cells, together with the flow cytometry data showing the % editing in primary human CD3+ T cells as measured by loss of surface expression of TCR.

Table 12.

			HEK (NGS)	
gRNA ID	Target	Coding vs non-coding targeted region	mean total % edit	SD
CR000789	TRBC2	Non-coding	62%	3%
CR000780	TRBC2	Non-coding	60%	9%

CR000734	TRBC1	Non-coding	59%	6%
CR000761	TRBC2	Non-coding	57%	2%
CR000776	TRBC2	Non-coding	54%	9%
CR000786	TRBC2	Non-coding	53%	7%
CR000785	TRBC2	Non-coding	52%	4%
CR000737	TRBC1	Non-coding	52%	5%
CR000775	TRBC2	Non-coding	51%	5%
CR000783	TRBC2	Non-coding	51%	5%
CR000823	TRBC2	Coding	51%	6%
CR000756	TRBC2	Non-coding	45%	2%
CR000798	TRBC2	Non-coding	44%	2%
CR000735	TRBC1	Non-coding	44%	7%
CR000731	TRBC1	Non-coding	44%	5%
CR000729	TRBC1	Non-coding	43%	4%
CR000774	TRBC2	Non-coding	43%	5%
CR000810	TRBC2	Coding	42%	9%
CR000800	TRBC2	Coding	41%	13%
CR000784	TRBC2	Non-coding	40%	3%
CR000762	TRBC2	Non-coding	40%	5%
CR000782	TRBC2	Non-coding	40%	4%
CR000815	TRBC2	Coding	39%	9%
CR000748	TRBC2	Non-coding	39%	3%
CR000760	TRBC2	Non-coding	38%	3%
CR000781	TRBC2	Non-coding	37%	4%
CR000812	TRBC2	Coding	37%	7%
CR000732	TRBC1	Non-coding	36%	5%
CR000788	TRBC2	Coding	36%	7%
CR000752	TRBC2	Non-coding	36%	13%
CR000745	TRBC1	Non-coding	34%	4%
CR000759	TRBC2	Non-coding	33%	7%
CR000813	TRBC2	Coding	32%	4%
CR000770	TRBC2	Non-coding	32%	7%
CR000738	TRBC1	Coding	31%	5%
CR000816	TRBC2	Coding	31%	8%
CR000744	TRBC1	Non-coding	31%	2%
CR000807	TRBC2	Coding	31%	4%
CR000811	TRBC2	Coding	30%	7%
CR000766	TRBC2	Non-coding	30%	2%
CR000787	TRBC2	Non-coding	30%	1%

CR000751	TRBC2	Non-coding	30%	6%
CR000730	TRBC1	Non-coding	29%	3%
CR000739	TRBC1	Non-coding	28%	6%
CR000768	TRBC2	Non-coding	28%	2%
CR000771	TRBC2	Non-coding	27%	4%
CR000763	TRBC2	Non-coding	26%	4%
CR000754	TRBC2	Non-coding	26%	7%
CR000755	TRBC2	Non-coding	24%	4%
CR000769	TRBC2	Non-coding	24%	1%
CR000777	TRBC2	Non-coding	23%	1%
CR000764	TRBC2	Non-coding	23%	6%
CR000749	TRBC2	Non-coding	23%	5%
CR000767	TRBC2	Non-coding	23%	5%
CR000791	TRBC2	Non-coding	23%	4%
CR000809	TRBC2	Coding	22%	8%
CR000773	TRBC2	Non-coding	22%	7%
CR000817	TRBC2	Coding	21%	6%
CR000746	TRBC1	Non-coding	21%	4%
CR000753	TRBC2	Non-coding	21%	1%
CR000757	TRBC2	Non-coding	21%	1%
CR000793	TRBC2	Non-coding	21%	4%
CR000743	TRBC1	Non-coding	20%	4%
CR000741	TRBC1	Non-coding	20%	2%
CR000819	TRBC2		20%	3%
CR000740	TRBC1	Non-coding	19%	2%
CR000814	TRBC2	Coding	19%	7%
CR000728	TRBC1	Non-coding	16%	6%
CR000742	TRBC1	Non-coding	14%	3%
CR000733	TRBC1	Non-coding	10%	4%
CR000747	TRBC1	Non-coding	8%	1%
CR000736	TRBC1	Non-coding	8%	1%

These data demonstrated that certain gRNA molecules, in combination with Cas9, were capable of creating indels within the TCR-beta sub-unit that result in loss of TCR expression on the surface of T cells.

Example 7: Editing of PDCD1 in HEK cells and primary human CD3+ T cells

Editing of CRISPR systems containting dgRNA molecules comprising targeting domains to sequences of PDCD1 were tested for editing in HEK (gRNA delivered to cells stably expressing Cas9) and CD3+ T cells (gRNA and Cas9 delivered as RNP) according to the methods described herein.

The results of editing in HEK cells are reported in Table 13. All mean editing % are as measured by NGS and are based on at least 3 experiments. Figure 16 shows the top gRNA molecules to PDCD1 as ranked according to the % editing in HEK cells. Figure 16 also shows % of cells with loss of PD-1 expression as measured by flow cytometry using an anti-PD-1 antibody (ceBioJ105, eBioscience). Briefly, primary human CD3+ T cells were activated with StemCell ImmunoCult beginning on day 0. RNP containing the indicated dgRNA were electroporated into the cells on day 3 (Neon; 1600 V, 10 ms, 3 pulses). 2 days after transfection (day 5), cells were stimulated with antiCD3/CD28 Dynabeads (1:3 cell:bead ratio). PD-1 expression was assessed on day 10.

Table 13.

		HEK (NGS) % Editing	
gRNA ID	target name	Mean	Std Dev
CR000847	PDCD1	77%	1%
CR000902	PDCD1	72%	8%
CR000852	PDCD1	72%	5%
CR000826	PDCD1	70%	7%
CR000904	PDCD1	70%	2%
CR000839	PDCD1	69%	10%
CR000828	PDCD1	69%	4%
CR000835	PDCD1	69%	6%
CR000829	PDCD1	68%	6%
CR000879	PDCD1	68%	8%
CR000870	PDCD1	66%	8%
CR000831	PDCD1	66%	13%
CR000848	PDCD1	65%	4%
CR000855	PDCD1	61%	21%
CR000838	PDCD1	61%	12%
CR000840	PDCD1	59%	5%
CR000884	PDCD1	59%	7%
CR000830	PDCD1	57%	12%
CR000871	PDCD1	57%	8%
CR000850	PDCD1	55%	9%
CR000869	PDCD1	55%	6%

CR000903	PDCD1	54%	8%
CR000824	PDCD1	54%	7%
CR000882	PDCD1	50%	11%
CR000918	PDCD1	50%	9%
CR000895	PDCD1	49%	10%
CR000832	PDCD1	49%	8%
CR000874	PDCD1	47%	5%
CR000868	PDCD1	47%	7%
CR000846	PDCD1	46%	6%
CR000887	PDCD1	46%	6%
CR000825	PDCD1	46%	6%
CR000892	PDCD1	45%	11%
CR000917	PDCD1	43%	9%
CR000896	PDCD1	42%	7%
CR000919	PDCD1	42%	8%
CR000863	PDCD1	40%	9%
CR000842	PDCD1	40%	15%
CR000827	PDCD1	39%	11%
CR000837	PDCD1	36%	8%
CR000915	PDCD1	35%	10%
CR000833	PDCD1	34%	5%
CR000853	PDCD1	33%	4%
CR000891	PDCD1	29%	11%
CR000849	PDCD1	29%	7%
CR000897	PDCD1	26%	2%
CR000872	PDCD1	26%	5%
CR000844	PDCD1	25%	3%
CR000854	PDCD1	24%	6%
CR000867	PDCD1	24%	4%
CR000856	PDCD1	23%	4%
CR000845	PDCD1	21%	6%
CR000881	PDCD1	21%	3%
CR000894	PDCD1	19%	3%
CR000834	PDCD1	19%	7%
CR000841	PDCD1	19%	1%
CR000858	PDCD1	16%	2%
CR000859	PDCD1	12%	3%
CR000898	PDCD1	11%	3%
CR000880	PDCD1	10%	2%

CR000893	PDCD1	10%	1%
CR000885	PDCD1	10%	1%
CR000883	PDCD1	9%	1%
CR000843	PDCD1	8%	2%
CR000864	PDCD1	7%	1%
CR000875	PDCD1	6%	2%
CR000899	PDCD1	5%	3%
CR000890	PDCD1	5%	2%
CR000914	PDCD1	5%	1%
CR000836	PDCD1	5%	1%
CR000916	PDCD1	5%	1%
CR000877	PDCD1	5%	1%
CR000888	PDCD1	4%	1%
CR000866	PDCD1	4%	1%
CR000851	PDCD1	4%	0%
CR000865	PDCD1	4%	1%
CR000889	PDCD1	3%	0%
CR000876	PDCD1	3%	0%
CR000886	PDCD1	2%	0%
CR000857	PDCD1	1%	0%
CR000878	PDCD1	1%	0%
CR000860	PDCD1	NA	NA
CR000861	PDCD1	NA	NA
CR000862	PDCD1	NA	NA
CR000873	PDCD1	NA	NA
CR000900	PDCD1	NA	NA
CR000901	PDCD1	NA	NA
CR000905	PDCD1	NA	NA
CR000906	PDCD1	NA	NA
CR000907	PDCD1	NA	NA
CR000908	PDCD1	NA	NA
CR000909	PDCD1	NA	NA
CR000910	PDCD1	NA	NA
CR000911	PDCD1	NA	NA
CR000912	PDCD1	NA	NA
CR000913	PDCD1	NA	NA

Next, editing of PDCD1 by RNPs comprising dgRNA molecules that include the targeting domain of the indicated CRxxxx ID was assayed in primary human CD3+ T cells as measured by NGS, and loss of PD-

1 surface expression was assayed by flow cytometry, as described herein. The results are reported at Figure 18. Several gRNA molecules show good editing and loss of PD-1. These same guides were then tested in CD3+ T cells from three different donors. The data is reported at Figure 19. As shown, gRNAs including the targeting domain of CR00852, CR00828, CR00870, CR00848, CR00855 and CR00838 show greater than 50% editing across at least 2 donors.

Example 8: Simultaneous and Sequential Knockout of TRAC and B2M in Primary Human CD3+ T Cells

Primary human CD3+ T cells were activated and electroporated with RNP containing gRNA to B2M (CR000442) and/or TRAC (CR000984). Briefly, RNPs targeting B2M and/or TRAC were electroporated into CD3+ T cells in the following ratios: B2M RNP only; TRAC RNP only; B2M RNP + TRAC RNP; 0.5X B2M RNP + 0.5X TRAC RNP; 0.5X B2M RNP + 1X TRAC RNP; 1X B2M RNP + 0.5X TRAC RNP; no RNPs. This allowed us to determine the effect of various amounts of RNP (1 or 2 targets) on cell viability and editing efficiency of the targeted genes. Cells were assessed by flow cytometry for both TCR expression and B2M expression. The results are showin in Figure 17A-17D. These results showed that RNPs targeting two separate targets could be delivered simultaneously to CD3+ T cells by electroporation without negative impact on viability or compromising the editing efficiency of either guide. Additionally, a high frequency of CD3+ T cells were successfully edited at both targets resulting in a CD3- B2M- population.

Next, the effect of editing two targets, B2M and TRAC by either simultaneous or sequential introduction of RNPs containing dgRNAs to B2M and TRAC. For this experiment, RNPs were generated as described above using a dgRNA comprising the targeting domain of CR000442 for targeting of B2M and using a dgRNA comprising the targeting domain of CR000984 for targeting TRAC. Briefly, CD3+ T cells were thawed, activated for 3 days (Immunocult CD3/CD28 T cell activator from StemCell Technologies). On day 3 and day 4 (sequential) or day 3 (Simultaneous), cells were electroporated to introduce RNPs, and maintained until day 5 post-delivery (Day 9), when expression of B2M and/or TCR was assessed by FACS (then by NGS following cell lysis). T cells were maintained in the presence of activating reagent throughout the electroporation and post-electroporation process. Expression of B2M and TCR were assessed by FACS (using anti-B2M clone 2M2 or anti-CD3 clone OKT3 at 1:200 dilution). Cells were subsequently lysed and editing of the targeted loci assessed by NGS. The results are reported at Figures 25 and 26. These results indicate that both sequential and simultaneous targeting of B2M and TRAC yield similar double knockout frequencies.

Example 9: Editing of FKBP1A

Editing of FKBP1A with dgRNAs targeted to the FKBP1A gene were assayed in HEK293 cells engineered to express Cas9, as described above. The data, including % editing and the % of frameshift (FS) edit, are reported in Figure 21, Figure 22, and Figure 23. Based on these results, the top 15 gRNA molecules were identified by highest percent FS edit. These gRNA molecules, including their targeting domains, are reported in Figure 23. Next, editing of FKBP1A in CD3+ T cells was assayed using RNPs comprising dual guides comprising the identified targeting domain to FKBP1A. Cells, RNPs and all methods were formed and performed as described above. The results are reported in Figure 24.

To follow up on the previous experiments, gRNAs comprising the targeting domains of the most efficient editing gRNAs were tested again in primary human T cells. Figure 52 shows the genomic editing of the FKBP1A locus resulting from human primary T cell electroporation with RNPs containing the indicated gRNAs targeting FKBP1A in dgRNA format (as described above). The frequency of insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence is shown. The results demonstrate a subset of gRNAs which are able to achieve high editing efficiency (> 80%) with a high proportion of frameshift edits (>65%). Figure 53 shows the top 5 most frequently observed sequence changes (indels) for each FKBP1A targeting gRNA used for primary human T cell editing.

Example 10: Editing of CIITA

Editing of CIITA with dgRNAs targeted to the CIITA gene were assayed in HEK293 cells engineered to express Cas9, as described above in Example 1. The data, including % editing and the % of frameshift (FS) edit, are reported below in Table 24.

Table 24. % editing (N=3) and % Frameshift edit (FS) as measured by NGS in HEK293 cells stably expressing Cas9 using dgRNAs that include the targeting domain to CIITA as indicated. gRNA molecules are ranked in the table by % edit.

		HEK293_Cas9 Cells				
ID	Target	Avg. % Edit	StdDev % Edit	Avg. % FS	StdDev % FS	Rank
CR002993	CIITA	60.16	6.68	48.86	4.24	1
CR002991	CIITA	59.11	9.04	51.40	8.37	2
CR002995	CIITA	52.74	11.49	43.64	9.45	3
CR002948	CIITA	52.71	7.63	48.08	6.93	4

CR002980	CIITA	50.30	13.62	42.41	11.48	5
CR002961	CIITA	50.29	6.60	38.41	4.64	6
CR003001	CIITA	47.64	11.32	43.30	10.38	7
CR002992	CIITA	46.54	12.64	31.23	7.79	8
CR002971	CIITA	45.94	13.74	33.61	9.92	9
CR002976	CIITA	45.36	14.84	37.66	12.71	10
CR002967	CIITA	44.47	21.39	38.77	18.85	11
CR003007	CIITA	43.64	12.08	32.22	8.81	12
CR002953	CIITA	43.60	11.37	34.95	9.42	13
CR002994	CIITA	42.35	8.53	31.32	5.55	14
CR002965	CIITA	41.85	16.72	29.63	10.99	15
CR002972	CIITA	41.06	12.07	28.56	9.07	16
CR003011	CIITA	38.96	19.22	22.19	10.64	17
CR002978	CIITA	38.34	18.04	34.11	16.14	18
CR003013	CIITA	37.75	11.18	29.94	8.82	19
CR002962	CIITA	37.71	10.14	26.10	7.04	20
CR002966	CIITA	37.12	18.00	31.49	15.77	21
CR002981	CIITA	36.28	15.11	29.98	12.29	22
CR002983	CIITA	35.90	10.82	33.83	10.53	23
CR002970	CIITA	35.40	15.32	25.50	10.63	24
CR002943	CIITA	35.24	3.38	26.47	2.47	25
CR002990	CIITA	35.19	11.07	24.08	7.77	26
CR003003	CIITA	35.07	16.21	27.91	12.76	27
CR002941	CIITA	34.89	4.47	21.77	3.02	28
CR002956	CIITA	34.30	9.28	29.66	8.14	29
CR002944	CIITA	34.04	2.10	22.26	1.09	30
CR002945	CIITA	33.37	9.71	17.29	4.42	31
CR002985	CIITA	32.99	11.62	29.52	10.46	32
CR002940	CIITA	32.80	8.06	22.25	6.09	33
CR002958	CIITA	32.78	8.06	22.49	4.77	34
CR003009	CIITA	32.69	14.75	25.62	11.60	35
CR003014	CIITA	32.51	14.39	26.93	11.72	36
CR002963	CIITA	32.48	13.28	26.80	11.02	37
CR002946	CIITA	31.12	11.15	14.20	4.24	38
CR002959	CIITA	30.79	8.79	29.78	8.64	39
CR002973	CIITA	30.60	11.08	23.55	8.17	40
CR003021	CIITA	29.94	10.67	26.88	9.37	41
CR003026	CIITA	29.63	6.59	20.05	4.52	42
CR002968	CIITA	29.53	17.36	22.22	12.73	43
CR003023	CIITA	29.38	7.13	16.83	3.71	44
CR002979	CIITA	28.91	13.80	23.07	10.56	45

CR003018	CIITA	27.72	9.36	26.54	9.18	46
CR002987	CIITA	27.56	11.04	24.06	9.81	47
CR003015	CIITA	27.40	7.88	24.05	6.97	48
CR002989	CIITA	27.38	13.31	8.45	4.26	49
CR002964	CIITA	26.56	11.21	19.56	7.74	50
CR003010	CIITA	25.45	10.54	14.37	5.52	51
CR002988	CIITA	25.29	13.48	11.35	5.56	52
CR002951	CIITA	25.09	6.28	16.13	3.91	53
CR003025	CIITA	24.52	6.66	19.21	4.70	54
CR002996	CIITA	23.91	7.13	17.83	5.34	55
CR003022	CIITA	23.73	11.35	17.96	8.69	56
CR003020	CIITA	23.67	9.57	16.44	6.58	57
CR002999	CIITA	23.50	12.38	18.58	9.69	58
CR002939	CIITA	22.02	5.58	17.27	4.64	59
CR003017	CIITA	21.90	4.21	15.22	2.47	60
CR003005	CIITA	21.11	6.97	18.08	5.97	61
CR002969	CIITA	20.82	14.36	14.85	9.88	62
CR003024	CIITA	20.40	6.26	16.33	4.88	63
CR003006	CIITA	19.46	9.28	14.66	6.72	64
CR002954	CIITA	19.43	7.05	6.28	2.27	65
CR003004	CIITA	19.43	7.68	15.63	6.01	66
CR002975	CIITA	19.31	3.56	15.82	2.58	67
CR002977	CIITA	19.11	9.48	12.99	6.31	68
CR003016	CIITA	17.86	4.27	13.55	3.56	69
CR002942	CIITA	17.14	1.59	8.91	0.97	70
CR002950	CIITA	16.64	4.84	8.65	2.46	71
CR002947	CIITA	15.86	4.03	8.10	2.13	72
CR003008	CIITA	15.30	10.49	10.91	7.58	73
CR003000	CIITA	12.83	7.31	10.53	5.76	74
CR003002	CIITA	11.85	4.06	9.78	3.32	75
CR003019	CIITA	11.80	2.88	9.74	2.19	76
CR003012	CIITA	10.67	6.52	7.51	4.18	77
CR002960	CIITA	10.56	3.88	6.96	2.14	78
CR002982	CIITA	10.45	4.28	9.05	3.66	79
CR002952	CIITA	10.37	4.96	8.22	4.17	80
CR002974	CIITA	8.99	2.67	6.92	1.79	81
CR002955	CIITA	7.88	3.56	5.04	2.25	82
CR002998	CIITA	4.95	6.44	4.84	6.27	83
CR002957	CIITA	3.73	0.70	3.15	0.48	84
CR002949	CIITA	2.39	0.64	1.83	0.32	85
CR002984	CIITA	2.33	0.18	2.19	0.17	86

CR002986	CIITA	1.77	0.51	1.48	0.27	87
CR002997	CIITA	N/A	N/A	N/A	N/A	88

Next, editing of the CIITA gRNA molecules with the highest Editing % was assessed in CD3+ primary human T cells, as described in Example 1. The results are shown in Table 32.

Table 32. % Editing and % Frameshift Edit (as measured by NGS) by dgRNA molecules targeting CIITA delivered as RNP to CD3+ T cells

	CD3+ NGS			
Targeting Domain ID	Editing %	Edit % Std. Dev.	Frameshift Edit %	Frameshift % Std. Dev.
CR002948	41.6	2.3	33.6	1.7
CR003001	36.3	1.8	32.0	1.3
CR002991	33.9	3.4	29.2	3.3
CR002993	33.8	2.6	27.2	1.7
CR003007	31.6	1.6	28.8	1.7
CR002961	30.3	2.0	24.7	1.2
CR002965	29.0	3.9	24.4	3.2
CR002967	28.0	0.7	25.6	0.5
CR002972	26.6	1.1	20.9	1.9
CR002994	22.0	2.7	18.1	2.3
CR002992	16.0	1.6	11.6	0.8
CR003013	11.5	0.9	9.0	0.6
CR002971	7.2	0.7	5.4	0.4
CR002980	6.1	0.5	3.6	0.6
CR003011	5.2	0.6	4.9	0.6
CR002953	5.1	0.7	4.8	0.7
CR002978	4.7	0.7	2.7	0.2
CR002976	4.0	0.3	3.6	0.3
CR002962	3.4	0.4	2.9	0.4
CR002995	3.1	0.2	2.5	0.4

Next, editing, and loss of MHC class II molecule expression, in response to a subset of gRNA molecules targeting CIITA was assessed in primary human T cells. Briefly, primary human T cells were prepared in culture and activated using CD3/CD28 bead stimulation (DynaBeads Invitrogen Cat#111.41D) at bead to cell ratio of 3:1. At day 2, RNP consisting of *S. pyogenes* Cas9 precomplexed with dgRNA molecules (using the crRNA and tracr sequences described above) comprising the indicated targeting domains were

electroporated into the T cells using the Neon electroporator at three different concentrations of RNP (0.3 uM, 1.0 uM and 3.0 uM; diluted after formation of RNP). On Day 5 and Day 7, % editing was assessed by loss of expression of HLA-DR, as assessed by flow cytometry. The results from Day 5 and Day 7 were comparable. % editing in T cells (e.g., % of cells which are CD3+ and HLA-DR-) at day 5 is shown in Figure 37. As shown, at the highest concentration tested, RNP that included dgRNA molecules CR02991, CR02993 and CR03007 each resulted in >50% editing, as measured by loss of HLA-DR surface staining. As shown below, the lack of editing observed for gRNA CR002961 was due to a mistake in the experimental protocol. When the experiment was repeated (data shown in Figure 39), RNP comprising gRNA CR002961 resulted in dose-responsive levels of reduction of HLA-DR expression.

The experiments described above were repeated for another set of gRNA molecules targeting CIITA. Figure 38 shows the results of this experiment, with genomic editing of the CIITA locus resulting from human primary T cell electroporation with RNP containing the indicated gRNA targeting the CIITA locus. The frequency of insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence is shown (%frameshift edits). The top 5 most frequently observed sequence changes are shown in detail in the bottom panel. These data indicate that gRNAs targeting CIITA are able to achieve >90% editing with up to 74% frameshift editing in primary human T cells.

The experiment was again performed using a third set of grNAs targeting CIITA at various concentrations of RNP. Figure 39 shows the % editing at Day 3 post electroporation in primary human T cells by RNPs that include the indicated dgRNA to CIITA (number indicates CR00xxxx identifier of targeting domain) at the indicated concentration, as measured by flow cytometry using an anti-HLA-DR reagent. % editing represents the expression of HLA-DR at the cell surface in cells electroporated with CIITA guide relative to the expression in cells electroporated without guide RNA. As mentioned above, activity of gRNA CR002961 was confirmed in this experiment. Figure 40 shows the frequency of insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence is shown (%frameshift edits). These data indicate that antoher set of gRNAs targeting CIITA is identified which are able to achieve >85% editing with up to 87% frameshift editing (CR002967) in primary human T cells. The top 5 most frequently observed sequence changes for each CIITA targeting gRNA used for primary human T cell editing are shown in Fgiure 41.

The experiment was again perfomed using a different set of gRNAs targeting CIITA, and compared to the highest performing gRNA (CR0002967) from the previous experiment. Figure 42 shows the results of %

editing at Day 3 post electroporation in primary human T cells by RNPs that include the indicated dgRNA to CIITA (number indicates CR00xxxx identifier of targeting domain) at the indicated concentration, as measured by flow cytometry using an anti-HLA-DR reagent. Figure 42 shows the frequency of insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence (%frameshift edits) when these gRNAs are used. Figure 44 shows the top 5 most frequently observed sequence changes (indels) for each of these CIITA targeting gRNA in primary human T cells. These data confirm the high editing/frameshift/loss of HLA-DR for RNP comprising dgRNA CR002967 and additionally identify other CIITA-targeted gRNAs which result in high editing (>90%) and high frameshift mutations (>80%) in primary human T cells.

Example 11: Editing of TCR (TRAC) and B2M in BCMA CAR T cells

Table 25: Reagents used for flow cytometry

Name	Catalog Number	Company	Nick name	Clone
R-PE Strepetavidin	016-110-084	Jackson Immuno Research	SAPE	
Streptavidin APC-eFluor780	47-43-17-82	ebiosciences	SA-APC-e780	
APC-Anti Hum B2Microglobulin	316312	Biolegend	B2M-APC	
PerCP-Cyanine5.5 Anti human CD3	45-0037-42	ebiosciences	CD3 PerCPcy5.5	OKT3
Anti Human CD8a APC	17-0087-42	ebiosciences	CD8 APC	SK1
Anti Human CD8a Alexafluor700	300920	Biolegend	CD8 Af700	
Anti Human HLA-DR efluor 450	48-9956-42	ebiosciences	HLA-DR V450	LN3
Anti Human CD8a eFluor 450	48-0086-42	ebiosciences	CD8 V450	OKT8
Anti Human CD4 eFluor 450	48-0047-42	ebiosciences	CD4 V450	SK3
Fixable Viability Dye eFlour780	65-0865-14	ebiosciences	L/D e780	

Table 26: T cell media components

Component	*Invitrogen Catalog #*	*Concentration*
RPMI 1640	22400-089	

FBS	16140	10% final
L-glutamine	25030-081	200 mM (100x stock)
Non-essential amino acids	11140-050	10 mM (100x stock)
Sodium pyruvate	11360-070	100 mM (100x stock)
HEPES buffer	15630-080	1 M (100x stock)
2-mercaptoethanol	21985-023	55 mM (1000x stock)

Editing of allogeneic T cell targets in T cells engineered to express a BCMA CART, and the function of edited cells was assessed. T cells, including TCR-B2M-/BCMA CAR+ T cells, used in these experiments were prepared as described schematically in Figure 27. Briefly, PBMC were isolated from human blood by using centrifugation method using Ficoll. Total T cells were isolated from these PBMC's (Hemacare) using human Pan T Cell Isolation Kit (Miltenyi Biotec #130-096-535). These cells were aliquoted and frozen using CRYOSTOR CS10 media (Biolife Solution-210102), and stored in liquid nitrogen. These frozen cell aliquots were then thawed in a 37 degree waterbath for 20 seconds and then transferred to a 50 ml conical tube with 10 ml of prewarmed T cell media and centrifuged at 300rpm for 5-10 mins at 24 degrees to remove the freezing media and resuspended with prewarmed T cell media. Cells were then transferred to a 24-well dish and activated by adding CD3/CD28 beads (DynaBeads Invitrogen Cat#111.41D) at bead to cell ratio of 3:1. Day1 post activation, lentivirus comprising sequence encoding CAR BCMA-13 (139112 from Table 23, above) was transduced into these cells at a multiplicity of infection (MOI) of 5. UTD (untransduced cells) were not treated with virus. Day 4 post activation, 250,000 cells per condition either CAR BCMA-13 or Untransduced T cells were then electroporated with RNP using BTX (settings: 1000V/ 0.6 ms /1 pulse) with or without guide RNA as indicated. For RNP generation, dgRNA molecules comprising tracr RNA and crRNA for TRAC and B2M were heated together at 95°C for 2 minutes and gradually were cooled to come to room temperature, upon which they were incubated with Cas9 Protein and 5X CCE buffer for 10 mins at 37°C. For TRAC editing the targeting domain of CR000985 (Sequence: CCGAAUCCUCCUCCUGAAAG (SEQ ID NO: 5593)) was used, and for B2M editing the targeting domain of CR000442 (Sequence: GGCCACGGAGCGAGACAUCU (SEQ ID NO: 5496)) was used. In each case, dgRNA were used with the crRNA sequence: [targeting domain]-GUUUUAGAGCUAUGCUGUUUUG (SEQ ID NO: 6607), and the tracr sequence: AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUUUUU (SEQ ID NO: 6660). After electroporation cells were returned to 0.5ml of T

cell media in a 24 well plate. Two days after electroporation, cells were split every other day to maintain cells at 0.5million/ml. Five days post electroporation, 100,000 cells were analyzed by flow cytometry (BD Fortessa) using FlowJo software. 100,000 cells were aliquoted to each well of round bottom 96 welled plate. Cells were taken from each sample, pipetted to dissociate them from beads, and beads were removed by using 96 welled plate magnet, and centrifuged with 100ul of FACS buffer (Miltenyi MACS buffer catalog # 130-092-987 with 0.5% BSA (Miltenyi- catalog# 130-091-376) to wash the cells. Cells were then incubated with different antibodies diluted in 100ul FACS buffer for 30 mins on ice. Cells were then washed two times with 200ul of FACS buffer. Cells were then resuspended in 150 ul of FACS buffer and run on 5 laser Fortessa flow cytometer (Becton Dickenson). Expression of TCR was detected by using anti- CD3-PercpCy5.5 (Ebiosciences 45-0037-42) and expression of B2M was detected by using anti-B2M-APC (316312 Biolegend). Cell surface expression of CAR was evaluated by staining with Biotinylated Protein L followed by Streptavidin-PE (016-110-084 Jackson Immuno Research). T cells were detected by staining CD4 using anti-CD4-V450 (48-0047-42 Ebiosciences) or CD8 using anti-CD8-alexa700 (300920 Biolegend). Expression of TCR (using anti- CD3-PercpCy5.5) and B2M (using anti-B2M-APC) is shown in Figure 28. T-cells transduced with BCMA CAR BCMA-13 are indicated as "CAR". Untransduced cells are indicated as "UTD". Cells electroporated with Cas9 but no guide RNA are indicated as "no guide". CD4 staining using anti-CD4-V450 is shown in the lower panels of Fig. 28 to verify that the loss of CD3 staining is due to loss of the TCR and not due to loss of T-cells. These results demonstrate that simultaneous introduction of CRISPR systems to B2M and TRAC can be used to generate a population of T cells which lack TCR expression and B2M expression in high yield, with 72% of T cell in the CAR-transduced set staining negative for both TCR and B2M. Next, the eding of TRAC and B2M was evaluated in the CAR+ subset of cells assessed in Fig. 28. The results are shown in Figure 29. Briefly, the cells from Figure 28 were analyzed by gating for CAR+ cells (stained using Biotinylated Protein L followed by Streptavidin-PE) for the left-hand panel or without CAR gating (total T-cells; right panel). Editing levels are similar in the CAR+ and total T-cell populations, indicating that CAR expression did not have an effect on editing efficiency.

Next, the cells from Figure 28 were analyzed for CAR expression by analyzing the PE channel. As shown in Figure 30, the percentage of CAR positive cells was similar in the cells receiving guide RNAs (TRAC and B2M) and those that did not (no guide), indicating that TCR and B2M editing did not have an effect on CAR expression. UTD indicates untransduced cells. CAR indicates cells that were transduced with BCMA CAR.

Next, the ability of T cells to proliferate in response to BCMA (the target antigen of the CAR molecule) was assessed. Briefly, cells were prepared as described above, were thawed and co-cultured with target

cells expressing BCMA (KMS11 (high), RPMI8226 (low)) or not expressing BCMA (Nalm6). T-cells transduced with CAR BCMA-13 are indicated as "BCMA CAR". Untransduced cells are indicated as "UTD". Cells electroporated with Cas9 but no guide RNA are indicated as "no guide". Cells electroporated with RNP containing B2M and TCR guides are indicated as "B2M+TCR". 25,000 irraduated target tumor cells were co-cultured with T cells at 1:1 ratio for 4 days followed by flow cytometry analysis. The number of T-cells (stained with anti-CD4-V450 and anti-CD8-alexa700) was determined by the number of CD4+ plus CD8+ cells relative to 3000 counting beads (Life technology, Catalog # C36950). As shown in Figure 31, both populations of cells transduced with BCMA CAR lentivirus exhibited proliferation in response to both BCMA-expressing cell types, with the population of cells receiving RNPs containing B2M and TRAC-targeting gRNA molecules exhibiting higher T cell counts after 4 days of co-culture. As shown in Figure 32, when proliferation of CAR+ CD4+ and/or CD8+ T cells was assessed seperately, results were similar, with CAR+ (gated by staining with biotinylated Protein L followed by Streptavidin-APC-efluor780) T cells proliferating in response to both BCMA-expressing cell types.The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention.

Example 12: Analysis of RNP concentration effects and indel patterns using RNPs targeting TCR or B2M, and generation of CIITA-/B2M-/TCR- CAR T cells

Methods

PBMC were isolated from human blood (Hemacare) by using centrifugation method using Ficoll. Total T cells were isolated from these PBMC's using human Pan T Cell Isolation Kit (Miltenyi Biotec #130-096-535). These cells were aliquoted and frozen. These frozen cell aliquots were then thawed and activated using CD3/CD28 beads (DynaBeads Invitrogen Cat#111.41D) at bead to cell ratio of 3:1. On day 2 or day 3 after bead activation, 200,000 cells were removed from culture for electroporation. RNP complex used for T cell genome editing was formed using a 1:2 molar ratio of Cas9 protein to RNA (crRNA and tracRNA). 100 µM crRNA and 100 µM tracrRNA were denatured separately at 95oC for 2 min and cooled to room temperature. In a final volume of 5 µL, 1.4 µL of Cas9 protein at a concentration of 5.9 µg/µL (NLS-Cas9-NLS) was mixed with 1.6 µL of Cas9 buffer (20 mM Tris, pH8.0; 200 mM KCL, 10 mM MgCL2) and mixed with 1 µL of 100 µM tracrRNA at room temperature. Next 1 µL of 100 µM crRNA was added, mixed and incubated for 10 min at 37oC. If more than one RNP was added during the electroporation step, each RNP with a crRNA targeting a different gene was assembled separately using the above method, then combined together with the addition of Cas9 buffer in order to obtain different RNP final concentrations for different conditions. For "triple editing", i.e. simultaneous addition of 3 RNPs targeting different genes, details of RNP quantities are provided in the figures. The assembled

RNPs were then mixed with 200,000 cells in 10 ul of T Buffer (neon transfection system 10ul Kit). Electroporation was performed by Neon electroporator using Neon® Transfection System 10 µL Kit (MPK1096) at 1600V, 10ms, 3 pulses. For CIITA, editing was quantitated by measuring loss of cell surface expression of HLA-DR by flow cytometry 3 days after electroporation. Cells were stained with anti-CD3 (PerCP-Cy5.5), anti-HLA-DR-V450, and a live/dead cell dye e780(APC-Cy7) and analyzed by flow cytometry. Editing of TRAC was quantitated by measuring loss of cell surface expression of CD3 epsilon by flow cytometry 3 days after electroporation using anti-CD3 antibody (PerCP-Cy5.5). Editing of B2M was measured by loss of cell surface expression using flow cytometry 4 days after electroporation using anti-B2M antibody-APC (316312 Biolegend). To evaluate the editing frequency and sequence changes resulting from gene editing in the above prepared T cells, genomic DNA was isolated and subjected to sequencing. Briefly, frozen cell pellets were thawed and processed using *DNeasy Blood & Tissue Kit (Qiagen, 69506)* to isolate genomic DNA. Eluted DNA was used to run PCR using *Titanium Taq PCR kit (Clontech Laboratories, 639211)* and primers in Table 27.

Table 27: primer design for PCR.

Target	**Forward Primer**	**SEQ ID NO:**	**Reverse Primer**	**SEQ ID NO:**
B2M	GCACGCGTTTAATATAAGTGGAGG	10819	GACCCTCCCGTCGCC	10832
FKBP12	CCTCATCTGTGCAGCGGGCAT	10820	CGAGGTACTAGGCAGAGCCGTGG	10833
TRAC (guides CR000961, CR000978)	CATCACGAGCAGCTGGTTTC	10821	GGACTGCCAGAACAAGGCTC	10834
TRAC (guides CR000979)	GAGCCGAGGTATCGGTCCTG	10822	ATTCAGGAGAGACCCCACCC	10835
TRAC guides (CR000984, CR000991, CR000992, CR000993)	TGTTTGTAAGGGGATATGCACAGA	10823	GTTTCAGGCCATTATTATTGCACA	10836
CIITA (guides CR002961, CR002967)	TGTTGTAGGTGTCAATTTTCTGCC	10824	AATTTCCCCTGATTGCCGTCTCTA	10837

CIITA (Guide CR002991)	CCCTCTTTCCAGAAATTTCCTTCTTC	10825	GACTGACGTGGCTCATGATGAAT	10838
CIITA (Guide CR003007)	AATAGAGACTCACCTTGGGCTTTC	10826	GTACATTTTAAGGCTCCTGTTGGC	10839
CIITA (Guide CR003001)	GCCTTCAGTTAGACCTTGTTGATT	10827	GAGTCTCTATTGTACCCACCTTGG	10840
CIITA (Guide CR002994)	TCCTTCTTCATCCAAGGGACTTTT	10828	CCCTTGCAATGATTTCTGTGGG	10841
CIITA (Guide CR002992, CR002993)	TTCTTCATCCAAGGGACTTTTCCT	10829	GACTGACGTGGCTCATGATGAAT	10842
CIITA (Guide CR002961, CR002967, CR002965)	TGTTGTAGGTGTCAATTTTCTGCC	10830	AATTTCCCCTGATTGCCGTCTCTA	10843
CIITA (Guide CR002972, CR002980, CR002976)	TGTAGGTGTCAATTTTCTGCCTCT	10831	GAATTTCCCCTGATTGCCGTCT	10844

PCR product was purified using *QIAquick PCR Purification Kit (Qiagen, 28104).* Purified PCR product was then used for T7E1 assay to detect base pair mismatches and confirm gene editing. PCR amplicons were subjected to standard Nextera NGS library prep (Illumina) and sequenced with paired-end reads on an Illumina MiSeq sequencer. Sequencing reads were aligned to the reference genome and variants were called.

Results

First, gRNAs targeting TRAC were evaluated for effects on cell surface TCR expression at various concentrations of Cas9 (RNP). Human primary T cells were electroporated on day 3 after CD3/CD28 bead activation with RNPs at the indicated concentrations (uM) containing the indicated gRNAs in dual guide format. Additional guide numbers indicate CRxxxxx identifier of targeting domain of the gRNA. Loss of TCR expression was evaluated by staining with anti-CD3 antibody and analysis by flow cytometry 3 days after electroporation (CD3 KO T cells (%). Figure 33A shows lss of CD3 staining upon electroporation of RNPs containing guides CR000961 (961), CR000978 (978), CR000984 (984), CR000992 (992), CR000985 (985), and CR000960 (gRNA1) and CR000979 (gRNA8). These data show

that nearly maximal editing (as shown by loss of CD3 staining) is achieved for RNPs with CR000961 and CR000984-containing gRNAs at RNP concentrations of between 0.2 and 0.3 uM. Other gRNAs achieved maximal editing at concentrations of 1 uM. Figure 33B shows loss of CD3 staining upon electroporation of RNPs containing guides CR000991 (991), CR000992 (992), CR000993 (993), and CR000978 (978). 991 and 992 are nearly superimposable. Here again, for RNP containing gRNAs 991, 992 and 993, maximum editing was observed at RNP concentrations of 0.3 uM, while gRNA 978 % editing continued to increase up to 1.1 uM. As shown in Figure 33C, electroporate of T cells with gRNA targeting the TRAC locus results in high levels of indel formation at the targeted sites (up to 97% editing) and high levels of frameshift mutations, which are predicted to result in loss of protein expression (up to 78%). Next, the mutations (indels) at each targeted locus were assessed by next generation sequencing. Figure 34A and Figure 34B show the top 5 most frequently observed sequence changes for each TRAC targeting dgRNA used for primary human T cell editing. Figures A and B are the outcome from 2 independently performed electroporation experiments. Data are the average from triplicate PCR products. These data show consistent patterns of editing across multiple experiments when the same gRNA format and RNP are used, in with the same delivery technique.

Next, similar experiments were performed with gRNAs (dual guide format) targeting B2M. The effect of RNP concentration was first assessed. Human primary T cells were electroporated on day 2 after CD3/CD28 bead activation with RNPs at the indicated concentrations containing the indicated gRNAs. Guide numbers indicate CR00xxx identifier of targeting domain. Loss of B2M expression was evaluated by staining with anti-B2M antibody and analysis by flow cytometry 4 days after electroporation (B2M negative cells). The results are reported in Figure 35, and demonstrate that >85% editing (as assayed by loss of B2M surface expression) was achieved by gRNA 442 at 0.2 uM, and at slightly higher RNP concentration (0.4 uM) for gRNA 442 and 455. As shown in Figure 36, RNPs comprising gRNAs CR000444 and CR000455 result in high levels of editing and high levels of frameshift editing in primary human T cells. Top ten indels produced by each gRNA are shown in the lower panel. Data are the average from triplicate PCR products.

Next, the simultaneous editing of TCR, B2M and CIITA was performed in CART cells, and the function of such CART cells was assessed. Figure 45 shows the schematic protocol that was followed for these experiments for preparation of primary human T cells edited at the B2M, TRAC, and CIITA loci (triple edited cells). Figure 46 shows the % loss of cell surface expression of CD3 epsilon, B2M, and HLA-DR, respectively, by flow cytometry (as indicators of editing at TRAC, B2M and CIITA, respectively). As expected, cells electroported with only single gRNA showed loss of only the expected protein. In cells

treated with 3 RNPs, each containing a gRNA to a different target, cells from each population exhibited over 80% loss of each of the target proteins, as well as >80% loss of both B2M and TRAC, with the exception of the lowest concentration of the CIITA-targetign gRNA (triple 4), which resulted in a lower loss of HLA-DR than when higher concentrations of this RNP are delivered to the cells. Figure 47 shows the genomic editing of the B2M, TRAC, and CIITA loci resulting from human primary T cell simultaneous electroporation with 3 RNPs containing gRNAs targeting the B2M, TRAC, and CIITA loci. The frequency of insertions or deletions is indicated (%indels) and the percentage of these edits that result in frameshifting of the coding sequence is shown in parentheses. Figure 48, Figure 49 and Figure 50 show the top 10 most frequently observed sequence changes at the B2M locus (in response to gRNA comprising CR000442), the TRAC locus (in response to gRNA comprising CR000961) and at the CIITA locus (in response to gRNA comprising CR002991), respectively, in primary human T cells in the context of simultaneous editing of 3 loci (triple editing) with different concentrations of each RNP as shown in the schematic in Figure 45. These data indicate that the efficient gRNA molecules used here efficiently knock out TRAC, CIITA and B2M in primary human T cells to with high efficiencies, and result in T cells which have reduced graft versus host disease capability (via loss of TCR) and reduced host versus graft disease capability (through loss of both B2M and CIITA), representing an important step toward an alloegenic, off-the-shelf T cell product.

Next, the effects fo the format of the gRNA molecule was assessed. Guide RNAs against TRAC (comprising the targeting domain of CR000961; upper panel) or B2M (comprising the targeting domain of CR00442; lower panel) were synthesized in the single guide or dual guide format with or without the indicated chemical modifications (PS (3 nt at both 5' and 3' ends are phosphorothioate) or OMePS (3 nt at both 5' and 3' ends are 2'-OMe and phosphorothioate); for dual guide RNA, both the crRNA and the tracr RNA comprised the modifications). RNPs were electroporated into human primary T cells at the indicated concentrations. Figure 51 shows the results of these experiments: editing efficiency was evaluated by analysis of cell surface staining of CD3 epsilon for TRAC editing (upper) and B2M protein for B2M editing (lower) by flow cytometry. As shownw in Figure 51, all formats were capable of achieving high efficiency editing at RNP concentration of 1 uM, however, sgRNA format was able to maintain high editing efficiencies at lower concentrations than dgRNA formats (down to 0.04 uM for gRNAs comprising the targeting domain of CR000961, and down to 0.1 uM for gRNAs comprising the targeting domain of CR000442). For the TRAC-targeting gRNA, chemical modification had no effect on editing efficiency at the rNP concentrations tested. For the B2M-targeting gRNA, chemical modification of the sgRNAs had an effect on editing efficiency at the lowest concentration tested, with the PS-modified sgRNA having the highest editing efficiency at 0.04 uM RNP concentration.

Example 13: T Cell Resistance to Immunosupression after genome editing of FKBP1A, and Funcational Assessment of TCR-/FKBP12- CART Cells

Without being bound by theory, as described herein, it is believed that another strategy for generating off-the-shelf ("universal") CART cells is to reduce or eliminate expression of TCR (to, e.g., reduce or suppress graft versus host disease), and also to reduce or eliminate expression of a target of an immunosuppressive agent (e.g., an mTor inhibitor). Subsequent treatment of a patient with such genome edited CART cells in combination with said immunosuppressive agent will inhibit the host immune response (e.g., thereby inhibiting host versus graft responses) without inhibiting the function of the CART cell (e.g., the antitumor function of the CART cell). Towards that end, function of T cells edited to make them TCR- and FKBP12- were assayed, including in the presence of the mTor inhibitor RAD001.

Methods:

After thawing, isolated human T cells were activated with CD3/CD28 beads for 3 days at a bead to cell ratio of 3:1. Cells were then electroporated with RNP containing dual guide RNA molecules (as indicated, as described above in these examples), and Cas9 protein using the Neon instrument with the 100 ul tip kit. RNPs were prepared in the following manner. crRNA and trRNA (10 ul of each at 100uM) were heated in separate tubes to 95 degrees C for two minutes and then cooled for 5 minutes at room temperature. Cas9 protein (1.5 mg/ml), 20 uM trRNA, and 20 uM crRNA and 17 ul of buffer (20mM Tris, PH8.0, 200nM KCI, 10mM MgCI2) were combined in a total of 50 ul volume and incubated at 37 degrees for 10 minutes. The RNP was then mixed with 100ul of cells at a cell count of 2 million cells per ml of T buffer (Invitrogen; Cat#: MPK1096). 100 ul of cells mixed with RNP was transferred to the Neon pipette tip and electroporated at 1600V, 10ms, 3 pulses. The RNP was at a final concentration of 3.3 uM as a measure of Cas9 protein.

After electroporation, cells were then transferred into a 6-well plate with 2 ml of T cell media with beads at a 3:1 bead to cell ratio. Fresh media was added every other day. On day 4 after electroporation, cells were debeaded and re-plated at a density of 0.5 million per well in a 96-well plate with 100 ul of media and fresh beads were added at a bead to cell ratio of 1:1 for 2 hours. To determine the functional effects of FKBP1A editing, cells were then treated with or without 2.5nM RAD001 (as indicated) for 3 hours. The phosphorylation of S6 was detected by flow cytometry, and was used as an indication of immunosuppressing by RAD001. For preparation of samples for flow cytometry, cells were spun down and washed with FACS buffer (MACS running buffer + 0.5%sBSA), the stained with Dead/live stain

(Zombie violet fixable viability kit, Biolegend, Catalog# 423114) for 10 minutes. Cells were then washed with FACS buffer and fixed overnight with Cytofix/Cytoperm solution (Becton Dickenson, Catalog # 554714). Cells were then washed twice with PBS and permeabilized with Cytofix/Cytoperm solution (Becton Dickenson, Catalog # 554714) for 20 minutes. Cells were then washed twice with PBS and incubated with PE conjugated anti-phospho-S6 antibody (phospho-S6 ribosomal protein Ser240/244 (D68F8) Rabbit mAb, Cell Signaling Technologies, Catalog# 14236) for 1 hour at 4 degrees. Cells were then washed twice with PBS and analyzed by flow cytometry on the Becton Dickenson LSR Fortessa using FloJo-V10 software.

Figure 54 shows the results of S6 phosphorylation in the presence or absence of mTor inhibitor RAD001 after exposure to gRNA targeted towards FKBP1A. T cells were edited with RNPs containing guide sequences targeting FKBP1A (CR002086, CR002097, CR002122; indicated as 2086, 2097, and 2112, respectively) or with negative controls: 442 (an irrelevant guide CR00442 targeting B2M); Cas9 (Cas9 alone with no trRNA or crRNA); trRNA (tracer RNA, but no crRNA or Cas9 protein); Cas9+trRNA (Cas9 and tracer RNA but no crRNA); EP (cells only with electroporation); no EP (cells only with no electroporation). After electroporation cells were treated with 2.5 nM RAD001 (upper panel) or left untreated (lower panel) and the impact on mTOR pathway inhibition was evaluated by analyzing S6 phosphorylation (pS6) by flow cytometry. The Y-axis indicates forward scatter (FSC) and the X-axis indicates the level of pS6. Positive staining for pS6 (shown in the gating trace) was determined by gating above the fluorescence level seen in a control stained with isotype antibody (not shown). Quantitation of S6 phosphorylation from the flow cytometry data is shown in the graph in the lower panel. These data demonstrate that editing of FKBP1A (and subsequence loss of FKBP12 protein) renders primary T cells refractory to the inhibitory effects of the rapalog RAD001.

Next, CART cells were generated which are TCR negative and FKBP12 negative, and their function evaluated. Briefly, PBMC were isolated from human blood by using centrifugation method using Ficoll. Total T cells were isolated from these PBMC's using human Pan T Cell Isolation Kit (Miltenyi Biotec #130-096-535). These cells were aliquoted and frozen. These frozen cell aliquots were then thawed and activated using CD3/CD28 beads (DynaBeads Invitrogen Cat#111.41D) at bead to cell ratio of 3:1. Day1 post activation, CAR BCMA-10 or CAR-CD19 (CTL019) virus was used to transduce these cells at MOI of 5. UTD (untransduced cells) were not treated with virus. Day 4 post activation, either CAR BCMA-10 or CAR-CD19 or untransduced T cells were then electroporated with RNP with the indicated guide RNAs or without guide RNA (no guide) as indicated using Neon electroporator. RNP were prepared as described above. For TRAC editing, CR000961 was used (indicated as 961) alone or with guides

targeting FKBP1A as indicated. For FKBP1A editing CR0002097 (indicated as 2097) or CR002097 and CR002086 together (indicated as 2097+2086) was used. The RNP (or RNPs) was then mixed with 100ul of cells at a cell count of 2 million cells per ml of T buffer (Invitrogen; Cat#: MPK1096). 100 ul of cells mixed with RNP was transferred to the Neon pipette tip and electroporated at 1600V, 10ms, 3 pulses. The RNP was at a final concentration of 3.3 uM as a measure of Cas9 protein. After electroporation, cells were then transferred into a 6-well plate with 2 ml of T cell media with beads at a 3:1 bead to cell ratio. Fresh media was added every other day. Five days after electroporation, 500,000 cells (for phosphor-S6 staining) or 50,000 cells for cell surface marker staining (eg CD3) were removed from culture and analyzed by flow cytometry (BD Fortessa) using FlowJo software. Expression of TCR was detected by using anti- CD3-PercpCy5.5 (Ebiosciences 45-0037-42). Cell surface expression of CAR was evaluated by staining with Biotinylated Protein L followed by Streptavidin-PE (016-110-084 Jackson Immuno Research). T cells were detected by staining CD4 using anti-CD4-V450 (48-0047-42 Ebiosciences) or CD8 using anti-CD8-APC (17-0087-42 eBiosciences).

To determine the functional effects of FKBP1A editing, on day 4 after electroporation, cells were debeaded and re-plated at a density of 0.5 million per well in a 96-well plate with 100 ul of T cell media and fresh beads were added at a bead to cell ratio of 1:1 for 2 hours. Cells were then treated with or without 2.5nM RAD001 (as indicated) for 3 hours. The phosphorylation of S6 was detected by flow cytometry. For preparation of samples for flow cytometry, cells were spun down and washed with FACS buffer (MACS running buffer + 0.5%sBSA), the stained with Dead/live stain (Zombie violet fixable viability kit, Biolegend, Catalog# 423114) for 10 minutes. Cells were then washed with FACS buffer and fixed overnight with Cytofix/Cytoperm solution (Becton Dickenson, Catalog # 554714). Cells were then washed twice with PBS and permeabilized with Cytofix/Cytoperm solution (Becton Dickenson, Catalog # 554714) for 20 minutes. Cells were then washed twice with PBS and incubated with PE conjugated anti-phospho-S6 antibody (phospho-S6 ribosomal protein Ser240/244 (D68F8) Rabbit mAb, Cell Signaling Technologies, Catalog# 14236) for 1 hour at 4 degrees. Cells were then washed twice with PBS and analyzed by flow cytometry on the Becton Dickenson LSR Fortessa using FloJo-V10 software.

To test the cytokine release from edited CART cells, effector cells (edited/unedited CART or untransduced cells) were thawed in media (RPMI, 5% FCS, 10 mM Hepes, 1x Pen/Strep, 1x Glutamine) on the day of the assay and counted on Cellometer (Nexelcom). These cells were then co-cultured with 30,000 target cells expressing BCMA (KMS11, RPMI8226) or cells expressing CD19 (Nalm6) at Effector: Target ratio of 1:1. 100ul of co-culture supernatant was harvested after 20 hours. These supernatants were then used measure the cytokines IL-2 and IFN-gamma released using Meso Scale

Discovery, Proinflammatory Panel 1 catalog # N05049A-1 system according to the manufacturer's protocol.

To measure the cytolytic capacity of effector cells (edited/unedited CART or untransduced cells), cells were thawed in media (RPMI, 5% FCS, 10 mM Hepes, 1x Pen/Strep, 1x Glutamine) on the day of the assay and counted on Cellometer (Nexelcom). These cells were then co-cultured for 20 hours with 30,000 target cells stably expressing the luciferase reporter gene and expressing BCMA (KMS11, RPMI8226) or cells expressing CD19 (Nalm6) at Effector: Target ratio of 1:1 in a 96 well assay plate black with clear bottom (Costar, cat# 3904). Luciferase signal was measured using Bright-Glo substrate (Promega, Ref# E263B) on the EnVision multiple plate reader instrument from Perkin Elmer. Cell killing was inferred from the decrease in luciferase signal and was calculated as follows:
Target cell killing (%) = 100 - (sample luminescence / average maximal luminescence) * 100

For the T cell proliferation assay, cells prepared as above were thawed and co-cultured with target cells expressing BCMA (KMS11, RPMI8226) or cells expressing CD19 (Nalm6). Irradiated target tumor cells were co-cultured with edited or unedited CART cells at an effector to target ratio of 1:1 for 4 days followed sample staining for CD4, CD8, and CAR as above and flow cytometry analysis Becton Dickenson LSR Fortessa and analyzed with FloJo-V10 software. The number of T-cells (stained with anti-CD4-V450 and anti-CD8-APC) was determined by the number of CD4+ plus CD8+ cells relative to 3000 counting beads (Life technology, Catalog # C36950). The number of CAR+ T cells was determined by gating the CAR+ cell population (stained with Biotinylated Protein L followed by Streptavidin-PE).

Results:
Cytokine production by CART cells in response to antigen exposure was determined. Gene editing was performed on CART cells using the CR000961 guide to target the TRAC locus and/or the CR002097 and CR002086 guides to target the FKBP1A locus (as indicated by cr961, 2097, and 2086, respectively). Figure 55A and 55B show interferon gamma release and IL-2 release, respectively, from edited/unedited CART cells. These data indicate that loss of FKBP12 and/or TCR through gene editing does not impair cytokine production in activated CART cells. Figure 56 shows the killing of antigen positive cancer cell lines by edited and unedited CART cells. These data indicate that loss of FKBP12 and/or TCR through gene editing does not impair the target cell killing capacity of CART cells. Figure 57 shows proliferation of edited and unedited CART cells in response to antigen exposure. These data indicate that loss of FKBP12 through gene editing does not impair the proliferation capacity of CART cells relative to cells treated with no guide. Finally, edited CART cells were investigated for their ability to resist

immunosuppression by the rapalog RAD001. The results are shown in Figure 58. These data indicate that editing of FKBP1A (and subsequence loss of FKBP12 protein) renders CART cells refractory to the inhibitory effects of the rapalog RAD001.

Example 14: Expression of HLA-G:B2M fusion protein

Without being bound by theory, it is believed that a cell that has been rendered TCR-/B2M-/CIITA- may be recognized as foreign by NK cells and targeted for destruction. Thus, an otherwise unmodified TCR-/B2M-/CIITA- allogeneic CART cell may be at risk for attack when administered to, for example, a cancer patient. Again, without being bound by theory, it is believed that expression of HLA-G on said cells should suppresss any NK cell activity against that cell. Because some forms of HLA-G require B2M, for cells in which expression of B2M has been reduced or eliminated, we investigated expression of a HLA-G:B2M fusion molecule.

The HLA-G/B2M fusion protein was synthesized as follows. β2 microglobulin and HLA-G amino acid sequences were obtained from databases. It is known that the HLA-G1 isoform of HLA-G forms a complex with B2M at the cell surface. In order to reconstitute this complex, for example, in a B2M- cell, the β2 microglobulin N terminal fusion polypeptide was linked to HLA-G1. Furthermore, B2M is linked to HLA-G1 through a glycine/serine (G4S)n linker (SEQ ID NO: 6629). The amino acid sequence was designed in the following order to create the fusion protein: B2M sequence – (G4S)3 - HLA-G1 ("(G4S)3" disclosed as SEQ ID NO: 6594). The fusion protein nucleotide sequence was codon optimized by GeneArt® GeneOptimizer® process (Thermo Fisher Scientific Inc) for mammalian cell expression. Optimized DNA was synthesized by Genescript. Synthesized DNA was amplified by PCR (NEB, Q5® Hot Start High-Fidelity DNA Polymerase, Catalog number: M0493L) and subcloned to pELPS vector by Gibson Assembly (NEB, Catalog number: E2611L). Subclone sequence was further verified by genewiz sequencing.

HLA-G-B2M Virus or HLA-G virus was generated using LentiX-293T cells. The cells were transfected with HLA-G-B2M or HLA-G lentiviral DNA plasmid along with packaging plasmid DNA (pRSV.REV (Rev expression plasmid), pMDLg/p.RRE (Gag/Pol expression plasmid), pVSV-G (VSV glycoprotein expression plasmid)) using Lipofectamine 2000 (Invitrogen). Media was changed after 12 hours post transfection. Fresh media was added to the cells and supernatants were harvested 30 hours post media change. Using LentiX concentrator, the virus was concentrated and aliquoted to be frozen. Virus was tittered using supT1 cells. Serial dilution of supernatant containing virus was incubated with 20,000 SupT1 cells for 3 days. Fresh media was added 24hr after transduction. Cells were harvested and washed

with FACS buffer and incubated with anti HLA-G-PE antibody. (335906 Biolegend) and cells were analyzed using BD Fortessa and flowJo Software.

Figure 59 shows the results of transduction of SupT1 cells with nucleic acid encoding the HLA-G:B2M fusion described above. The HLA-G/B2M fusion protein was introduced into SupT1 cells by lentiviral transduction. Cells surface expression of HLA-G was detected by flow cytometry. The light gray histogram indicates the background fluorescence in the PE channel in untransduced cells. The dark gray histogram indicates fluorescence in the PE channel from cells transduced with HLA-G/B2M. This indicates successful expression and surface location of HLA-G:B2M fusion protein in T cells.

Example 15: Edting of CD3-epsilon (CD3E) in HEK-293(Cas9) Cells

dgRNA molecules comprising the indicated targeting domain were chemically synthesized, and editing assessed in HEK-293 cells by NGS as described in Example 1. The results of the editing experiments are shown in Table 28. This Example shows gRNA molecules targeting CD3E are capable of editing the target locus when delivered as RNP at frequencies ranging from 3% to over 75%. Several gRNA moleucles were able to edit more than 50% of the cells, including producing a frameshift mutation in more than 50% of the cells.

Table 28: % Edit and % Frameshift Edit with dgRNA to CD3E in HEK-293(Cas9) Cells

Targeting Domain ID	Avg. % Edit (any indel)	Std. Dev. % Edit	Avg. Frameshift %	Std. Dev. Frameshift
CR002275	76.01	5.72	15.70	0.95
CR002282	67.86	4.87	49.37	3.04
CR002272	64.58	4.15	46.13	2.53
CR002317	64.37	8.01	52.67	7.38
CR002242	62.63	14.18	60.27	13.41
CR002254	60.61	11.17	57.40	10.85
CR002253	60.56	12.93	57.47	12.22
CR002238	59.48	9.56	47.73	8.60
CR002316	58.02	6.94	33.73	1.04
CR002244	57.67	8.32	55.70	7.45
CR002273	56.67	14.54	41.70	12.21
CR002269	55.71	9.82	39.57	6.98
CR002234	53.46	5.59	48.40	4.19
CR002306	52.44	2.86	39.37	2.12
CR002294	50.53	2.60	43.10	2.51
CR002239	49.40	10.43	41.43	9.15
CR002263	49.02	10.60	46.10	9.98

CR002257	48.84	4.53	27.40	1.85
CR002312	48.83	5.89	41.00	6.08
CR002292	48.53	2.67	26.27	0.91
CR002262	46.30	9.31	40.53	7.39
CR002248	44.72	11.44	29.47	7.17
CR002243	43.63	5.20	42.90	5.22
CR002276	43.24	8.71	24.47	5.10
CR002286	42.49	12.84	34.50	8.76
CR002313	42.09	16.14	32.37	11.91
CR002280	41.57	6.24	35.23	4.77
CR002305	41.32	4.80	29.00	2.55
CR002293	40.95	13.91	33.93	10.96
CR002250	40.13	8.00	29.93	5.62
CR002274	39.19	4.25	21.20	4.16
CR002270	39.10	9.71	20.90	4.78
CR002287	38.67	4.82	31.63	3.42
CR002237	38.48	8.58	33.90	7.32
CR002233	37.97	16.11	30.65	13.22
CR002240	37.60	8.12	27.67	5.78
CR002268	37.55	6.09	33.63	5.30
CR002309	36.78	11.88	25.40	6.76
CR002235	35.81	13.86	31.33	11.72
CR002304	35.42	4.37	31.63	3.45
CR002258	34.45	3.18	28.67	2.30
CR002266	34.31	8.23	28.87	7.65
CR002308	33.64	6.64	25.73	6.48
CR002281	33.35	4.23	26.00	4.04
CR002310	31.16	12.69	20.73	8.20
CR002256	31.04	5.30	27.83	4.20
CR002271	30.93	10.56	21.93	7.31
CR002288	30.39	6.64	20.43	4.56
CR002236	29.27	12.38	25.90	10.78
CR002289	29.10	7.53	20.63	4.28
CR002307	29.04	5.90	22.00	4.74
CR002284	29.02	7.03	24.33	6.11
CR002279	28.69	2.73	27.30	2.63
CR002291	28.24	5.73	24.50	4.72
CR002241	27.78	8.43	24.37	7.27
CR002277	27.37	6.06	20.43	3.67
CR002260	26.89	7.90	21.93	5.79
CR002245	26.47	5.52	22.97	4.95

CR002303	26.17	6.27	22.43	5.61
CR002267	26.14	6.26	23.83	5.66
CR002249	25.67	12.15	15.37	7.09
CR002299	25.37	3.62	15.03	3.63
CR002283	24.47	6.84	19.07	5.75
CR002297	24.19	3.09	13.80	1.90
CR002252	22.37	4.23	12.57	1.43
CR002290	21.69	7.77	16.60	5.82
CR002285	21.07	10.10	15.70	7.20
CR002298	20.74	6.51	19.13	6.60
CR002230	20.64	10.21	20.10	10.02
CR002232	20.62	5.79	20.30	5.63
CR002311	20.48	3.46	12.73	1.10
CR002300	19.46	11.73	15.07	9.41
CR002259	19.23	6.38	15.27	5.03
CR002296	18.26	2.92	17.33	2.61
CR002261	17.11	3.65	15.50	3.08
CR002251	16.52	2.59	13.03	2.44
CR002302	14.54	3.42	12.93	3.02
CR002231	13.83	4.08	12.37	3.70
CR002295	13.11	9.91	5.20	3.90
CR002246	12.89	5.72	12.07	5.35
CR002265	12.38	4.56	10.20	3.46
CR002278	11.66	4.48	7.47	3.23
CR002301	10.91	1.00	4.70	0.26
CR002255	7.38	2.00	6.43	1.85
CR002315	5.97	0.49	5.63	0.47
CR002264	5.96	1.05	5.57	0.83
CR002247	3.92	1.09	3.43	0.96
CR002314	3.43	0.99	3.40	0.95

Example 16: Evaluation of Cas9 Variants

Evaluation in CD34+ hematopoietic stem cells

We evaluated 14 purified *Streptococcus pyogenes* Cas9 (SPyCas9) proteins by measuring their efficiency of knocking out the beta-2-microglobulin (B2M) gene in primary human hematopoietic stem cells (HSCs). These proteins were divided into 3 groups: the first group consisted of SPyCas9 variants with improved selectivity (Slaymaker et al. 2015, Science 351: 84 (e1.0, e1.1 and K855A); Kleinstiver et al. 2016, Nature 529: 490 (HF)). The second group consisted of wild type SPyCas9 with different numbers

and/or positions of the SV40 nuclear localization signal (NLS) and the 6xHistidine (His6) (SEQ ID NO: 10795) or 8xHistidine (His8) (SEQ ID NO: 10796) tag with or without a cleavable TEV site, and a SPyCas9 protein with two cysteine substitutions (C80L, C574E), which have been reported to stabilize Cas9 for structural studies (Nishimasu et al. 2014, Cell 156:935). The third group consisted of the same recombinant SPyCas9 produced by different processes (Fig 60). B2M knockout was determined by FACS and next generation sequencing (NGS).

Methods

Materials

1. Neon electroporation instrument (Invitrogen, MPK5000)
2. Neon electroporation kit (Invitrogen, MPK1025)
3. crRNA (targeting domain of CR00441 (SEQ ID NO: 5495) fused to SEQ ID NO: 6607)
4. tracrRNA (SEQ ID NO: 6660)
5. Cas9 storage buffer: 20 mM Tris-Cl, pH 8.0, 200mM KCl, 10mM $MgCl_2$
6. Bone marrow derived CD34+ HSCs (Lonza, 2M-101C)
7. Cell culture media (Stemcell Technologies, StemSpam SFEM II with StemSpam CC-100)
8. FACS wash buffer: 2% FCS in PBS
9. FACS block buffer: per mL PBS, add 0.5 ug mouse IgG, 150 ug Fc block, 20 uL FCS
10. Chelex suspension: 10% Chelex 100 (bioRad, Cat# 142-1253) in H_2O
11. Anti-B2M antibody: Biolegend, cat# 316304

Process

Thaw and grow the cells following Lonza's recommendations, add media every 2-3 days. On day 5, pellet the cells at 200 x g for 15 min, wash once with PBS, resuspend the cells with T-buffer from NEON kit at $2x10^4$/uL, put on ice. Dilute Cas 9 protein with Cas9 storage buffer to 5 mg/ml. Reconstitute crRNA and tracrRNA to 100 uM with H_2O. The ribonucleoprotein (RNP) complex is made by mixing 0.8 uL each of CAS 9 protein, crRNA and tracrRNA with 0.6 uL of Cas9 storage buffer, incubate at room temperature for 10 min. Mix 7 uL of HSCs with RNP complex for two minutes and transfer the entire 10 uL into a Neon pipette tip, electroporate at 1700v, 20 ms and 1 pulse. After electroporation, immediately transfer cells into a well of 24-well plate containing 1 ml media pre-calibrated at 37°C, 5% CO_2. Harvest cells 72 hrs post-electroproation for FACS and NGS analysis.

FACS: take 250 uL of the cells from each well of 24-well plate, to wells of 96-well U-bottom plate and pellet the cells. Wash once with 2% FCS (fetal calf serum)-PBS. Add 50 uL FACS block buffer to the

cells and incubate on ice for 10 minutes, add 1 uL FITC labeled B2M antibody and incubate for 30 minutes. Wash with 150 uL FACS wash buffer once followed by once more with 200 uL FACS wash buffer once. Cells were resuspended in 200 uL FACS buffer FACS analysis.

NGS sample prep: transfer 250 uL of cell suspension from each well of the 24-well plate to a 1.5 ml Eppendorf tube, add 1 mL PBS and pellet the cells. Add 100 uL of Chelex suspension, incubate at 99°C for 8 minutes and vortex 10 seconds followed by incubating at 99°C for 8 minutes, vortex 10 seconds. Pellet down the resin by centrifuging at 10,000 x g for 3 minutes and the supernatant lysate is used for PCR. Take 4 uL lysate and do PCR reaction with the b2m primers (b2mg67F: CAGACAGCAAACTCACCCAGT (SEQ ID NO: 10807), b2mg67R: CTGACGCTTATCGACGCCCT (SEQ ID NO: 10808)) using Titanium kit (Clonetech, cat# 639208) and follow the manufacturer's instruction. The following PCR conditions are used: 5 minutes at 98°C for 1 cycle; 15 seconds at 95°C, 15 seconds at 62°C, and 1 minute at 72°C for 30 cycles; and finally 3 minutes at 72°C for 1 cycle. The PCR product was used for NGS.

Statistics: The percentage of B2M KO cells by FACS and the percentage of indels by NGS are used to evaluate the CAS 9 cleavage efficiency. The experiment was designed with Cas9 as fixed effect. Each experiment is nested within donors, as nested random effects. Therefore, the mixed linear model was applied for the analysis of FACS and NGS data.

Results

In order to normalize the experimental and donor variations, we graphed the relative activity of each protein to iProt105026, the original design with two SV40 NLS flanking the wild type SPyCas9 and the His6 tag (SEQ ID NO: 10795) at the C-terminal of the protein (Fig 60). The statistical analysis shows that compared with the reference Cas9 protein iProt105026, iProt106331, iProt106518, iProt106520 and iProt106521 are not significantly different in knocking out B2M in HSCs, while the other variants tested (PID426303, iProt106519, iProt106522, iProt106545, iProt106658, iProt106745, iProt106746, iProt106747, iProt106884) are highly significantly different from the reference iProt105026 in knocking out B2M in HSCs. We found that moving the His6 tag (SEQ ID NO: 10795) from the C-terminal to N-terminal (iProt106520) did not affect the activity of the protein (Fig. 60). One NLS was sufficient to maintain activity only when it was placed at the C-terminal of the protein (iProt106521 vs. iProt106522, Fig. 60). Proteins purified from process 1 had consistent higher knockout efficiency than those from processes 2 and 3 (iProt106331 vs. iProt106545 & PID426303, Fig. 60). In general, the SPyCas9 variants with a reported improved selectivity were not as active as the wild type SPyCas9 (iProt106745, iProt106746 and iProt106747, Fig. 60). Interestingly iProt106884 did not cut the targeting site. This is

consistent with the report by Kleinstiver et al that this variant failed to cut up to 20% of the legitimate targeting sites in mammalian cells (Kleinstiver et al. 2016, Nature 529: 490). Finally, the Cas9 variant with two cysteine substitutions (iProt106518) maintained high levels of enzymatic activity (Fig. 60).

Evaluation in T cells

Methods

The different S Pyogenes Cas9 variants shown in Table 29 were used in these experiments. The structures are also shown in Figure 60.

Table 29: Cas9 variants (NLS = SV40 NLS; Cas9 = S. Pyogenes Cas9 wild type, with any mutations indicated in parenthesis; Cas9e1.1 (as described in Slaymaker et al. 2015, Science 351: 84); GGS = glycine-glycine-serine).

iprot	CAS9 (His6 disclosed as SEQ ID NO: 10795)	Size (Daltons)	Conc (ug/ml)	Molar conc. [uM]
106520	His6-GGS-NLS-CAS9-NLS	161696.22	6.2	38.34
106518	NLS-CAS9(C80L, C574E)-NLS-His6	161531.04	6.5	40.24
106521	NLS-CAS9-His6	160629.9	6	37.12
106745	NLS-CAS9(K855A)-NLS-His6	161437.94	5.9	36.55
106747	NLS-CAS9e1.1-NLS-His6	161295.74	6.5	40.3
106154 (also referred to as 105026)	NLS-CAS9-NLS-His6	161495.04	5.9	36.54

PBMC were isolated from human blood (obtained from Hemacare/ALL Cells) by using centrifugation method using Ficoll (GE Healthcare catalog# 17-1440-03) . Total T cells were isolated from these PBMC's using human Pan T Cell Isolation Kit (Miltenyi Biotec #130-096-535). These cells were aliquoted, frozen using CRYOSTOR CS10 media (Biolife Solution-210102), and stored in liquid nitrogen. These frozen cell aliquots were then thawed in a 37 degree C water bath for 20 secs and then transferred to a 50 ml conical tube in 10 ml of pre-warmed T cell media and centrifuged at 300 rpm for 5-10 mins at 24 degrees C to remove the freezing media and resuspended with prewarmed T cell media. These are then activated by using CD3/CD28 beads (DynaBeads Invitrogen Cat#111.41D) at a bead to cell ratio of 3:1 at keeping the cell concentration at 0.5 million/ml and activated using CD3/CD28 beads (DynaBeads Invitrogen Cat#111.41D) at bead to cell ratio of 3:1 at 0.5million/ml concentration of cells.

On Day3 post bead activation, the 200,000 cells are used per electroporation. RNP complex used for T cell genome editing was formed using a 1:2 molar ratio of Cas9 protein to RNA (crRNA and tracRNA). 100 µM crRNA ([targeting domain]-[SEQ ID NO: 6607]) and 100 µM tracrRNA (SEQ ID NO: 6660) were denatured separately at 95°C for 2 min and cooled to room temperature. In a final volume of 5 µL, 1.4 µL of Cas9 proteins at a concentration of 5.9 µg/µL was mixed with 1.6 µL of reaction buffer (20 mM Tris, pH8.0; 200 mM KCL, 10 mM MgCl2) and mixed with 1 µL of 100 µM tracrRNA at room temperature. Next 1 µL of 100 µM crRNA was added, mixed and incubated for 10 min at 37 °C. The targeting domain for B2M was CR000442, and for TRAC was CR000961. These RNP's at higher concentrations were used to generate samples of RNP serial dilutions. These RNP dilutions were then used to mix with 200,000 cells in 10 ul of T Buffer (neon transfection system 10ul Kit). Electroporation was performed by Neon electroporator using *Neon® Transfection System 10 µL Kit (MPK1096)* at 1600V, 10ms, 3 pulses. Cells were cultured in T cell media without antibiotics. Cells were taken from each sample pipetted to dissociate them from beads and beads were removed by using 96 welled plate magnet and centrifuged with 100ul of FACS buffer (Miltenyi MACS buffer catalog # 130-092-987 with 0.5% BSA (Miltenyi- catalog# 130-091-376) to wash the cells. Cells were then incubated with different antibodies diluted in 100ul FACS buffer for 30 mins on ice. Cells were then washed two times with 200ul of FACS buffer. Cells are then resuspended in 150ul of FACS buffer and run on BD 5 laser Fortessa. Expression of TCR was detected by using anti- CD3-PercpCy5.5 (Ebiosciences 45-0037-42) and expression of B2M was detected by using anti-B2M-APC (316312 Biolegend). Flow cytometry data was analyzed using FlowJo Software.

Results

Generation of low concentrations of RNP, and highest editing efficiency, proceeded well when RNP was generated at high concentration, and then diluted to the desired concentrations. 6 different Cas9 proteins were tested for efficiency of editing using the B2M guide CR00442 in primary T cells. Editing efficiency was measured using cell surface detection by flow cytometry of the B2M protein and the results are shown in Figure 61 (Y-axis; % Editing of B2M) 3 days after RNP electroporation at the indicated concentrations of RNP (X-axis). The different Cas9 proteins tested are indicated by their "iprot" ID numbers (see Figure 60 and Table . The results are shown in Figure 61. These data indicate that all of these variants of Cas9 are active, but Cas9 proteins 106521, 106518, and 106154 (also referred to as 105026) show higher activity in T cells, as evidenced by their greater activity at lower concentrations of RNP. Next, two different Cas9 proteins, 106884 or 106154 (also referred to as 105026), as indicated, were tested for editing efficiency using the B2M targeting guide CR00442 (Figure 62, left panel) or the TRAC targeting guide CR000961 (Figure 62, right panel) by using different concentrations of RNP as

indicated on the X-axis. Editing efficiency (% editing) was measured by flow cytometry by measuring the loss of cell surface expression of B2M (Figure 62, left panel) or TCR using CD3 epsilon antibody (Figure 62, right panel).

Example 17: Off-Target Evaluation

T cell culture and CRISPR/Cas9 genome editing

Peripheral blood mononuclear cells (PBMC) were isolated from human blood (HemaCare, Cat # PB000) using standard Ficoll density gradient centrifugation methods. Total T cells were isolated from PBMC using the Pan T Cell Isolation Kit for human cells (Miltenyi Biotec, Cat #130-096-535) following manufacturer's recommendations and stored at -80°C. T cells were thawed and activated using Dynabeads Human T-Activator CD3/CD28 for T Cell Expansion and Activation (Thermo Fisher Scientific, Cat # 11131D) at a 3:1 bead to cell number ratio following manufacturer's recommendations. T cells were cultured in antibiotic-free complete T cell medium (RPMI 1640 with L-glutamine, Lonza, Cat # 12-702F; 10% FBS, GE HyClone, Cat # SH30071; 200 mM L-glutamine, GE HyClone, Cat # SH30034.01; 10 mM non-essential amino acids, GE HyClone, Cat # 13-114E; 100 mM sodium pyruvate, Invitrogen, Cat # 11360-070; 1 M HEPES buffer, GE HyClone, Cat # 17-737E and 55 mM 2-mercaptoethanol, Invitrogen, Cat # 21985-023) at 37°C, 5% CO_2 for 3 days prior to genome editing.

RNP complex used for T cell genome editing was formed using a 1:2 molar ratio of Cas9 protein to gRNA (crRNA and tracRNA). Chemically synthesized crRNA at a concentration of 100 µM ([targeting domain]-[SEQ ID NO: 6607]) and tracr (SEQ ID NO: 6660) at a concentration of 100 µM were denatured separately at 95°C for 2 min and cooled to room temperature. In a final volume of 5 µ buffer (20 mM Tris, pH8.0; 200 mM KCL, 10 mM $MgCl_2$), Cas9 protein (NLS-Cas9-NLS-His6 ("His6" disclosed as SEQ ID NO: 10795); iPROT105026; NLS = SV40 NLS; Cas9 = wt S. Py Cas9) was first mixed with tracrRNA at room temperature and then mixed with crRNA and incubated for 5 min at 37°C. Final concentrations of Cas9 protein, tracrRNA and crRNA used were 10 µM, 20 µM and 20 µM respectively. Bead activated T cells were collected by centrifugation and resuspended in the Neon electroporation kit T buffer (Invitrogen; Cat # MPK1096) at a cell density of 20 x 10^6/mL. 5 µL of RNP was mixed with 10 µL of T cells by gentle pipetting and incubated at room temperature for 5 min. The RNP T cell mixture was transferred into a 10 µL Neon electroporation tip probe. Electroporation was performed using the Neon transfection system (Invitrogen; MPK5000S) using the following conditions: 3 pulses of 1600 volts/10 milliseconds. Duplicate 10 µL electroporation reactions were performed. Electroporated T cells were then immediately transferred into 200 µL pre-warmed antibiotics-free complete T cell medium in a 96 well plate and incubated at 37°C, 5% CO_2 for 2 days. T cells were then diluted at 1:1 volume using

antibiotics-free complete T cell medium and transferred to a 24 well plate and cultured an additional 4-7 days at 37°C, 5% CO_2. In parallel activated T cells without RNP treatment were similarly cultured to serve as untreated control samples. T cells were then collected by centrifugation and genomic DNA was isolated from 1-2 million cells using the DNeasy Blood & Tissue Kit (Qiagen, Cat # 69506) following the manufacturer's recommendations. Genome editing was performed for gRNAs comprising the targeting domain sequences of CR00442, CR00444, CR000961 and CR000984 generating two treated and one untreated replicate per gRNA.

***In silico* identification of potential gRNA off-target loci**

For gRNAs CR00442, CR00444, CR000961 and CR000984, potential off-target loci were identified by aligning the 20 nucleotide gRNA protospacer sequence to the human genome reference sequence (build GRCh38) using the BFAST sequence aligner (version 0.6.4f, Homer et al, PLoS One, 2009, 4(11), e7767, PMID: 19907642) using standard parameters allowing up to 5 nucleotide mismatches. Loci identified were filtered to only contain sites that are 5' adjacent to the Cas9 canonical 5'-NGG-3' PAM sequence (i.e. 5'-off-target locus-PAM-3'). Using the BEDTools script (version 2.11.2, Quinlan and Hall, Bioinformatics, 2010 26(6):841-2, PMID: 20110278) sites with 5 nucleotide mismatches were further filtered against RefSeq gene annotations (Pruitt et al, Nucleic Acids Res., 2014 42(Database issue):D756-63, PMID: 24259432) to only contain loci annotated as exons. Counts of the potential off-target loci identified for each gRNA are shown in Table 30.

Table 30. Counts of *in silico* off-target loci identified for gRNAs CR00442, CR00444, CR000961 and CR00098 with 0, 1, 2, 3 and 4 nucleotide mismatches and 5 nucleotide mismatches within RefSeq exons are shown.

		Number of off-targets with N mismatches						
Gene	**gRNA name**	**0**	**1**	**2**	**3**	**4**	**5 RefSeq exons**	**Total**
B2M	CR00442	0	0	0	7	72	71	150
	CR00444	0	0	0	2	24	33	59
TRAC	CR000961	0	0	2	23	224	63	312
	CR000984	0	0	0	3	40	15	58

PCR primer design for targeted amplification of potential off-target sites

PCR amplicons targeting potential off-target loci (and the on-target locus) identified for gRNAs CR00442, CR00444, CR000961 and CR00098 were design using Primer3 (version 2.3.6, Untergasser et al, Nucleic Acids Res., 2012 40(15):e115, PMID: 22730293) using default parameters aiming for an amplicon size range of approximately 160-300bp in length with the gRNA protospacer sequence located in the center of the amplicon. Resulting PCR primer pairs and amplicon sequences were checked for uniqueness by BLAST searching (version 2.2.19, Altschul et al, J Mol Biol., 1990, 215(3):403-10, PMID: 2231712) sequences against the human genome reference sequence (build GRCh38). Primer pairs resulting in more than one amplicon sequence were discarded and redesigned. Table 31 provides a count of successful primer pairs designed for each gRNA.

Illumina sequencing library preparation, quantification and sequencing

Genomic DNA from RNP treated (2 replicates per gRNA) and untreated (1 replicate per gRNA) T-cell samples was quantified using the Quant-iT PicoGreen dsDNA kit (Thermo Fisher, Cat # P7581) using manufacture's recommendations. Illumina sequencing libraries targeting individual off-target loci (and the on-target locus) were generated for each sample using two sequential PCR reactions. The first PCR amplified the target locus using target specific PCR primers (designed above) that were tailed with universal Illumina sequencing compatible sequences. The second PCR added additional Illumina sequencing compatible sequences to the first PCR amplicon, including sample barcodes to enable multiplexing during sequencing. PCR 1 was performed in a final volume of 10 µL with each reaction containing 6 ng of gDNA (equivalent to approximately 1000 cells), PCR 1 primer pairs (Integrated DNA Technologies) at a final concentration of 0.25 µM and 1x final concentration of Q5 Hot Start Master Mix (New England BioLabs, Cat # 102500-140). PCR 1 left primers were 5' tailed (i.e. 5'-tail-target specific left primer-3') with sequence 5'-TCGTCGGCAGCGTCAGATGTGTATAAGAGACAG-3' (SEQ ID NO: 10810) and right primers were 5' tailed (i.e. 5'-tail- target specific right primer-3') with sequence 5'-GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAG-3' (SEQ ID NO: 10811). PCR 1 was performed on a thermocycler using the following cycling conditions: 1 cycle of 98°C for 1 min; 25 cycles of 98°C for 10 sec, 63°C for 20 sec, and 72°C for 30 sec; 1 cycle at 72°C for 2 min. PCR 1 was then diluted 1 in 100 using nuclease free water (Ambion, Cat # AM9932) and used as input into PCR 2. PCR 2 was performed in a final volume of 10 µL with each reaction containing 2 µL of diluted PCR 1 product, PCR 2 primer pairs (Integrated DNA Technologies) at a final concentration of 0.5 µM and 1x final concentration of Q5 Hot Start Master Mix (New England BioLabs, Cat # 102500-140). PCR 2 left primer sequence used was 5'-AATGATACGGCGACCACCGAGATCTACACNNNNNNNNTCGTCGGCAGCGTC-3' (SEQ ID NO: 10812) and PCR 2 right primer sequence used was 5'-

CAAGCAGAAGACGGCATACGAGATNNNNNNNNGTCTCGTGGGCTCGG-3' (SEQ ID NO: 10813) where the NNNNNNNN denote an 8 nucleotide barcode sequence used for sample multiplexing as part of the standard Illumina sequencing process. PCR 2 was performed on a thermocycler using the following cycling conditions: 1 cycle of 72°C for 3 min; 1 cycle of 98°C for 2 min; 15 cycles of 98°C for 10 sec, 63°C for 30 sec, and 72°C for 2 min. PCR 2 amplicons, now viable Illumina sequencing libraries, were cleaned up using Agencourt AMPure XP beads (Beckman Coulter, Cat # A63882) following the manufacture's recommendations. The cleaned Illumina sequencing libraries were then quantified using standard qPCR quantification methods using Power SYBR Green PCR master mix (Life Technologies, Cat # 4367660) and primers specific to the Illumina sequencing library ends (forward primer sequence 5'- CAAGCAGAAGACGGCATACGA-3' (SEQ ID NO: 10814) and reverse primer sequence 5'-AATGATACGGCGACCACCGAGA-3' (SEQ ID NO: 10815)). Illumina sequencing libraries were then pooled equimolar and subjected to Illumina sequencing on a MiSeq instrument (Illumina, Cat # SY-410-1003) with 300 base paired-end reads using a MiSeq Reagent Kit v3 (Illumina, Cat # MS-102-3003) following the manufacture's recommendations. A minimum of 1000-fold sequence coverage was generated for each locus. PCR, cleanup, pooling and sequencing of treated and untreated samples were performed separately to avoid any possibility of cross contamination between treated and untreated samples or PCR amplicons generated therefrom.

Illumina sequencing data QC and variant analysis

Using default parameters, the Illumina MiSeq analysis software (MiSeq reporter, version 2.6.2, Illumina) was used to generate amplicon specific FASTQ sequencing data files (Cock et al, Nucleic Acids Res. 2010, 38(6):1767-71, PMID: 20015970). FASTQ files were then processed through an internally developed variant analysis pipeline consisting of a series of public domain software packages joined together using a standard Perl script wrapper. The workflow used was divided into five stages.

Stage1, PCR primer and on- and off-target sequence QC: For both on- and off- target sites the 20 nucleotide gRNA protospacer sequence plus PAM sequence and target specific PCR primer sequences (left and right without the additional Illumina sequenced) were aligned to the human genome reference sequence (build GRCh38) using a BLAST search (version 2.2.29+, Altschul et al, J Mol Biol., 1990, 215(3):403-10, PMID: 2231712). On- and off-target sites with multiple genomic locations were flagged.

Stage 2, sequencer file decompression: Illumina sequencer generated FASTQ.GZ files were decompressed to FASTQ files using the gzip script (version 1.3.12) and number of reads per file was calculated. Files with no reads were excluded from further analysis.

Stage 3, sequence read alignment and quality trimming: Sequencing reads in FASTQ files were aligned to the human genome reference sequence (build GRCh38) using the BWA-MEM aligner (version 0.7.4-r385, Li and Durbin, Bioinformatics, 2009, 25(14):1754-60, PMID: 19451168) using 'hard-clipping' to trim 3' ends of reads of Illumina sequences and low quality bases. Resulting aligned reads, in the BAM file format (Li et al, Bioinformatics, 2009 25(16):2078-9, PMID: 19505943), were converted to FASTQ files using the SAMtools script (version 0.1.19-44428cd, Li et al, Bioinformatics, 2009 25(16):2078-9, PMID: 19505943). FASTQ files were then aligned again to the human genome reference sequence (build GRCh38) using the BWA-MEM aligner, this time without 'hard-clipping'.

Stage 4, variant (SNP and INDEL) analysis: BAM files of aligned reads were processed using the VarDict variant caller (version 1.0 'Cas9 aware' modified by developer ZhangWu Lia, Lai et al, Nucleic Acids Res., 2016, 44(11):e108, PMID: 27060149) with allele frequency detection limit set at >=0.0001 to identify variants (SNPs and INDELs). The Cas9 aware VarDict caller is based on a public domain package but able to move ambiguous variant calls, generated due to repetitive sequences in the alignment region of the variant events, toward the potential Cas9 nuclease cut site in the gRNA protospacer sequence located 3 bases 5' of the PAM sequence. The SAMtools script was used to calculate read coverage per sample amplicon to determine whether the on- and off-target sites were covered at >1000-fold sequence coverage. Sites with <1000-fold sequence coverage were flagged and more sequencing data was generated.

Stage 5, dbSNP filtering and treated/untreated differential analysis: Variants identified were filtered for known variants (SNPs and INDELs) found in dbSNP (build 142, Shery et al, Nucleic Acids Res. 2001, 29(1):308-11, PMID: 11125122). Variants in the treated samples were further filtered to exclude: 1) variants identified in the untreated control samples; 2) variants with a VarDict strand bias of 2:1 (where forward and reverse read counts supporting the reference sequence are balanced but imbalanced for the non-reference variant call); 3) variants located outside a 100bp window around the potential Cas9 cut site; 4) single nucleotide variants within a 100bp window around the potential Cas9 cut site. Finally only sites with a combined INDEL frequency of >2% (editing in more than approximately 20 cells) in a 100bp window of the potential Cas9 cut site were considered. Potential active editing sites were further examined at the read alignment level using the Integrative Genome Viewer (IGV version 2.3, Robinson et al, Nat Biotechnol. 2011, 9(1):24-6, PMID: 21221095) that allows for visual inspection of read alignments to the genome reference sequence. Sites identified to have potential off-target activity were reworked a second time through the entire laboratory (starting with PCR) and analysis process.

On- and off-target analysis results

On-target sites for gRNA CR00442, CR00444, CR000961 and CR000984 all showed robust editing at the intended Cas9 cut site in both treated biological replicates with an average variant frequency of 96%, 84%, 81%, and 98% respectively. No editing was observed in any of the untreated control samples. Table 31 shows number of off-target sites identified and characterized. Uncharacterized sites either failed in PCR primer design or PCR amplification and are currently still under investigation.

gRNA CR00442: The on-target site for gRNA CR00442 showed robust editing at the intended Cas9 cut site in both treated biological replicates with an average INDEL frequency of 96%. No editing was observed in the untreated control sample. Table 31 shows the number of off-target sites characterized. Uncharacterized sites failed in PCR primer design or PCR amplification and are currently still under investigation. Characterization of potential off-target sites identified two weak off-target sites for gRNA CR00442 with average INDEL frequencies of 3.7% and 4.4% in the 100bp window around the proposed Cas9 cut site. One site has 3 mismatches relative to the on-target gRNA protospacer sequence (5'-GGCaACaGAGCGAGACAaCT-PAM-3', PAM = GGG (SEQ ID NO: 10816)) and is located in intron 1 of the zinc finger protein 440 gene (ZNF440) on chromosome 19 at base pair position 11,815,253-11,815,275, approximately 0.9kb away from exon 1. The second site also has 3 mismatches relative to the on-target gRNA protospacer sequence (5'-GGCgACaGAaCGAGACATCT-PAM-3', PAM = CGG (SEQ ID NO: 10817)) and is located in intron 9 of the epithelial cell-transforming sequence 2 oncogene-like gene (ECT2L) on chromosome 6 at base pair position 138,856,234-138,856,256, approximately 2kb away from exon 9. Manual inspection of both sites showed typical INDEL patterns surrounding the proposed Cas9 cut sites typical of Cas9 mediated double stranded break non homologous end joining DNA repair. Reamplification and sequencing of both sites gave similar results. It is unclear whether editing at either site identified has any detrimental effect on gene expression or cell viability, further analysis is required.

gRNA CR00444: The on-target site for gRNA CR00444 showed robust editing at the intended Cas9 cut site in both treated biological replicates with an average INDEL frequency of 84%. No editing was observed in the untreated control sample. Table 31 shows the number of off-target sites successfully characterized. Uncharacterized sites failed in PCR primer design or PCR amplification and are currently still under investigation. To date no significant off-target activity was observed for gRNA CR00444 at sites examined. However, as Table 31 shows, there are still two sites that have not yet been characterized, one with 4 mismatches located in an intergenic region and another with 5 mismatches located in exon 4 of the non-coding dynamin 1 pseudogene 46 gene (DNM1P46). Based on the high number of mismatches in these sites it is expected that these sites will likely not show any significant editing, however further analysis is required to confirm this.

gRNA CR000961: The on-target site for gRNA CR000961 showed robust editing at the intended Cas9 cut site in both treated biological replicates with an average INDEL frequency of 81%. No editing was observed in the untreated control sample. Table 31 shows the number of off-target sites successfully characterized. Uncharacterized sites failed in PCR primer design or PCR amplification and are currently still under investigation. Characterization of potential off-target sites identified one weak off-target site for gRNA CR000961 with an average INDEL frequency of 5.5% in the 100bp window around the proposed Cas9 cut site. The site has 3 mismatches relative to the gRNA protospacer sequence (5'-AaAGTCaCaCAGCTGGTACA-PAM-3', PAM = TGG (SEQ ID NO: 10818)) and is located in intron 12 of the doublecortin domain-containing protein 1 gene (DCDC1) on chromosome 11 at base pair position 31,102,920-31,102,942, approximately 0.6kb away from exon 13. Manual inspection of the site showed typical INDEL patterns surrounding the proposed Cas9 cut sites typical of Cas9 mediated double stranded break non homologous end joining DNA repair. Reamplification and sequencing of the site gave similar results. It is unclear whether editing at this site has any detrimental effect on gene expression or cell viability, however further analysis is required.

gRNA CR000984: The on-target site for gRNA CR000984 showed robust editing at the intended Cas9 cut site in both treated biological replicates with an average INDEL frequency of 98%. No editing was observed in the untreated control sample. Table 31 the shows the number of off-target sites successfully characterized. Uncharacterized sites failed in PCR primer design or PCR amplification and are currently still under investigation. Characterization of off-target sites identified no significant off-target activity for gRNA CR000984 at sites examined. However, as Table 31 shows, there is still one site that has not yet been characterized. The site has 5 mismatches and is located in an exon of an uncharacterized long non-coding RNA (LOC440896). Based on the high number of mismatches it is expected that this site will likely not show any significant editing, however further analysis is required to confirm this.

Table 31. Counts of total number of potential off-target sites, number of successfully characterized off-target sites and number of active off- target sites identified for gRNAs CR00442, CR00444, CR000961 and CR000984 are shown.

Gene	Targeting domain gRNA name	Total number of off-target sites	Number of off-target sites characterized	Number of active off-target sites identified
B2M	CR00442	150	147 (98%)	2
	CR00444	59	57 (97%)	0
TRAC	CR000961	312	306 (98%)	1

	CR000984	58	57 (98%)	0

GUIDE-Seq hit validation results

Potential off-target loci identified using the GUIDE-seq method (Tsai et al, Nat Biotechnol. 2015, 33(2):187-97, PMID: 25513782) were characterized in RNP treated and untreated T cells using the same methods described for *in silico* identified sites. GUIDE-Seq identified 2 potential sites for gRNA CR00442, 1 potential site for CR00444 and 1 potential site for gRNA CR000984. No active sites were identified for gRNA CR000961. Target sequencing analysis of all potential GUIDE-seq sites showed no significant activity in RNP treated T cells tested.

Off-Target Editing Assessment by Insertional Analysis

An oligo insertion based assay (See, e.g., Tsai et al., *Nature Biotechnology.* **33**, 187–197; 2015) was used to determine potential off-target genomic sites cleaved by Cas9 targeting B2M TRAC, TRBC2, PDCD1, CIITA, and FKBP1A. A total of 34 guideRNAs (dual guide RNAs comprising the indicated targeting domain, modified or unmodified, as indicated) targeting B2M (5), TRAC (9), TRBC2 (2), PDCD1 (8), FKBP1A (5), or CIITA (5) were screened in the Cas9-expressing HEK293 cells described above in Example 1, and the results are plotted in Figure 63 and Figure 64. The assay detected high-efficiency editing at the expected target sequences. No off-target editing was observed for the B2M-targeting gRNA comprising the targeting domain of CR00444 or the targeting domain of CR00441, and only a single very low-efficiency off-target edit was detected using the B2M-targeting gRNA comprising the targeting domain of CR00442. The results show that for gRNAs targeting TRAC comprising the targeting domain of CR00961, CR00978, CR00984, CR00991 and CR00992, each resulted in high-efficiency editing of the target sequence wihout editing at any off-target location. As well, no off-target editing was detected for the PDCD1-targeting gRNA comprising the targeting domain of CR00902. With respect to gRNA molecules which demonstrated potential off-target editing in this assay, deep sequencing will be used to determine whether the potential sites are bona fide off-target sites cleaved by Cas9. As well, any potential off-target edit will be assessed for presence and frequency in T-cells.

Example 18: Editing of CD3 delta and CD3 gamma in primary human CD3+ cells

Editing of CRISPR systems containting dgRNA molecules comprising targeting domains to sequences of CD3 delta and CD3 gamma were tested for editing in primary CD3+ T cells (gRNA/Cas9 RNP delivered by electroporation) according to the methods described herein. Surface expression of CD3 after editing was assayed by flow cytometry. Briefly, edited CD3+ cells were stained with antibodies against CD3

(OKT3, BioLegend) at day 7 post-electroporation. Expression of CD3 in live cells (identified using 7AAD exclusion) relative to the un-edited controls was used to determine frequency of RNP editing. The results are reported in Figure 65 and Figure 66, which include flow cytometry data showing the % editing in primary human CD3+ T cells as measured by loss of surface expression of CD3. Notably, the dgRNA comprising the targeting domain of CR005334 resulted in 98% loss of CD3.

The present invention is not to be limited in scope by the exemplified constructs, since the exemplified embodiments are intended to illustrate only certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. Various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

It is understood that the application of the teachings of the present invention to a specific problem or situation will be within the capabilities of one having ordinary skill in the art in light of the teachings contained herein.

The disclosures of each and every citation in the specification are expressly incorporated herein by reference.

This application is being filed with a sequence listing. To the extent there are any discrepancies between the sequence listing and any sequence recited in the specification, the sequence recited in the specification should be considered the correct sequence. Unless otherwise indicated, all genomic locations are according to hg38.

Claims:

1. A gRNA molecule comprising a tracr and crRNA, wherein the crRNA comprises a targeting domain that is complementary with a target sequence of an allogeneic T-cell target selected from B2M, CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, TRBC2, HLA-A, HLA-B, HLA-C, DCK, CD52, FKBP1A, CIITA, NLRC5, RFXANK, RFX5, RFXAP, or NR3C1.

2. A gRNA molecule of claim 1, wherein:

(a) the allogeneic T-cell target is B2M, and the targeting domain comprises any one of SEQ ID NO: 1 to SEQ ID NO: 83 or SEQ ID NO: 5492 to SEQ ID NO: 5527;

(b) the allogeneic T-cell target is TRAC, and the targeting domain comprises any one of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965;

(c) the allogeneic T-cell target is TRBC1, and the targeting domain comprises any one of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097;

(d) the allogeneic T-cell target is TRBC2, and the targeting domain comprises any one of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226;

(e) the allogeneic T-cell target is CD247, and the targeting domain comprises any one of SEQ ID NO: 84 to SEQ ID NO: 392;

(f) the allogeneic T-cell target is CD3D, and the targeting domain comprises any one of SEQ ID NO: 393 to SEQ ID NO: 532 or SEQ ID NO: 10780 to SEQ ID NO: 10794;

(g) the allogeneic T-cell target is CD3E, and the targeting domain comprises any one of SEQ ID NO: 533 to SEQ ID NO: 839 or SEQ ID NO: 10677 to SEQ ID NO: 10764;

(h) the allogeneic T-cell target is CD3G, and the targeting domain comprises any one of SEQ ID NO: 840 to SEQ ID NO: 968 or SEQ ID NO: 10765 to SEQ ID NO: 10779;

(i) the allogeneic T-cell target is HLA-A, and the targeting domain comprises any one of SEQ ID NO: 969 to SEQ ID NO: 1345;

(j) the allogeneic T-cell target is HLA-B, and the targeting domain comprises any one of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(k) the allogeneic T-cell target is HLA-C, and the targeting domain comprises any one of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(l) the allogeneic T-cell target is DCK, and the targeting domain comprises any one of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(m) the allogeneic T-cell target is CD52, and the targeting domain comprises any one of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(n) the allogeneic T-cell target is FKBP1A, and the targeting domain comprises any one of SEQ ID NO: 6325 to SEQ ID NO: 6583 or SEQ ID NO: 6662 to SEQ ID NO: 6749;

(o) the allogeneic T-cell target is NR3C1, and the targeting domain comprises any one of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(p) the allogeneic T-cell target is CIITA, and the targeting domain comprises any one of SEQ ID NO: 6750 to SEQ ID NO: 7716 or SEQ ID NO: 7717 to SEQ ID NO: 7804; or

(q) the allogeneic T-cell target is NLRC5, and the targeting domain comprises any one of SEQ ID NO: 8622 to SEQ ID NO: 10089.

3. The gRNA molecule of any of claims 1-2, wherein the allogeneic T-cell target is TRAC, and the targeting domain comprises SEQ ID NO: 5569, SEQ ID NO: 5585, SEQ ID NO: 5587, SEQ ID NO: 5592, SEQ ID NO: 5601, SEQ ID NO: 5589, SEQ ID NO: 5600, SEQ ID NO: 5594, SEQ ID NO: 5571, SEQ ID NO: 5593, SEQ ID NO: 5574,SEQ ID NO: 5598, SEQ ID NO: 5586, SEQ ID NO: 5599, SEQ ID NO: 5591, SEQ ID NO: 5610, SEQ ID NO: 5608, SEQ ID NO: 5617, SEQ ID NO: 5619, or SEQ ID NO: 5620.

4. The gRNA molecule of claim 3, wherein the allogeneic T cell target is TRAC, and the targeting domain comprises SEQ ID NO: 5569, SEQ ID NO: 5586, SEQ ID NO: 5587, SEQ ID NO: 5592, SEQ ID NO: 5599, or SEQ ID NO: 5600.

5. The gRNA molecule of any of claims 1-2, wherein the allogeneic T-cell target is TRBC2, and the targeting domain comprises SEQ ID NO: 5719, SEQ ID NO: 5694, SEQ ID NO: 5706, SEQ ID NO: 5696, SEQ ID NO: 5711, SEQ ID NO: 5708, SEQ ID NO: 5709, SEQ ID NO: 5712, SEQ ID NO: 5703, SEQ ID NO: 5707, SEQ ID NO: 5687, SEQ ID NO: 5705, SEQ ID NO: 5713, SEQ ID NO: 5715, or SEQ ID NO: 5710.

6. The gRNA molecule of any of claims 1-2, wherein the allogeneic T-cell target is B2M, and the targeting domain comprises SEQ ID NO: 5519, SEQ ID NO: 5497, SEQ ID NO: 5499, SEQ ID NO: 5498, SEQ ID NO: 5503, SEQ ID NO: 5496, SEQ ID NO: 5507, SEQ ID NO: 5515, SEQ ID NO: 5493, SEQ ID NO: 5506, SEQ ID NO: 5509, SEQ ID NO: 5517, SEQ ID NO: 5521, SEQ ID NO: 5520, SEQ ID NO: 5500, SEQ ID NO: 5494, SEQ ID NO: 5508, SEQ ID NO: 5514, or SEQ ID NO: 5492.

7. The gRNA molecule of claim 6, wherein the allogeneic T-cell target is B2M, and the targeting domain comprises SEQ ID NO: 5496, SEQ ID NO: 5498, or SEQ ID NO: 5509.

8. The gRNA molecule of any one of clams 1-2, wherein the allogeneic T-cell target is CIITA, and the targeting domain comprises SEQ ID NO: 7771, SEQ ID NO: 7769, SEQ ID NO: 7773, SEQ ID NO: 7726, SEQ ID NO: 7758, SEQ ID NO: 7739, SEQ ID NO: 7779, SEQ ID NO: 7770, SEQ ID NO: 7749, SEQ ID NO: 7754, SEQ ID NO: 7745, SEQ ID NO: 7785, SEQ ID NO: 7731, SEQ ID NO: 7772, SEQ ID NO: 7743, or SEQ ID NO: 7750.

9. The gRNA molecule of claim 8, wherein the targeting domain comprises SEQ ID NO: 7769, SEQ ID NO: 7771, SEQ ID NO: 7739, or SEQ ID NO: 7785.

10. The gRNA molecule of any of claims 1-4, wherein the allogeneic T-cell target is TRAC, and the targeting domain comprises SEQ ID NO: 5569, SEQ ID NO: 5587, SEQ ID NO: 5592 or SEQ ID NO: 5586.

11. The gRNA molecule of any of claims 1-4 or 10, wherein the allogeneic T-cell target is TRAC, and the targeting domain comprises SEQ ID NO: 5569.

12. The gRNA molecule of any of claims 1-2, wherein the allogeneic T-cell target is CD3E, and the targeting domain comprises SEQ ID NO: 10729, SEQ ID NO: 10719, SEQ ID NO: 10764, SEQ ID NO: 10789, SEQ ID NO: 10701, SEQ ID NO: 10700, or SEQ ID NO: 10722.

13. The gRNA molecule of any of claims 1-2, wherein the allogeneic T-cell target is FKBP1A, and the targeting domain comprises SEQ ID NO: 6693, SEQ ID NO: 6705, SEQ ID NO: 6694, SEQ ID NO: 6708, or SEQ ID NO: 6699.

14. A gRNA molecule comprising a tracr and a crRNA, wherein the crRNA comprises a targeting domain that is complementary with a target sequence of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule selected from CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT,

LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, or PTPN11.

15. The gRNA molecule of claim 14, wherein:

(a) the inhibitory molecule is CD274 (PD-L1), and the targeting domain comprises any one of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(b) the inhibitory molecule is HAVCR2 (TIM3), and the targeting domain comprises any one of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(c) the inhibitory molecule is LAG3, and the targeting domain comprises any one of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(d) the inhibitory molecule is PDCD1 (PD-1), and the targeting domain comprises any one of SEQ ID NO: 4033 to SEQ ID NO: 4589 or SEQ ID NO: 5720 to SEQ ID NO: 5815; or

(e) the downstream effector of signaling through an inhibitory molecule is PTPN1, and the targeting domain comprises any one of SEQ ID NO: 4590 to SEQ ID NO: 5277.

16. The gRNA molecule of any of claims 14-15, wherein the inhibitory molecule is PDCD1, and the targeting domain comprises SEQ ID NO: 5743, SEQ ID NO: 5798, SEQ ID NO: 5748, SEQ ID NO: 5722, SEQ ID NO: 5800, SEQ ID NO: 5735, SEQ ID NO: 5724, SEQ ID NO: 5731, SEQ ID NO: 5725, SEQ ID NO: 5775, SEQ ID NO: 5766, SEQ ID NO: 5727, SEQ ID NO: 5744, SEQ ID NO: 5751, or SEQ ID NO: 5734.

17. The gRNA molecule of any of claims 14-15, wherein the inhibitory molecule is PDCD1, and the targeting domain comprises SEQ ID NO: 5775.

18. The gRNA molecule of any of claims 2-13 or 15-16, wherein the targeting domain comprises 17, 18, 19, 20, 21, 22, 23, or 24 consecutive nucleic acids of any one of the recited targeting domain sequences.

19. The gRNA molecule of any of claims 2-13 or 15-16, wherein the targeting domain consists of 17, 18, 19, 20, 21, 22, 23, or 24 consecutive nucleic acids of any one of the recited targeting domain sequences.

20. The gRNA molecule of claim 18 or 19, wherein the 17, 18, 19, 20, 21, 22, 23, or 24 consecutive nucleic acids of any one of the recited targeting domain sequences are the 17, 18, 19, 20, 21, 22, 23, or 24 consecutive nucleic acids disposed at the 3' end of the recited targeting domain sequence.

21. The gRNA molecule of claim 18 or 19, wherein the 17, 18, 19, 20, 21, 22, 23, or 24 consecutive nucleic acids of any one of the recited targeting domain sequences are the 17, 18, 19, 20, 21, 22, 23, or 24 consecutive nucleic acids disposed at the 5' end of the recited targeting domain sequence.

22. The gRNA molecule of claim 18 or 19, wherein the 17, 18, 19, 20, 21, 22, 23, or 24 consecutive nucleic acids of any one of the recited targeting domain sequences do not comprise either the 5' or 3' nucleic acid of the recited targeting domain sequence.

23. The gRNA molecule of any of claims 2-13 or 15-16, wherein the targeting domain consists of the recited targeting domain sequence.

24. The gRNA molecule of any of the previous claims, wherein a portion of the crRNA and a portion of the tracr hybridize to form a flagpole comprising SEQ ID NO: 6584 or SEQ ID NO: 6585.

25. The gRNA molecule of claim 24, wherein the flagpole further comprises a first flagpole extension, located 3' to the crRNA portion of the flagpole, wherein said first flagpole extension comprises SEQ ID NO: 6586.

26. The gRNA molecule of claim 24 or 25, wherein the flagpole further comprises a second flagpole extension located 3' to the crRNA portion of the flagpole and, if present, the first flagpole extension, wherein said second flagpole extension comprises SEQ ID NO: 6587.

27. The gRNA molecule of any of claims 1-26, wherein the tracr comprises:

(a) SEQ ID NO: 7820, optionally further comprising, at the 3' end, an additional 1, 2, 3, 4, 5, 6, or 7 uracil (U) nucleotides;

(b) SEQ ID NO: 6660; or

(c) SEQ ID NO: 6661.

28. The gRNA molecule of claim 27, wherein the crRNA portion of the flagpole comprises SEQ ID NO: 6607 or SEQ ID NO: 6608.

29. The gRNA molecule of any of claims 1-26, wherein the tracr comprises SEQ ID NO: 6589 or SEQ ID NO: 6590, and optionally, if a first flagpole extension is present, a first tracr extension, disposed 5' to SEQ ID NO: 6589 or SEQ ID NO: 6590, said first tracr extension comprising SEQ ID NO: 6591.

30. The gRNA molecule of any of claims 19-20, wherein the targeting domain and the tracr are disposed on separate nucleic acid molecules.

31. The gRNA molecule of any of claims 1-23, wherein the crRNA comprises, from 5' to 3', [targeting domain]-:

a) SEQ ID NO: 6584;

b) SEQ ID NO: 6585;

c) SEQ ID NO: 6605;

d) SEQ ID NO: 6606;

e) SEQ ID NO: 6607;

f) SEQ ID NO: 6608; or

g) SEQ ID NO: 7806.

32. The gRNA molecule of any of claims 1-23 or 31, wherein the tracr comprises, from 5' to 3':

a) SEQ ID NO: 6589;

b) SEQ ID NO: 6590;

c) SEQ ID NO: 6609;

d) SEQ ID NO: 6610;

e) SEQ ID NO: 6660;

f) SEQ ID NO: 6661;

g) SEQ ID NO: 7820;

h) SEQ ID NO: 7807;

i) SEQ ID NO: 7808;

j) SEQ ID NO: 7809;

k) any of a) to j), above, further comprising, at the 3' end, at least 1, 2, 3, 4, 5, 6 or 7 uracil (U) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 uracil (U) nucleotides;

l) any of a) to k), above, further comprising, at the 3' end, at least 1, 2, 3, 4, 5, 6 or 7 adenine (A) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 adenine (A) nucleotides; or

m) any of a) to l), above, further comprising, at the 5' end (e.g., at the 5' terminus), at least 1, 2, 3, 4, 5, 6 or 7 adenine (A) nucleotides, e.g., 1, 2, 3, 4, 5, 6, or 7 adenine (A) nucleotides.

33. The gRNA molecule of any of claims 1-23, wherein the targeting domain and the tracr are disposed on separate nucleic acid molecules, and wherein the nucleic acid molecule comprising the targeting domain comprises SEQ ID NO: 6607, optionally disposed immediately 3' to the targeting domain, and the nucleic acid molecule comprising the tracr comprises, e.g., consists of, SEQ ID NO: 6660.

34. The gRNA molecule of any of claims 27-28, wherein the targeting domain and the tracr are disposed on a single nucleic acid molecule, and wherein the tracr is disposed 3' to the targeting domain.

35. The gRNA molecule of claim 34, further comprising a loop, disposed 3' to the targeting domain and 5' to the tracr.

36. The gRNA molecule of claim 35, wherein the loop comprises SEQ ID NO: 6588.

37. The gRNA molecule of any of claims 1-23, comprising, from 5' to 3', [targeting domain]-:

(a) SEQ ID NO: 6601;

(b) SEQ ID NO: 6602;

(c) SEQ ID NO: 6603;

(d) SEQ ID NO: 6604;

(e) SEQ ID NO: 7811; or

(f) any of (a) to (e), above, further comprising, at the 3' end, 1, 2, 3, 4, 5, 6 or 7 uracil (U) nucleotides.

38. The gRNA molecule of any of claims 1-23, wherein the targeting domain and the tracr are disposed on a single nucleic acid molecule, and wherein said nucleic acid molecule comprises, e.g., consists of, said targeting domain and SEQ ID NO: 6601, optionally disposed immediately 3' to said targeting domain.

39. The gRNA molecule of any of claims 1-23, wherein the targeting domain and the tracr are disposed on a single nucleic acid molecule, and wherein said nucleic acid molecule comprises, e.g., consists of, said targeting domain and SEQ ID NO: 7811, optionally disposed immediately 3' to said targeting domain.

40. The gRNA molecule of any of claims 1-39 wherein one, or optionally more than one, of the nucleic acid molecules comprising the gRNA molecule comprises:

a) a, e.g., three, phosphorothioate modification(s) at the 3' end of said nucleic acid molecule or molecules;

b) a, e.g., three, phosphorothioate modification(s) at the 5' end of said nucleic acid molecule or molecules;

c) a, e.g., three, 2'-O-methyl modification(s) at the 3' end of said nucleic acid molecule or molecules;

d) a, e.g., three, 2'-O-methyl modification(s) at the 5' end of said nucleic acid molecule or molecules;

e) a 2' O-methyl modification at each of the 4th-to-terminal, 3rd-to-terminal, and 2nd-to-terminal 3' residues of said nucleic acid molecule or molecules; or

f) any combination thereof.

41. A gRNA molecule of any of claims 1-40, wherein when a CRISPR system (e.g., an RNP as described herein) comprising the gRNA molecule is introduced into a cell, an indel is formed at or near the target sequence complementary to the targeting domain of the gRNA molecule.

42. The gRNA molecule of claim 41, wherein the indel is a frameshift mutation.

43. The gRNA molecule of any of claims 41-42, wherein the indel is an indel listed in any of Figure 34A, Figure 34B, Figure 36, Figure 38, Figure 41, Figure 44, Figure 48, Figure 49, Figure 50 or Figure 53.

43. A gRNA molecule of any of claims 1-40, wherein when a CRISPR system (e.g., an RNP as described herein) comprising the gRNA molecule is introduced into a population of cells, an indel is formed at or near the target sequence complementary to the targeting domain of the gRNA molecule in at least about 40%, e.g., at least about 50%, e.g., at least about 60%, e.g., at least about 70%, e.g., at least about 80%, e.g., at least about 90%, e.g., at least about 95%, e.g., at least about 96%, e.g., at least about 97%, e.g., at least about 98%, e.g., at least about 99%, of the cells of the population.

44. A gRNA molecule of any of claims 1-40, wherein when a CRISPR system (e.g., an RNP as described herein) comprising the gRNA molecule is introduced into a population of cells, an indel that is a frameshift mutation is formed at or near the target sequence complementary to the targeting domain of the gRNA molecule in at least about 20%, e.g., at least about 30%, e.g., at least about 35%, e.g., at least about 40%, e.g., at least about 45%, e.g., at least about 50%, e.g., at least about 55%, e.g., at least about 60%,

e.g., at least about 65%, e.g., at least about 70%, e.g., at least about 75%, e.g., at least about 80%, e.g., at least about 85%, e.g., at least about 90%, e.g., at least about 95%, e.g., at least about 99%, of the cells of the population.

45. The gRNA molecule of any of claims 43-44, wherein in at least about 30%, e.g., least about 40%, e.g., at least about 50%, e.g., at least about 60%, e.g., at least about 70%, e.g., at least about 80%, e.g., at least about 90%, e.g., at least about 95%, e.g., at least about 96%, e.g., at least about 97%, e.g., at least about 98%, e.g., at least about 99%, of the cells of the population, the indel is an indel listed in any of Figure 34A, Figure 34B, Figure 36, Figure 38, Figure 41, Figure 44, Figure 48, Figure 49, Figure 50 or Figure 53.

46. The gRNA molecule of any of claims 43-45, wherein the five most frequently detected indels in said population of cells comprise three or more, e.g., four, e.g., five, of the indels associated with any gRNA listed in any of Figure 34A, Figure 34B, Figure 36, Figure 38, Figure 41, Figure 44, Figure 48, Figure 49, Figure 50 or Figure 53.

47. The gRNA molecule of any of claims 41-46, wherein the indel is as measured by next generation sequencing (NGS).

48. A gRNA molecule of any of claims 1-47, wherein when a CRISPR system (e.g., an RNP as described herein) comprising the gRNA molecule is introduced into a cell, expression of the gene comprising the target sequence complementary to the targeting domain of the gRNA molecule is reduced or eliminated in said cell.

49. A gRNA molecule of any of claims 1-48, wherein when a CRISPR system (e.g., an RNP as described herein) comprising the gRNA molecule is introduced into a population of cells, expression of the gene comprising the target sequence complementary to the targeting domain of the gRNA molecule is reduced or eliminated in at least about 40%, e.g., at least about 50%, e.g., at least about 60%, e.g., at least about 70%, e.g., at least about 80%, e.g., at least about 90%, e.g., at least about 95%, e.g., at least about 96%, e.g., at least about 97%, e.g., at least about 98%, e.g., at least about 99%, of the cells of the population.

50. The gRNA molecule of any of claims 48-49, wherein the reduced or eliminated expression is measured by flow cytometry.

51. The gRNA molecule of any of claims 41-50, wherein when a CRISPR system (e.g., an RNP as described herein) comprising the gRNA molecule is introduced into a cell, no off-target indels are formed in said cell, e.g., as detectible by next generation sequencing and/or a nucleotide insertional assay.

52. The gRNA molecule of any of claims 41-50, wherein when a CRISPR system (e.g., an RNP as described herein) comprising the gRNA molecule is introduced into a population of cells, an off-target indel is detected in no more than about 5%, e.g., no more than about 1%, e.g., no more than about 0.1%, e.g., no more than about 0.01%, of the cells of the population of cells e.g., as detectible by next generation sequencing and/or a nucleotide insertional assay.

53. The gRNA molecule of any of claims 41-52, wherein the cell is (or population of cells comprises) a mammalian, primate, or human cell, e.g., is a human cell.

54. The gRNA molecule of claim 53, wherein the cell is (or population of cells comprises) an immune effector cell.

55. The gRNA molecule of claim 54, wherein the immune effector cell is (or population of cells comprises) a T cell or NK cell, e.g., is a T cell.

56. The gRNA molecule of claim 55, wherein the T cell is (or population of cells comprises) a CD4+ T cell, a CD8+ T cell, or a combination thereof.

57. The gRNA molecule of any of claims 52-55, wherein the cell (or population of cells) has been, or will be, engineered to express a chimeric antigen receptor (CAR).

58. The gRNA molecule of claim 57, wherein the CAR is:

(a) a CD19 CAR; or

(b) a BCMA CAR.

59. The gRNA molecule of 58, wherein:

(a) the CAR is a CD19 CAR comprising an antigen binding domain comprising any one of SEQ ID NO: 7883 to SEQ ID NO: 7898;

(b) the CAR is a CD19 CAR comprising SEQ ID NO: 7909 or SEQ ID NO: 7920;

(c) the CAR is a BCMA CAR comprising an antigen binding domain comprising any one of SEQ ID NO: 7939 to SEQ ID NO: 8112, e.g., comprising an antigen binding domain of SEQ ID NO: 7949; or

(d) the CAR is a BCMA CAR comprising any one of SEQ ID NO: 8549 to SEQ ID NO: 8621, e.g., comprising SEQ ID NO: 8559.

60. The gRNA molecule of any of claims 41-59, wherein the cell is allogeneic with respect to a patient to be administered said cell.

61. A composition comprising a first gRNA molecule of any of claims 1-60, further comprising a Cas9 molecule.

62. The composition of claim 61, wherein the Cas9 molecule comprises, e.g., consists of, any one of SEQ ID NO: 6611 or SEQ ID NO: 7821 to SEQ ID NO: 7831.

63. The composition of claim 61, wherein the Cas9 molecule is an active or inactive *s. pyogenes* Cas9.

64. The composition of any of claims 61-63, wherein the first gRNA molecule and Cas9 molecule are present in a ribonuclear protein complex (RNP).

65. The composition of any of claims 61-64, further comprising a second gRNA molecule; a second gRNA molecule and a third gRNA molecule; or a second gRNA molecule, a third gRNA molecule, and a fourth gRNA molecule, wherein the second gRNA molecule, the third gRNA molecule (if present), and the fourth gRNA molecule (if present) are a gRNA molecule of any of claims 1-26, and wherein each gRNA molecule of the composition is complementary to a different target sequence.

66. The composition of claim 65, wherein the first gRNA molecule, the second gRNA molecule, the third gRNA molecule (if present), and the fourth gRNA molecule (if present) are complementary to target sequences within the same gene.

67. The composition of claim 65 or 66, wherein the first gRNA molecule, the second gRNA molecule, the third gRNA molecule (if present), and the fourth gRNA molecule (if present) are complementary to target sequences not more than 20000 nucleotides, not more than 10000 nucleotides, not more than 6000, not more than 5000 nucleotides, not more than 4000, not more than 1000 nucleotides, not more than 500 nucleotides, not more than 400 nucleotides, not more than 300 nucleotides, not more than 200 nucleotides, not more than 100 nucleotides, not more than 90 nucleotides, not more than 80 nucleotides, not more than 70 nucleotides, not more than 60 nucleotides, not more than 50 nucleotides, not more than 40 nucleotides, not more than 30 nucleotides, not more than 20 nucleotides or not more than 10 nucleotides apart.

68. The composition of claim 65, wherein the first gRNA molecule, the second gRNA molecule, the third gRNA molecule (if present), and the fourth gRNA molecule (if present) are complementary to target sequence within different genes.

69. The composition of claim 68 comprising a first gRNA molecule, a second gRNA molecule and a third gRNA molecule, wherein the first gRNA molecule is the gRNA molecule of any of claims 2(b), 2(c), 2(d), 2(d), 2(e), 2(f), 2(g) or 2(h); and the second gRNA molecule is the gRNA molecule of any of claims 2(a), 2(i), 2(j), 2(k) or 2(q); and the third gRNA molecule is the gRNA molecule of any of claims 15(a), 15(b), 15(c), 15(d), or 15(e).

70. The composition of claim 69 comprising a first gRNA molecule, a second gRNA molecule and a third gRNA molecule, wherein the first gRNA molecule is the gRNA molecule of any of claims 2(b), 2(c), 2(d), 2(d), 2(e), 2(f), 2(g) or 2(h); and the second gRNA molecule is the gRNA molecule of any of claims 2(l), 2(m), 2(n), or 2(o); and the third gRNA molecule is the gRNA molecule of any of claims 15(a), 15(b), 15(c), 15(d), or 15(e).

71. The composition of claim 70 comprising a first gRNA molecule and a second gRNA molecule, wherein the first gRNA molecule is the gRNA molecule of any of claims 2(b), 2(c), 2(d), 2(d), 2(e), 2(f), 2(g) or 2(h); and the second gRNA molecule is the gRNA molecule of any of claims 2(l), 2(m), 2(n), or 2(o).

72. The composition of claim 70 comprising a first gRNA molecule and a second gRNA molecule, wherein the first gRNA molecule is the gRNA molecule of any of claims 2(b), 2(c), 2(d), 2(d), 2(e), 2(f), 2(g) or 2(h); and the second gRNA molecule is the gRNA molecule of any of claims 2(a), 2(i), 2(j), or 2(k).

73. The composition of claim 70 comprising a first gRNA molecule and a second gRNA molecule, wherein the first gRNA molecule is the gRNA molecule of any of claims 2(b), 2(c), 2(d), 2(d), 2(e), 2(f), 2(g) or 2(h); and the second gRNA molecule is the gRNA molecule of any of claims 15(a), 15(b), 15(c), 15(d), or 15(e).

74. The composition of claim 70 comprising a first gRNA molecule and a second gRNA molecule, wherein the first gRNA molecule is the gRNA molecule of any of claims 15(a), 15(b), 15(c), 15(d), or 7(e); and the second gRNA molecule is the gRNA molecule of any of claims 15(a), 15(b), 15(c), 15(d), or 15(e).

75. The composition of claim 74, further comprising a third gRNA molecule, wherein the third gRNA molecule is the gRNA molecule of any of claims 15(a), 15(b), 15(c), 15(d), or 15(e).

76. The composition of any of claims 65-68, 71, 72, 73, or 74, consisting of two gRNA molecules of any of claims 1-60.

77. The composition of any of claims 65-70, or 75, consisting of three gRNA molecules of any of claims 1-60.

78. A composition comprising:

a) a first gRNA molecule of any of claims 1-60, wherein the targeting domain of said first gRNA molecule is a targeting domain of any of claims 2(a), 2(i), 2(j), or 2(k); and

b) a second gRNA molecule of any of claims 1-60, wherein the targeting domain of said second gRNA molecule is a targeting domain of any of claims 2(b), 2(c), 2(d), 2(f), 2(g), 2(h), or 2(i).

79. The composition of claim 78, wherein:

a) the targeting domain of said first gRNA molecule is a targeting domain of claim 6; and

b) the targeting domain of said second gRNA molecule is a targeting domain of claim 3.

80. The composition of claim 78, wherein:

a) the targeting domain of said first gRNA molecule is a targeting domain of claim 7; and

b) the targeting domain of said second gRNA molecule is a targeting domain of claim 4.

81. The composition of claim 78, wherein:

a) the targeting domain of said first gRNA molecule is a targeting domain of claim 7; and

b) the targeting domain of said second gRNA molecule is a targeting domain of claim 11.

82. The composition of claim 78, wherein:

a) the targeting domain of said first gRNA molecule is a targeting domain of claim 7; and

b) the targeting domain of said second gRNA molecule is a targeting domain of claim 12.

83. The composition of any of claims 78-82, further comprising a third gRNA molecule of any of claims 1-60, wherein the targeting domain of said third gRNA molecule is a targeting domain of any of claims 2(n) or 2(q).

84. The composition of claim 83, wherein the targeting domain of said third gRNA molecule is a targeting domain of claim 8.

85. The composition of claim 83, wherein the targeting domain of said third gRNA molecule is a targeting domain of claim 9.

86. The composition of any of claims 78-85, further comprising a fourth gRNA molecule, wherein the targeting domain of said fourth gRNA molecule is complementary to a target sequence of a target of an NK inhibitory molecule.

87. The composition of claim 86, wherein the target of an NK inhibitory molecule is LILRB1.

88. The composition of claim 87, wherein the targeting domain of said fourth gRNA molecule comprises, e.g., consists of:

a) any one of SEQ ID NO: 10090 to SEQ ID NO: 10673;
b) 17, 18, 19, 20, 21, 22, 23, or 24 consecutive nucleotides, preferably 20 consecutive nucleotides, of any one of SEQ ID NO: 10090 to SEQ ID NO: 10673.
c) The 5' 17, 18, 19, 20, 21, 22, 23 or 24 nucleotides, preferably 20 nucleotides, of any one of SEQ ID NO: 10090 to SEQ ID NO: 10673; or
d) The 3' 17, 18, 19, 20, 21, 22, 23 or 24 nucleotides, preferably 20 nucleotides, of any one of SEQ ID NO: 10090 to SEQ ID NO: 10673.

89. The composition of any one of claims 78-88, wherein each of said gRNA molecules is in a ribonuclear protein complex (RNP) with a Cas9 molecule described herein.

90. The composition of any of claims 61-89, formulated in a medium suitable for electroporation.

91. The composition of any of claims 61-90, wherein each of said gRNA molecules is in a RNP complex with a Cas9 molecule described herein, and wherein each of said RNP complexes is at a concentration of less than about 10uM, e.g., less than about 3uM, e.g., less than about 1uM, e.g., less than about 0.5uM, e.g., less than about 0.3uM, e.g., less than about 0.1uM.

92. The composition of claim 91, further comprising a cell, e.g., a population of cells, e.g., an immune effector cell, e.g., a CAR-expressing immune effector cell, e.g., described herein.

93. A nucleic acid sequence that encodes a gRNA molecule of any of claims 1-60 or a, e.g., all, components of a composition of any of claims 61-92.

94. The nucleic acid sequence of claim 93, wherein the nucleic acid comprises a promoter operably linked to the sequence that encodes the gRNA molecule.

95. The nucleic acid sequence of claim 94, wherein the promoter is a promoter recognized by an RNA polymerase II or RNA polymerase III.

96. The nucleic acid sequence of claim 95, wherein the promoter is a U6 promoter or an HI promoter.

97. The nucleic acid sequence of any of claims 93-96, wherein the nucleic acid further encodes a Cas9 molecule.

98. The nucleic acid sequence of claim 97, wherein said nucleic acid comprises a promoter operably linked to the sequence that encodes a Cas9 molecule.

99. The nucleic acid sequence of claim 98, wherein the promoter is an EF-1 promoter, a CMV IE gene promoter, an EF-1α promoter, an ubiquitin C promoter, or a phosphoglycerate kinase (PGK) promoter.

100. A vector comprising the nucleic acid of any of claims 93-99.

101. The vector of claim 80, wherein in the vector is selected from the group consisting of a lentiviral vector, an adenoviral vector, an adeno-associated viral (AAV) vector, a herpes simplex virus (HSV) vector, a plasmid, a minicircle, a nanoplasmid, and an RNA vector.

102. A composition comprising a gRNA molecule of any of claims 1-60, and nucleic acid encoding a Cas9 molecule.

103. A composition comprising nucleic acid encoding a gRNA molecule of any of claims 1-60, and a Cas9 molecule.

104. The composition of any of claims 61-92 or 102-103, further comprising a template nucleic acid.

105. The composition of claim 104, wherein the template nucleic acid comprises a nucleotide that corresponds to a nucleotide of a target sequence of the gRNA molecule.

106. The composition of any of claims 104-105, wherein the template nucleic acid comprises nucleic acid encoding a chimeric antigen receptor (CAR).

107. The composition of claim 106, wherein the CAR is:

(a) a CD19 CAR, e.g., as described in WO2012/079000 or WO2014/153270; or

(b) a BCMA CAR, e.g., as described herein, e.g., a BCMA CAR comprising SEQ ID NO: 8559.

108. the composition of any of claims 104-107, wherein the template nucleic acid comprises nucleic acid encoding an NK inhibitory molecule.

109. A method of altering e.g., altering the structure, e.g., sequence of, a target sequence of a cell, comprising contacting said cell with:

a) a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 1-60 and a Cas9 molecule;

b) a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 1-60 and nucleic acid encoding a Cas9 molecule;

c) nucleic acid encoding a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 1-60 and a Cas9 molecule;

d) nucleic acid encoding a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 1-60 and nucleic acid encoding a Cas9 molecule;

e) any of a) to d), above, and a template nucleic acid;

f) any of a) to d) above, and nucleic acid comprising sequence encoding a template nucleic acid;

g) the composition of any of claims 61-92 or 102-108; or

h) the vector of any of claims 100-101.

110. The method of claim 109, wherein the gRNA molecule or nucleic acid encoding the gRNA molecule, and the Cas9 molecule or nucleic acid encoding the Cas9 molecule, are formulated in a single composition.

111. The method of claim 109, wherein the gRNA molecule or nucleic acid encoding the gRNA molecule, and the Cas9 molecule or nucleic acid encoding the Cas9 molecule, are formulated in more than one composition.

112. The method of claim 111, wherein the more than one composition are delivered simultaneously or sequentially.

113. The method of any of claims 109-112, wherein the cell is an animal cell.

114. The method of any of claims 109-112, wherein the cell is a mammalian, primate, or human cell.

115 The method of claim 114, an immune effector cell (e.g., a population of immune effector cells).

116. The method of claim 115, wherein the immune effector cell is a T cell or NK cell.

117. The method of any of claims 115-116, wherein the immune effector cell is a T cell.

118. The method of claim 1178, wherein the T cell is a CD4+ T cell, a CD8+ T cell, or a combination thereof.

119. The method of any of claims 113-119, wherein the cell has been, or will be, engineered to express a chimeric antigen receptor (CAR).

120. The method of claim 119, wherein the CAR is:

(a) a CD19 CAR; or

(b) a BCMA CAR.

121. The method of claim 120, wherein the CAR is a CD19 CAR comprising an antigen binding domain comprising any one of SEQ ID NO: 7883 to SEQ ID NO: 7898.

122. The method of any of claims 120 and 121, wherein the CAR is a CD19 CAR and comprises any one of SEQ ID NO: 7908 to SEQ ID NO: 7920.

123. The method of claim 120, wherein the CAR is a BCMA CAR comprising an antigen binding domain comprising any one of SEQ ID NO: 7939 to SEQ ID NO: 8112.

124. The method of any of claims 120 and 123, wherein the CAR is a BCMA CAR and comprises any one of SEQ ID NO: 8549 to SEQ ID NO: 8621, e.g., comprises SEQ ID NO: 8559.

125. The method of any of claims 113-124, wherein the cell is autologous or allogeneic with respect to a patient to be administered said cell.

126. A cell, altered by the method of any of claims 109-124.

127. A cell, comprising a first gRNA molecule of any of claims 1-60, or a composition of any of claims 61-92 or 102-108, a nucleic acid of any of claim 93-99, or a vector of any of claims 100-101.

128. The cell of any of claims 126 or 127, wherein the cell is an animal cell.

129. The cell of any of claims 126-128, wherein the cell is a mammalian, primate, or human cell.

130. The cell of claim 129, wherein the cell is an immune effector cell (e.g., a population of immune effector cells).

131. The cell of claim 130, wherein the immune effector cell is a T cell or NK cell.

132. The cell of any of claims 130-131, wherein the immune effector cell is a T cell.

133. The cell of claim 132, wherein the T cell is a CD4+ T cell, a CD8+ T cell, or a combination thereof.

134. The cell of any of claims 126-133, wherein the cell has been, or will be, engineered to express a chimeric antigen receptor (CAR).

135. The cell of any of claims 126-134, wherein the cell is autologous with respect to a patient to be administered said cell.

136. The cell of any of claims 126-134, wherein the cell is allogeneic with respect to a patient to be administered said cell.

137. The cell of any of claims 126-136, wherein the cell comprises, has comprised, or will comprise a second gRNA molecule of any of claims 1-60, or a nucleic acid encoding the second gRNA molecule of any of claims 1-60, wherein the first gRNA molecule and second gRNA molecule comprise nonidentical targeting domains.

138. The cell of claim 137, wherein the first gRNA molecule comprises a targeting domain complementary with a target sequence of an allogeneic T-cell target (e.g., a targeting domain described in Tables 1, 3, 4 or 5), and the second gRNA molecule comprises a targeting domain complementary with a target sequence of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule (e.g., comprises a targeting domain described in Table 2 or Table 6).

139. The cell of claim 138, wherein the inhibitory molecule or downstream effector of signaling through an inhibitory molecule is CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, or PTPN11.

140. The cell of claim 137, wherein the first gRNA molecule comprises a targeting domain complementary with a target sequence of TRAC, TRBC1, TRBC2, CD247, CD3D, CD3E, or CD3G, and the second gRNA molecule comprises a targeting domain complementary with a target sequence of NLRC5, e.g., comprises a targeting domain comprising (e.g., consisting of) any one of SEQ ID NO: 8622 to SEQ ID NO: 10089.

141. The cell of claim 137, wherein the first gRNA molecule comprises a targeting domain complementary with a target sequence of TRAC, TRBC1, TRBC2, CD247, CD3D, CD3E, or CD3G, and the second gRNA molecule comprises a targeting domain complementary with a target sequence of B2M, HLA-A, HLA-B or HLA-C.

142. The cell of any of claims 137 and 141, wherein the cell further comprises, has comprised, or will comprise a third gRNA molecule of any of claims 1-60, or a nucleic acid encoding the third gRNA molecule of any of claims 1-60, wherein the first gRNA molecule, the second gRNA molecule and the third gRNA molecule comprise nonidentical targeting domains.

143. The cell of claim 142, wherein the third gRNA molecule comprises a targeting domain complementary with a target sequence of CIITA, RFXANK, RFX5, or RFXAP.

144. The cell of claim 143, wherein the third gRNA molecule comprises a targeting domain complementary with a target sequence of CIITA.

145. The cell of claim 144, wherein the third gRNA molecule comprises a targeting domain comprising, e.g., consisting of, any one of SEQ ID NO: 7717 to SEQ ID NO: 7804, e.g., comprises a targeting domain comprising, e.g., consisting of, any one of SEQ ID NO: 7769, SEQ ID NO: 7771, or SEQ ID NO: 7785.

146. The cell of any of claims 142-145, wherein the first gRNA molecule comprises a targeting domain complementary with a target sequence of TRAC; the second gRNA molecule comprises a targeting domain complementary with a target sequence of B2M; and the third gRNA molecule comprises a targeting domain complementary with a target sequence of CIITA.

147. The cell of any of claims 142-145, wherein the first gRNA molecule comprises a targeting domain complementary with a target sequence of TRAC; the second gRNA molecule comprises a targeting domain complementary with a target sequence of NLRC5; and the third gRNA molecule comprises a targeting domain complementary with a target sequence of CIITA.

148. The cell of claim 137, wherein the first gRNA molecule comprises a targeting domain complementary with a target sequence of TRAC, TRBC1, TRBC2, CD247, CD3D, CD3E, or CD3G, and the second gRNA molecule comprises a targeting domain complementary with a target sequence of NR3C1, DCK, CD52 or FKBP1A.

149. The cell of claim 137 wherein:

(1) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(2) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(3) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(4) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(5) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(6) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(7) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(8) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(9) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide

RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(10) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(11) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(12) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(13) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(14) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(15) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(16) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(17) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(18) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(19) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(20) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(21) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(22) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(23) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(24) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide

RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(25) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(26) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(27) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(28) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(29) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(30) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(31) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(32) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(33) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain

selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(34) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(35) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(36) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(37) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(38) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(39) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(40) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(41) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(42) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(43) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(44) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(45) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(46) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(47) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324;

(48) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583;

(49) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 83 and SEQ ID NO: 5492 to SEQ ID NO: 5527;

(50) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 969 to SEQ ID NO: 1345;

(51) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1346 to SEQ ID NO: 1698;

(52) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 1699 to SEQ ID NO: 2068;

(53) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2069 to SEQ ID NO: 2941;

(54) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5278 to SEQ ID NO: 5491;

(55) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6227 to SEQ ID NO: 6324; or

(56) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 6325 to SEQ ID NO: 6583.

150. The cell of claim 149, further comprising a third gRNA molecule comprising a targeting domain complementary with a target sequence of an inhibitory molecule or downstream effector of signaling through an inhibitory molecule, wherein the inhibitory molecule or downstream effector of signaling through an inhibitory molecule is CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, or PTPN11.

151. The cell of claim 150, wherein the third gRNA molecule is the third gRNA molecule of claim 15.

152. The cell of claim 137, wherein:

(1) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide

RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(2) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(3) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(4) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(5) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5528 to SEQ ID NO: 5623 or SEQ ID NO: 5816 to SEQ ID NO: 5965, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(6) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(7) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(8) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(9) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(10) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5624 to SEQ ID NO: 5643 or SEQ ID NO: 5966 to SEQ ID NO: 6097, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(11) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(12) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(13) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(14) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(15) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 5644 to SEQ ID NO: 5719 or SEQ ID NO: 6098 to SEQ ID NO: 6226, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(16) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(17) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(18) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(19) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(20) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 84 to SEQ ID NO: 392, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(21) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(22) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(23) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(24) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(25) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 393 to SEQ ID NO: 532, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(26) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(27) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(28) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(29) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815;

(30) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 533 to SEQ ID NO: 839, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277;

(31) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 2942 to SEQ ID NO: 3270;

(32) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3271 to SEQ ID NO: 3541;

(33) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 3542 to SEQ ID NO: 4032;

(34) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4033 to SEQ ID NO: 4589 and SEQ ID NO: 5720 to SEQ ID NO: 5815; or

(35) the first gRNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 840 to SEQ ID NO: 968, and the second guide RNA molecule comprises a targeting domain selected from the group consisting of SEQ ID NO: 4590 to SEQ ID NO: 5277.

153. The cell of claim 137 or claim 142, wherein the targeting domain of the first gRNA molecule, the targeting domain of the second gRNA molecule, and, if present, the targeting domain of the third gRNA molecule, comprise, e.g., consist of, the sequences of any of:

a) Combination A1 to combination A72 of Table 33;
b) Combination B1 to combination B84 of Table 34;
c) Combination C1 to combination C42 of Table 35;
d) Combination D1 to combination D36 of Table 36;
e) Combination E1 to combination E30 of Table 37; or
f) Combination F1 to combination F60 of Table 38.

154. The cell of claim 137, wherein the first gRNA molecule comprises a targeting domain comprising SEQ ID NO: 5569, SEQ ID NO: 5592, or SEQ ID NO: 5586, and the second gRNA molecule comprises a targeting domain comprising SEQ ID NO: 5775.

155. The cell of any of claims 126-154, wherein a gene comprising a target sequence complementary to the targeting domain of the first gRNA molecule, and, optionally, a gene comprising a target sequence complementary to the targeting domain of the second gRNA molecule, has been altered such that expression of a functional product of the gene comprising a target sequence complementary to the targeting domain of the first gRNA molecule, and, optionally, the gene comprising a target sequence complementary to the targeting domain of the second gRNA molecule, has been reduced or eliminated.

156. A method of providing an anti-tumor immunity in a subject, the method comprising administering to the subject an effective amount of a cell of any of claims 126 to 155.

157. A method of treating a subject having a disease associated with expression of a tumor antigen, e.g., a proliferative disease, a precancerous condition, a cancer, and a non-cancer related indication associated

with expression of the tumor antigen, the method comprising administering to the subject an effective amount of a cell of any of claims 126 to 155.

158. The method of claim 157, wherein the disease associated with expression of a tumor antigen is cancer or a non-cancer related indication.

159. The method of claim 158, wherein the disease is cancer selected from colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers, chronic lymphocytic leukemia (CLL), acute leukemias, acute lymphoid leukemia (ALL), B-cell acute lymphoid leukemia (B-ALL), T-cell acute lymphoid leukemia (T-ALL), chronic myelogenous leukemia (CML), acute myeloid leukemia (AML), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, Hodgkin’s lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and pre-leukemia, combinations of said cancers, and metastatic lesions of said cancers.

160. The method of any of claims 156-159, wherein the method further comprises administering a chemotherapeutic agent.

161. The method of claim 160, wherein the chemotherapeutic agent is cyclophosphamide, fludarabine, or cyclophosphamide and fludarabine.

162. The method of any of claims 156-161, wherein the method comprises administering a lymphodepleting agent or immunosuppressant prior to administering to the subject an effective amount of the cell of any of claims 126 to 155.

163. A method of preparing cells (e.g., a population of cells) for immunotherapy comprising: (a) modifying cells by reducing or eliminating expression of a component of a T-cell receptor (TCR) comprising introducing into said cells a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 2b to 2h, e.g., a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 3, 4, 5, 10, 11 or 12; (b) modifying cells by reducing or eliminating expression of an HLA (e.g., HLA-A, HLA-B, and/or HLA-C) or B2M comprising introducing into said cells a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 2a, 2i, 2j or 2k, e.g., a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 6 or 7; and (c) expanding said cells.

164. The method of claim 163, further comprising modifying said cells by reducing or eliminating expression of CIITA comprising introducing into said cells a gRNA molecule, e.g., more than one gRNA molecule, of claim 2p, e.g., a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 8 or 9, wherein said modifying optionally takes place before the step of expanding said cells.

165. A method of preparing cells (e.g., a population of cells) for immunotherapy comprising: (a) modifying cells by reducing or eliminating expression of a component of a T-cell receptor (TCR) comprising introducing into said cells a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 2b to 2h, e.g., a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 3, 4, 5, 10, 11 or 12; (b) modifying cells by reducing or eliminating expression of a target for an immunosuppressant comprising introducing into said cells a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 2l, 2m, 2n or 2o, e.g., a gRNA molecule, e.g., more than one gRNA molecule, of claim 13; and (c) expanding said cells.

166. The method of any of claims 163-165, further comprising (d) modifying cells by reducing or eliminating expression of a first inhibitory molecule or downstream effector of signaling through an inhibitory molecule comprising introducing into said cells a gRNA molecule, e.g., more than one gRNA molecule, of claim 14; wherein said modifying optionally takes place before the step of expanding said cells.

167. A method of preparing cells (e.g., a population of cells) for immunotherapy comprising: (a) modifying cells by reducing or eliminating expression of a first inhibitory molecule or downstream effector of signaling through an inhibitory molecule comprising introducing into said cells a gRNA

molecule, e.g., more than one gRNA molecule, of claim 14, e.g., a gRNA molecule, e.g., more than one gRNA molecule, of any of claims 15-17; and (c) expanding said cells.

168. The method of any of claims 166-167, further comprising (e) modifying cells by reducing or eliminating expression of a second inhibitory molecule or downstream effector of signaling through an inhibitory molecule comprising introducing into said cells a gRNA molecule, e.g., more than one gRNA molecule, of claim 14, wherein the first inhibitory molecule or downstream effector of signaling through an inhibitory molecule and second inhibitory molecule or downstream effector of signaling through an inhibitory molecule are different.

169. The method of any of claims 163-168, wherein the introduction of each of the gRNA molecules is simultaneous or sequential.

170. The method of claim 169, wherein the introduction of each of the gRNA molecules is sequential, and separated by a period of at least 24 hours, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days or 10 days.

171. The method of any of claims 163-170, wherein the method further comprises introducing into the cells nucleic acid encoding a chimeric antigen receptor (CAR), e.g., described herein.

172. The method of claim 171, wherein the nucleic acid encoding a CAR is disposed on a template nucleic acid.

173. The method of claim 171, wherein the nucleic acid encoding a CAR is disposed on a RNA vector.

174. The method of claim 171, wherein the nucleic acid encoding a CAR is disposed on a lentiviral vector.

175. The method of any of claims 163-166 or 169-174, wherein the method further comprises isolating cells which are negative for TCR expression.

176. The method of claim 175, wherein the isolating results in a population of cells in which greater than about 90%, 91%, 92%, 93, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% of the cells are negative for TCR expression.

177. The method of claim 175 or 176 wherein the step of isolating cells which are negative for TCR expression comprises contacting the cell population with a composition comprising an antibody specific for a component of a T cell receptor (TCR), optionally bound to a solid support or detectable label, and isolating the cells which do not bind to said antibody.

178. The method of any of claims 163-177, wherein the cells are immune effector cells.

179. The method of claim 178, wherein the cells are T cells or NK cells.

180. The method of claim 178, wherein the cells are T cells.

181. The method of any of claims 163-180, wherein the cells are isolated from a healthy donor, e.g., a donor which does not suffer from a condition associated with expression of a tumor antigen.

182. The method of any of claims 163-181, wherein steps (a) and/or (b) are performed ex vivo.

183. The method of claim 182, wherein step (c) is performed ex vivo.

184. The method of any of claims 163-183, wherein the expansion of step (c) is performed for a period of at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 days, or for a period of 2-15, 2-14, 2-13, 2-12, 2-11, 2-10, 3-10, 2-9, 3-9, 2-8, 3-8, 2-7, 3-7, 2-6, 3-6, 2-5, or 3-5 days.

185. A method of treating a subject in need thereof comprising administering cells (e.g., population of cells) prepared by the method of any of claims 163-164.

186. A method of treating a subject in need thereof comprising administering cells (e.g., population of cells) prepared by the method of claim 165 in combination with an immunosuppressive agent.

187. The method of any of claims 185-186, wherein the cells (e.g., population of cells) are autologous to the subject.

188. The method of claims 185-186, wherein the cells (e.g., population of cells) are allogeneic to the subject.

189. The method of any of claims 185-188, wherein the subject has a disease associated with expression of a tumor antigen, e.g., a proliferative disease, a precancerous condition, a cancer, and a non-cancer related indication associated with expression of the tumor antigen, wherein said administration treats said disease associated with expression of a tumor antigen.

190. The method of claim 189, wherein the disease associated with expression of a tumor antigen is cancer or a non-cancer related indication.

191. The method of claim 190, wherein the disease is cancer selected from colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or

neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers, chronic lymphocytic leukemia (CLL), acute leukemias, acute lymphoid leukemia (ALL), B-cell acute lymphoid leukemia (B-ALL), T-cell acute lymphoid leukemia (T-ALL), chronic myelogenous leukemia (CML), acute myeloid leukemia (AML), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, Hodgkin’s lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and pre-leukemia, combinations of said cancers, and metastatic lesions of said cancers.

192. A method of treating a patient suffering from a disease comprising:

(a) providing a population of cells from an allogeneic donor;

(b) introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a first gRNA molecule (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in a gene selected from CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, and TRBC2;

(c) optionally, selecting those cells in which expression of functional TCR has been reduced or eliminated;

(d) transducing the cells with nucleic acid encoding a CAR; and

(e) administering the cells to a patient in need thereof, e.g., a patient who has a disease associated with expression of an antigen recognized by the CAR.

193. The method of claim 192, wherein the first gRNA molecule to CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, or TRBC2 is a gRNA molecule of any of claims 2(b)-2(h), e.g., is a gRNA molecule of any of claims 3, 4, 5, 10, 11 or 12.

194. The method of any of claims 192-193, further comprising introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a second gRNA molecule (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in a gene selected from B2M, HLA-A, HLA-B or HLA-C.

195. The method of claim 194, wherein the second gRNA to B2M, HLA-A, HLA-B or HLA-C is a gRNA molecule of any of claims 2(a) or 2(i)-2(k), e.g., is a gRNA molecule of any of claims 6 or 7.

196. The method of any of claims 192-195, further comprising introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a third gRNA molecule (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in a gene selected from CIITA, RFXANK, RFXAP, RFX5, HLA-DM, HLA-DO, HLA-DR, HLA-DQ and HLA-DP.

197. The method of claim 196, wherein the third gRNA molecule is a gRNA molecule of any of claims 2(a) or 2(i)-2(k), e.g., is a gRNA molecule of any of claims 6 or 7.

198.The method of any of claims 192-193, further comprising introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a second gRNA molecule (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in a gene selected from DCK, CD52, FKBP1A or NR3C1.

199. The method of claim 198, wherein the second gRNA molecule to DCK, CD52, FKBP1A or NR3C1 is a second gRNA molecule of any of claims 2(l)-2(o), e.g., is a second gRNA molecule of claim 13.

200. The method of any of claims 198-199, wherein the second gRNA is to DCK, the method further comprising administering a nucleoside analog-based drug to said patient.

201. The method of claim 200, wherein the nucleoside analog-based drug is cytarabine or gemcitabine.

202. The method of any of claims 198-199, wherein the second gRNA is to CD52, the method further comprising administering an anti-CD52 antibody or antigen-binding fragment thereof to said patient.

203. The method of claim 202, wherein the anti-CD52 antibody or antigen-binding fragment thereof is alemtuzumab (CAMPATH®).

204. The method of any of claims 198-199, wherein the second gRNA is to FKBP1A, the method further comprising administering FK506, cyclosporine, rapamycin or rapalog, or mTor inhibitor such as RAD001, to said patient.

205. The method of any of claims 198-199, wherein the second gRNA is to NR3C1, the method further comprising administering a corticosteroid to said patient.

206. The method of claim 205, wherein the corticosteroid is dexamethasone.

207.The method of any of claims 192-206, further comprising introducing into the cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a fourth gRNA molecule (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in a gene selected from CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD113), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD107), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta, or PTPN11.

208. The method of claim 207, wherein the fourth gRNA molecule is to CD274, HAVCR2, LAG3, PDCD1 or PTPN11, and is a gRNA molecule of any of claims 15(a)-(e), e.g., a gRNA molecule of any of claims 15-17.

209. A method of treating a patient suffering from a disease comprising:

(a) providing a population of immune effector cells;

(b) introducing into the population of cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a first gRNA molecule (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in a gene selected from CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, and TRBC2;

(c) introducing into the population of cells a CRISPR System (e.g., an *S. pyogenes* Cas9 CRISPR system) comprising a second gRNA molecule (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in a gene selected from B2M, HLA-A, HLA-B and HLA-C;

(d) optionally, selecting those cells in which expression of functional TCR, functional B2M, or both functional TCR and B2M has been reduced or eliminated;

(d) introducing into the population of cells a nucleic acid encoding a CAR; and

(e) administering the population of cells to a patient in need thereof, e.g., a patient who has a disease associated with expression of an antigen recognized by the CAR.

210. The method of claim 209, further comprising:

(f) introducing into the population of cells a CRISPR System (e.g., an S. pyogenes Cas9 CRISPR system) comprising a third gRNA molecule (or nucleic acid encoding said gRNA molecule) comprising a targeting domain complementary to a target sequence in a gene selected from CIITA, RFXANK, RFX5, and RFXAP.

211. The method of claim 209-210, wherein the first gRNA molecule comprises a targeting domain complementary to a target sequence in a gene selected from TRAC, TRBC1 and TRBC2.

212. The method of claim 209-211, wherein the second gRNA molecule comprises a targeting domain complementary to a target sequence in a B2M gene.

213. The method of claim 210-212, wherein the third gRNA molecule comprises a targeting domain complementary to a target sequence in a CIITA gene.

214. The method of any of claims 209-213, wherein the first gRNA molecule targets a sequence of a TRAC gene, and comprises a targeting domain comprising, e.g., consisting of, any one of SEQ ID NO: 5569, SEQ ID NO: 5585, SEQ ID NO: 5592, SEQ ID NO: 5601, SEQ ID NO: 5589, SEQ ID NO: 5600, SEQ ID NO: 5594, SEQ ID NO: 5571, SEQ ID NO: 5593, SEQ ID NO: 5574,SEQ ID NO: 5598, SEQ ID NO: 5586, SEQ ID NO: 5599, SEQ ID NO: 5591, SEQ ID NO: 5610, SEQ ID NO: 5608, SEQ ID NO: 5617, SEQ ID NO: 5619, or SEQ ID NO: 5620.

215. The method of claim 214, wherein the first gRNA molecule comprises a targeting domain comprising, e.g., consisting of, any one of SEQ ID NO: 5569, SEQ ID NO: 5592, SEQ ID NO: 5587, SEQ ID NO: 5599, SEQ ID NO: 5600, SEQ ID NO: 5586, e.g., SEQ ID NO: 5569, SEQ ID NO: 5586, or SEQ ID NO: 5592.

216. The method of any of claims 209-215, wherein the second gRNA molecule targets a sequence of a B2M gene, and comprises a targeting domain comprising, e.g., consisting of, any one of SEQ ID NO: 5519, SEQ ID NO: 5497, SEQ ID NO: 5499, SEQ ID NO: 5498, SEQ ID NO: 5503, SEQ ID NO: 5496, SEQ ID NO: 5507, SEQ ID NO: 5515, SEQ ID NO: 5493, SEQ ID NO: 5506, SEQ ID NO: 5509, SEQ ID NO: 5517, SEQ ID NO: 5521, SEQ ID NO: 5520, SEQ ID NO: 5500, SEQ ID NO: 5494, SEQ ID NO: 5508, SEQ ID NO: 5514, or SEQ ID NO: 5492.

217. The method of claim 216, wherein the second gRNA molecule comprises a targeting domain comprising, e.g., consisting of, SEQ ID NO: 5496, SEQ ID NO: 5498 or SEQ ID NO: 5509.

218. The method of any of claims 210-217, wherein the third gRNA molecule targets a sequence of a CIITA gene, and comprises a targeting domain comprising, e.g., consisting of, any one of SEQ ID NO:

7771, SEQ ID NO: 7769, SEQ ID NO: 7773, SEQ ID NO: 7726, SEQ ID NO: 7758, SEQ ID NO: 7739, SEQ ID NO: 7779, SEQ ID NO: 7770, SEQ ID NO: 7749, SEQ ID NO: 7754, SEQ ID NO: 7745, SEQ ID NO: 7785, SEQ ID NO: 7731, SEQ ID NO: 7772, SEQ ID NO: 7743, or SEQ ID NO: 7750.

219. The method of claim 218, wherein the third gRNA molecule comprises a targeting domain comprising, e.g., consisting of, any one of SEQ ID NO: 7769, SEQ ID NO: 7771, SEQ ID NO: 7739 or SEQ ID NO: 7785.

220. The method of any of claims 209-219, further comprising introducing into said cells a nucleic acid molecule encoding an NK inhibitory molecule, e.g., a nucleic acid molecule encoding an HLA-G:B2M fusion, e.g., a nucleic acid molecule encoding SEQ ID NO: 10674.

221. The method of any of claims 209-220, wherein the population of immune effector cells is a population of T cells.

222. The method of claim 221, wherein the population of immune effector cells is allogeneic relative to the patient.

223. The method of any of claims 209-222, wherein the CAR is a CD19 CAR.

224. The method of any of claims 209-222, wherein the CAR is a BCMA CAR.

225. The method of claim 224, wherein the BCMA CAR comprises an antigen recognition domain comprising any one of SEQ ID NO: 7939 to SEQ ID NO: 8112 or SEQ ID NO: 8155 to SEQ ID NO: 8166, e.g., comprises an antigen recognition domain comprising, e.g., consisting of, SEQ ID NO: 7949.

226. The method of claim 224, wherein the BCMA CAR comprises any one of SEQ ID NO: 8549 to SEQ ID NO: 8621, e.g., comprises, e.g., consists of, SEQ ID NO: 8559.

227. A modified cell, which has reduced or eliminated expression of:

a) a component of the T cell receptor;

b) B2M; and/or

c) CIITA,

relative to an unmodified cell of the same type.

228. The cell of claim 227, wherein the component of the T cell receptor is a TCR alpha chain or a TCR beta chain.

229. The cell of claim 227, wherein the component of the T cell receptor is a TCR alpha chain.

230. The cell of claim 227, wherein the component of the TCR is CD3 delta, CD3 epsilon, or CD3 gamma, e.g., is CD3 epsilon.

231. A modified cell, comprising an insertion or deletion of a base pair, e.g., more than one base pair, at or near:

a) a gene encoding a component of the T cell receptor;

b) B2M; and/or

c) CIITA;

relative to an unmodified cell of the same type.

232. The modified cell of claim 231, wherein each of said insertions or deletions is an indel.

233. The modified cell of any of claims 231-232, wherein each of said insertion or deletion is a frameshift mutation.

234. A population of cells comprising the modified cell of any of claims 231-233, wherein in at least about 30% of the cells, at least one said insertion or deletion is a frameshift mutation, e.g., as measured by NGS.

235. The modified cell (or population of cells) of any of claims 231 to 234, wherein the modified cell has reduced or eliminated expression of a component of the T cell receptor, B2M and CIITA.

236. A cell comprising (e.g., a population of cells comprising a cell, e.g., more than one cell, comprising):

(g) Nucleic acid sequence encoding a CAR, e.g., as described herein;

(h) Optionally, nucleic acid sequence encoding an NK inhibitory molecule, e.g., as described herein, e.g., nucleic acid encoding an HLA-G or HLA-G:B2M fusion as described herein;

(i) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3E, CD3D or CD3G, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to a component of a TCR (e.g., TRAC, TRBC1, TRBC2, CD3E, CD3D, or CD3G e.g. TRAC), e.g., comprising a targeting domain listed in Table 1, Table 4, Table 5, Table 6e, Table 6f, or Table 6g;

(j) An indel at or near a sequence of the gene encoding B2M or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to B2M, e.g., comprising a targeting domain listed in Table 1 or Table 3;

(k) Optionally, an indel at or near a sequence of the gene encoding CIITA or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to CIITA, e.g., comprising a targeting domain listed in Table 1 or Table 6c; and

(l) Optionally, an indel at or near a sequence of the gene encoding LILRB1 or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to LILRB1, e.g., comprising a targeting domain listed in Table 6d;

Wherein the cell (or population of cells comprising said cell) expresses the CAR and, optionally, the NK inhibitory molecule, and exhibits reduced or eliminated expression and/or function of one or more of: i) a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), ii) B2M, iii) CIITA, and/or iv) LILRB1.

237. A cell comprising (e.g., a population of cells comprising a cell, e.g., more than one cell, comprising):

(g) Nucleic acid sequence encoding a CAR, e.g., as described herein;

(h) Optionally, nucleic acid sequence encoding an NK inhibitory molecule, e.g., as described herein, e.g., nucleic acid encoding an HLA-G as described herein;

(i) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), e.g., comprising a targeting domain listed in Table 1, Table 4, Table 5, Table 6e, Table 6f, or Table 6g;

(j) An indel at or near a sequence of the gene encoding NLRC5 or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to NLRC5, e.g., comprising a targeting domain listed in Table 1;

(k) Optionally, an indel at or near a sequence of the gene encoding CIITA or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to CIITA, e.g., comprising a targeting domain listed in Table 1 or Table 6c; and

(l) Optionally, an indel at or near a sequence of the gene encoding LILRB1 or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to LILRB1, e.g., comprising a targeting domain listed in Table 6d;

Wherein the cell (or population of cells comprising one or more of said cells) expresses the CAR and, optionally, the NK inhibitory molecule, and exhibits reduced or eliminated expression and/or function of one or more of: i) a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), ii) B2M, iii) NLRC5, and/or iv) LILRB1.

238. A cell comprising (e.g., a population of cells comprising a cell, e.g., more than one cell, comprising):

(d) Nucleic acid sequence encoding a CAR, e.g., as described herein;
(e) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), e.g., comprising a targeting domain listed in Table 1, Table 4, Table 5, Table 6e, Table 6f, or Table 6g; and
(f) An indel at or near a sequence of the gene encoding FKBP1A or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to FKBP1A, e.g., comprising a targeting domain listed in Table 1 or Table 6b;

Wherein the cell (or population of cells comprising a cell, e.g., more than one cell, comprising) expresses the CAR, and exhibits reduced or eliminated expression and/or function of one or more of: i) a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), and/or ii) FKBP12.

239. A cell comprising (e.g., a population of cells comprising a cell, e.g., more than one cell, comprising):

(d) Nucleic acid sequence encoding a CAR, e.g., as described herein;
(e) Nucleic acid sequence encoding a rapamycin-resistant mTor, e.g., as described herein, e.g., nucleic acid sequence encoding an mTor comprising a S2035 mutation, e.g., an S2035I mutation; and;
(f) An indel at or near a sequence of a gene encoding a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC) or its regulatory elements, e.g., an indel at or near a target sequence of a gRNA comprising a targeting domain to a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC), e.g., comprising a targeting domain listed in Table 1, Table 4, Table 5, Table 6e, Table 6f, or Table 6g;

Wherein the cell (or population of cells comprising said cell, e.g., more than one of said cell,) expresses the CAR and the rapamycin-resistant mTor, and exhibits reduced or eliminated expression and/or function of a component of a TCR (e.g., TRAC, TRBC1 TRBC2, CD3D, CD3E or CD3G, e.g. TRAC).

240. A cell of any one of claims 236 to 239, wherein the gRNA comprising a targeting domain to a component of a TCR comprises a targeting domain comprising (e.g., consisting of) any one of SEQ ID NO: 5569, SEQ ID NO: 5568, SEQ ID NO: 5601, SEQ ID NO: 5592, SEQ ID NO: 5586, SEQ ID NO: 5587, SEQ ID NO: 5599, SEQ ID NO: 5600, e.g., SEQ ID NO: 5569, SEQ ID NO: 5586, SEQ ID NO: 5587 or SEQ ID NO: 5592.

241. A cell of any one of claims 236 or 240, wherein the gRNA comprising a targeting domain to B2M comprises a targeting domain comprising (e.g., consisting of) any one of SEQ ID NO: 5496, SEQ ID NO: 5498, or SEQ ID NO: 5509.

242. A cell of any one of claims 236, 237, 239, 240 or 241, wherein the gRNA comprising a targeting domain to CIITA comprises a targeting domain comprising (e.g., consisting of) any one of SEQ ID NO: 7739, SEQ ID NO: 7769, SEQ ID NO: 7771 or SEQ ID NO: 7785.

243. A cell of any one of claims 238, 240 or 241, wherein the gRNA comprising a targeting domain to KFBP1A comprises a targeting domain comprising (e.g., consisting of) any one of SEQ ID NO: 6693, SEQ ID NO: 6705, SEQ ID NO: 6694, SEQ ID NO: 6699 or SEQ ID NO: 6708.

244. A cell of any one of claims 236-239 or 241-243, wherein the gRNA comprising a targeting domain to a component of a TCR comprises a targeting domain comprising (e.g., consisting of) a targeting domain listed in Table 6e, Table 6f or Table 6g, e.g., Table 6e, e.g., any one of SEQ ID NO: 10729, SEQ ID NO: 10719, SEQ ID NO: 10764, SEQ ID NO: 10689, SEQ ID NO: 10701, SEQ ID NO: 10700, or SEQ ID NO: 10722.

245. A cell of claim 236, wherein the targeting domain of the gRNA molecule to a component of the TCR, the targeting domain of the gRNA molecule to B2M, and the targeting domain of the gRNA molecule to CIIRA comprise, e.g., consists of, respectively:

a) the targeting domain sequences for said gRNA molecules listed in any combination of A1 to A72 in Table 33; or

b) the targeting domain sequences for said gRNA molecules listed in any combination of F1 to F60 in Table 38.

246. A cell of claim 236, wherein the targeting domain of the gRNA molecule to a component of the TCR, the targeting domain of the gRNA molecule to B2M, and the targeting domain of the gRNA molecule to CIIRA comprise, e.g., consists of, respectively, the targeting domain sequence for each gRNA molecule listed in any combination of B1 to B84 in Table 34.

247. A cell of claim 238, wherein the targeting domain of the gRNA molecule to a component of the TCR, and the targeting domain of the gRNA molecule to FKBP1A comprise, e.g., consists of, respectively, the targeting domain sequences for said gRNA molecules listed in any combination of C1 to C42 in Table 35.

248. A cell of claim 238, wherein the targeting domain of the gRNA molecule to a component of the TCR, and the targeting domain of the gRNA molecule to FKBP1A comprises, e.g., consists of, respectively:

a) the targeting domain sequences for said gRNA molecules listed in any combination of D1 to D36 in Table 36; or

b) the targeting domain sequences for said gRNA molecules listed in any combination of E1 to E30 in Table 37.

249. The cell of any of claims 236-248, wherein each of said indels in said cell is made by introducing into said cell a gRNA molecule, e.g., more than one gRNA molecule, (e.g., a CRISPR system, e.g., more than one CRISPR system, comprising said gRNA molecule, e.g., each of said more than one gRNA molecules), each comprising a targeting domain which is complementary to a target sequence at or near each of said indels.

250. A population of cells, wherein at least about 30% of the cells of the population are the cell of any of claims 236-249.

251. A population of cells, wherein at least about 50% of the cells of the population are the cell of any of claims 236-249.

252. A population of cells, wherein at least about 75% of the cells of the population are the cell of any of claims 236-249.

253. A population of cells, wherein at least about 90% of the cells of the population are the cell of any of claims 236-249.

254. A population of cells, comprising the cell of any of claims 236-249, wherein in at least about 30% of said cells (e.g., in at least about 40%, e.g., in at least about 50%, e.g., in at least about 60%, e.g., in at least about 70%, e.g., in at least about 80%, e.g., in at least about 90%, e.g., in at least about 95%, e.g., in at least about 99%), each of said indels is a frameshift mutation.

255. A cell (or population of cells) of any one of claims 236 to 254, comprising an indel listed in Figure 34A, Figure 34B or Figure 49.

256. A cell (or population of cells) of any one of claims 236 or 239-255, comprising an indel listed in Figure 36 or Figure 48.

257. A cell (or population of cells) of any one of claims 236, 237, or 239-256, comprising an indel listed in Figure 38, Figure 41, Figure 44 or Figure 50.

258. A cell (or population of cells) of any one of claims 238-257, comprising an indel listed in Figure 53.

259. A population of cells comprising the cell of any one of claims 255-258.

260. A population of cells, wherein at least about 20% of the cells of the population of cells is a cell of any one of claims 255-258.

261. The population of cells of claim 260, wherein at least about 50% of the cells of the population of cells is a cell of any one of claims 255-258.

262. The population of cells of any of claims 259-261, wherein less than about 5%, e.g., less than about 1%, e.g., less than about 0.01%, of the cells of the population of cells comprises an off-target indel.

263. The cell (or population of cells) of any of claims 227-235, engineered to express a chimeric antigen receptor.

264. The cell (or population of cells) of any of claims 236-263, wherein the CAR is a CD19 CAR.

265. The cell (or population of cells) of any of claims 236-263, wherein the CAR is a BCMA CAR.

266. The cell (or population of cells) of claim 265, wherein the BCMA CAR comprises an antigen recognition domain comprising any one of SEQ ID NO: 7939 to SEQ ID NO: 8112 or SEQ ID NO: 8155 to SEQ ID NO: 8166, e.g., comprises an antigen recognition domain comprising, e.g., consisting of, SEQ ID NO: 7949.

267. The cell (or population of cells) of claim cell 265, wherein the BCMA CAR comprises any one of SEQ ID NO: 8549 to SEQ ID NO: 8621, e.g., comprises, e.g., consists of, SEQ ID NO: 8559.

268. The cell (or population of cells) of claim cell 264, wherein the CD19 CAR comprises an antigen binding domain comprising any one of SEQ ID NO: 7883 to SEQ ID NO: 7898.

269. The cell (or population of cells) of claim cell 264, wherein the CD19 CAR comprises SEQ ID NO: 7909 or SEQ ID NO: 7920.

270. The cell (or population of cells) of any of claims 227-269, wherein the cell is an animal cell.

271. The cell (or population of cells) of any of claims 227-270, wherein the cell is a mammalian, primate, or human cell, e.g., a human cell.

272. The cell (or population of cells) of any of claims 227-271, an immune effector cell (e.g., a population of immune effector cells).

273. The cell (or population of cells) of claim 272, wherein the immune effector cell is a T cell or NK cell.

274. The cell (or population of cells) of any of claims 272-273, wherein the immune effector cell is a T cell.

275. The cell (or population of cells) of claim 274, wherein the T cell is a CD4+ T cell, a CD8+ T cell, or a combination thereof.

276. The cell (or population of cells) of any of claims 227-275, wherein the cell is isolated from a healthy human subject.

277. The cell (or population of cells) of any of claims 227-276, wherein the cell allogeneic relative to a patient to be administered said cell.

278. A method of treating a disease, e.g., a cancer, in a patient in need thereof, comprising administering the cell of any of claims 227-277.

279. A method of claim 278, comprising administering the cell of any of claims 227-277 in combination with an immunosuppressant, e.g., RAD001.

280. A gRNA molecule of any of claims 1-60, a composition of any of claims 61-92 or 102-108, a nucleic acid of any of claims 93-99, a vector of any of claims 100-101, or a cell (or population of cells) of any of claims 126-155 or 227-277, for use as a medicament.

281. A gRNA molecule of any of claims 1-60, a composition of any of claims 61-92 or 102-108, a nucleic acid of any of claims 93-99, a vector of any of claims 100-101, or a cell (or population of cells) of any of claims 126-155 or 227-277, for use in the manufacture of a medicament.

282. A gRNA molecule of any of claims 1-60, a composition of any of claims 61-92 or 102-108, a nucleic acid of any of claims 93-99, a vector of any of claims 100-101, or a cell (or population of cells) of any of claims 126-155 or 227-277, for use in the treatment of a disease.

283. A gRNA molecule of any of claims 1-60, a composition of any of claims 61-92 or 102-108, a nucleic acid of any of claims 93-99, a vector of any of claims 100-101, or a cell (or population of cells) of any of claims 126-155 or 227-277, for use in the treatment of a disease, wherein the disease is a disease associated with expression of a tumor antigen, e.g., a proliferative disease, a precancerous condition, a cancer, and a non-cancer related indication associated with expression of the tumor antigen.

284. A gRNA molecule of any of claims 1-60, a composition of any of claims 61-92 or 102-108, a nucleic acid of any of claims 93-99, a vector of any of claims 100-101, or a cell (or population of cells) of any of claims 126-155 or 227-277, for use in the treatment of a cancer, wherein the cancer is a hematologic cancer selected from the group consisting of chronic lymphocytic leukemia (CLL), acute leukemias, acute lymphoid leukemia (ALL), B-cell acute lymphoid leukemia (B-ALL), T-cell acute lymphoid leukemia (T-ALL), chronic myelogenous leukemia (CML), acute myeloid leukemia (AML), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin’s lymphoma, Hodgkin’s lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and pre-leukemia.

285. A gRNA molecule of any of claims 1-60, a composition of any of claims 61-92 or 102-108, a nucleic acid of any of claims 93-99, a vector of any of claims 100-101, or a cell (or population of cells) of any of claims 126-155 or 227-277, for use in the treatment of a cancer, e.g., wherein the cancer is selected from the group consisting of mesothelioma, adenocarcinoma, glioblastoma, colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of

the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers, combinations of said cancers, and metastatic lesions of said cancers.

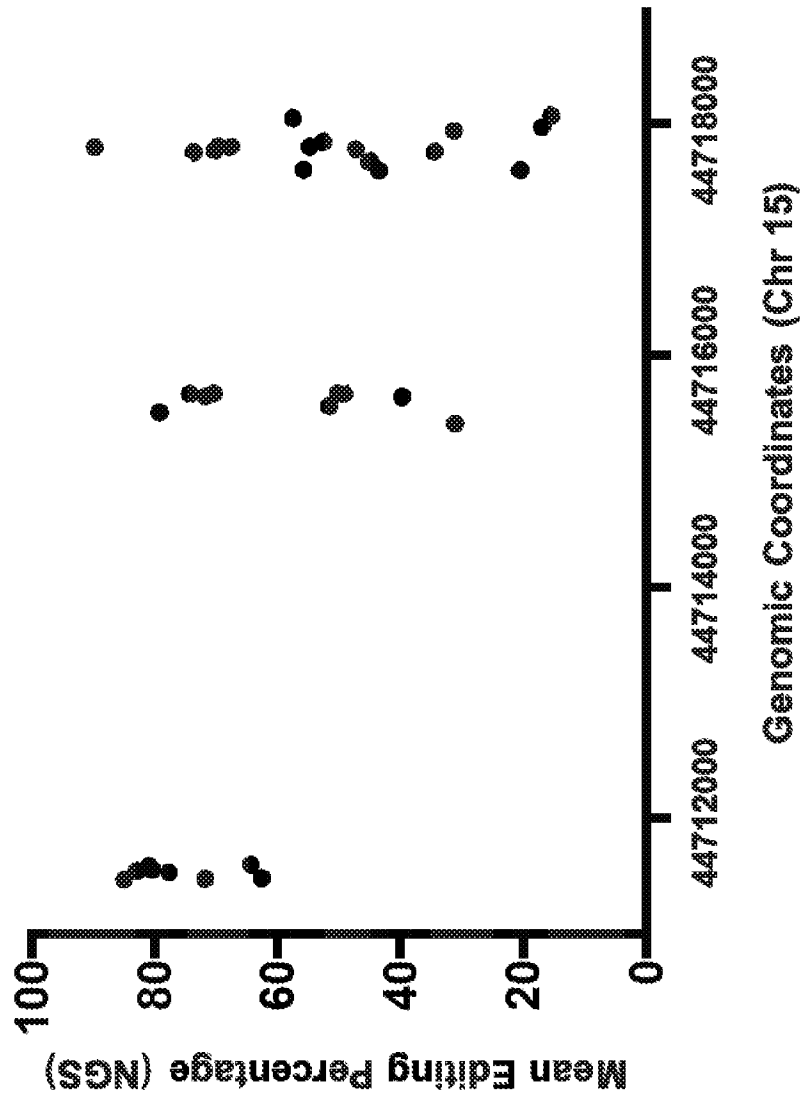

B2M Editing Efficiency by Location
Mean Editing Percentage (NGS)
100
80
60
40
20
0
44712000
44714000
44716000
44718000
Genomic Coordinates (Chr 15)

FIG. 1

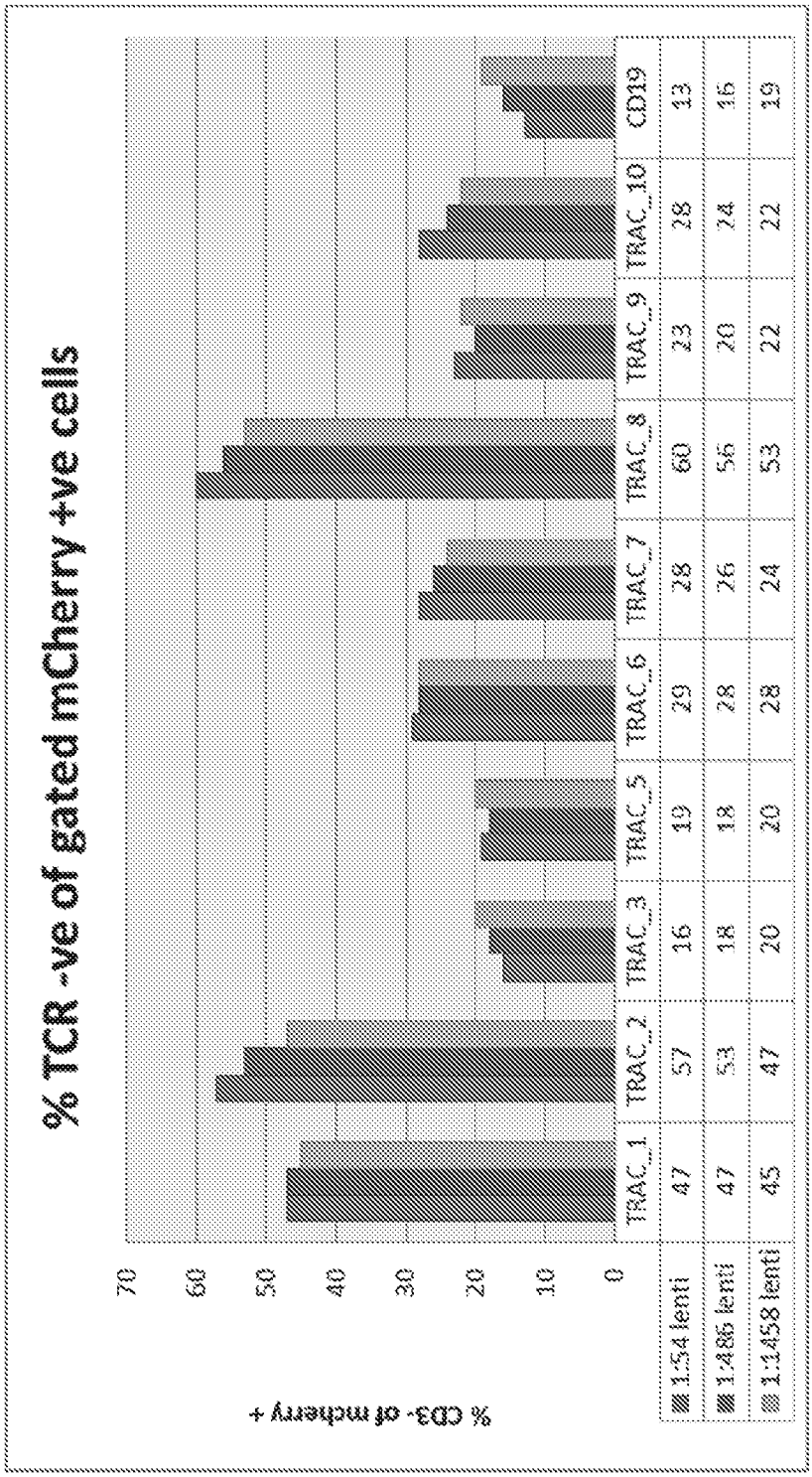

% TCR -ve of gated mCherry +ve cells
% CD3- of mcherry +
70
60
50
40
30
20
10
0
1:54 lenti
1:486 lenti
1:1458 lenti
TRAC_1 TRAC_2 TRAC_3 TRAC_5 TRAC_6 TRAC_7 TRAC_8 TRAC_9 TRAC_10 CD19
47 57 16 19 29 28 60 23 28 13
47 53 18 18 28 26 56 20 24 16
45 47 20 20 28 24 53 22 22 19

FIG.2

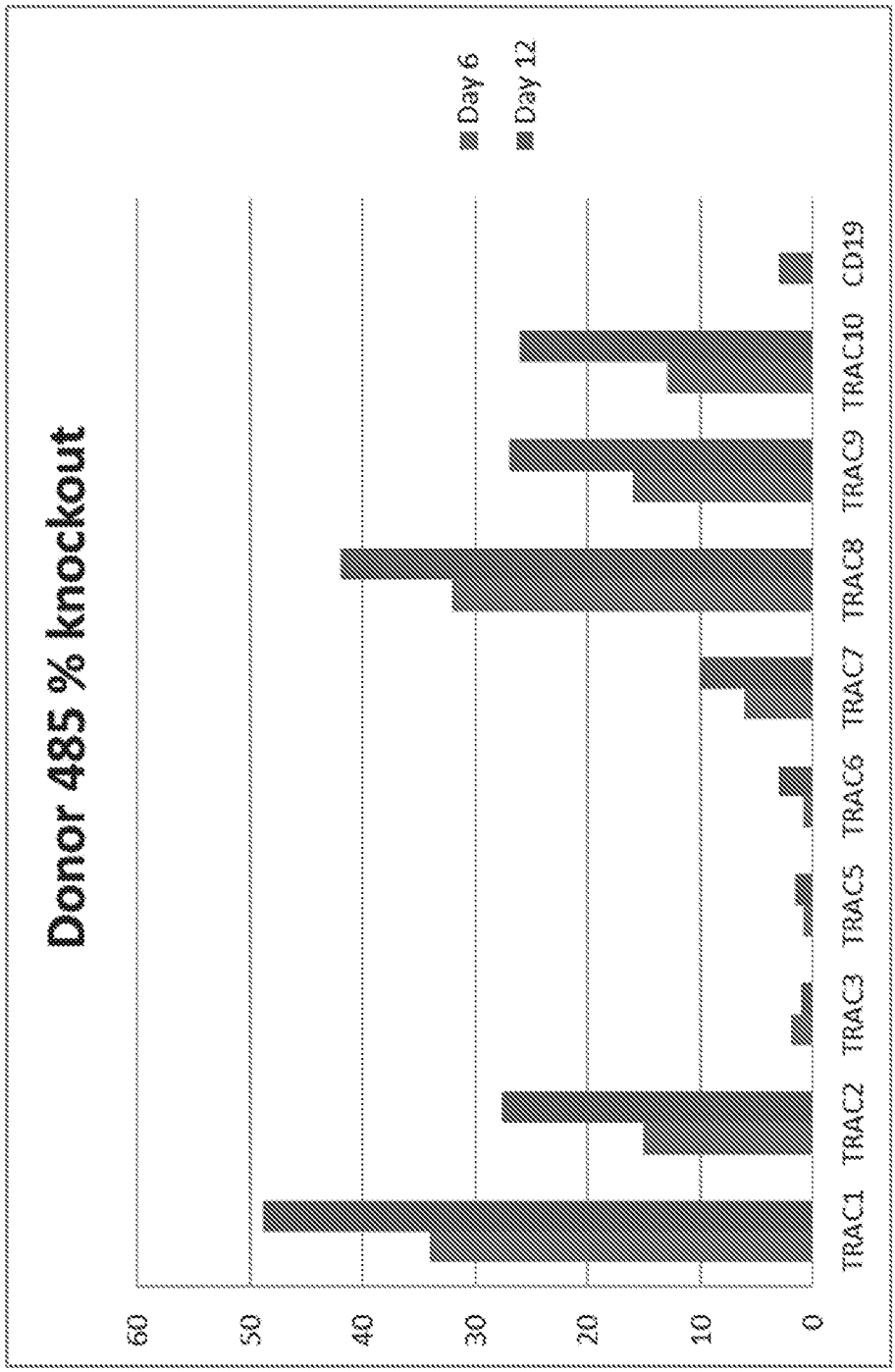

Donor 485 % knockout
Day 6
Day 12
60
50
40
30
20
10
0
TRAC1
TRAC2
TRAC3
TRAC5
TRAC6
TRAC7
TRAC8
TRAC9
TRAC10
CD19

FIG.3

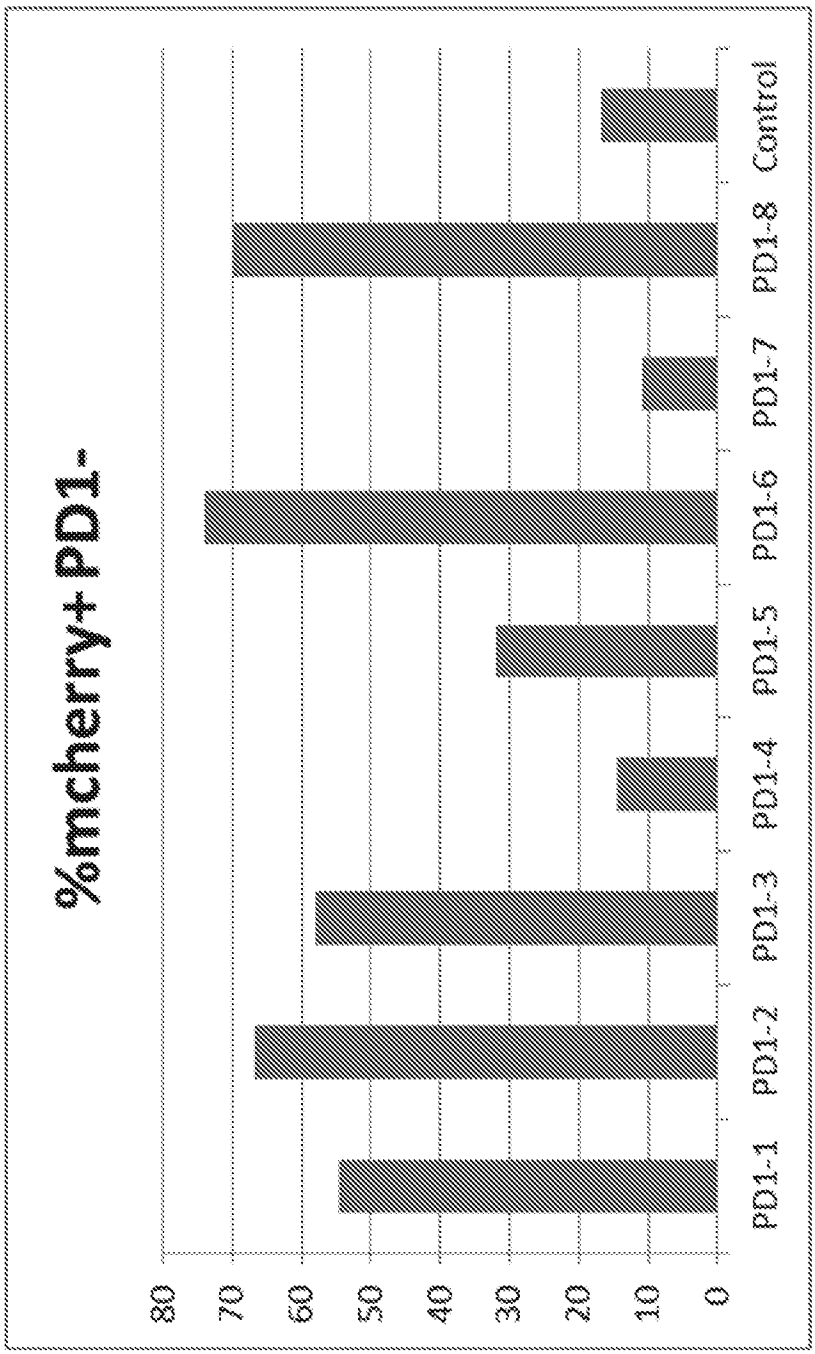

%mcherry+ PD1-
80
70
60
50
40
30
20
10
0
PD1-1
PD1-2
PD1-3
PD1-4
PD1-5
PD1-6
PD1-7
PD1-8
Control

FIG.4

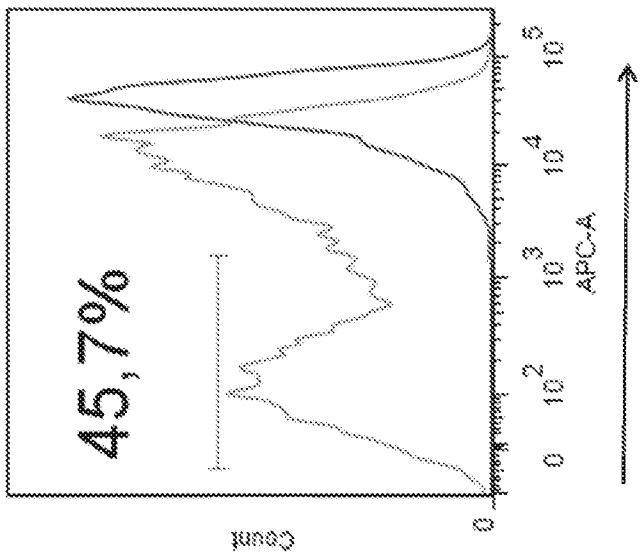


FIG.5A

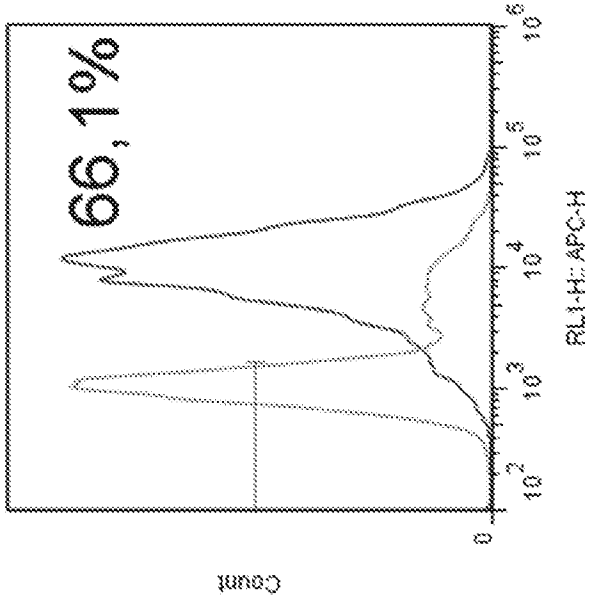


FIG.5B

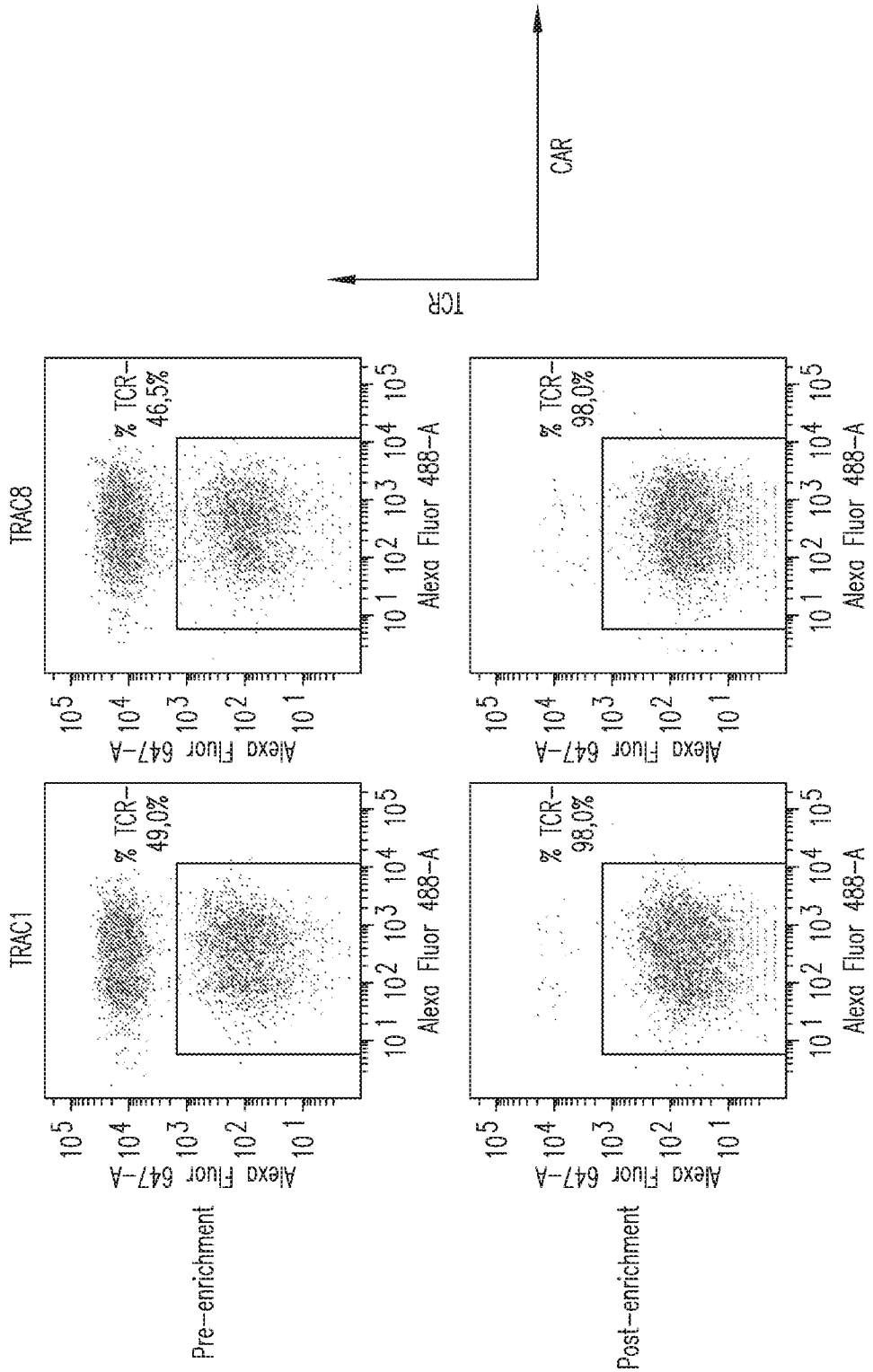

TCR
CAR
TRAC8
TRAC1
% TCR-
46,5%
49,0%
98,0%
98,0%
Alexa Fluor 647-A
Alexa Fluor 488-A
Pre-enrichment
Post-enrichment

FIG.6

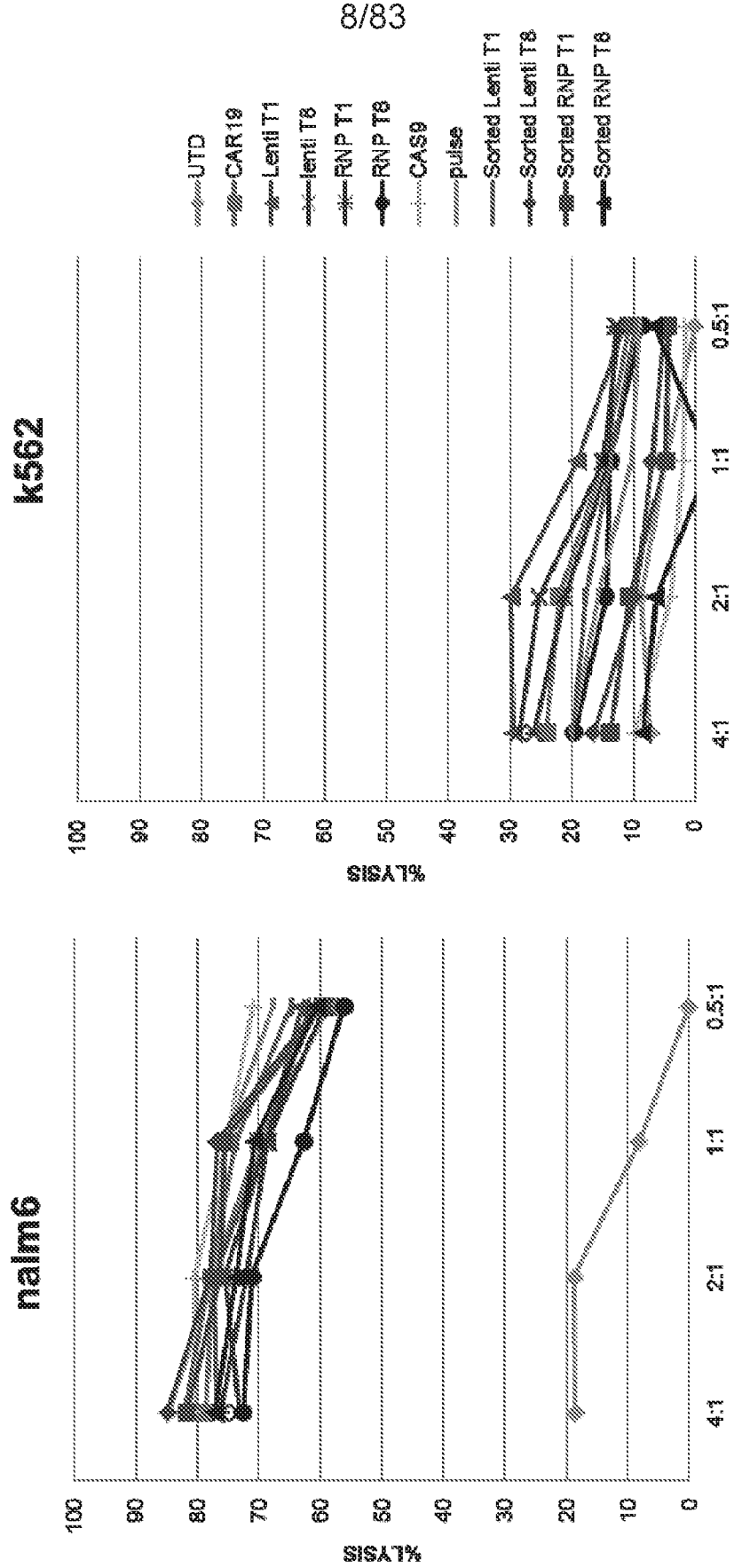

k562
nalm6
UTD
CAR19
Lenti T1
lenti T8
RNP T1
RNP T8
CAS9
pulse
Sorted Lenti T1
Sorted Lenti T8
Sorted RNP T1
Sorted RNP T8
%LYSIS
100
90
80
70
60
50
40
30
20
10
0
4:1
2:1
1:1
0.5:1

FIG. 7

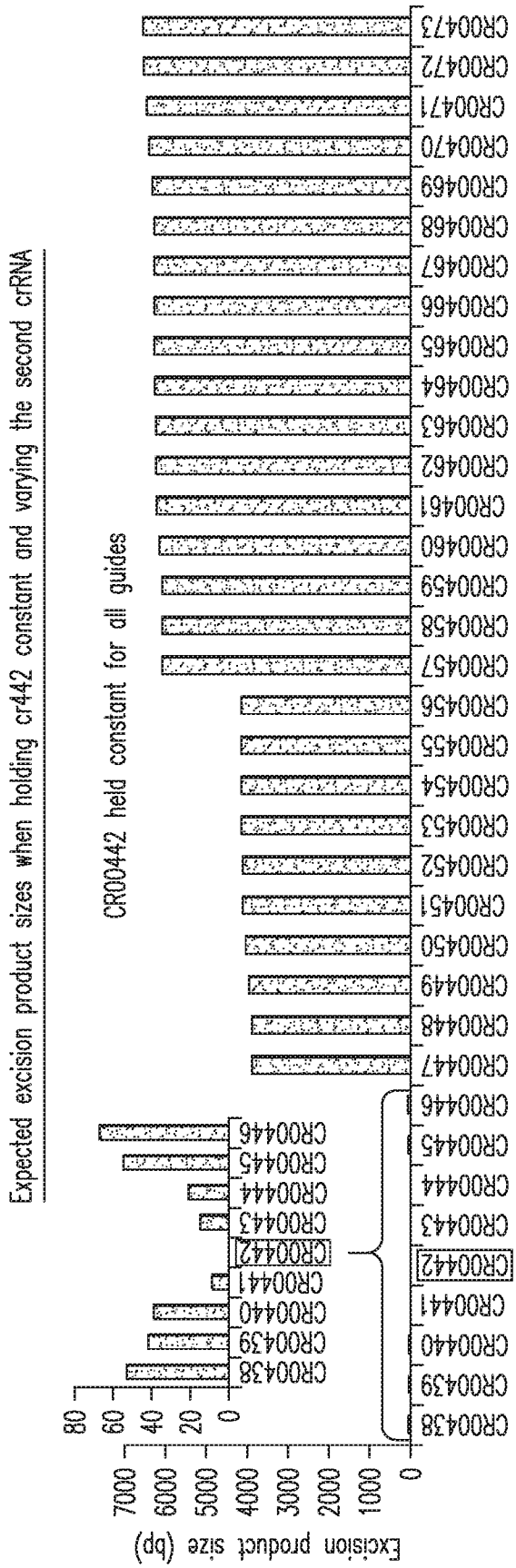

Expected excision product sizes when holding cr442 constant and varying the second crRNA
CR00442 held constant for all guides
Excision product size (bp)
0
1000
2000
3000
4000
5000
6000
7000
0
20
40
60
80
CR00438
CR00439
CR00440
CR00441
CR00442
CR00443
CR00444
CR00445
CR00446
CR00447
CR00448
CR00449
CR00450
CR00451
CR00452
CR00453
CR00454
CR00455
CR00456
CR00457
CR00458
CR00459
CR00460
CR00461
CR00462
CR00463
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CR00467
CR00468
CR00469
CR00470
CR00471
CR00472
CR00473

FIG.8

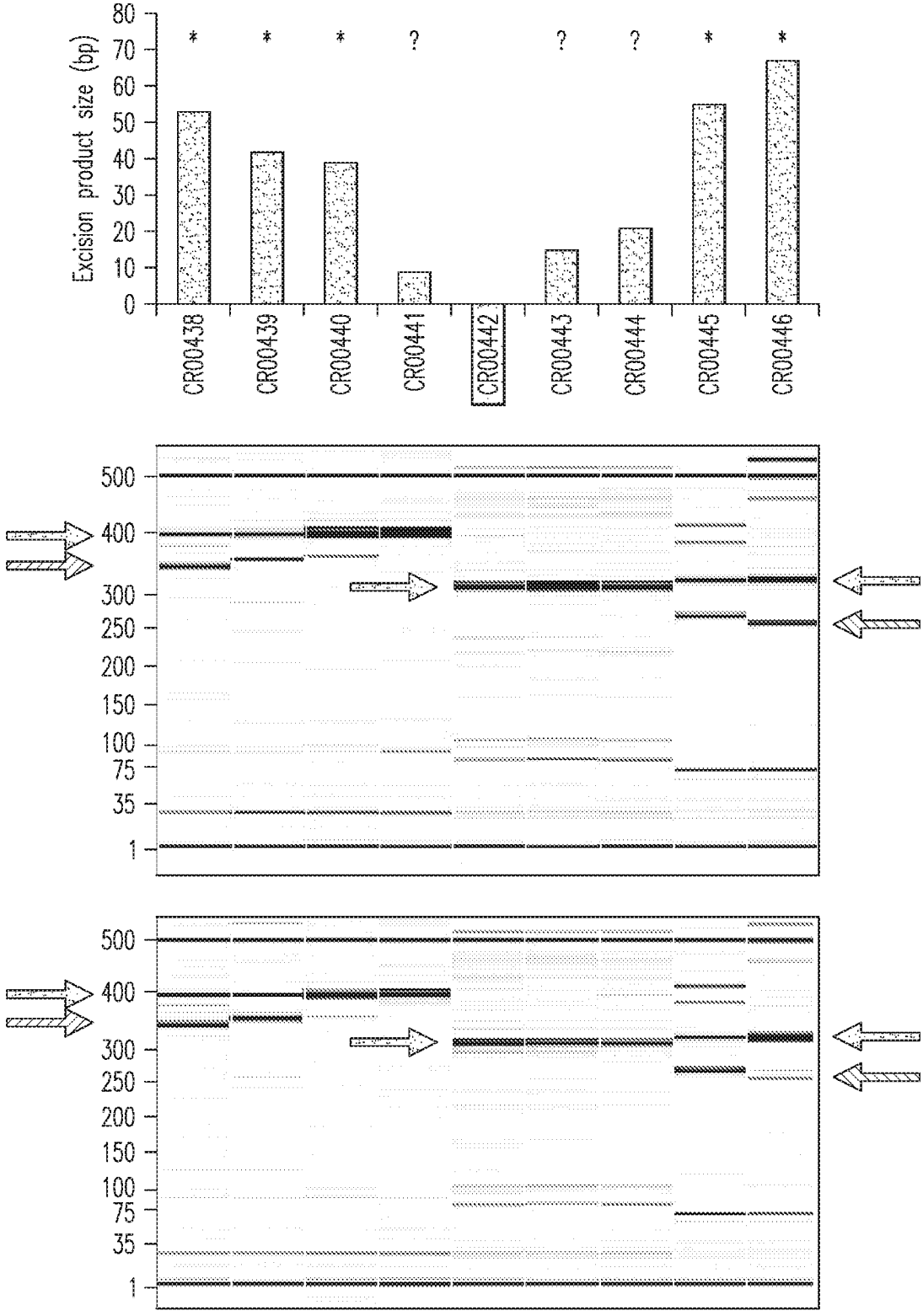

Excision product size (bp)
80
70
60
50
40
30
20
10
0
* * * ? ? ? * *
CR00438
CR00439
CR00440
CR00441
CR00442
CR00443
CR00444
CR00445
CR00446
500
400
300
250
200
150
100
75
35
1

FIG.9

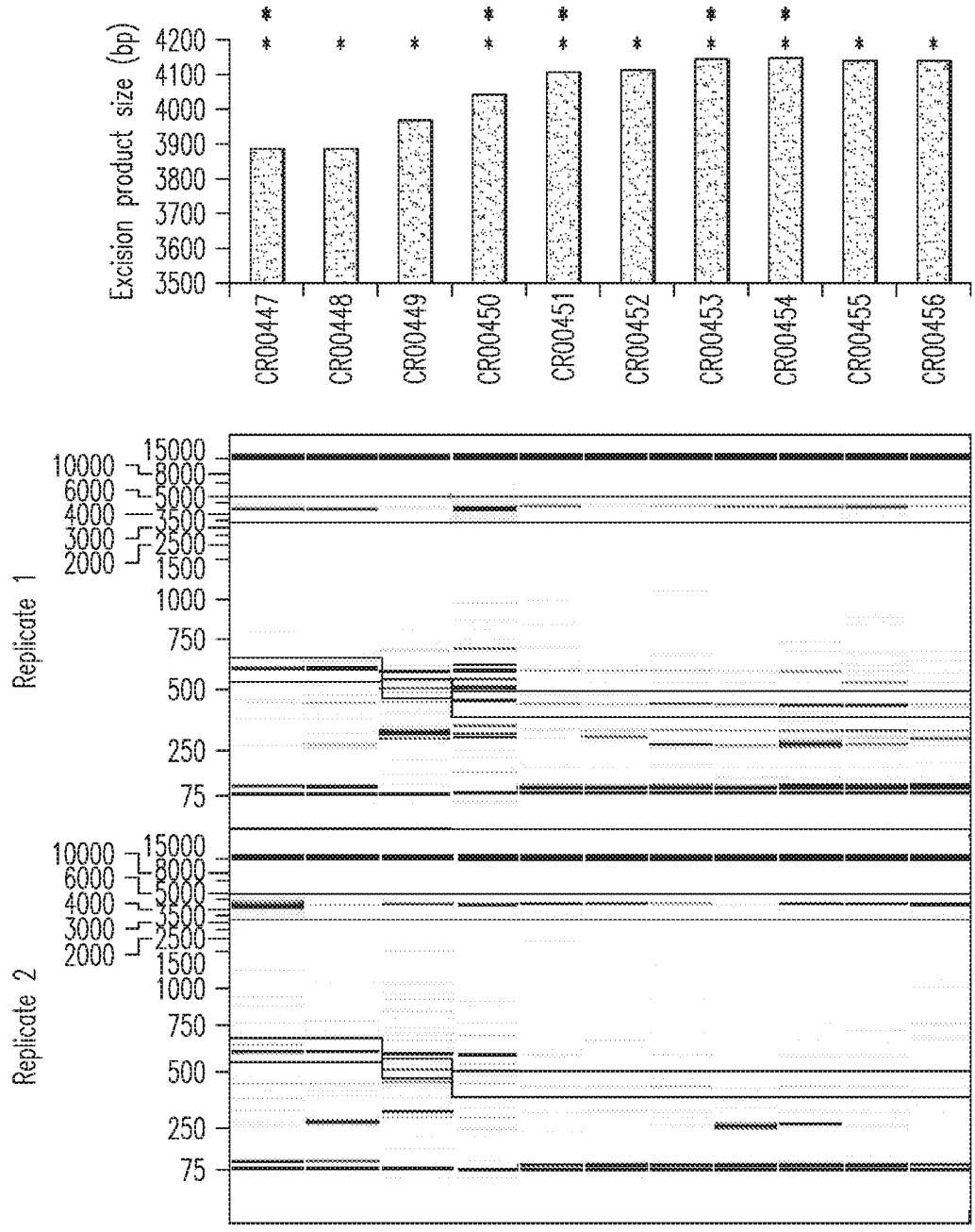

Excision product size (bp)
4200
4100
4000
3900
3800
3700
3600
3500
CR00447
CR00448
CR00449
CR00450
CR00451
CR00452
CR00453
CR00454
CR00455
CR00456
Replicate 1
Replicate 2
15000
10000
8000
6000
5000
4000
3500
3000
2500
2000
1500
1000
750
500
250
75

FIG.10

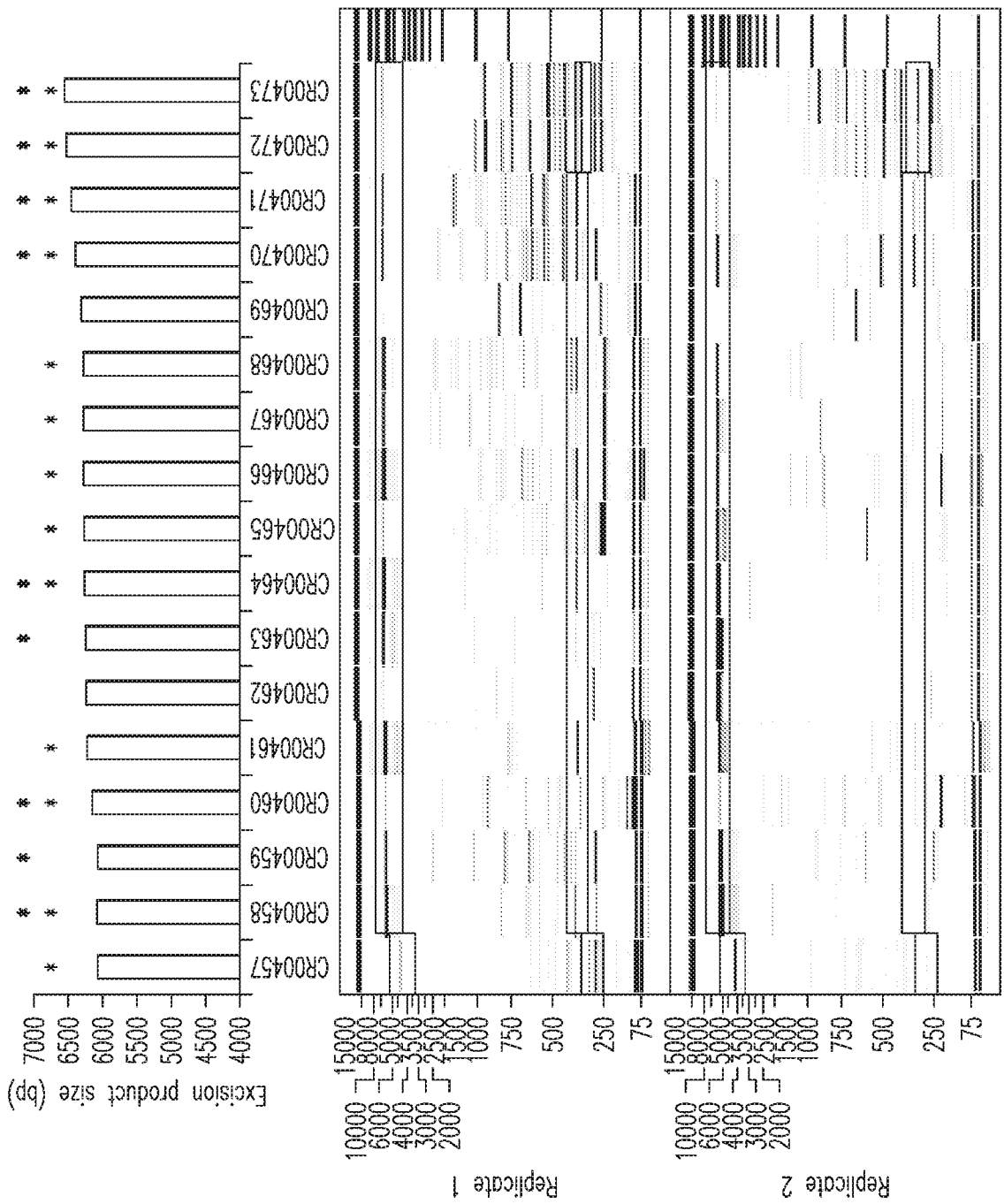
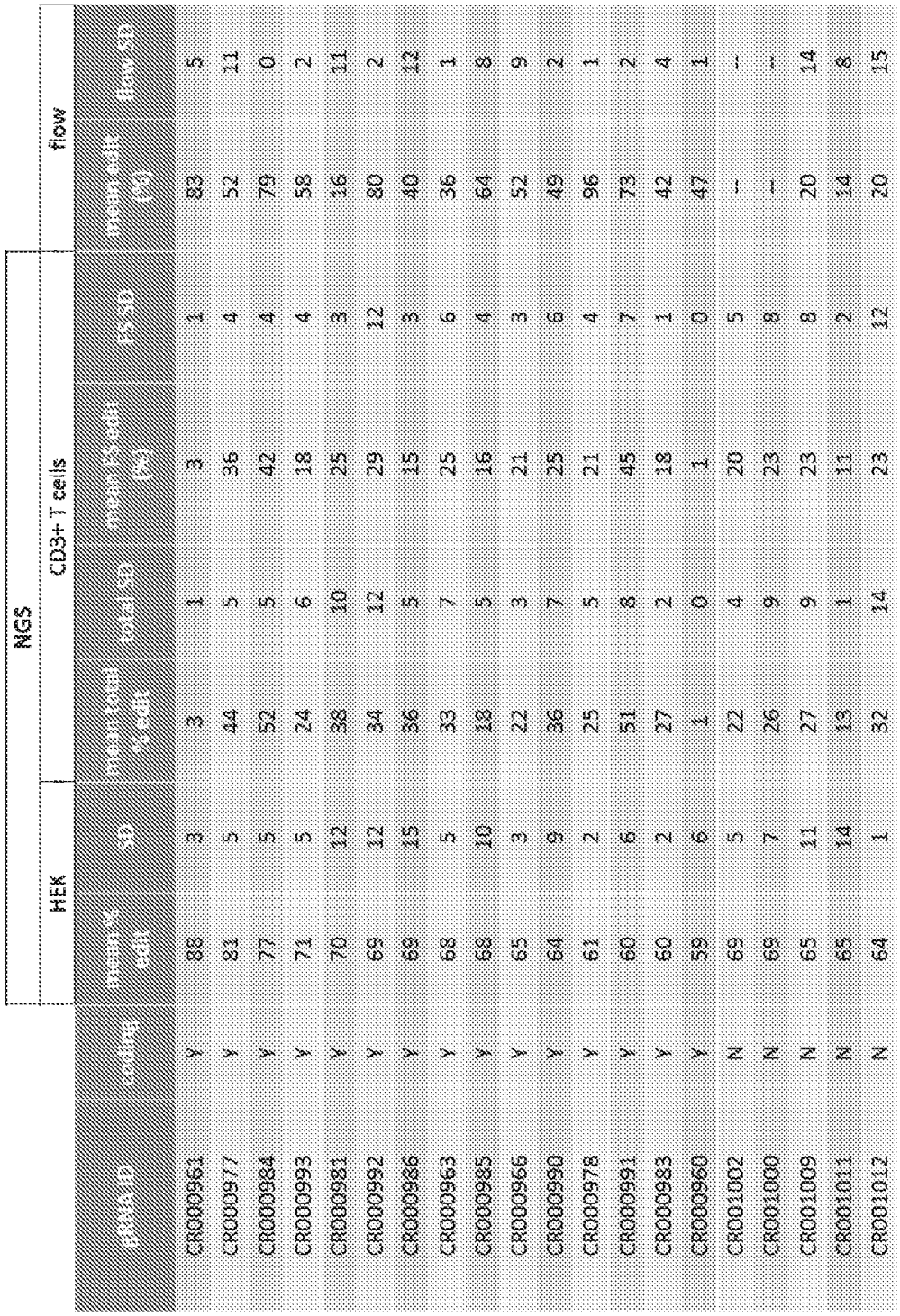
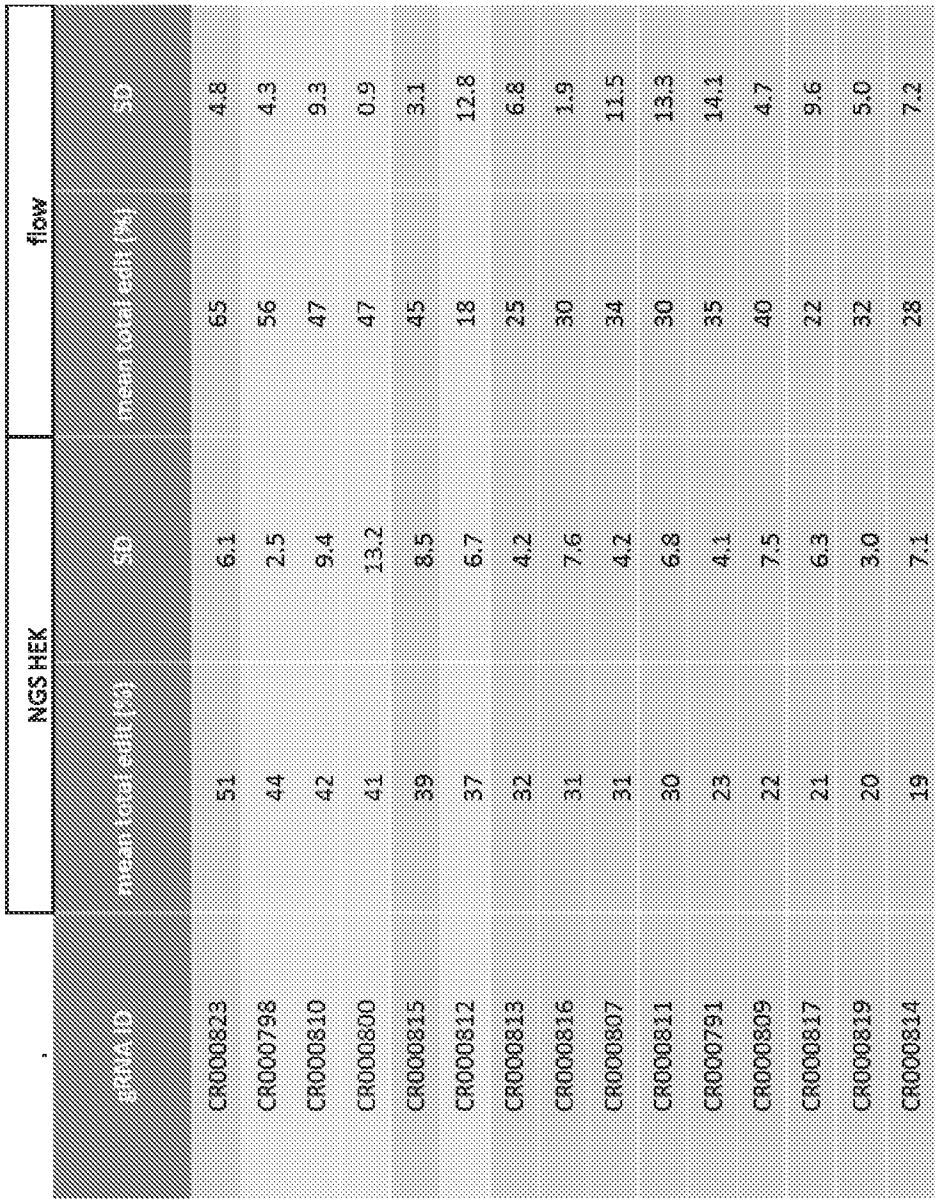

Excision product size (bp)
7000
6500
6000
5500
5000
4500
4000
CR00457
CR00458
CR00459
CR00460
CR00461
CR00462
CR00463
CR00464
CR00465
CR00466
CR00467
CR00468
CR00469
CR00470
CR00471
CR00472
CR00473
Replicate 1
Replicate 2
15000
8000
5000
3500
2500
1500
1000
750
500
250
75
10000
6000
4000
3000
2000

FIG.11



		NGS								flow	
		HEK		CD3+ T cells							
amplicon	coding	mean % indel	SD	mean % indel	total SD	mean % indel (bi)	SD bi	mean % indel (bi)	flow SD
CR000961	Y	88	3	3	1	3	1	83	5
CR000977	Y	81	5	44	5	36	4	52	11
CR000984	Y	77	5	52	5	42	4	79	0
CR000993	Y	71	5	24	6	18	4	58	2
CR000981	Y	70	12	38	10	25	3	16	11
CR000992	Y	69	12	34	12	29	12	80	2
CR000986	Y	69	15	36	5	15	3	40	12
CR000963	Y	68	5	33	7	25	6	36	1
CR000985	Y	68	10	18	5	16	4	64	8
CR000966	Y	65	3	22	3	21	3	52	9
CR000990	Y	64	9	36	7	25	6	49	2
CR000978	Y	61	2	25	5	21	4	96	1
CR000991	Y	60	6	51	8	45	7	73	2
CR000983	Y	60	2	27	2	18	1	42	4
CR000960	Y	59	6	1	0	1	0	47	1
CR001002	N	69	5	22	4	20	5	--	--
CR001000	N	69	7	26	9	23	8	--	--
CR001009	N	65	11	27	9	23	8	20	14
CR001011	N	65	14	13	1	11	2	14	8
CR001012	N	64	1	32	14	23	12	20	15

FIG.12



	NGS HEK		flow	
RNA-10	mean coverage (x)	SD	mean coverage (x)	SD
CR000823	51	6.1	65	4.8
CR000798	44	2.5	56	4.3
CR000810	42	9.4	47	9.3
CR000800	41	13.2	47	0.9
CR000815	39	8.5	45	3.1
CR000812	37	6.7	18	12.8
CR000813	32	4.2	25	6.8
CR000816	31	7.6	30	1.9
CR000807	31	4.2	34	11.5
CR000811	30	6.8	30	13.3
CR000791	23	4.1	35	14.1
CR000809	22	7.5	40	4.7
CR000817	21	6.3	22	9.6
CR000819	20	3.0	32	5.0
CR000814	19	7.1	28	7.2

FIG. 13

			MiSeq				Ion Proton			
			HEK		CD34+		cells			
gRNA ID	Target	Target Sequence (PAM=NGG)	HR Modification		NHEJ		HR Modification		NHEJ	
CR00442	B2M	Chr15:44711536-44711558	78	2	63	5	51	2	39	3
CR00444	B2M	Chr15:44711557-44711579	90	6	56	11	45	2	39	3
CR00455	B2M	Chr15:44715677-44715699	70	11	25	5	43	3	19	2
CR00446	B2M	Chr15:44711603-44711625	64	6	37	5	21	2	19	2
CR00445	B2M	Chr15:44711591-44711613	81	8	38	6	18	6	19	2
CR00449	B2M	Chr15:44715507-44715529	79	5	25	4	16	2	13	2
CR00443	B2M	Chr15:44711551-44711573	83	3	45	3	13	2	13	2
CR00441	B2M	Chr15:44711534-44711556	NA	NA	25	NA	13	4	13	4
CR00453	B2M	Chr15:44715672-44715694	74	4	20	4	13	3	13	3
CR00452	B2M	Chr15:44715649-44715671	72	11	15	5	4	3	4	3
CR00438	B2M	Chr15:44711472-44711494	NA	NA	59	7	4	1	4	1
CR00439	B2M	Chr15:44711483-44711505	72	13	45	8	2	1	2	1
CR00467	B2M	Chr15:44717809-44717831	70	12	13	3	2	2	2	2
CR00440	B2M	Chr15:44711486-44711508	63	9	15	4	1	1	1	1
CR00463	B2M	Chr15:44717776-44717798	70	7	13	2	1	1	1	1
CR00454	B2M	Chr15:44715673-44715695	49	17	24	3	1	1	1	1
CR00465	B2M	Chr15:44717805-44717827	90	2	46	5	1	1	1	1
CR00460	B2M	Chr15:44717681-44717703	45	10	16	3	1	0	1	0
CR00466	B2M	Chr15:44717808-44717830	68	11	12	3	1	0	1	0
CR00461	B2M	Chr15:44717763-44717785	74	5	12	1	0	0	0	0

FIG. 14

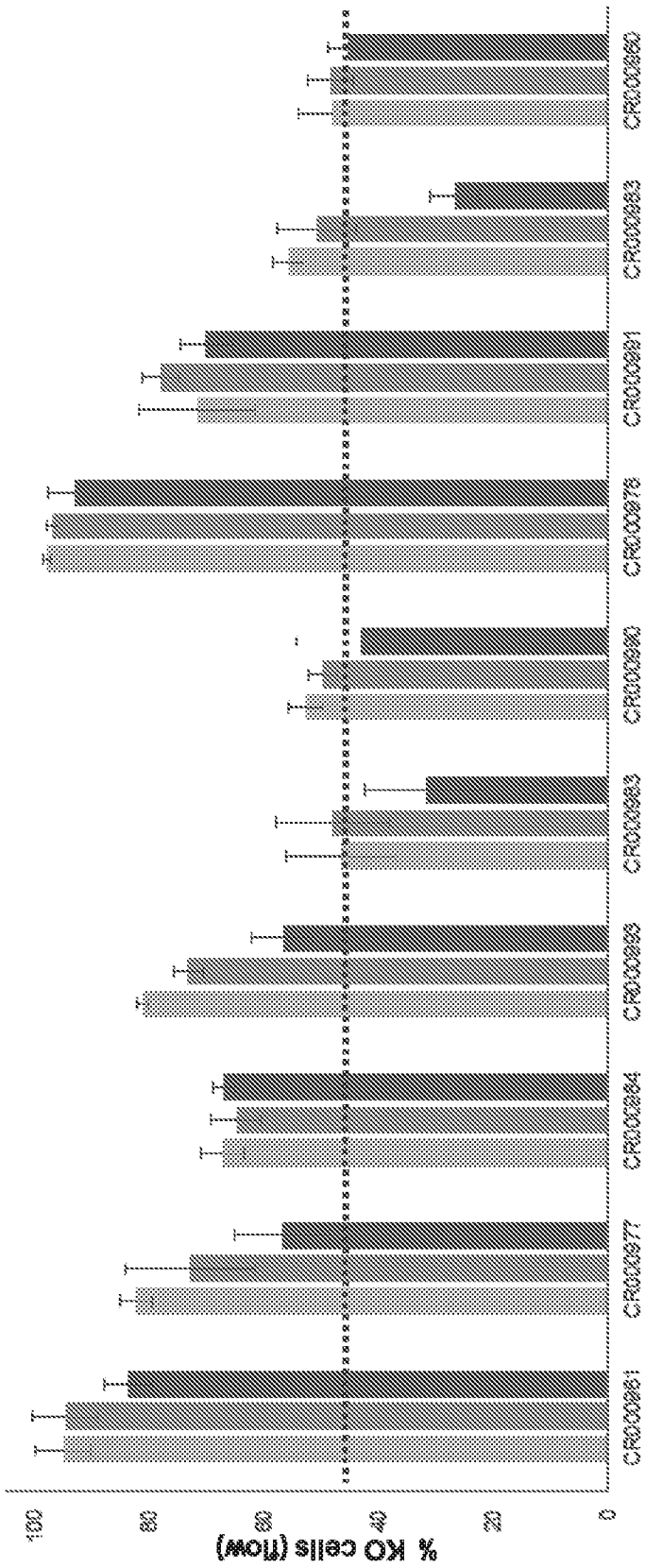

% KO cells (flow)
100
80
60
40
20
0
CR000861
CR000877
CR002864
CR000865
CR000883
CR000890
CR000878
CR000891
CR000883
CR000860

FIG. 15

gRNA Targeting Sequence ID	Targeting Sequence	Strand	Target Sequence Location	HEK (NGS)				CD34+ (Flow)	
					MonoEdit (%)	SubEx1 (%)	MonoEdit + SubEx1 (%)		
CR000828	PDCD1	h	+	Chr2:241858861-241858883	69	4.5	86.0		0.6
CR000848	PDCD1	h	-	Chr2:241852910-241852932	65	4.2	67.5		4.1
CR000907	PDCD1	h	+	Chr2:241857759-241857781	72	8.3	67.4		1.6
CR000870	PDCD1	h	-	Chr2:241852743-241852765	66	8.1	65.0		4.6
CR000855	PDCD1	h	+	Chr2:241853825-241852847	61	20.8	62.0		2.3
CR000839	PDCD1	h	-	Chr2:241858780-241858802	69	9.8	60.7		6.8
CR000838	PDCD1	h	-	Chr2:241858781-241858803	61	12.0	57.2		13.7
CR000852	PDCD1	h	+	Chr2:241852877-241852899	72	5.1	56.8		6.3
CR000879	PDCD1	h	-	Chr2:241852695-241852717	68	7.9	48.4		4.7
CR000847	PDCD1	h	+	Chr2:241852910-241852932	77	0.9	47.5		1.3
CR000829	PDCD1	h	-	Chr2:241858849-241858871	68	6.2	39.1		2.7
CR000831	PDCD1	h	-	Chr2:241858845-241858867	66	13.0	37.7		8.4
CR000835	PDCD1	h	-	Chr2:241858793-241858815	69	5.7	35.0		2.6
CR000904	PDCD1	h	-	Chr2:241852257-241852279	70	2.5	20.1		1.7
CR000876	PDCD1	h	+	Chr2:241858868-241858890	70	7.5	19.0		2.3

FIG.16

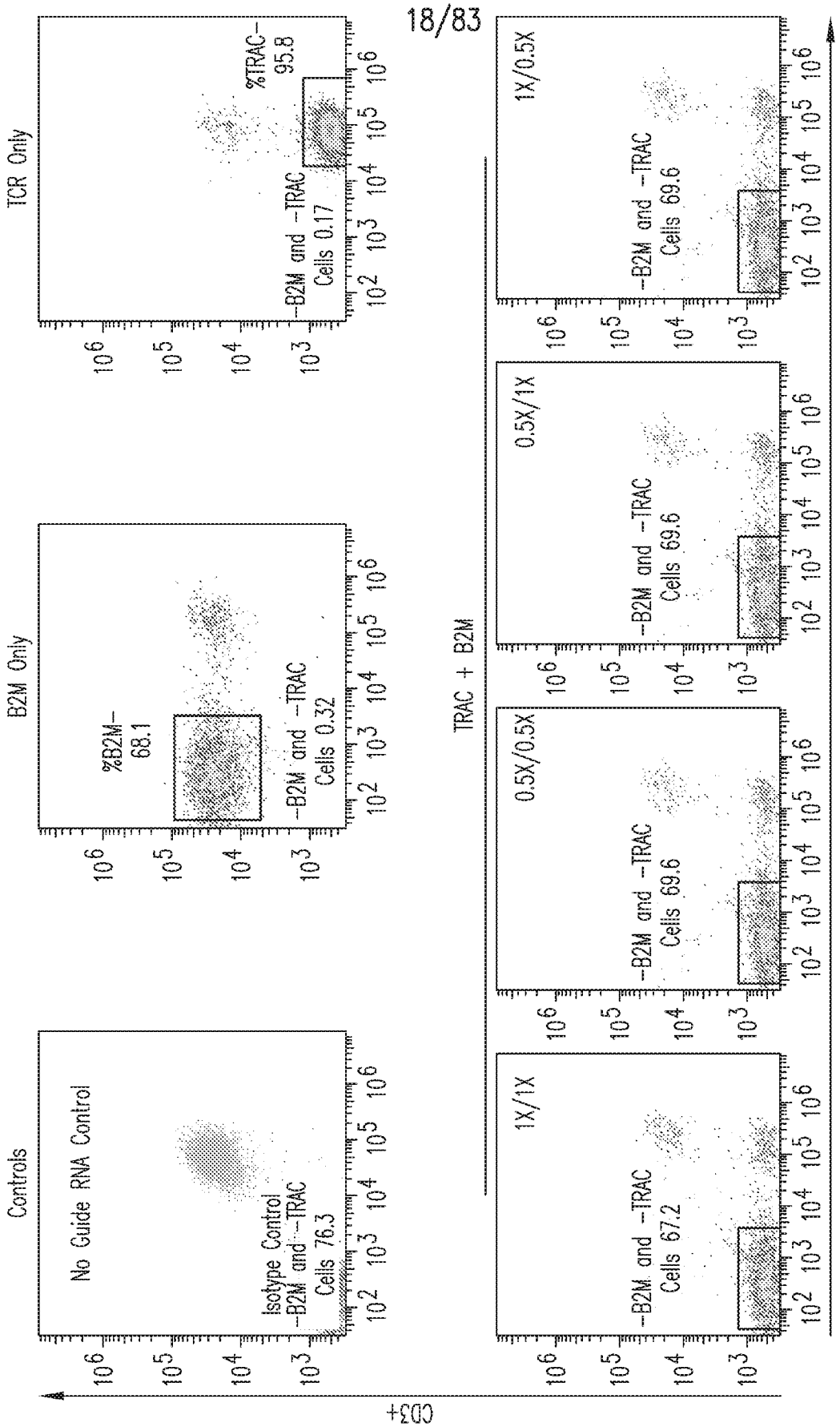

Controls
No Guide RNA Control
Isotype Control
-B2M and -TRAC
Cells 76.3
B2M Only
%B2M-
68.1
-B2M and -TRAC
Cells 0.32
TCR Only
%TRAC-
95.8
-B2M and -TRAC
Cells 0.17
TRAC + B2M
1X/1X
-B2M and -TRAC
Cells 67.2
0.5X/0.5X
-B2M and -TRAC
Cells 69.6
0.5X/1X
-B2M and -TRAC
Cells 69.6
1X/0.5X
-B2M and -TRAC
Cells 69.6
CD3+
B2M

FIG.17A

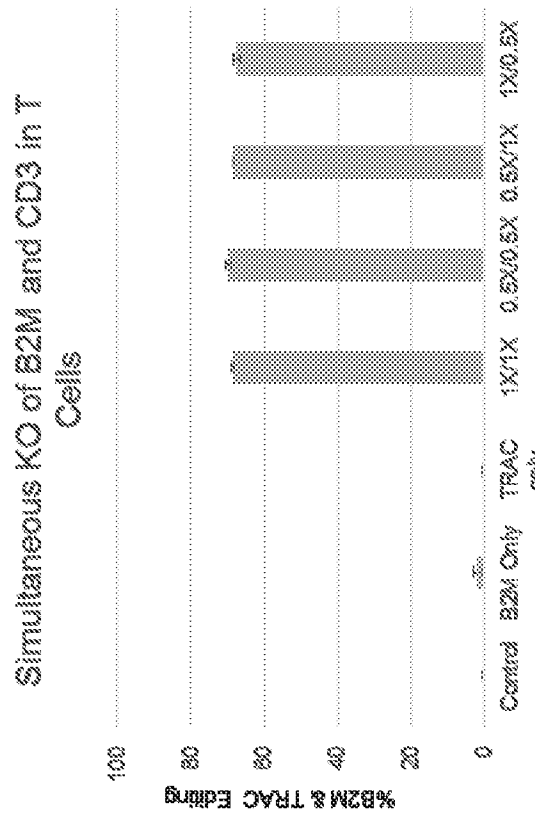

Simultaneous KO of B2M and CD3 in T Cells
%B2M & TRAC Editing
100
80
60
40
20
0
Control
B2M Only
TRAC only
1X/1X
0.5X/0.5X
0.5X/1X
1X/0.5X

FIG. 17B

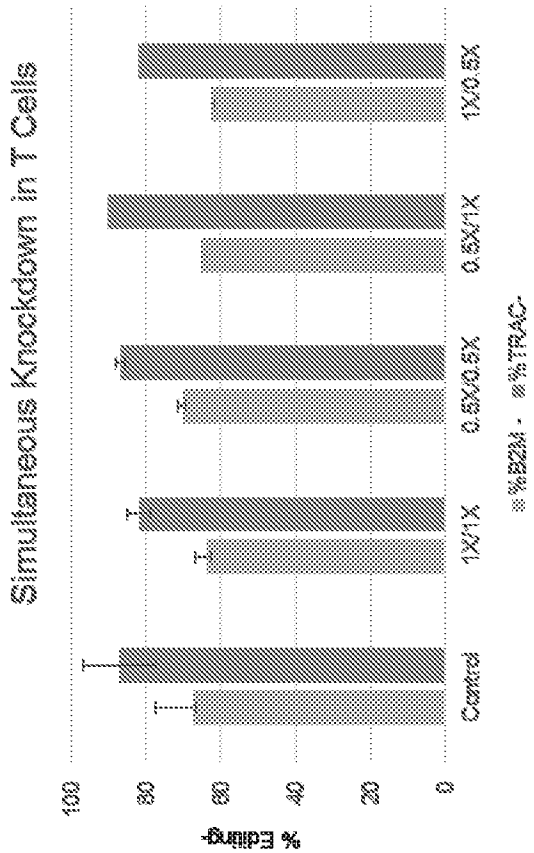

Simultaneous Knockdown in T Cells
% Editing
100
80
60
40
20
0
Control
1X/1X
0.5X/0.5X
0.5X/1X
1X/0.5X
%B2M - %TRAC-

FIG. 17C

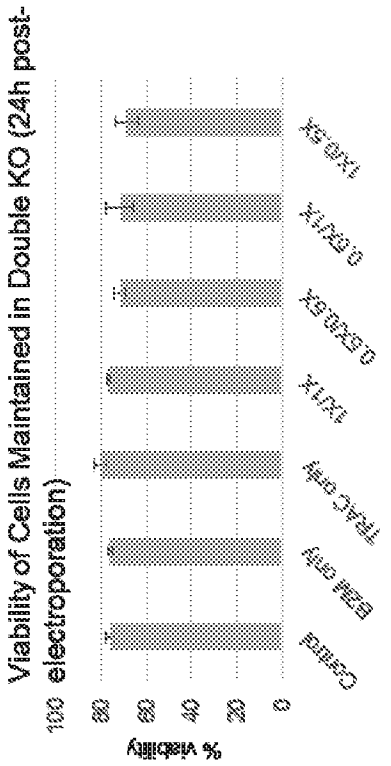

Viability of Cells Maintained in Double KO (24h post-electroporation)
% viability
100
80
60
40
20
0
Control
Edit only
TRAC only
TRAC
CD52
PD1
TRAC
CD52
PD1

FIG. 17D

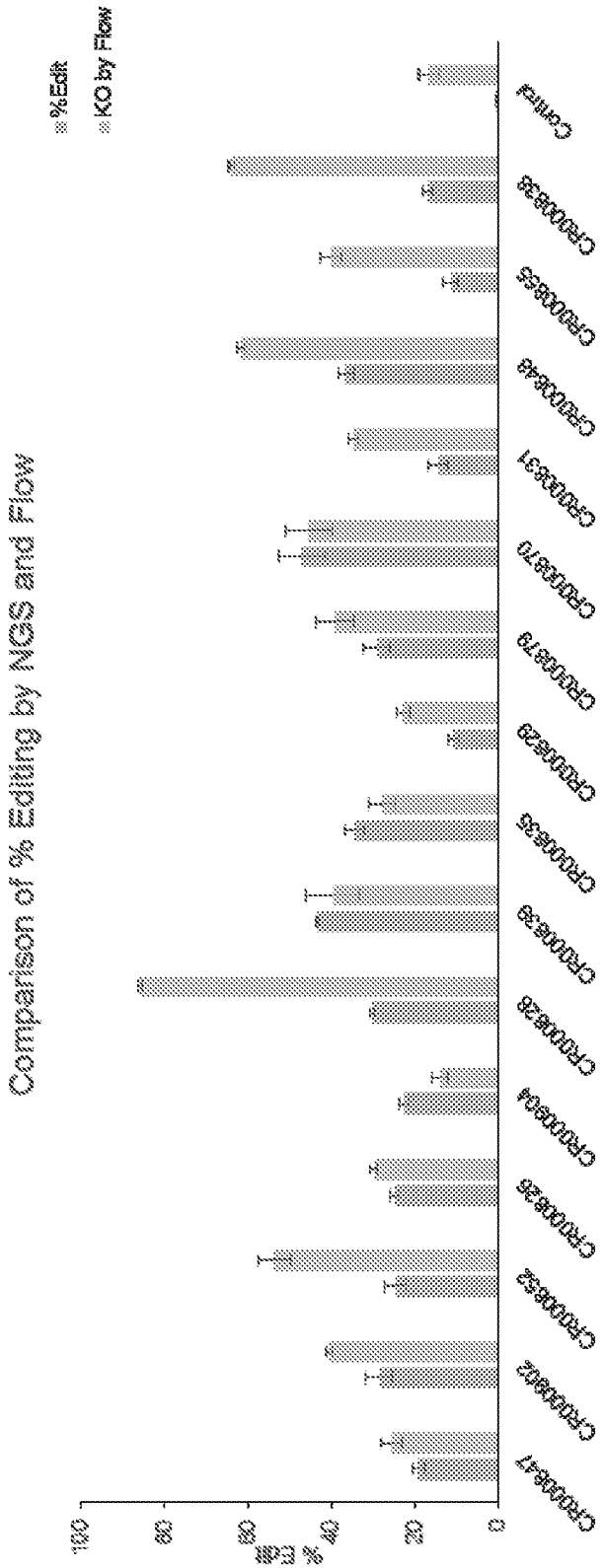

Comparison of % Editing by NGS and Flow
%Edit
KO by Flow
% Edit
100
80
60
40
20
0
Control
CR000838
CR000835
CR000848
CR000831
CR000870
CR000879
CR000829
CR000835
CR000839
CR000828
CR000804
CR000825
CR000832
CR000842
CR000847

FIG. 18

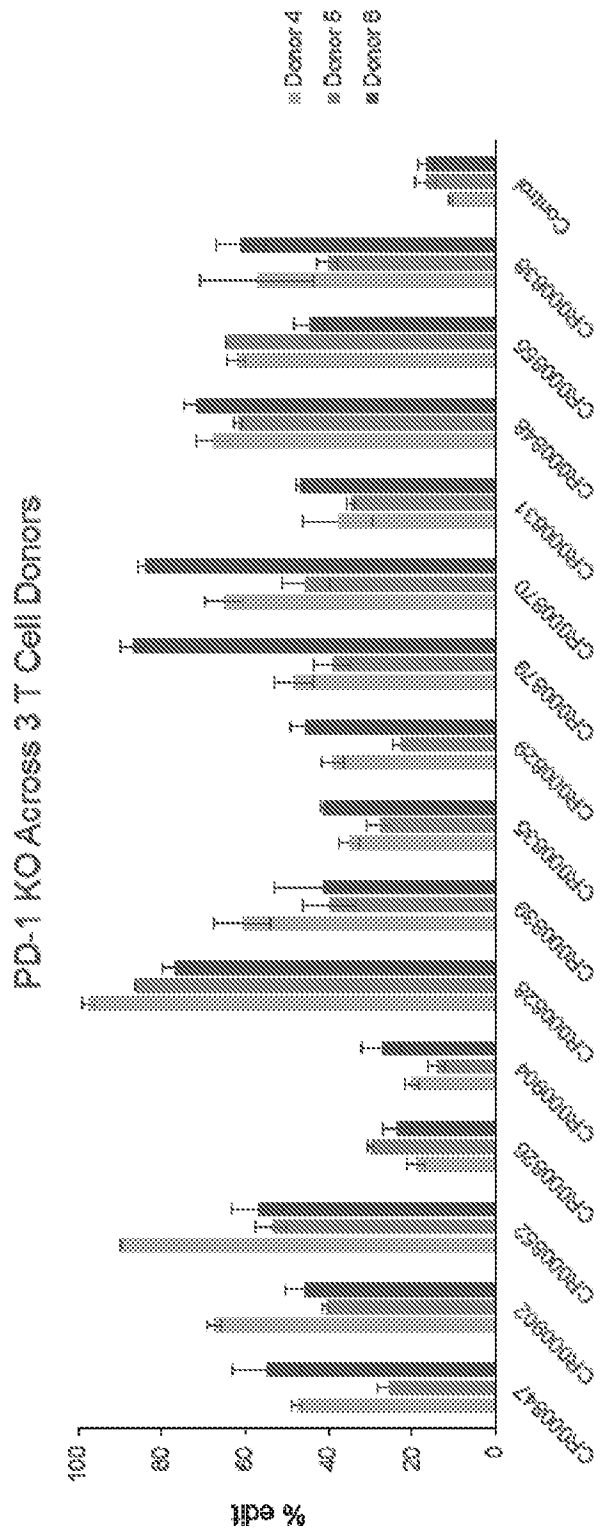

PD-1 KO Across 3 T Cell Donors
Donor 4
Donor 6
Donor 8
% edit
100
80
60
40
20
0
Control
CRISPR2
CRISPR3
CRISPR4
CRISPR5
CRISPR6
CRISPR7
CRISPR8
CRISPR9
CRISPR10
CRISPR11
CRISPR12
CRISPR13
CRISPR14
CRISPR15
CRISPR16
CRISPR17

FIG.19

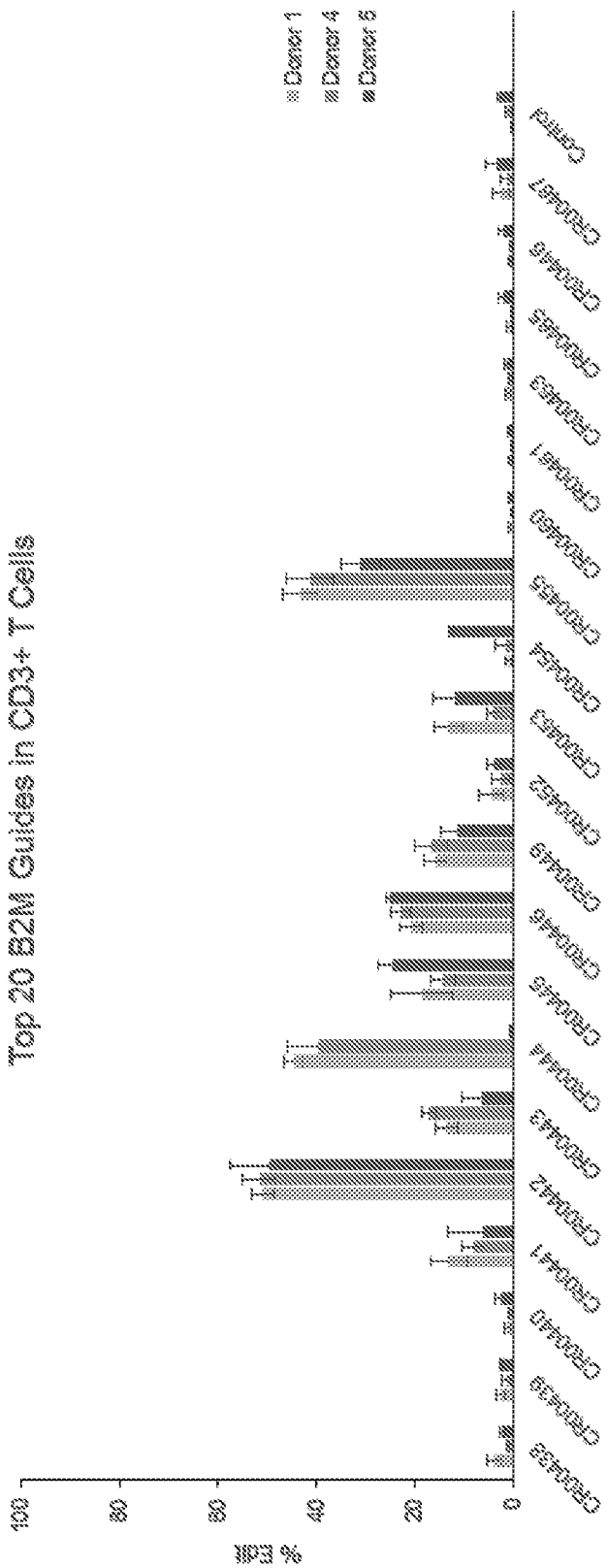

Top 20 B2M Guides in CD3+ T Cells
Donor 1
Donor 4
Donor 8
% EdIt
100
80
60
40
20
0
CRISPR39
CRISPR40
CRISPR41
CRISPR42
CRISPR43
CRISPR44
CRISPR45
CRISPR46
CRISPR47
CRISPR48
CRISPR49
CRISPR50
CRISPR51
CRISPR52
CRISPR53
CRISPR54
CRISPR55
CRISPR56
CRISPR57
CRISPR58
Control

FIG.20

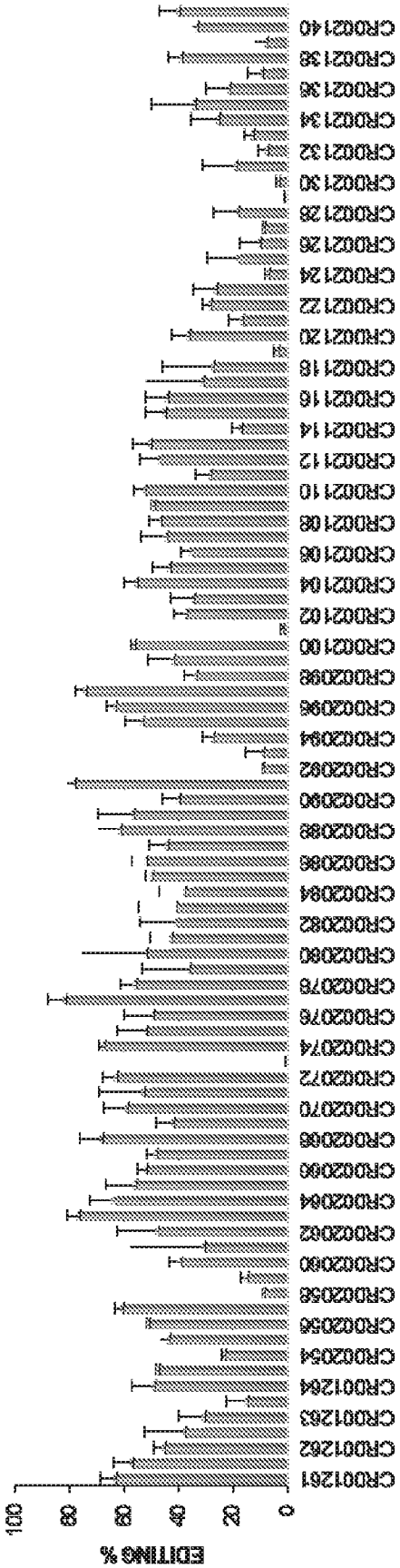

EDITING %
100
80
60
40
20
0
CR001261
CR001262
CR001263
CR001264
CR002054
CR002056
CR002058
CR002060
CR002062
CR002064
CR002066
CR002068
CR002070
CR002072
CR002074
CR002076
CR002078
CR002080
CR002082
CR002084
CR002086
CR002088
CR002090
CR002092
CR002094
CR002096
CR002098
CR002100
CR002102
CR002104
CR002106
CR002108
CR002110
CR002112
CR002114
CR002116
CR002118
CR002120
CR002122
CR002124
CR002126
CR002128
CR002130
CR002132
CR002134
CR002136
CR002138
CR002140

FIG.21

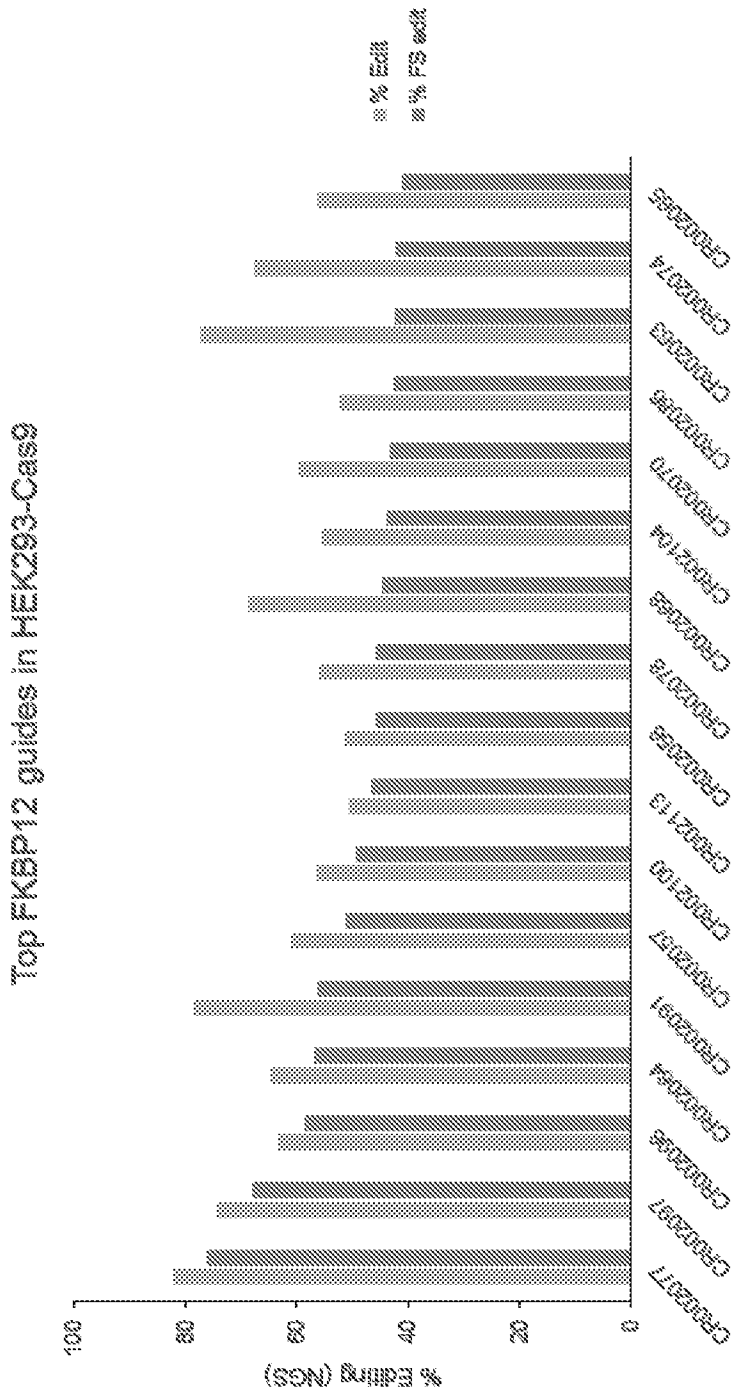

Top FKBP12 guides in HEK293-Cas9
% Edit
% FS edit
% Editing (NGS)
0
20
40
60
80
100
CR00207T
CR00208T
CR00209S
CR00210A
CR00207A
CR00208S
CR00207G
CR00210A
CR00208S
CR00207S
CR00208A
CR00207C
CR00210G
CR00210T
CR00208T
CR00208A
CR00209A
CR00208G
CR00209S

FIG.22

gRNA ID	Species	Strand	Location	Avg % Edit	SD Edit	Editing Rank	Ave % FS	SD FS	FS rank
CR0020077	h	+	Chr20:13929381393020	82.22	5.96	1	76.13	4.34	1
CR0020097	h	-	Chr20:13928461392868	74.27	3.87	4	67.97	3.89	2
CR0020096	h	+	Chr20:13928471392869	63.30	3.03	8	58.53	2.29	3
CR0020064	h	+	Chr20:13930531393075	64.65	7.97	7	56.80	6.95	4
CR0020091	h	-	Chr20:13928801392902	78.42	2.47	2	56.20	2.70	5
CR0020057	h	-	Chr20:13931171393139	61.01	2.06	9	51.13	2.00	6
CR0020100	h	+	Chr20:13928141392836	56.42	0.99	11	49.20	0.95	7
CR0020113	h	-	Chr20:13755131375535	50.51	5.97	17	46.47	5.85	8
CR0020056	h	-	Chr20:13931181393140	51.26	0.23	16	45.73	0.99	9
CR0020078	h	-	Chr20:13929951393017	56.06	5.31	13	45.70	4.44	10
CR0020068	h	+	Chr20:13930391393061	68.55	7.79	5	44.70	4.09	11
CR0020104	h	-	Chr20:13755651375587	55.58	4.38	14	43.87	5.22	12
CR0020070	h	+	Chr20:13930181393040	59.50	8.10	10	43.17	4.19	13
CR0020086	h	-	Chr20:13929671392989	52.13	4.69	15	42.63	2.94	14
CR0020063	h	-	Chr20:13930571393079	77.18	3.99	3	42.43	1.37	15

FIG. 23

	CD3+ T cells (NGS)					
gRNA ID	% Edit	Stdev	% FS edit	StDev		
CR002100	56.3	2.3	46.1	2.3		
CR002097	46.0	4.5	38.7	4.5		
CR002091	51.2	7.9	35.7	7.9		
CR002085	39.5	7.1	30.4	7.1		
CR002086	33.6	1.9	29.3	1.9		
CR002089	40.2	1.9	28.3	1.9		
CR002088	33.6	2.4	26.2	2.4		
CR002096	23.8	3.0	22.3	3.0		
CR002095	29.1	4.0	20.1	4.0		
CR002080	29.7	7.5	18.9	1.5		
CR002109	25.2	3.4	16.4	3.4		
CR002112	21.8	0.7	15.7	0.7		
CR002110	15.3	1.4	13.8	1.4		
CR002108	19.2	1.4	13.7	1.4		
CR002104	18.2	0.7	13.1	0.7		
CR002115	16.3	1.8	12.4	1.8		
CR002116	10.2	0.2	8.6	0.2		
CR002087	12.5	0.8	8.3	0.6		
CR002107	6.7	0.6	5.9	0.6		
CR002113	6.3	0.7	5.3	0.7		

FIG.24

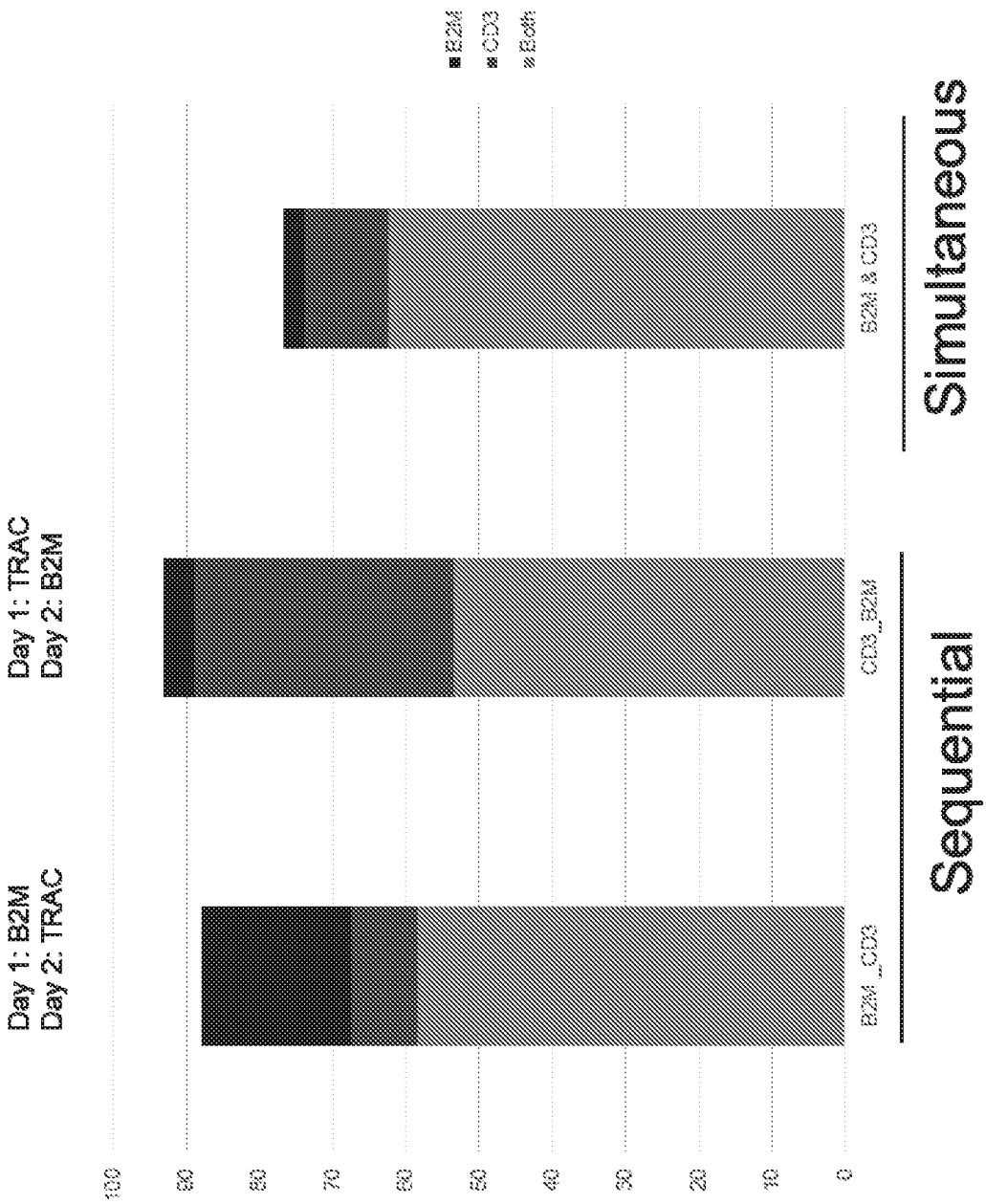

B2M
CD3
Both
Day 1: B2M
Day 2: TRAC
Day 1: TRAC
Day 2: B2M
B2M _CD3
CD3_B2M
B2M & CD3
Sequential
Simultaneous
100
90
80
70
60
50
40
30
20
10
0

FIG.25

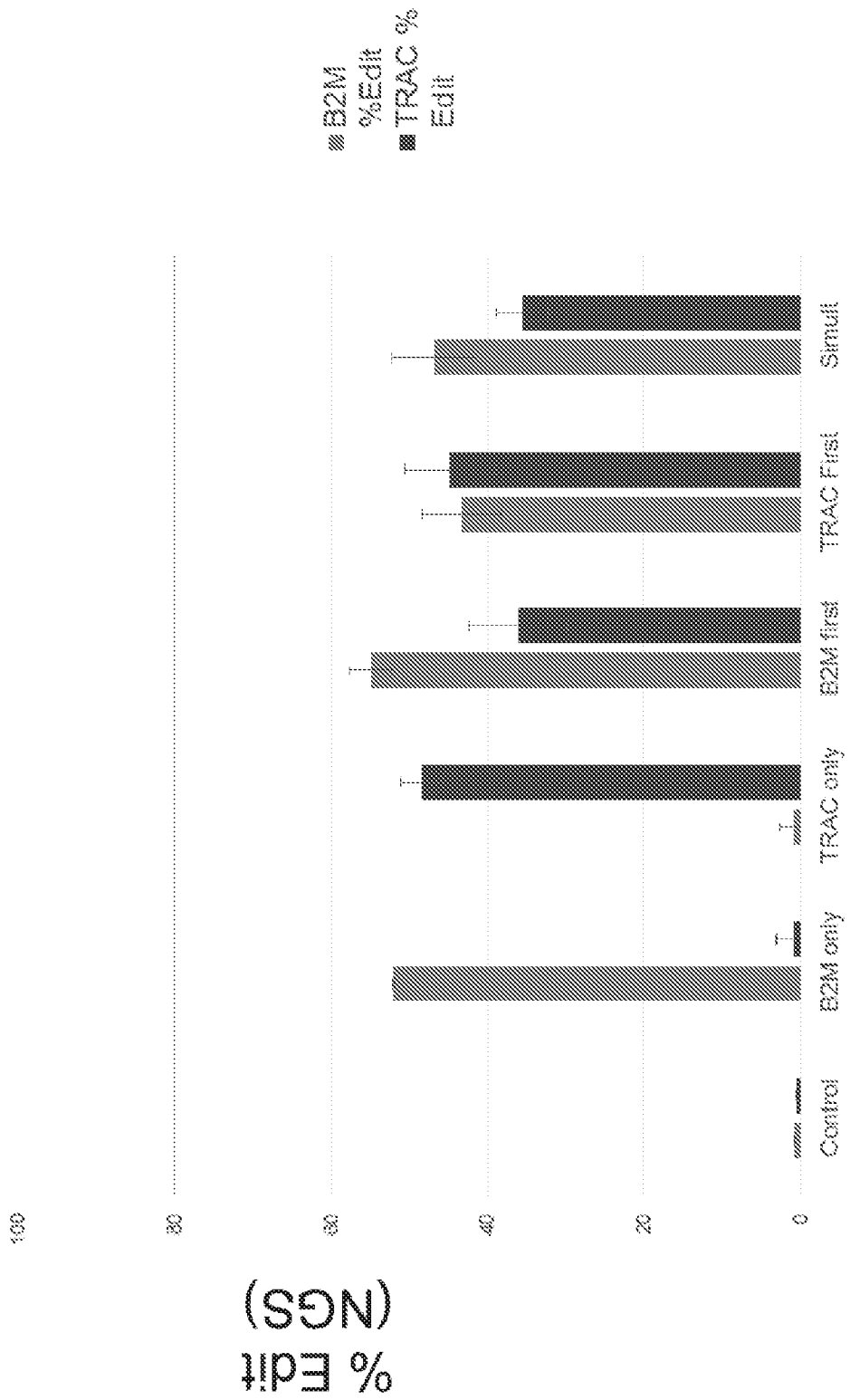

B2M %Edit
TRAC % Edit
Control
B2M only
TRAC only
B2M first
TRAC First
Simult
0
20
40
60
80
100
% Edit (NGS)

FIG.26

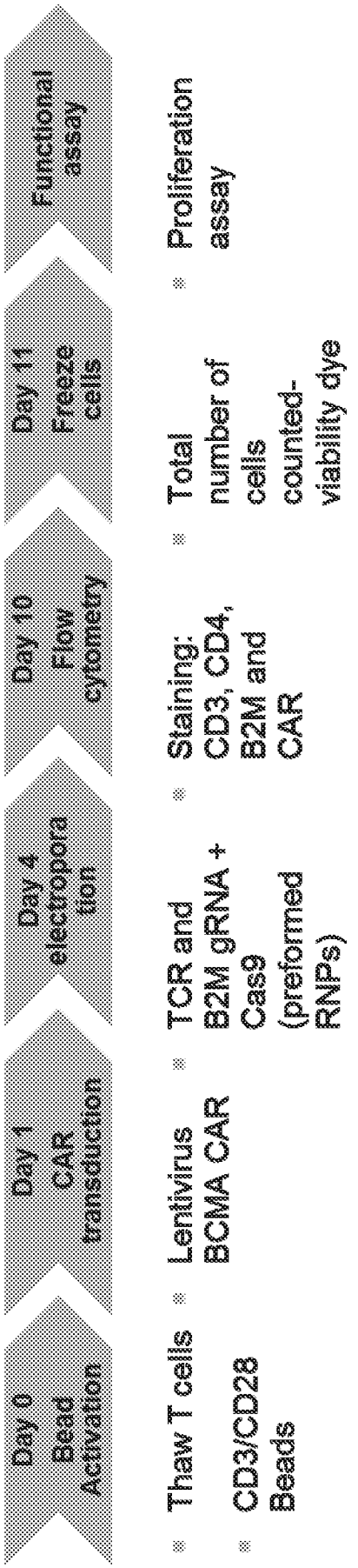

Day 0
Bead Activation
Thaw T cells
CD3/CD28 Beads
Day 1
CAR transduction
Lentivirus BCMA CAR
Day 4
electropora tion
TCR and B2M gRNA + Cas9 (preformed RNPs)
Day 10
Flow cytometry
Staining: CD3, CD4, B2M and CAR
Day 11
Freeze cells
Total number of cells counted- viability dye
Functional assay
Proliferation assay

FIG.27

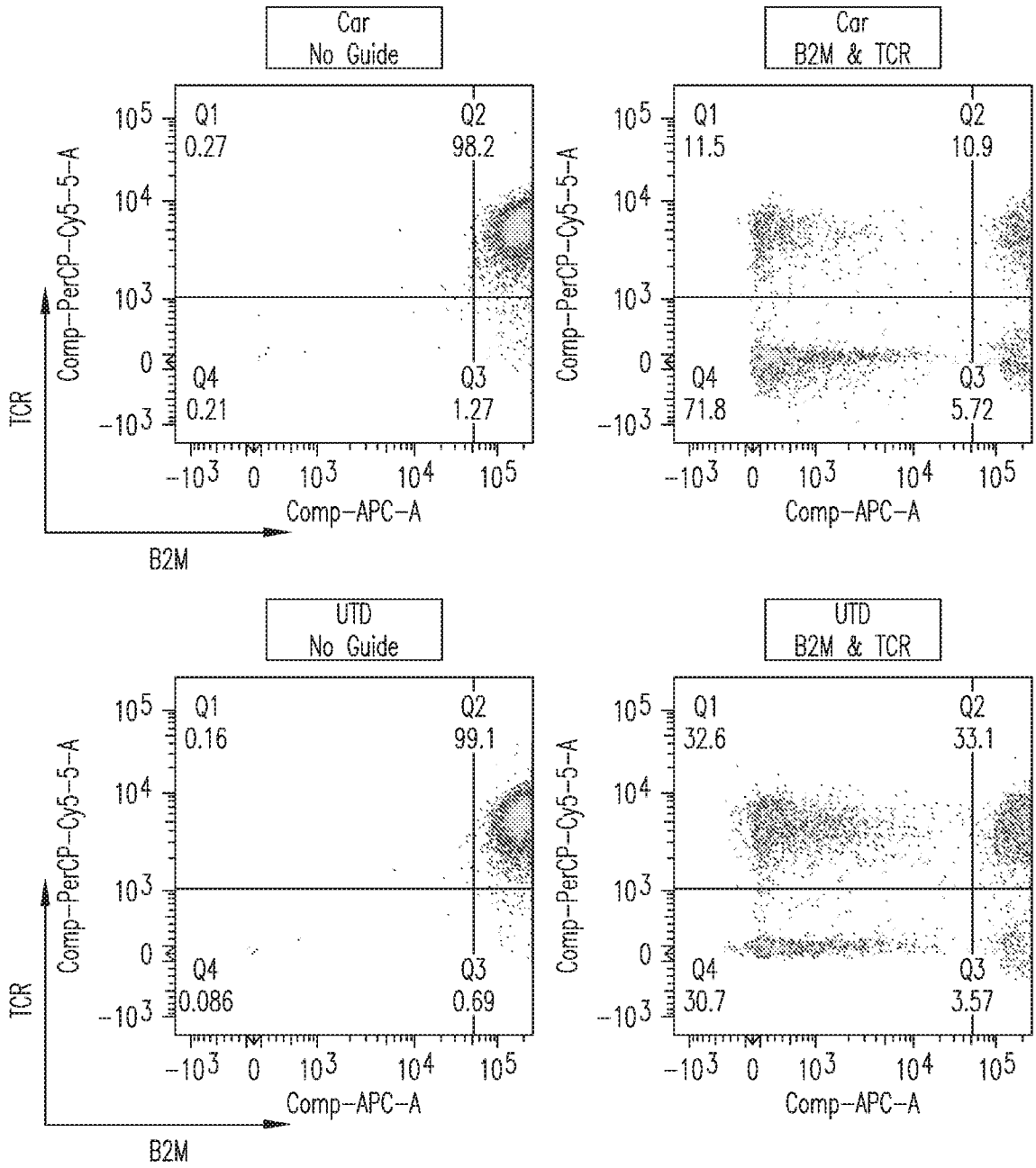

Car
No Guide
Car
B2M & TCR
UTD
No Guide
UTD
B2M & TCR
Q1
0.27
Q2
98.2
Q4
0.21
Q3
1.27
Q1
11.5
Q2
10.9
Q4
71.8
Q3
5.72
Q1
0.16
Q2
99.1
Q4
0.086
Q3
0.69
Q1
32.6
Q2
33.1
Q4
30.7
Q3
3.57
Comp-PerCP-Cy5-5-A
Comp-APC-A
TCR
B2M
10^5
10^4
10^3
0
-10^3

FIG.28A

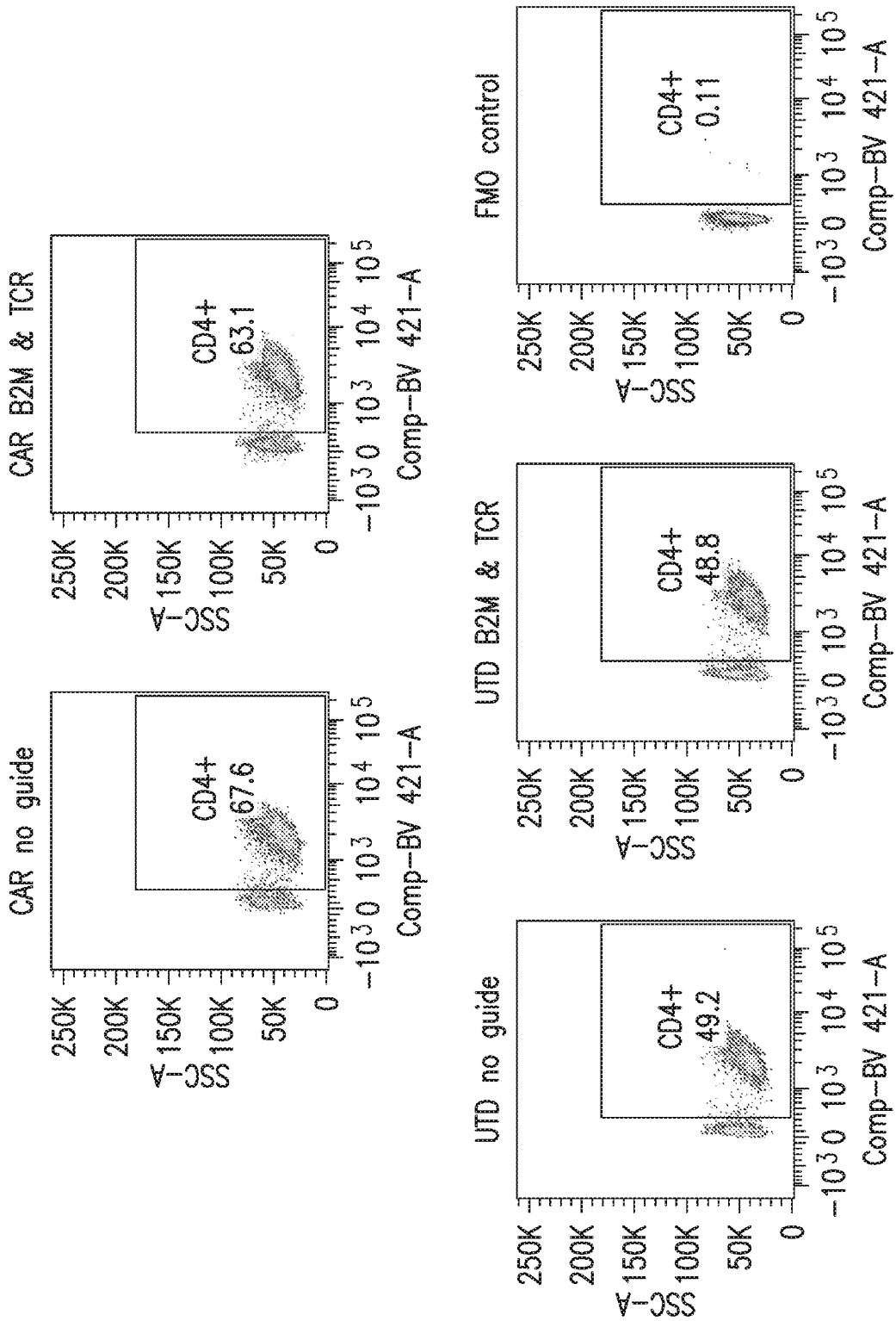

CAR no guide
CD4+
67.6
CAR B2M & TCR
CD4+
63.1
UTD no guide
CD4+
49.2
UTD B2M & TCR
CD4+
48.8
FMO control
CD4+
0.11
SSC-A
250K
200K
150K
100K
50K
0
-10^3 0 10^3 10^4 10^5
Comp-BV 421-A

FIG.28B

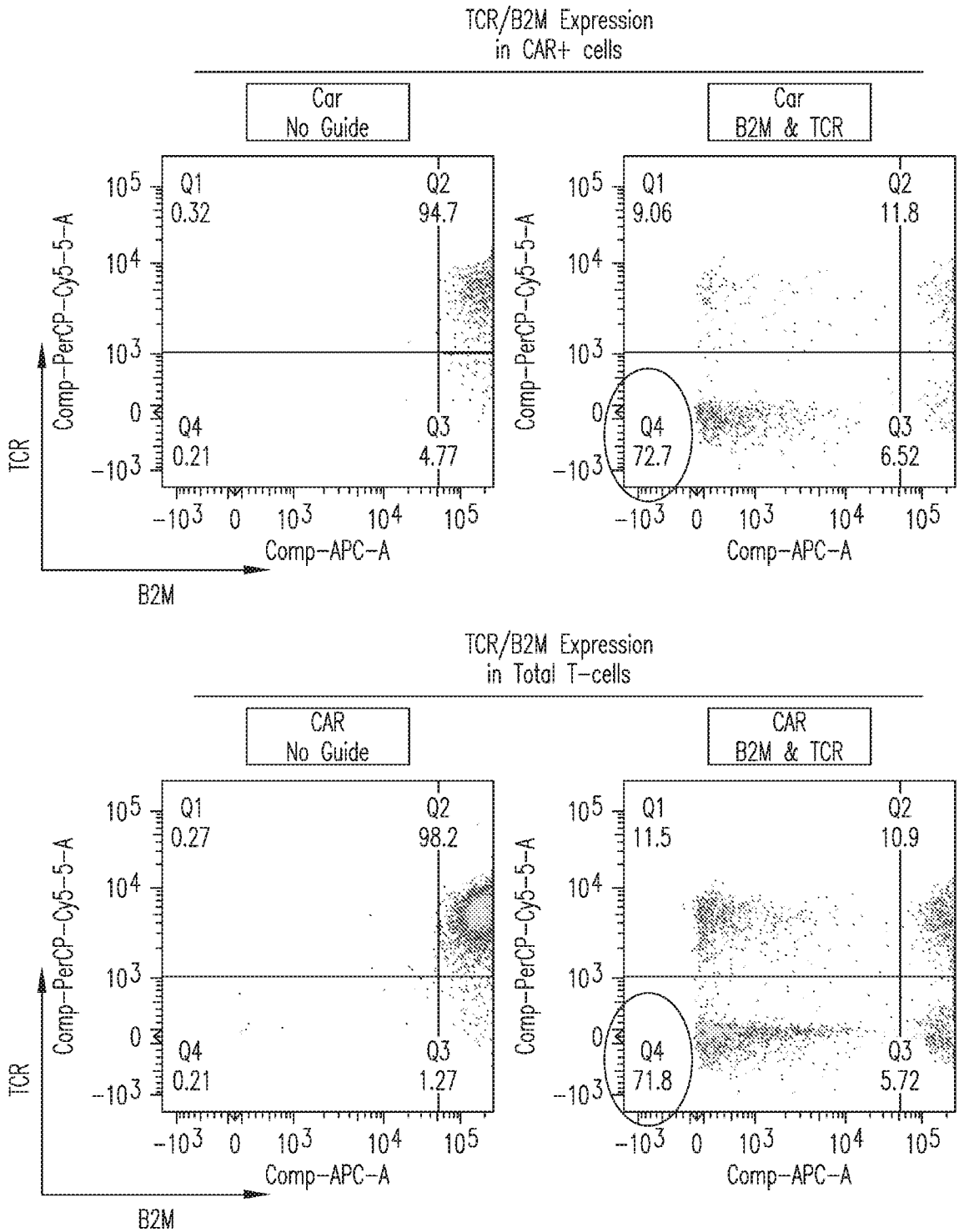

TCR/B2M Expression
in CAR+ cells
Car
No Guide
Car
B2M & TCR
Q1
0.32
Q2
94.7
Q4
0.21
Q3
4.77
Q1
9.06
Q2
11.8
Q4
72.7
Q3
6.52
Comp-PerCP-Cy5-5-A
Comp-APC-A
TCR
B2M
TCR/B2M Expression
in Total T-cells
CAR
No Guide
CAR
B2M & TCR
Q1
0.27
Q2
98.2
Q4
0.21
Q3
1.27
Q1
11.5
Q2
10.9
Q4
71.8
Q3
5.72
Comp-PerCP-Cy5-5-A
Comp-APC-A
TCR
B2M

FIG.29

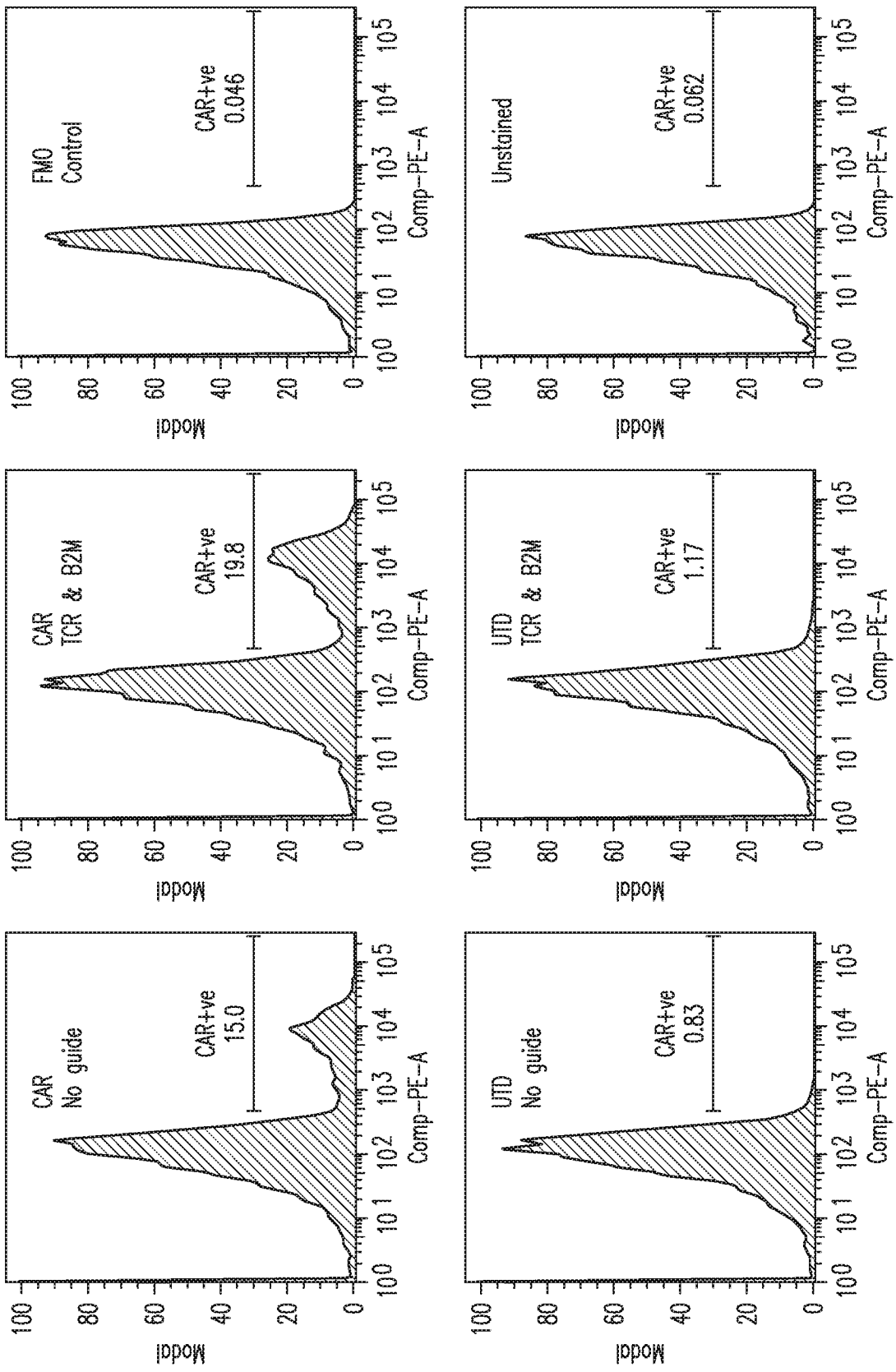

FMO
Control
CAR+ve
0.046
Unstained
CAR+ve
0.062
CAR
TCR & B2M
CAR+ve
19.8
UTD
TCR & B2M
CAR+ve
1.17
CAR
No guide
CAR+ve
15.0
UTD
No guide
CAR+ve
0.83
Modal
Comp-PE-A
0
20
40
60
80
100
10^0
10^1
10^2
10^3
10^4
10^5

FIG.30

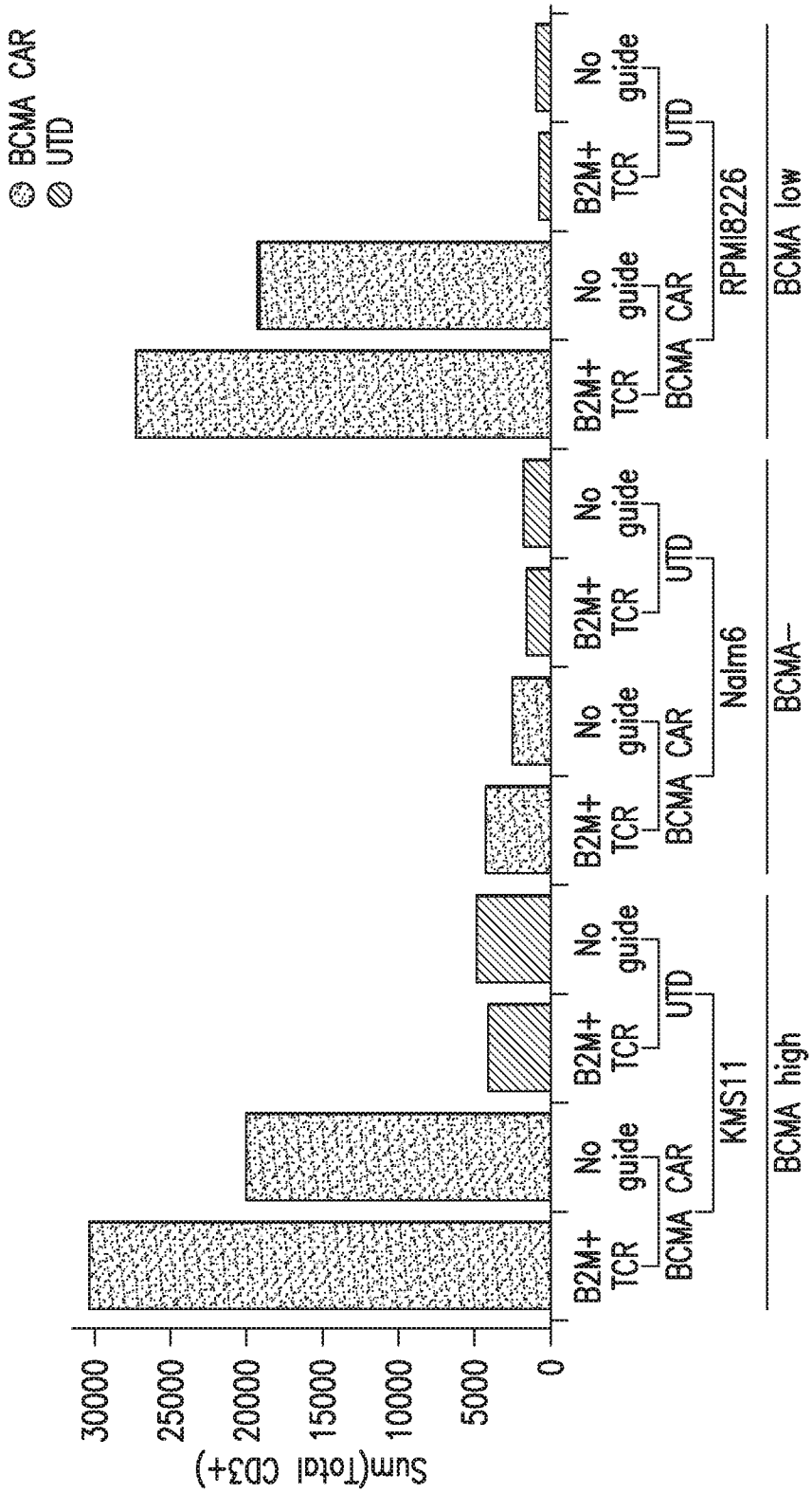

BCMA CAR
UTD
Sum(Total CD3+)
30000
25000
20000
15000
10000
5000
0
B2M+ TCR
No guide
BCMA CAR
B2M+ TCR
No guide
UTD
KMS11
BCMA high
B2M+ TCR
No guide
BCMA CAR
B2M+ TCR
No guide
UTD
Nalm6
BCMA−
B2M+ TCR
No guide
BCMA CAR
B2M+ TCR
No guide
UTD
RPMI8226
BCMA low

FIG.31

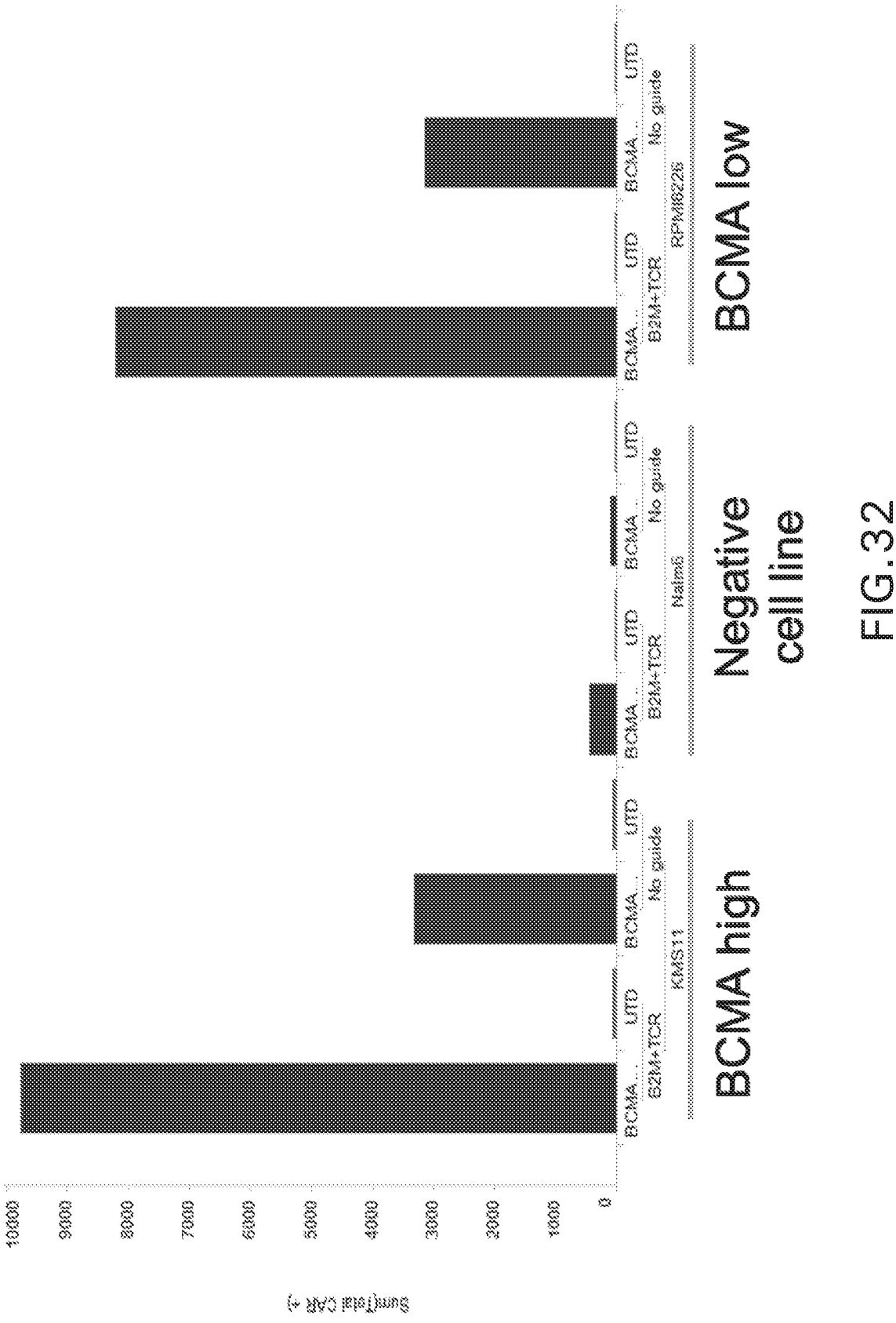

BCMA high
Negative cell line
BCMA low
KMS11
Nalm6
RPMI8226
B2M+TCR
No guide
UTD
BCMA
Sum(Total CAR +)
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000

FIG. 32

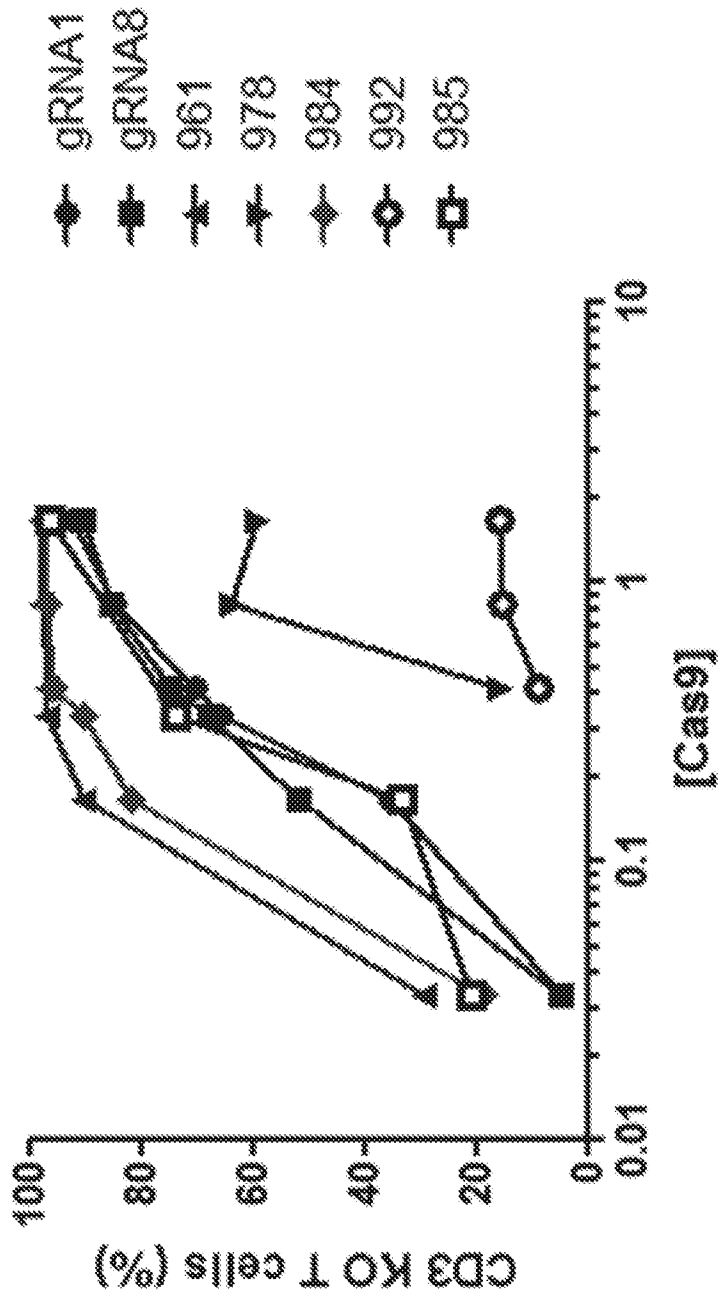

gRNA1
gRNA8
961
978
984
992
985
CD3 KO T cells (%)
100
80
60
40
20
0
0.01
0.1
1
10
[Cas9]

FIG.33A

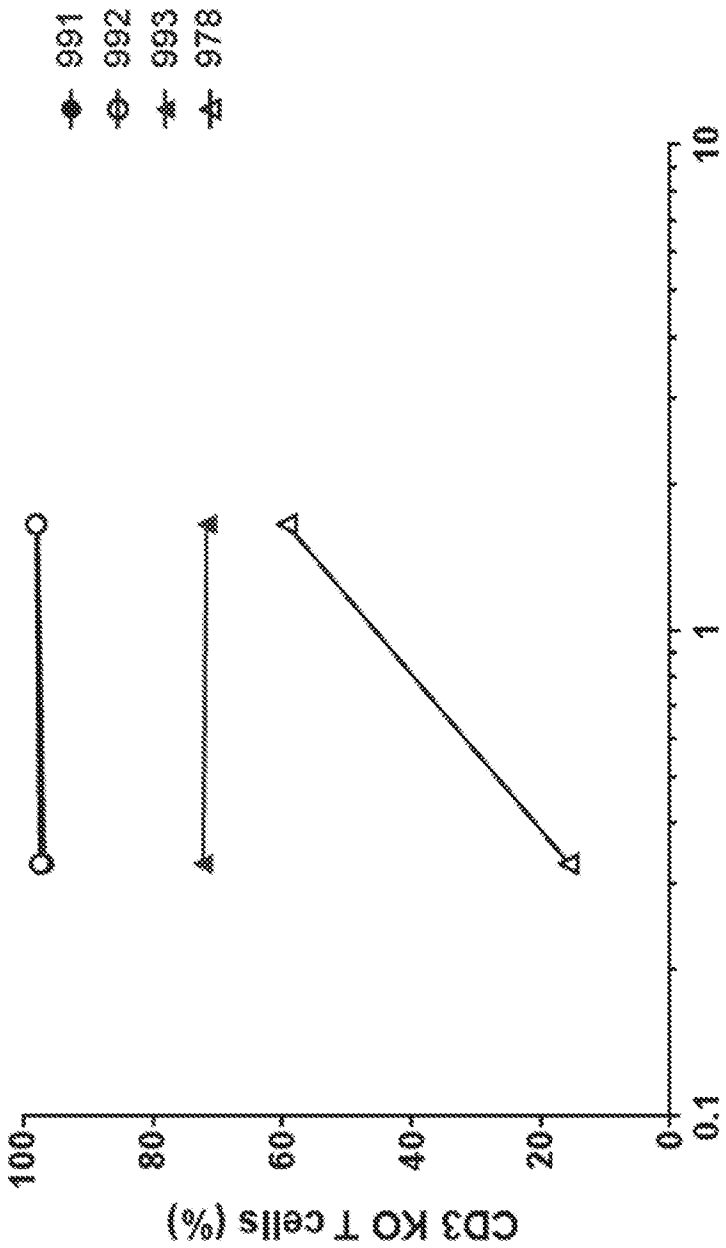


FIG.33B

Guide RNA	% indels (avg) Expt. 1	% indels (avg) Expt. 2	% frameshift edits (avg) Expt. 2
CR000961	96.95	96.54	77.27
CR000978	86.31	93.97	46.86
CR000984	96.96		
CR000992	14.97	95.57	65.73
CR000960	95.12		
CR000979	91.03		
CR000991		96.65	52.14
CR000993		97.14	37.88

FIG. 33C

Guide-Treatment	Variant Read	Avg(Indel Length)	Frequency (avg)	UniqueConcatenate(Call)
CR000960	CCCTGATCCTCTTGTCCCACAGATATCCAGAACCCTGACCCTGCCGT ACCAGCTGAGAGACTCTAAATCCAGTGACAA	-2	9.61%	Frameshift
CR000960	CCCTGATCCTCTTGTCCCACAGATATCCAGAACCCTGACCCTGCC TGTACCAGCTGAGAGACTCTAAATCCAGTGACAA	-1	6.04%	Frameshift
CR000960	CCCTGATCCTCTTGTCCCACAGATATCCAG----------CTGAGAGACTCTAAATCCAGTGACAA	-24	4.58%	In Frame
CR000960	CCCTGATCCTCTTGTCCCACAGATATCCAGAACCCTGACC----------AGCTGAGAGACTCTAAATCCAGTGACAA	-12	4.22%	In Frame
CR000960	CCCTGATCCTCTTGTCCCACAGATATCCAGAACCCTGA----------GAGACTCTAAATCCAGTGACAA	-20	3.82%	Frameshift
CR000961	GATCCTCTTGTCCCACAGATATCCAGAACCCTGACCCTGCCGTGTAcCAGCTGAGAGACTCTAAATCCAGTGACAAGTCT	1	48.07%	Frameshift
CR000961	GATCCTCTTGTCCCACAGATATCCAGAACCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTCT	1	3.14%	Frameshift
CR000961	GATCCTCTTGTCCCACAGATATCCAGAACCCTGACCC----------AGCTGAGAGACTCTAAATCCAGTGACAAGTCT	-11	2.87%	Frameshift
CR000961	GATCCTCTTGTCCCACAGATATCCAG----------TGACAAGTCT	-44	1.94%	Frameshift
CR000961	GATCCTCTTGTCCCACAGATATCCAGAACCCTGACCCTGC----------TGAGAGACTCTAAATCCAGTGACAAGTCT	-11	1.48%	Frameshift
CR000978	AACAACAGCAATATTCCAGAAGACACCTTCTTCCCCAGCCCAGG----GCAGCTTTGGTGCCTTCGCAGGCTGTTTCCT	-5	8.51%	Frameshift
CR000978	AACAACAGCAATATTCCAGAAGACACCTTCTTCCCCAGC----------TTTGGTGCCTTCGCAGGCTGTTTCCT	-15	8.36%	In Frame
CR000978	AACAACAGCAATATTCCAGAAGACACCTTCTTCCCCAGCCCAGGTA-GGCCAGCTTTGGTGCCTTCGCAGGCTGTTTCCT	-1	7.47%	Frameshift
CR000978	AACAACAGCAATATTCCAGAAGACACCTTCTTCCCCAGCCCAG----CTTTGGTGCCTTCGCAGGCTGTTTCCT	-10	6.57%	Frameshift
CR000978	AACAACAGCAATATTCCAGAAGACACCTTCTTCCCCAGCCCAGGT----------GCCTTCGCAGGCTGTTTCCT	-15	2.91%	In Frame
CR000979	TGTTTTCCTTTTACAAAAGTTCCTGTGATGTCCAGGTTGGTCAAAGCTTTGAAACAGGTAAGACAGGGGTCTAGCCT	1	10.57%	Frameshift
CR000979	TGTTTTCCTTTTACAAAAGTTCCTGTGATGTCA-GCTGGTCGAGAAAAGCTTTGAAACAGGTAAGACAGGGGTCTAGCCT	-1	7.21%	Frameshift
CR000979	TGTTTTCCTTTTACAAAAGTTCCTG----------GTCGAGAAAAGCTTTGAAACAGGTAAGACAGCGGTCTAGCCT	-13	6.80%	Frameshift
CR000979	TGTTTTCCTTTTACAAAAGTTCCTGTGATGTC----------CAGAAAAGCTTTGAAACAGGTAAGACAGCGGTCTAGCCT	-9	5.76%	In Frame
CR000979	TGTTTTCCTTTTACAAAAG----------AAACAGGTAAGACAGGGGTCTAGCCT	-35	3.85%	Frameshift
CR000984	GCCTCTTGTTTTACAGATACGAACCTAAACTTTCAAAACCTGTCAaGTGATTGGGTTCCGAATCCTCCTCCTGAAAGTGG	1	32.51%	Frameshift
CR000984	GCCTCTTGTTTTACAGATACGAACCTAAACTTTCAAAACCTGTCA TGATTGGGTTCCGAATCCTCCTCCTGAAAGTGG	-1	7.36%	Frameshift
CR000984	GCCTCTTGTTTTACAGATACGAACCTAAACTTTCAAAACCTGTC-GTGATTGGGTTCCGAATCCTCCTCCTGAAAGTGG	-1	7.19%	Frameshift
CR000984	GCCTCTTGTTTTACAGATACGAACCTAAACTTTCAAAACCTGTCA----TTGGGTTCCGAATCCTCCTCCTGAAAGTGG	-4	5.70%	Frameshift
CR000984	GCCTCTTGTTTTACAGATACGAACCTAAACTTTCAAAACCTGTCAG-ATTGGGTTCCGAATCCTCCTCCTGAAAGTGG	-2	2.86%	Frameshift
CR000992	TGTCAGTGATTGGGTTCCGAATCCTCCTCCTGAAAGTGGCCGGGTTTAATCTGCTCATGACGCTGCGGCTGTGGTCCAGC	1	5.28%	Frameshift
CR000992	TGTCAGTGATTGGGTTCCGAAATCCTCCTCCTGAAAGTGGCCGGGTT-AATCTGCTCATGACGCTGCGGCTGTGGTCCAGC	-1	1.78%	Frameshift
CR000992	TGTCAGTGATTGGGTTCCGAATCCgCCTCCTGAAAGTGGCCGGGTTTAATCTGCTCATGACGCTGCGGCTGTGGTCCAGC	0	0.56%	In Frame
CR000992	TGTCAGTGATTGGGTTCCGAATCCTCCgCCTGAAAGTGGCCGGGTTTAATCTGCTCATGACGCTGCGGCTGTGGTCCAGC	0	0.40%	In Frame
CR000992	TGTCAGTGATTGGGTTCCGAATCCTCCTCCTGAAAGTGGC----------TCATGACGCTGCGGCTGTGGTCCAGC	-14	0.36%	Frameshift

FIG.34A

Guide-Treatment	Variant Read	Frequency(Avg)	Avg(Indel Length)	UniqueConcatenate(Call)
CR000961	GATCCTCTTGTCCCACAGATATCCAGAACCCTGACCCTGCCGTGTAaCCAGCTGAGAGACTCTAAATCCAGTGACAAGTCT	55.23%	1	Frameshift
CR000961	GATCCTCTTGTCCCACAGATATCCAGAACCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTCT	2.91%	1	Frameshift
CR000961	GATCCTCTTGTCCCACAGATATCCAGAACCCTGACCC----------AGCTGAGAGACTCTAAATCCAGTGACAAGTCT	1.77%	-11	Frameshift
CR000961	GATCCTCTTGTCCCACAGATATCCAGAACCCTGACCCTGCC------AGCTGAGAGACTCTAAATCCAGTGACAAGTCT	1.47%	-7	Frameshift
CR000961	GATCCTCTTGTCCCACAGATATCCAGAACCCTGACCCTGCCGTGTgACCAGCTGAGAGACTCTAAATCCAGTGACAAGTCT	0.90%	1	Frameshift
CR000978	AACAACAGCATATTCCAGAAGACACCTTCTTCCCCAGCCCAG----GCAGCTTTGGTGCCTTCGCAGGCTGTTTCCT	12.73%	-5	Frameshift
CR000978	AACAACAGCATATTCCAGAAGACACCTTCTTCCCCAGCCCAG----------TTGGTGCCTTCGCAGGCTGTTTCCT	8.55%	-15	In Frame
CR000978	AACAACAGCATATTCCAGAAGACACCTTCTTCCCCAGCCCAG----------CTTGGTGCCTTCGCAGGCTGTTTCCT	7.03%	-10	Frameshift
CR000978	AACAACAGCATATTCCAGAAGACACCTTCTTCCCCAGCCCAGGTA-GGGCAGCTTTGGTGCCTTCGCAGGCTGTTTCCT	5.26%	-1	Frameshift
CR000978	AACAACAGCATATTCCAGAAGACACCTTCTTCCCCAGCCCAG----------GCCTTCGCAGGCTGTTTCCT	4.12%	-15	In Frame
CR000991	CTTTCAAAACCTGTCAGTGATTGGGTTCCGAATCCTCCTCCTGAA-GTGGCCGGGTTTAATCTGCTCATGACGCTGCGGC	8.61%	-1	Frameshift
CR000991	CTTTCAAAACCTGTCAGTGATTGGGTTCCGAATCCTCCTCCTGAAA-TGGCCGGGTTTAATCTGCTCATGACGCTGCGGC	6.68%	-1	Frameshift
CR000991	CTTTCAAAACCTGTCAGTGATTGGGTTCCGAATCCTCCTCCTGAAAaaGTGGCCGGGTTTAATCTGCTCATGACGCTGCGGC	6.56%	2	Frameshift
CR000991	CTTTCAAAACCTGTCAGTGATTGCCTTCCGAATCCTCCTCCTGCTGAA-TCGCCCGGTTTAATCTGCTCATGACGCTGCGGC	4.99%	-2	Frameshift
CR000991	CTTTCAAAACCTGTCAGTGATTGGGTTCCGAATCCTCCTCCTGAAAaGTGGCCGGGTTTAATCTGCTCATGACGCTGCGGC	4.40%	1	Frameshift
CR000992	TGTCAGTGATTGGGTTCCGAATCCTCCTCCTGAAAGTGGCCGGGTT-AATCTGCTCATGACGCTGCGGCTGTGGTCCAGC	16.80%	-1	Frameshift
CR000992	TGTCAGTGATTGGGTTCCGAATCCTCCTCCTGAAAGTGGCCGGGTTTAAATCTGCTCATGACGCTGCGGCTGTGGTCCAGC	9.93%	1	Frameshift
CR000992	TGTCAGTGATTGGGTTCCGAATCCTCCTCCTGAAAGTGGCCGGGT-AATCTGCTCATGACGCTGCGGCTGTGGTCCAGC	3.44%	-2	Frameshift
CR000992	TGTCAGTGATTGGGTTCCGAATCCTCCTCCTGAAAGTGGCC----------TCATGACGCTGCGGCTGTGGTCCAGC	2.98%	-14	Frameshift
CR000992	TGTCAGTGATTGGGTTCCGAATCCTCCTCCTGAAAGTGC----------CTCATGACGCTGCGGCTGTGGTCCAGC	2.95%	-15	In Frame
CR000993	CTCCTGAAAGTGGCCGGGTTTAATCTGC----------CGCTGGTCCAGCTGAGGTGAGGGGCCTTGAAGCTGGGA	17.31%	-12	In Frame
CR000993	CTCCTGAAAGTGGCCGGGTTTAATCTGCTCATGACGgCTGGCGCTGTGGTCCAGCTGAGGTGAGGGGCCTTGAAGCTGGGA	7.53%	1	Frameshift
CR000993	CTCCTGAAAGTGGCCGGGTTTAATCTGCTCATGAC-TGTGGCTGTGGTCCAGCTGAGGTGAGGGGCCTTGAAGCTGGGA	4.72%	-2	Frameshift
CR000993	CTCCTGAAAGTGGCCGGGTTTAATCTGCTCATGAC-CTGCGGCTGTGGTCCAGCTGAGGTGAGGGGCCTTGAAGCTGGGA	4.33%	-1	Frameshift
CR000993	CTCCTGAAAGTGGCCGGGTTTAATCTGCTCATG----CGGCTGTGGTCCAGCTGAGGTGAGGGGCCTTGAAGCTGGGA	2.79%	-6	In Frame

FIG.34B

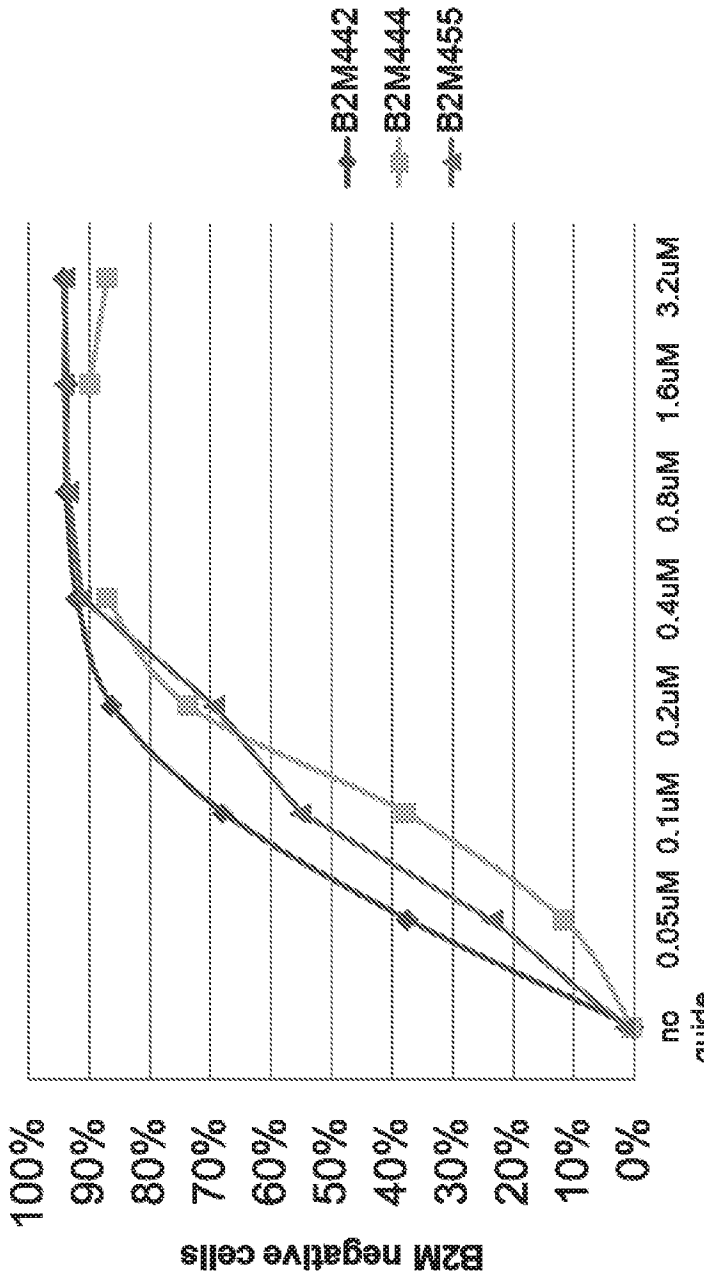

B2M442
B2M444
B2M455
B2M negative cells
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
no guide
0.05uM
0.1uM
0.2uM
0.4uM
0.8uM
1.6uM
3.2uM
RNP concentration

FIG.35

Guide RNA	% indels (avg)	% frameshift edits (avg)
CR00444	72.81	42.61
CR00455	86.95	43.38

Guide-Treatment	Variant Read	Avg(Indel Length)	Avg(Hit % All reads)	UniqueConcatenate(Call)
CR00444	GAAGCTGACAGCATTCGGGCCGAGATGTCTCGC----------GCTACTCTCTCTTTCTGGCCTGGA	-23	3.34%	Frameshift
CR00444	GAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCGGTGGCCTAGCaTGTGCTCGCGCTACTCTCTCTTTCTGGCCTGGA	1	2.81%	Frameshift
CR00444	GAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCGTGGC----------TACTCTCTCTTTCTGGCCTGGA	-17	2.60%	Frameshift
CR00444	GAAGCTGACAGCATTCGGGCCGAGATGTCTCGCT----------ACTCTCTCTTTCTGGCCTGGA	-25	2.53%	Frameshift
CR00444	GAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCTAG—TGCTCGCGCTACTCTCTCTTTCTGGCCTGGA	-3	2.45%	In Frame
CR00444	GAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCGTGGC----------TCGCGCTACTCTCTCTTTCTGGCCTGGA	-11	1.85%	Frameshift
CR00444	GAAGCTGACAGCATTCGGGCCGAGATGTCTCGC----------GCGCTACTCTCTCTTTCTGGCCTGGA	-19	1.77%	Frameshift
CR00444	GAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCTAGCTACTCTCTCTTTCTGGCCTGGA	2	1.68%	Frameshift
CR00444	GAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCGTGGC----------GCTACTCTCTCTTTCTGGCCTGGA	-15	1.60%	In Frame
CR00444	GAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCTAGCT----CGCGCTACTCTCTCTTTCTGGCCTGGA	-5	1.60%	Frameshift
CR00455	CCGTGTGAACCATGTGACTTTGTCACAGCCCAAG----TTAAGTGGGGTAAGTCTTACATTCTTTTGTAAGCTGCTGAAA	-4	7.82%	Frameshift
CR00455	CCGTGTGAACCATGTGACTTTGTCACAGCCCAAGaaTAGTTAAGTGGGGTAAGTCTTACATTCTTTTGTAAGCTGCTGAAA	1	6.93%	Frameshift
CR00455	CCGTGTGAACCATGTGACTTTGT----------TAAGTGGGGTAAGTCTTACATTCTTTTGTAAGCTGCTGAAA	-18	4.71%	Frameshift
CR00455	CCGTGTGAACCATGTGACTTTGTCACAGCCCAAG----------TGGGGTAAGTCTTACATTCTTTTGTAAGCTGCTGAAA	-8	3.88%	In Frame
CR00455	CCGTGTGAACCATGTGACTTTGTC----------TTACATTCTTTTGTAAGCTGCTGAAA	-30	3.40%	In Frame
CR00455	CCGTGTGAACCATGTGACTTTGT----------GGGGTAAGTCTTACATTCTTTTGTAAGCTGCTGAAA	-21	2.85%	In Frame
CR00455	CCGTGTGAACCATGTGACTT----------ACATTCTTTTGTAAGCTGCTGAAA	-36	2.84%	In Frame
CR00455	CCGTGTGAACCATGTGACTTTGTCACAGCCCAAG-TAGTTAAGTGGGGTAAGTCTTACATTCTTTTGTAAGCTGCTGAAA	-1	2.43%	Frameshift
CR00455	CCGTGTGAACCATGTG----------GGGTAAGTCTTACATTCTTTTGTAAGCTGCTGAAA	-29	2.42%	Frameshift
CR00455	CCGTGTGAACCATGTGACTTTGTCACAGCCCAAGA-GTTAAGTGGGGTAAGTCTTACATTCTTTTGTAAGCTGCTGAAA	-2	1.88%	Frameshift

FIG. 36

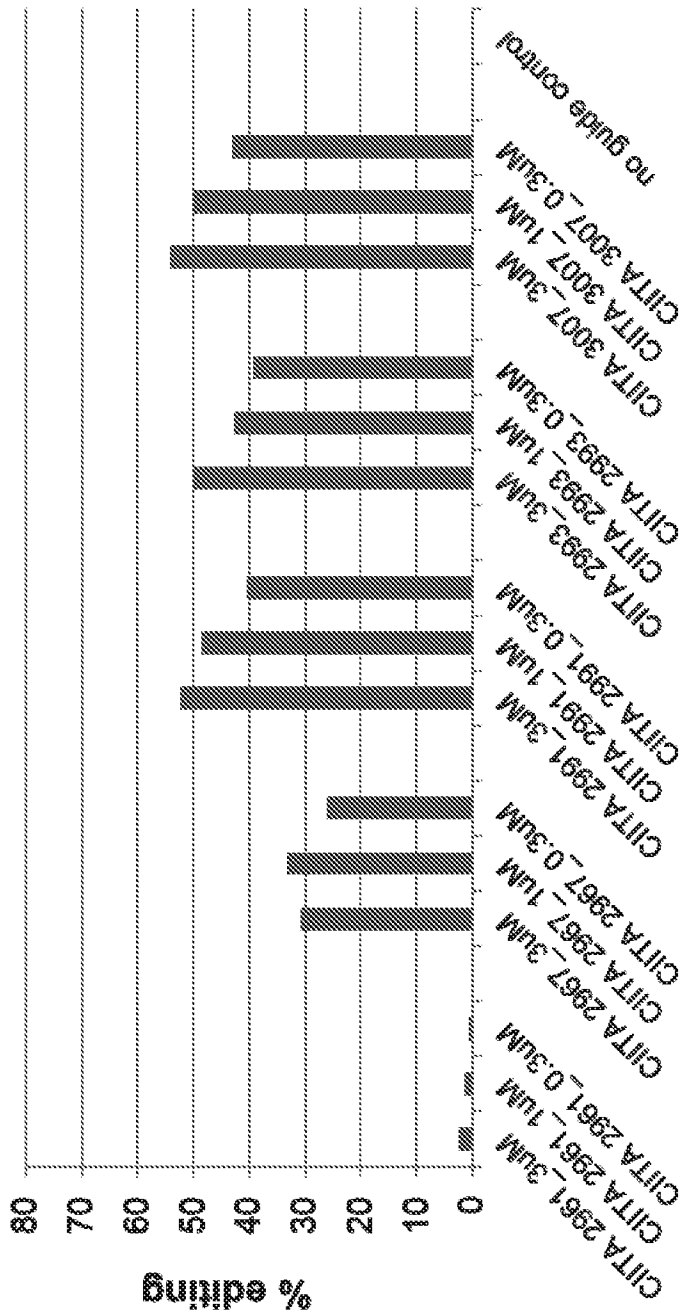

% editing
0
10
20
30
40
50
60
70
80
CIITA 2961_3uM
CIITA 2961_1uM
CIITA 2961_0.3uM
CIITA 2967_3uM
CIITA 2967_1uM
CIITA 2967_0.3uM
CIITA 2991_3uM
CIITA 2991_1uM
CIITA 2991_0.3uM
CIITA 2993_3uM
CIITA 2993_1uM
CIITA 2993_0.3uM
CIITA 3007_3uM
CIITA 3007_1uM
CIITA 3007_0.3uM
no guide control

FIG. 37

Guide RNA	% indels (avg)	% frameshift edits (avg)
CR002967	89.74	74.04
CR002991	93.51	64.76
CR002993	90.08	56.92
CR003007	93.09	58.37

Guide-Treatment	Variant Read	Frequency (avg)	Avg(Indel Length)	Unique Conce lands(Cell)
CR002967	AGCTCACAGTGTGCCACCATGGAGTTGGGGCCCTAGAAGGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCCCT	31.26%	1	Frameshift
CR002967	AGCTCACAGTGTGCCACCATGGAGTTGG----------CTACCTGGAGCTTCTTAACAGCGATGCTGACCCCCT	7.01%	-10	Frameshift
CR002967	AGCTCACAGTGTGCCACCATGGAGTTGGGGC----------TACCTGGAGCTTCTTAACAGCGATGCTGACCCCCT	4.58%	-14	Frameshift
CR002967	AGCTCACAGTGTGCCACCATGGAGTTGGGG---TAGAAGGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCCCT	3.64%	-4	Frameshift
CR002967	AGCTCACAGTGTGCCACCATGGAG----------CTTCTTAACAGCGATGCTGACCCCCT	3.70%	-20	In Frame
CR002991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGACATTGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	19.51%	1	Frameshift
CR002991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGA----------TGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	11.37%	-12	In Frame
CR002991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGAC-TGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	4.53%	-1	Frameshift
CR002991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGACA-GGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	3.55%	-1	Frameshift
CR002991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGA--TGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	3.49%	-2	Frameshift
CR002993	CAGGCTGTTGTGTGACATGGAAGGTGATGAAGAG-CCAGGGAGGCTTATGCCAATATCGGTGAGGAAGACACCTGAGCCCA	9.29%	-1	Frameshift
CR002993	CAGGCTGTTGTGTGACATGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGCCCA	5.57%	1	Frameshift
CR002993	CAGGCTGTTGTGTGACATGGAAGG----------CTTATGCCAATATCGGTGAGGAAGCACCTGAGCCCA	4.47%	-20	Frameshift
CR002993	CAGGCTGTTGTGTGACA----------GGGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGCCCA	4.29%	-21	In Frame
CR002993	CAGGCTGTTGTGTGACATGGAAGGTGAGGA----------GGCACCTGAGCCCA	4.17%	-36	In Frame
CR003007	TTTCTCAAAGTAGAGCACATAGGACCAGATGAAGTTGATCGGTGAGAGATATGCAGATGCCAGCAGAAGTTGGGCAGAAAAG	23.89%	1	Frameshift
CR003007	TTTCTCAAAGTAGAGCACATAGGACCAGATGA----------GAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAAAG	4.82%	-12	In Frame
CR003007	TTTCTCAAAGTAGAGCACATAGGACCAGAT----------CGGTGAGAGTATGGCAGCAGAAGTTGGGCAGAAAAG	3.57%	-8	Frameshift
CR003007	TTTCTCAAAGTAGAGCACATAGGACCAGA----------GTATGGAGATGCCAGCAGAAGTTGGGCAGAAAAG	1.65%	-17	Frameshift
CR003007	TTTCTCAAAGTAGAGCACATAGGACCAGATGA----TCGGTGAGAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAAAG	1.82%	-5	Frameshift

FIG. 38

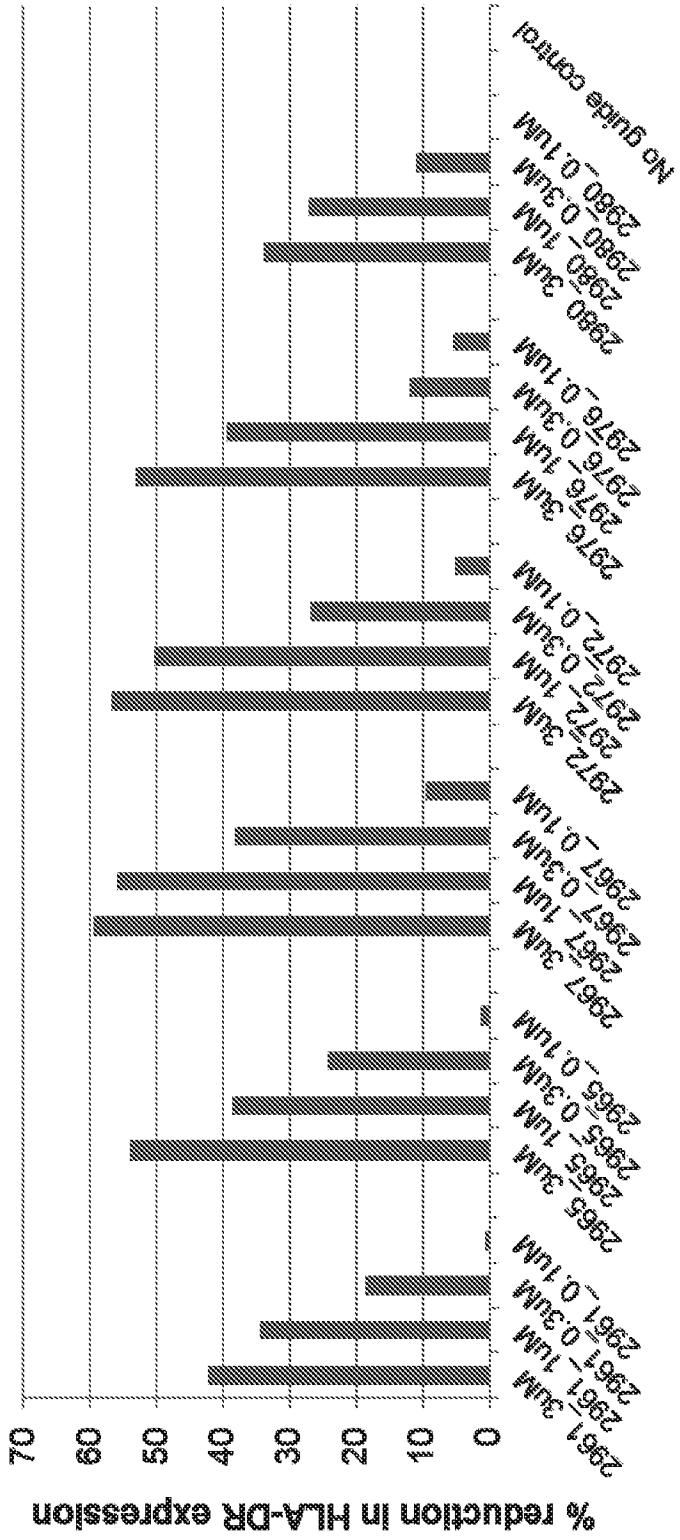

% reduction in HLA-DR expression
0
10
20
30
40
50
60
70
No guide control
2980_0.1uM
2980_0.3uM
2980_1uM
2980_3uM
2976_0.1uM
2976_0.3uM
2976_1uM
2976_3uM
2972_0.1uM
2972_0.3uM
2972_1uM
2972_3uM
2967_0.1uM
2967_0.3uM
2967_1uM
2967_3uM
2965_0.1uM
2965_0.3uM
2965_1uM
2965_3uM
2961_0.1uM
2961_0.3uM
2961_1uM
2961_3uM

FIG. 39

Guide RNA	% indels (avg)	% frameshift edits (avg)
CR002961	91.38	66.88
CR002965	92.49	75.36
CR002967	99.24	87.58
CR002972	88.41	64.76
CR002976	90.40	61.85
CR002980	68.81	27.07

FIG. 40

Guide-Treatment	Variant Read	Frequency (avg)	Avg(Incel Length)	UniqueConcatenate(Call)
CR002965	TGAGCATTGTCTTCCCTCCCAGGCAGCTCACAGTGTGCC----------CCTAGAAGGTGGCTACCTGGAGCT	7.58%	-17	Frameshift
CR002965	TGAGCATTGTCTTCCCTCCCAGGCAGCTCACAGTGTGCCACCATGGAGTTGGGGCCCCTAGAAGGTGGCTACCTGGAGCT	7.49%	1	Frameshift
CR002965	TGAGCATTGTCTTCCCTCCCAGGCAGCTCACAGTGTGGCAGCCA-GCAGTTGGGGCCCCTAGAAGGTGGCTACCTGGAGCT	6.37%	-1	Frameshift
CR002965	TGAGCATTGTCTTCCCTCCCAGGCAGCTCACAGTGTGCCACCA-GAGTTGGGGCCCCTAGAAGGTGGCTACCTGGAGCT	2.96%	-2	Frameshift
CR002965	TGAGCATTGTCTTCCCTCCCAGGC----------TCCTAGAAGGTGGCTACCTGGAGCT	2.18%	-31	Frameshift
CR002972	GGGGGTCAGCATCGCTGTTAAGAAGCTCCAGGTAGCCACT-GTAGGGGCCCCAACTCCATGGTGGCACACTGTGAGCTG	14.04%	-1	Frameshift
CR002972	GGGGGTCAGCATCGCTGTTAAGAAGCTCCAGGTAGCCAC-TCTAGGGGCCCCAACTCCATGGTGGCACACTGTGAGCTG	6.14%	-2	Frameshift
CR002972	GGGGGTCAGCATCGCTGTTAAGAAGCTCCAGGTAGCC----------CCAACTCCATGGTGGCACACTGTGAGCTG	4.55%	-14	Frameshift
CR002972	GGGGGTCAGCATCGCTGTTAAGAAGCTCCAGGTAGCCACTCCTGTAGGGGCCCCAACTCCATGGTGGCACACTGTGAGCTG	4.22%	1	Frameshift
CR002972	GGGGGTCAGCATCGCTGTTAAGAAGCTCCAGGTAGCCA--TCTAGGGGCCCCAACTCCATGGTGGCACACTGTGAGCTG	3.59%	-3	In Frame
CR002976	GGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCCCTGTGgCCTCTACCACTTCTATGACCAGATGGACCTGGCTGG	18.87%	1	Frameshift
CR002976	GGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCCCT----CTACCACTTCTATGACCAGATGGACCTGGCTGG	6.60%	-6	In Frame
CR002976	GGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACC----------AGTTCTATGACCAGATGGACCTGGCTGG	3.32%	-15	In Frame
CR002976	GGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCCCTGTGC-TCTACCACTTCTATGACCAGATGGACCTGGCTGG	2.30%	-1	Frameshift
CR002976	GGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCCCTGTGC--TACCACTTCTATGACCAGATGGACCTGGCTGG	1.92%	-3	In Frame
CR002980	AGCTTCTTAACAGCGATGCTGACCCCCTGTGC----------GATGGACCTGGCTGGAGAAGAAGAGATT	13.83%	-12	In Frame
CR002980	AGCTTCTTAACAGCGATGCTGACCCCCTGTGCCTCTACCA----------ATGGACCTGGCTGGAGAAGAAGAGATT	4.51%	-3	In Frame
CR002980	AGCTTCTTAACAGCGATGCTGACCCCCTGTGC----------AGATGGACCTGGCTGGAGAAGAAGAGATT	3.22%	-16	In Frame
CR002980	AGCTTCTTAACAGCGATGCTGACCCCCTGTGCCTCTACCACTT--ATGACCAGATGGACCTGGCTGGAGAAGAAGAGATT	2.50%	-2	Frameshift
CR002980	AGCTTCTTAACAGCGATGCTGACCCCCTGTGCCTCTACCACTT-TATGACCAGATGGACCTGGCTGGAGAAGAAGAGATT	2.09%	-1	Frameshift
CR003007	TTTTCTCAAAGTAGAGCACATAGGACCATGGAGTTGGGGCAGAAGTTGGGCAGAAA	44.74%	1	Frameshift
CR003007	TTTTCTCAAAGTAGAGCACATAGGACCATGGA----------GAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAA	3.33%	-12	In Frame
CR003007	TTTTCTCAAAGTAGAGCACATAGGACCAGAT----------CGGTGAGATGGCCAGCAGAAGTTGGGCAGAAA	2.98%	-8	Frameshift
CR003007	TTTTCTCAAAGTAGAGCACATAGGACCAGATGA-TGATCGGTGAGAGTATGGCCAGCAGAAGTTGGGCAGAAA	2.28%	-2	Frameshift
CR003007	TTTTCTCAAAGTAGAGCACATAGGACCAGATGA----TGATCGGTGAGAGTATGGCCAGCAGAAGTTGGGCAGAAA	1.88%	-3	In Frame
CR002961	GCATTGTCTTCCCTCCCAGGCAGCTCACAGTGTGCCA----TGGAGTTGGGGCCCCTAGAAGGTGGCTACCTGGAGCTTCT	10.61%	-3	In Frame
CR002961	GCATTGTCTTCCCTCCCAGGCAGCTCACAGTGTGCCAGCCATGGAGTTGGGGCCCCTAGAAGGTGGCTACCTGGAGCTTCT	7.18%	1	Frameshift
CR002961	GCATTGTCTTCCCTCCCAGGCAGCTCACAGTGTGCCA-ATGGAGTTGGGGCCCCTAGAAGGTGGCTACCTGGAGCTTCT	5.68%	-2	Frameshift
CR002961	GCATTGTCTTCCCTCCCAGGCAGCTCACAGTGTGCC-CCATGGAGTTGGGGCCCCTAGAAGGTGGCTACCTGGAGCTTCT	5.24%	-1	Frameshift
CR002961	GCATTGTCTTCCCTCCCAGGCAGCTCACAGTGTGCCAC-ATGGAGTTGGGGCCCCTAGAAGGTGGCTACCTGGAGCTTCT	4.01%	-1	Frameshift
CR002967	GCAGCTCACAGTGTGCCACCATGGAGTTGGGGCCCTAGAAGGTGGCTACCTGGAGCTGCTGACCCC	36.83%	1	Frameshift
CR002967	GCAGCTCACAGTGTGCCACCATGGAGTTGGGGCCC-AGAAGGTGGCTACCTGGAGCTTCTAACAGCGATGCTGACCCC	4.96%	-1	Frameshift
CR002967	GCAGCTCACAGTGTGCCACCATGGAGTTGGGG----TAGAAGGTGGCTACCTGGAGCTTCTAACAGCGATGCTGACCCC	4.74%	-4	Frameshift
CR002967	GCAGCTCACAGTGTGCCACCATGGAG----------CTTCTAACAGCGATGCTGACCCC	4.12%	-30	In Frame
CR002967	GCAGCTCACAGTGTGCCACCATGGAGTTGC----------CTACCTGGAGCTTCTTAACAGCGATGCTGACCCC	3.67%	-16	Frameshift

FIG.41

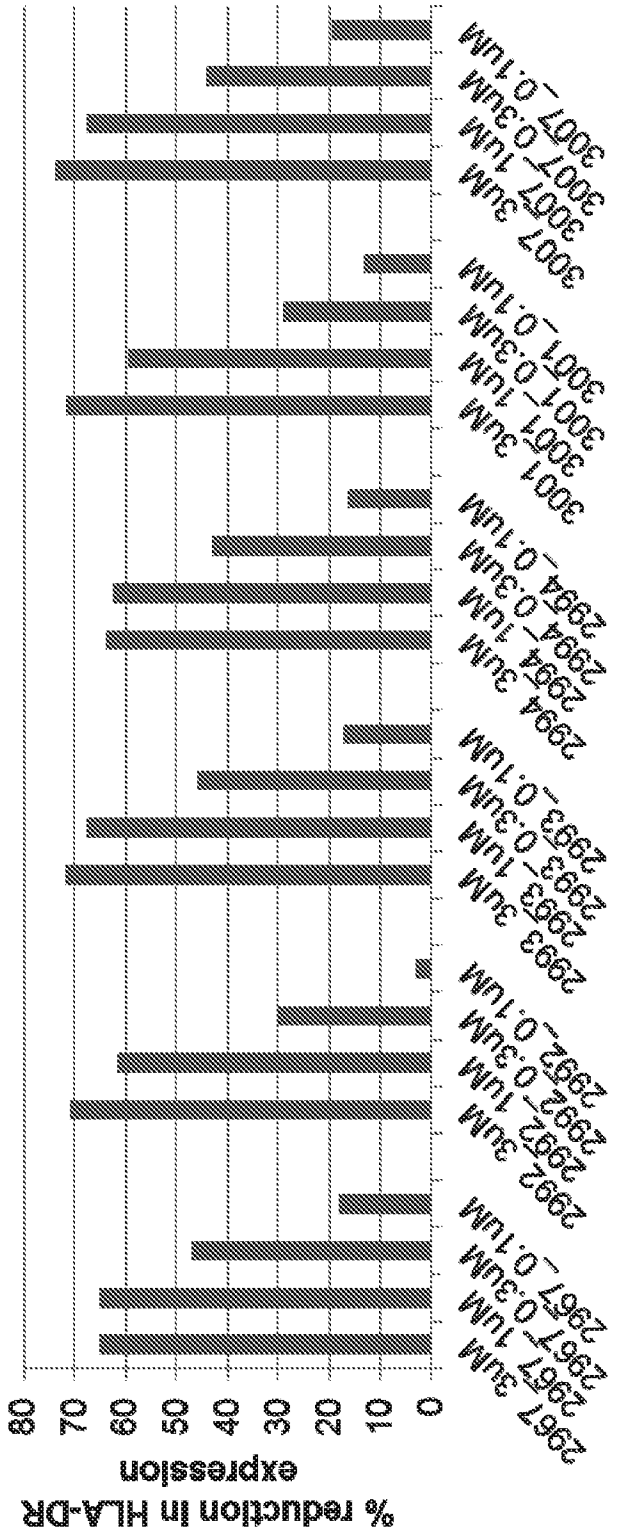

% reduction in HLA-DR expression
0
10
20
30
40
50
60
70
80
2967_3uM
2967_1uM
2967_0.3uM
2967_0.1uM
2992_3uM
2992_1uM
2992_0.3uM
2992_0.1uM
2993_3uM
2993_1uM
2993_0.3uM
2993_0.1uM
2994_3uM
2994_1uM
2994_0.3uM
2994_0.1uM
3001_3uM
3001_1uM
3001_0.3uM
3001_0.1uM
3007_3uM
3007_1uM
3007_0.3uM
3007_0.1uM

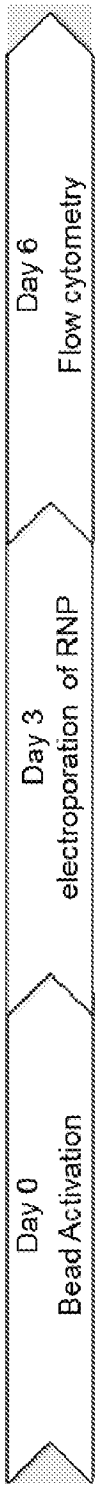
FIG.42

Guide RNA	% indels (avg)	% frameshift edits (avg)
CR002967	95.35	84.59
CR002992	94.82	60.91
CR002993	96.09	65.11
CR003007	96.16	82.93

FIG.43

Guide-Treatment	Variant Read	Frequency (avg)	Avg(Indel Length)	UniqueConsensus(Call)
CR002987	GCAGCTCACAGTGTGCCACCATGGAGTTGGGCCCCTAGAAGGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCC	36.70%	1	Frameshift
CR002987	GCAGCTCACAGTGTGCCACCATGGAGTTGGG---TAGAAGGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCC	4.83%	-4	Frameshift
CR002987	GCAGCTCACAGTGTGCCACCATGGAGTTGGGCCCC-AGAAGGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCC	2.38%	-1	Frameshift
CR002987	GCAGCTCACAGTGTGCCACCATGGAG----------CTTCTTAACAGCGATGCTGACCCC	2.52%	-30	In Frame
CR002987	GCAGCTCACAGTGTGCCACCATGGAGTTGGGGC----------TACCTGGAGCTTCTTAACAGCGATGCTGACCCC	2.30%	-14	Frameshift
CR002987	GCAGCTCACAGTGTGCCACCATGGAGTTGGG----TAGAAGGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCC	2.01%	-5	Frameshift
CR002987	GCAGCTCACAGTGTGCCACCATGGAGTTGG----------CTACCTGGAGCTTCTTAACAGCGATGCTGACCCC	1.90%	-16	Frameshift
CR002987	GCAGCTCACAGTGTGCCACC----------TGGAGCTTCTTAACAGCGATGCTGACCCC	1.85%	-31	Frameshift
CR002987	GCAGCTCACAGTGTGCCACCATGGAGTTGGGCCC-TAGAAGGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCC	1.82%	-1	Frameshift
CR002987	GCAGCTCACAGTGTGCCACCATGGAGTTGGGG----AGAAGGTGGCTACCTGGAGCTTCTTAACAGCGATGCTGACCCC	1.81%	-5	Frameshift
CR002992	CAGCAGGCTGTTGTGTGACATGGAAGGTGATGAAGA-CCAGGGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGC	6.88%	-2	Frameshift
CR002992	CAGCAGGCTGTTGTGTGACATGGAAGGTGATGAAGA-ACCAGGGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGC	4.03%	-1	Frameshift
CR002992	CAGCAGGCTGTTGTGTGACATGGAAGG----------GAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGC	3.52%	-15	Frameshift
CR002992	CAGCAGGCTGTTGTGTGACATGGAAGAG----------GCTTATGCCAATATCGGTGAGGAAGCACCTGAGC	3.35%	-9	In Frame
CR002992	CAGCAGGCTGTTGTGTGACATGGAAGG----------CTTATGCCAATATCGGTGAGGAAGCACCTGAGC	3.06%	-20	Frameshift
CR002992	CAGCAGGCTGTTGTGTGACATGGAAGGTGATGAAGAG--CAGGGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGC	2.59%	-2	Frameshift
CR002992	CAGCAGGCTGTTGTGTGACATGGAAGGTGATGAAG----GGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGC	2.19%	-7	Frameshift
CR002992	CAGCAGGCTGTTGTGTGACA----------GGGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGC	2.04%	-21	In Frame
CR002992	CAGCAGGCTGTTGTGTGACATGGAAGGTGA----------GGAAGCACCTGAGC	2.02%	-36	In Frame
CR002992	CAGCAGGCTGTTGTGTGACATGGAAGGTGATGAA---CCAGGGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGC	2.01%	-4	Frameshift
CR002993	AGCAGGCTGTTGTGTGACATGAAGAG-CCACGGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGCC	16.80%	-1	Frameshift
CR002993	AGCAGGCTGTTGTGTGACATGGAAGGTGATGAAGAGaCCAGGGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGCC	8.07%	1	Frameshift
CR002993	AGCAGGCTGTTGTGTGACATGGAAGGTGA----------GGAAGCACCTGAGCC	4.44%	-36	In Frame
CR002993	AGCAGGCTGTTGTGTGACATGGAAGG----------CTTATGCCAATATCGGTGAGGAAGCACCTGAGCC	3.00%	-20	Frameshift
CR002993	AGCAGGCTGTTGTGTGACATGGAAGGTGATG----------CCAATATCGGTGAGGAAGCACCTGAGCC	2.77%	-21	In Frame
CR002993	AGCAGGCTGTTGTGTGACATGGAAGGTGATGAAGAG----------GCTTATGCCAATATCGGTGAGGAAGCACCTGAGCC	2.71%	-9	In Frame
CR002993	AGCAGGCTGTTGTGTGACATGGAAGG----------GAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGCC	2.48%	-16	Frameshift
CR002993	AGCAGGCTGTTGTGTGACATGGAAGGTGATGAAGA-CCAGGGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGCC	2.15%	-2	Frameshift
CR002993	AGCAGGCTGTTGTGTGACATGGAAGGTGATGAAG----------GCAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGCC	1.97%	-7	Frameshift
CR002993	AGCAGGCTGTTGTGTGACATGGAAGGTGATGAAGAGAC-AGGGAGGCTTATGCCAATATCGGTGAGGAAGCACCTGAGCC	1.77%	-1	Frameshift
CR003007	TTTTTCTCAAAGTAGAGCACATAGGACCAGATGAAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAA	46.85%	1	Frameshift
CR003007	TTTTTCTCAAAGTAGAGCACATAGGACCAGAT----------CGGTGAGAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAA	4.85%	-8	Frameshift
CR003007	TTTTTCTCAAAGTAGAGCACATAGGACCAGATGA--TGATCGGTGAGAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAA	2.52%	-2	Frameshift
CR003007	TTTTTCTCAAAGTAGAGCACATAGGACCAGATGA----TCGGTGAGAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAA	2.28%	-5	Frameshift
CR003007	TTTTTCTCAAAGTAGAGCACATAGGACCAGATGA----------GAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAA	2.18%	-12	In Frame
CR003007	TTTTTCTCAAAGTAGAGCACATAGGACCAGATGAAG--ATCGGTGAGAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAA	1.84%	-2	Frameshift
CR003007	TTTTTCTCAAAGTAGAGCACATAGGACCAGATGAA-TGATCGGTGAGAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAA	1.42%	-1	Frameshift
CR003007	TTTTTCTCAAAGTAGAGCACATAGGACCAGATG---TGATCGGTGAGAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAA	1.38%	-3	In Frame
CR003007	TTTTTCTCAAAGTAGAGCACATAGGACCAGAT----TGATCGGTGAGAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAA	1.09%	-4	Frameshift
CR003007	TTTTTCTCAAAGTAGAGCACATAGGACCAGATGA---GATCGGTGAGAGTATGGAGATGCCAGCAGAAGTTGGGCAGAAA	0.99%	-3	In Frame

FIG. 44



	Controls		single editing controls [RNP] uM			Triple Editing conditions [RNP] uM			
Dual gRNAs	No EP	No Guide	B2M	TRAC	CIITA	Triple 1	Triple 2	Triple 3	Triple 4
TRAC CR000961				0.3		1	0.3	0.3	0.3
B2M CR00442			0.4			1	0.4	0.4	0.4
CIITA CR002991					1	1	2.3	1	0.3
Total RNP in cells	0	0	0.4	0.3	1	3	3	1.7	1

FIG.45

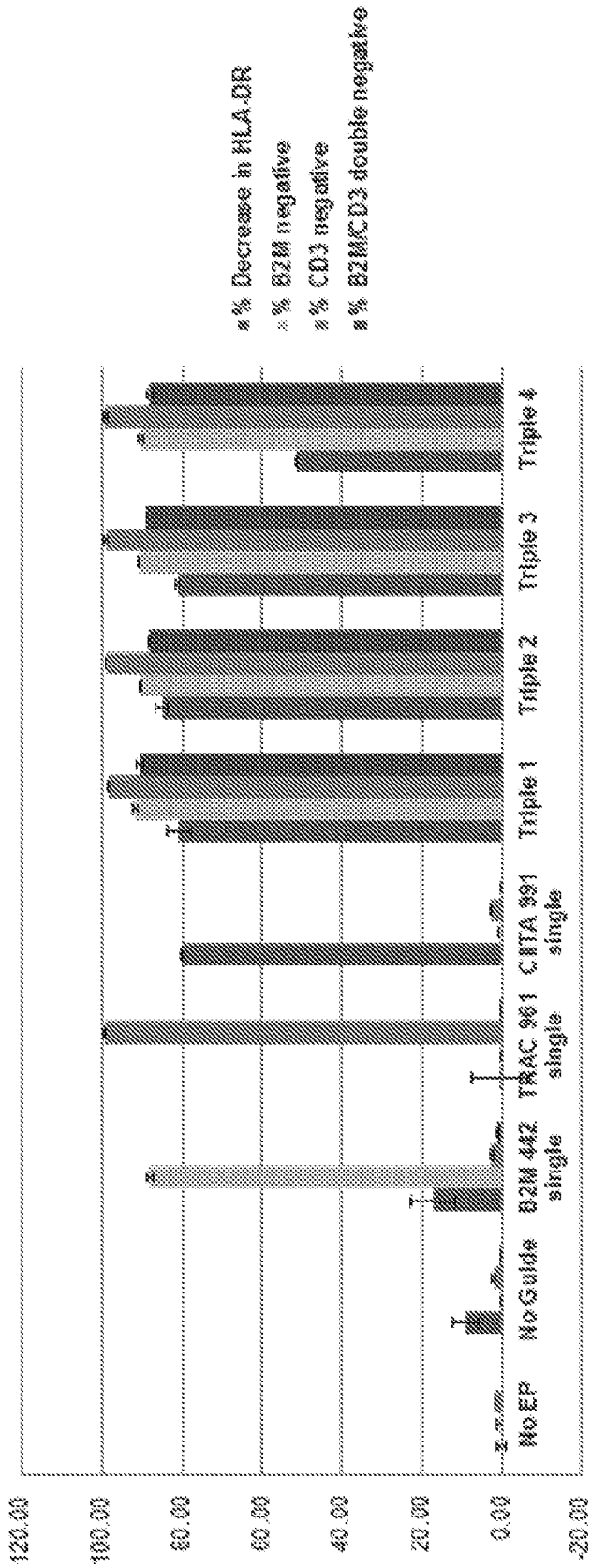

% Decrease in HLA-DR
% B2M negative
% CD3 negative
% B2M/CD3 double negative
120.00
100.00
80.00
60.00
40.00
20.00
0.00
-20.00
No EP
No Guide
B2M 442 single
TRAC 961 single
CIITA 991 single
Triple 1
Triple 2
Triple 3
Triple 4

FIG.46

%indels (frameshifts)

	Triple 1	Triple 2	Triple 3	Triple 4
B2M locus *	92.71 (39.46)	84.51 (38.33)	94.75 (39.20)	94.94 (39.16)
TRAC locus	93.11 (74.95)	93.89 (77.08)	94.82 (76.85)	96.08 (77.97)
CIITA locus	90.59 (60.87)	96.44 (63.63)	90.78 (60.79)	58.69 (40.69)

*Frameshift calculation for this guide does not include edits that alter or remove the start codon, so is an underestimate of disruptions of the coding sequence

FIG. 47

Guide Treatment	Variant Read	Avg(Indel Length)	Avg(Hit % of reads)	UniqueConcatCall)
triple1_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	1	10.10%	Frameshift
triple1_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCG----------CTCGGTGGCCTTAGCTGTGCTCGCGCT	-15	8.68%	In Frame
triple1_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCG----------TGGCCTTAGCTGTGCTCGCGCT	-15	6.97%	In Frame
triple1_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCC----------TAGCTGTGCTCGCGCT	-21	6.08%	In Frame
triple1_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	-1	5.63%	Frameshift
triple1_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGAT-GTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	-2	3.99%	Frameshift
triple1_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGC----------TCGGTGGCCTTAGCTGTGCTCGCGCT	-21	3.75%	In Frame
triple1_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCG----------TGGCCTTAGCTGTGCTCGCGCT	-20	1.92%	Frameshift
triple1_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCAT----------CCGTGGCCTTAGCTGTGCTCGCGCT	-20	1.69%	Frameshift
triple1_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGAATGTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	1	1.38%	Frameshift
triple2_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCG----------CTCGTGGCCTTAGCTGTGCTCGCGCT	-15	10.73%	In Frame
triple2_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	1	10.00%	Frameshift
triple2_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCG----------TGGCCTTAGCTGTGCTCGCGCT	-15	7.84%	In Frame
triple2_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCC----------TAGCTGTGCTCGCGCT	-21	5.96%	In Frame
triple2_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGA-GTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	-1	4.33%	Frameshift
triple2_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGC----------TCGTGGCCTTAGCTGTGCTCGCGCT	-21	3.80%	In Frame
triple2_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGAT-CTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	-2	3.42%	Frameshift
triple2_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGAATGTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	1	1.61%	Frameshift
triple2_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCAT----------CCGTGGCCTTAGCTGTGCTCGCGCT	-20	1.58%	Frameshift
triple2_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCG----------TGGCCTTAGCTGTGCTCGCGCT	-20	1.46%	Frameshift
triple3_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	1	10.50%	Frameshift
triple3_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCG----------CTCGTGGCCTTAGCTGTGCTCGCGCT	-15	10.46%	In Frame
triple3_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCG----------TGGCCTTAGCTGTGCTCGCGCT	15	8.53%	In Frame
triple3_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCC----------TAGCTGTGCTCGCGCT	-21	6.17%	In Frame
triple3_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGA-GTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	-1	4.40%	Frameshift
triple3_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGAT-CTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	-2	3.40%	Frameshift
triple3_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGC----------TCGTGGCCTTAGCTGTGCTCGCGCT	-21	3.17%	In Frame
triple3_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCG----------TGGCCTTAGCTGTGCTCGCGCT	-20	1.61%	Frameshift
triple3_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCAT----------CCGTGGCCTTAGCTGTGCTCGCGCT	-20	1.47%	Frameshift
triple3_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGAATGTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	-13	1.31%	Frameshift
triple4_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCG----------CTCGTGGCCTTAGCTGTGCTCGCGCT	-15	10.52%	In Frame
triple4_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGATGTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	1	9.54%	Frameshift
triple4_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCG----------TGGCCTTAGCTGTGCTCGCGCT	-15	7.74%	In Frame
triple4_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCC----------TAGCTGTGCTCGCGCT	-21	5.82%	In Frame
triple4_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGA-GTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	-1	5.30%	Frameshift
triple4_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGC----------TCGTGGCCTTAGCTGTGCTCGCGCT	-21	3.35%	In Frame
triple4_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGAT-CTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	-2	3.21%	Frameshift
triple4_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGAATGTCTCGCTCCGGTGGCCTTAGCTGTGCTCGCGCT	1	1.63%	Frameshift
triple4_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCG----------TGGCCTTAGCTGTGCTCGCGCT	-20	1.58%	Frameshift
triple4_442	GTCGCGCTGGCGGGGCATTCCTGAAGCTGACAGCATTCGGGCC----------TCGTGGCCTTAGCTGTGCTCGCGCT	-13	1.46%	Frameshift

FIG. 48

Guide-Treatment	Variant Read	AvgIndel Length)	Avg(Hit % All reads)	UniqueConcatenated(Call)
tripe1_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	53.44%	Frameshift
tripe1_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	2.87%	Frameshift
tripe1_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-11	2.11%	Frameshift
tripe1_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTgAGCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	1.20%	Frameshift
tripe1_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-7	1.09%	Frameshift
tripe1_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGC----TGAGAGACTCTAAATCCAGTGACAAGTC	-11	0.99%	Frameshift
tripe1_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGAC----TCTAAATCCAGTGACAAGTC	-24	0.83%	In Frame
tripe1_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-12	0.77%	In Frame
tripe1_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTG----ACAGACTCTAAATCCAGTGACAAGTC	-14	0.76%	Frameshift
tripe1_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGT-CAGCTGAGAGACTCTAAATCCAGTGACAAGTC	-2	0.70%	Frameshift
tripe2_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	55.11%	Frameshift
tripe2_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	3.23%	Frameshift
tripe2_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-11	2.29%	Frameshift
tripe2_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTgACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	1.41%	Frameshift
tripe2_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-7	0.80%	Frameshift
tripe2_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGC----TGAGAGACTCTAAATCCAGTGACAAGTC	-11	0.79%	Frameshift
tripe2_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTA---GCTGAGAGACTCTAAATCCAGTGACAAGTC	-3	0.70%	In Frame
tripe2_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTTAGC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-12	0.62%	In Frame
tripe2_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTG----ACAGACTCTAAATCCAGTGACAAGTC	-14	0.58%	Frameshift
tripe2_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	2	0.54%	Frameshift
tripe3_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	53.07%	Frameshift
tripe3_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	3.40%	Frameshift
tripe3_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-11	2.26%	Frameshift
tripe3_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-7	1.56%	Frameshift
tripe3_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTgACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	1.34%	Frameshift
tripe3_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGC----TGAGAGACTCTAAATCCAGTGACAAGTC	-11	1.26%	Frameshift
tripe3_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGAGC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-12	0.95%	In Frame
tripe3_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGT-CAGCTGAGAGACTCTAAATCCAGTGACAAGTC	-2	0.72%	Frameshift
tripe3_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTAaCCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	2	0.61%	Frameshift
tripe3_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTG-ACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	0.55%	Frameshift
tripe4_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	54.94%	Frameshift
tripe4_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	3.18%	Frameshift
tripe4_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-11	2.55%	Frameshift
tripe4_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-7	1.29%	Frameshift
tripe4_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTG----TGAGAGACTCTAAATCCAGTGACAAGTC	-11	1.21%	Frameshift
tripe4_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTGTgACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	1	1.16%	Frameshift
tripe4_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTGCCGTG-ACCAGCTGAGAGACTCTAAATCCAGTGACAAGTC	-1	0.69%	Frameshift
tripe4_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACCCTG----AGAGACTCTAAATCCAGTGACAAGTC	-14	0.68%	Frameshift
tripe4_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGAC----TCTAAATCCAGTGACAAGTC	-24	0.61%	In Frame
tripe4_961	TGATCCTCTTGTCCCACAGATATCCAGAACCTGACC----AGCTGAGAGACTCTAAATCCAGTGACAAGTC	-12	0.59%	In Frame

FIG.49

Guide-Treatment	Variant Read	Avg(Indel Length)	Avg(Hit reads)	% All Unique Constructs	Effect(Call)
triple1_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGACATGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	1	29.49%		Frameshift
triple1_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGA----------TGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-12	8.62%		In Frame
triple1_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGACA-GGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-1	5.91%		Frameshift
triple1_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGAC-TGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-1	3.56%		Frameshift
triple1_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTG----------ATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-14	2.56%		Frameshift
triple1_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGAC--GGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-2	1.80%		Frameshift
triple1_2991	AACTGCGACCAGTTCAGCAGCCTGTTGTGTGA----------AGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-15	1.39%		In Frame
triple1_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGA-TGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-2	1.24%		Frameshift
triple1_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTG----GAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-5	1.08%		Frameshift
triple1_2991	AACTGCGACCAGTTCAGCAGG----------TGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-20	1.02%		Frameshift
triple2_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGACATGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	1	29.14%		Frameshift
triple2_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGA----------TGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-12	9.96%		In Frame
triple2_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGACA-GGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-1	7.00%		Frameshift
triple2_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGAC-TGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-1	4.57%		Frameshift
triple2_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTG----------ATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-14	3.04%		Frameshift
triple2_2991	AACTGCGACCAGTTCAGCAGCCTGTTGTGTGA----------AGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-15	1.59%		In Frame
triple2_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTG----GAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-2	1.44%		Frameshift
triple2_2991	AACTGCGACCAG----------GGAGGCTTATGCCAATATCGGTGA	-44	1.33%		Frameshift
triple2_2991	AACTGCGACCAGTTCAGCAGCCTGTTGTC----GAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-5	1.29%		Frameshift
triple2_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGA-TGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-3	1.21%		Frameshift
triple3_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGACATGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	1	30.73%		Frameshift
triple3_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGA----------TGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-12	9.24%		In Frame
triple3_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGACA-GGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-1	6.04%		Frameshift
triple3_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGAC-TGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-1	3.21%		Frameshift
triple3_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTG----------ATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-14	2.79%		Frameshift
triple3_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGAC-GGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	2	1.72%		Frameshift
triple3_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGA----------ATGAAGACCAGGGAGGCTTATGCCAATATCGGTGA	-15	1.45%		In Frame
triple3_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGA--TGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-2	1.10%		Frameshift
triple3_2991	AACTGCGACCAGTTCAGCAGC----------GACGCTTATGCCAATATCGGTGA	-36	0.83%		In Frame
triple3_2991	AACTGCGACCAG----------GGAGGCTTATGCCAATATCGGTGA	-44	0.82%		Frameshift
triple4_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGACATGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	1	22.66%		Frameshift
triple4_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGA----------TGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-12	4.92%		In Frame
triple4_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTGACA-GGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-1	4.45%		Frameshift
triple4_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGAC-TGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-1	1.83%		Frameshift
triple4_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGAC--GGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-2	1.08%		Frameshift
triple4_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGTC----------ATGAACAGACCAGGGAGGCTTATGCCAATATCGGTGA	-14	0.79%		Frameshift
triple4_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGA--TGGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-2	0.74%		Frameshift
triple4_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTG----GGAAGGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-4	0.65%		Frameshift
triple4_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGA----------AGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-15	0.60%		In Frame
triple4_2991	AACTGCGACCAGTTCAGCAGGCTGTTGTGA----------ACGTGATGAAGAGACCAGGGAGGCTTATGCCAATATCGGTGA	-6	0.57%		In Frame

FIG. 50

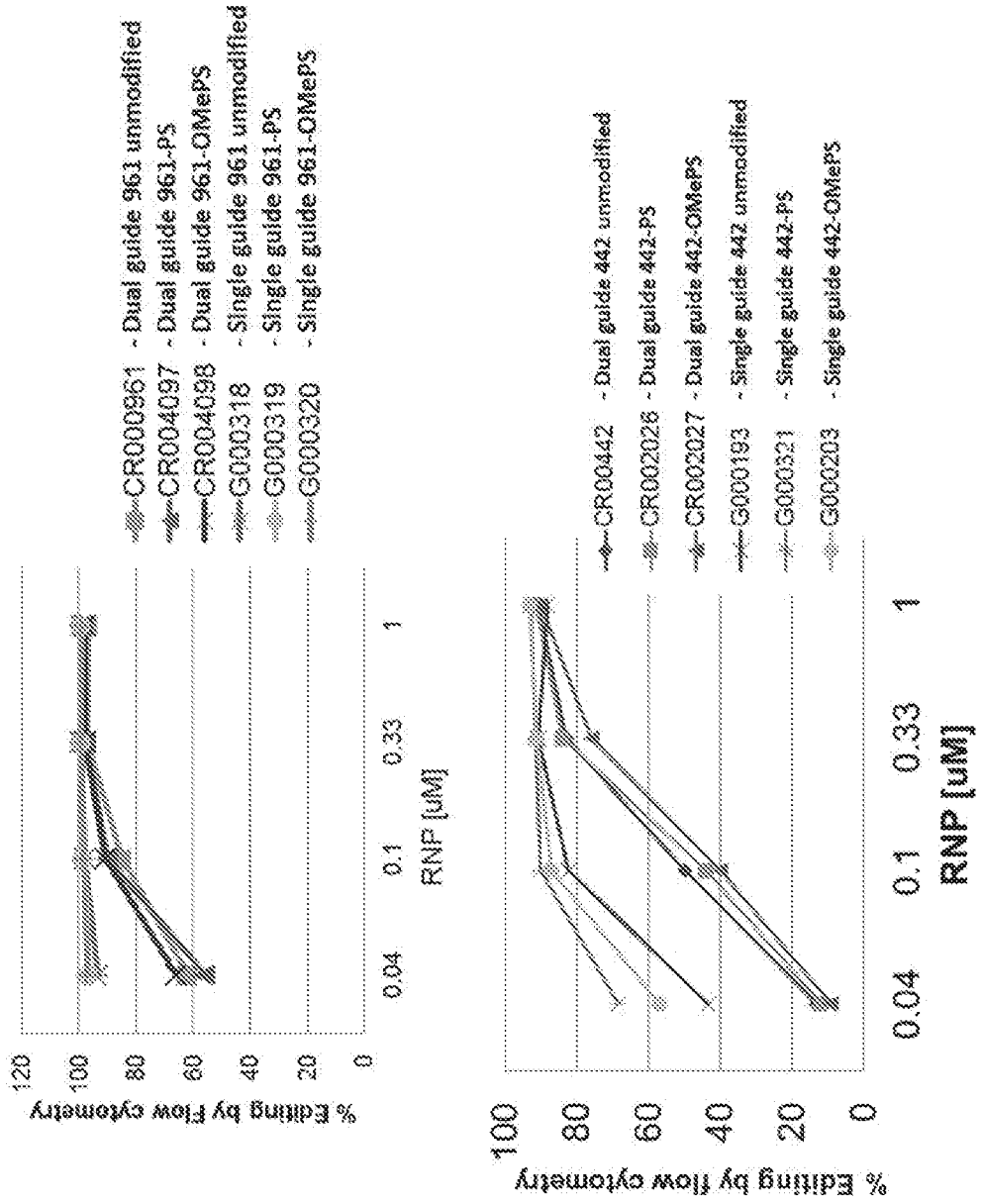

% Editing by flow cytometry
120
100
80
60
40
20
0
0.04
0.1
0.33
1
RNP [uM]
CR000961 - Dual guide 961 unmodified
CR004097 - Dual guide 961-PS
CR004098 - Dual guide 961-OMePS
G000318 - Single guide 961 unmodified
G000319 - Single guide 961-PS
G000320 - Single guide 961-OMePS
% Editing by flow cytometry
100
80
60
40
20
0
0.04
0.1
0.33
1
RNP [uM]
CR00442 - Dual guide 442 unmodified
CR002026 - Dual guide 442-PS
CR002027 - Dual guide 442-OMePS
G000193 - Single guide 442 unmodified
G000321 - Single guide 442-PS
G000203 - Single guide 442-OMePS

FIG.51

Guide RNA	% indels (avg)	% frameshift edits (avg)
CR002100	91.11	73.28
CR002097	90.89	81.82
CR002091	89.72	68.92
CR002086	81.52	67.04
CR002085	85.33	64.22

FIG. 52

Guide-Treatment	Variant Read	Indel frequency (avg)	Indel length (avg)	Unique Concatenate(Call)
CR002100	CCCCTCCCCGCTGGCCCCCGACTCACCGGTGTAGTGCACCACGCAGGTCTGGCCGCGCT	27.04%	1	Frameshift
CR002100	CCCCTCCCCGCTGGCCCCCGA-TCACCGGTGTAGTGCACCACGCAGGTCTGGCCGCGCT	5.77%	-1	Frameshift
CR002100	CCCCTCCCCGCTGGCCCCCGAC--ACCGGTGTAGTGCACCACGCAGGTCTGGCCGCGCT	3.92%	-2	Frameshift
CR002100	CCCCTCCCCGCTGGCCCCCCG--TCACCGGTGTAGTGCACCACGCAGGTCTGGCCGCGCT	3.59%	-2	Frameshift
CR002100	CCCCTCCCCG----------GTGTAGTGCACCACGCAGGTCTGGCCGCGCT	3.31%	-19	Frameshift
CR002097	CTGGGCCCCCCGACTCACCGGTGTAGTGCACCACGCAaGGTCTGGCCGCGCTTGGGGAAGGT	59.62%	1	Frameshift
CR002097	CTGGGCCCCCCGACTCACCGGTGTAGTGCACCACGCA--CTGGCCGCGCTTGGGGAAGGT	2.24%	-3	In Frame
CR002097	CTGGGCCCCCCGACTCACCGGTGTAGTGCACCACGCA---TGGCCGCGCTTGGGGAAGGT	1.94%	-4	Frameshift
CR002097	CTGGGCCCCCCGACTCACCGGTGTAGTGCACCACGCA--TCTGGCCGCGCTTGGGGAAGGT	1.86%	-2	Frameshift
CR002097	CTGGGCCCCCCGACTCACCGGTGTAGTGCACCACGC----------TTGGGGAAGGT	1.47%	-14	Frameshift
CR002091	CAGGTCTGGCCGCGCTTGGGGAAGGTGCGCCCTGAG-AGACAGAGACGGGCATGCTGAGC	40.37%	-1	Frameshift
CR002091	CAGGTCTGGCCGCGCTTGGGGAAGGTGCGCCCTGAGGgAGACAGAGACGGGCATGCTGAGC	9.41%	1	Frameshift
CR002091	CAGGTCTGGCCGCGCTTGGGGAAGGTGCGCCCTGAG--ACAGAGACGGGCATGCTGAGC	7.55%	-3	In Frame
CR002091	CAGGTCTGGCCGCGCTTGGGGAAGGTGCGCCCTG-GGAGACAGAGACGGGCATGCTGAGC	4.87%	-1	Frameshift
CR002091	CAGGTCTGGCCGCGCTTGGGGAAGGTGCGCCCTGA----CAGAGACGGGCATGCTGAGC	1.61%	-5	Frameshift
CR002086	GAGCCGCCGCGCGCCACTACTCACCGTCTCCTGGG-AGATGGTTTCCACCTGCACTCCCA	28.55%	-1	Frameshift
CR002086	GAGCCGCCGCGCGCCACTACTCACCGTCTCCTGGC---ATGGTTTCCACCTGCACTCCCA	5.26%	-3	In Frame
CR002086	GAGCCGCCGCGCGCCACTACTCACCGTCTCCTGG--AGATGGTTTCCACCTGCACTCCCA	4.68%	-2	Frameshift
CR002086	GAGCCGCCGCGCGCCACTACTCACC----------TGCACTCCCA	4.21%	-25	Frameshift
CR002086	GAGCCGCCGCGCGCCACTACTCACCGTCTCCTG----------CACTCCCA	3.91%	-19	Frameshift
CR002085	GGGAGATGGTTTCCACCTGCACTCC-ATGGCGGCGGCGACGCTGAGCGCGGCGGCG	31.48%	-1	Frameshift
CR002085	GGGAGATGGTTTCCACCTGCACTC--ATGGCGGCGGCGACGCTGAGCGCGGCGGCG	6.10%	-2	Frameshift
CR002085	GGGAGATGGTTTCCACCTGCACTCCATGGCGGCGGCGACGCTGAGCGCGGCGGCG	4.66%	0	In Frame
CR002085	GGGAGATGGTTTCCACCTGCAC--CCATGGCGGCGGCGACGCTGAGCGCGGCGGCG	4.62%	-2	Frameshift
CR002085	GGGAGATGGTTTCCACCTGCAC---CATGGCGGCGGCGACGCTGAGCGCGGCGGCG	1.70%	-3	In Frame

FIG.53

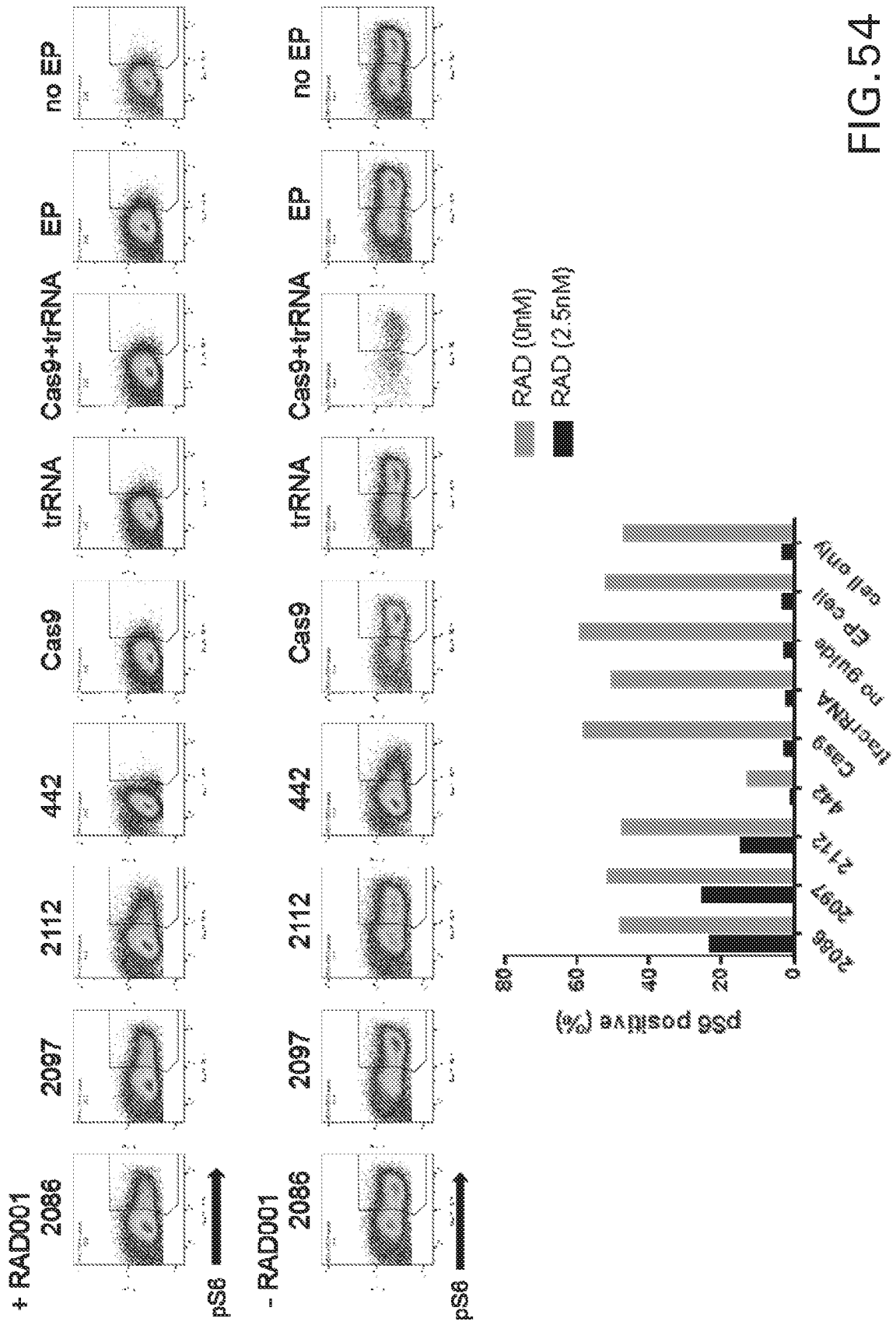

+ RAD001
- RAD001
2086
2097
2112
442
Cas9
trRNA
Cas9+trRNA
EP
no EP
pS6
RAD (0nM)
RAD (2.5nM)
pS6 positive (%)
0
20
40
60
80
2086
2097
2112
442
Cas9
trRNA
no Guide
EP cell
cell only

FIG.54

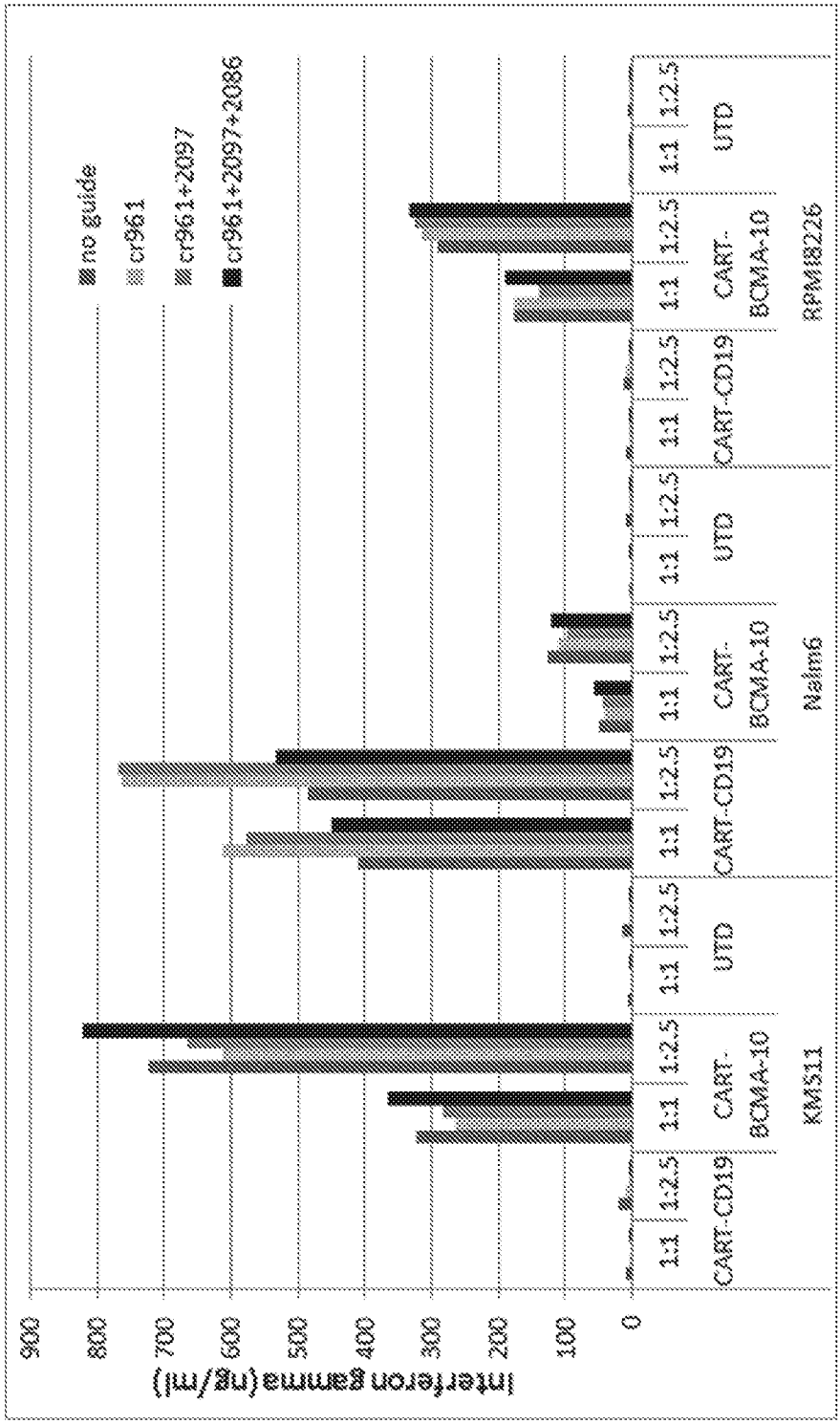

interferon gamma (ng/ml)
900
800
700
600
500
400
300
200
100
0
no guide
cr961
cr961+2097
cr961+2097+2086
1:1
1:2.5
CART-CD19
CART-BCMA-10
UTD
KMS11
Nalm6
RPMI8226

FIG.55A

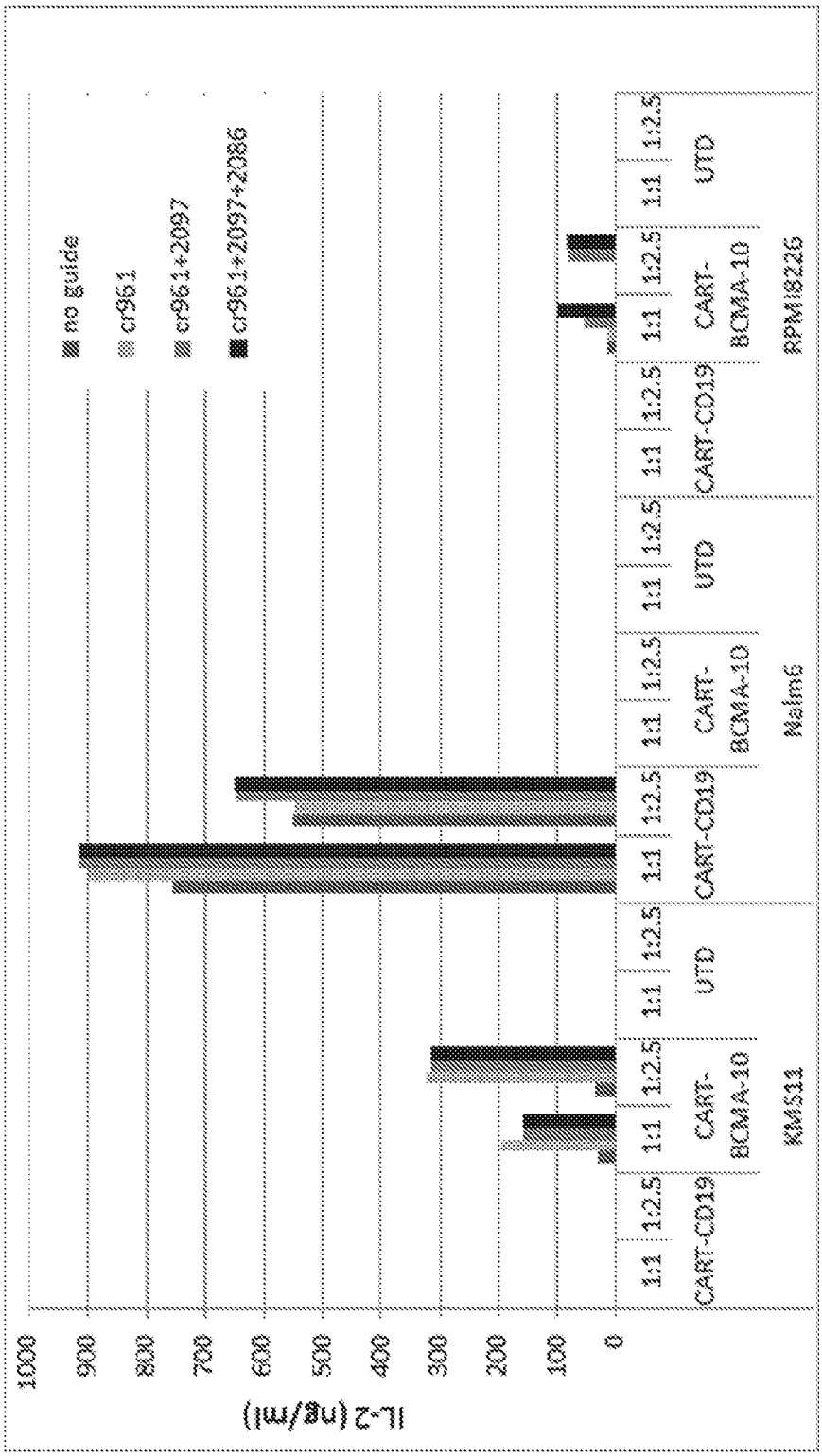

IL-2 (ng/ml)
1000
900
800
700
600
500
400
300
200
100
0
no guide
cr961
cr961+2097
cr961+2097+2086
CART-CD19
CART-BCMA-10
UTD
1:1
1:2.5
KMS11
Nalm6
RPMI8226

FIG. 55B

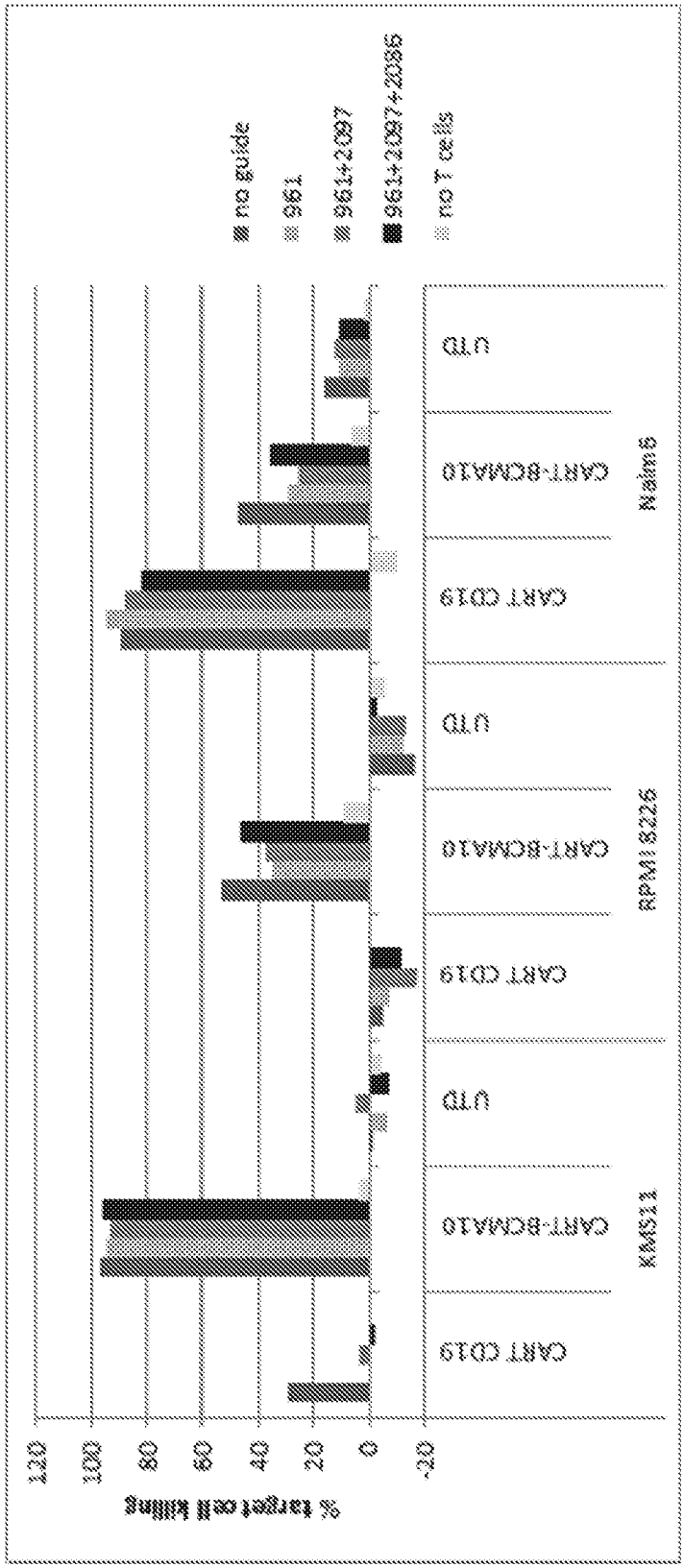

no guide
961
961+2097
961+2097+2086
no T cells
% target cell killing
120
100
80
60
40
20
0
-20
CART CD19
CART-BCMA10
UTD
KMS11
CART CD19
CART-BCMA10
UTD
RPMI 8226
CART CD19
CART-BCMA10
UTD
Naima

FIG.56

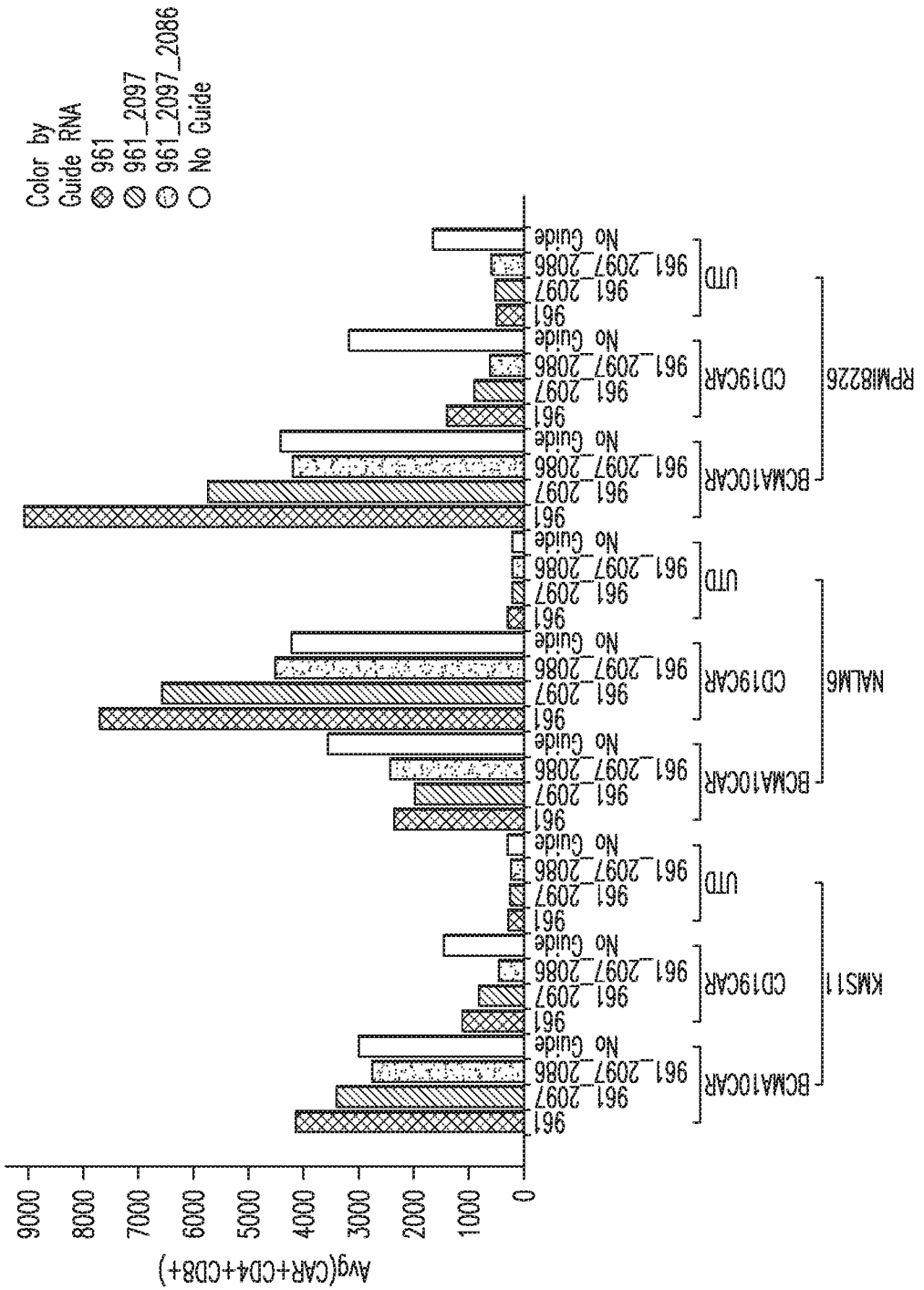

Color by
Guide RNA
961
961_2097
961_2097_2086
No Guide
Avg(CAR+CD4+CD8+)
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
KMS11
NALM6
RPMI8226
BCMA10CAR
CD19CAR
UTD
961
961_2097
961_2097_2086
No Guide
Target, Effector, Guide RNA

FIG.57

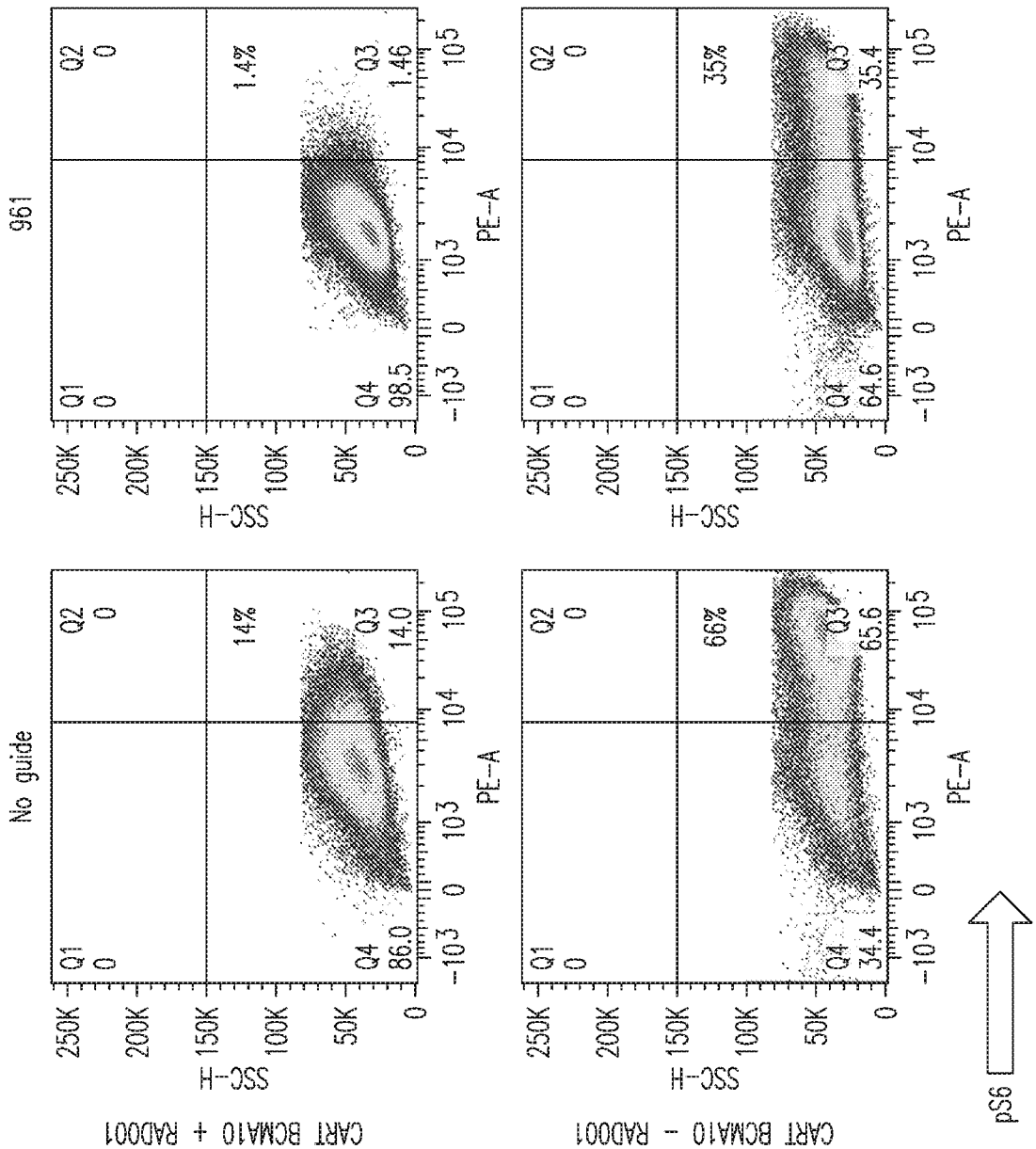

961
No guide
CART BCMA10 + RAD001
CART BCMA10 - RAD001
SSC-H
PE-A
Q1
Q2
Q3
Q4
1.4%
98.5
1.46
14%
86.0
14.0
35%
64.6
35.4
66%
34.4
65.6
pS6

FIG.58A-1

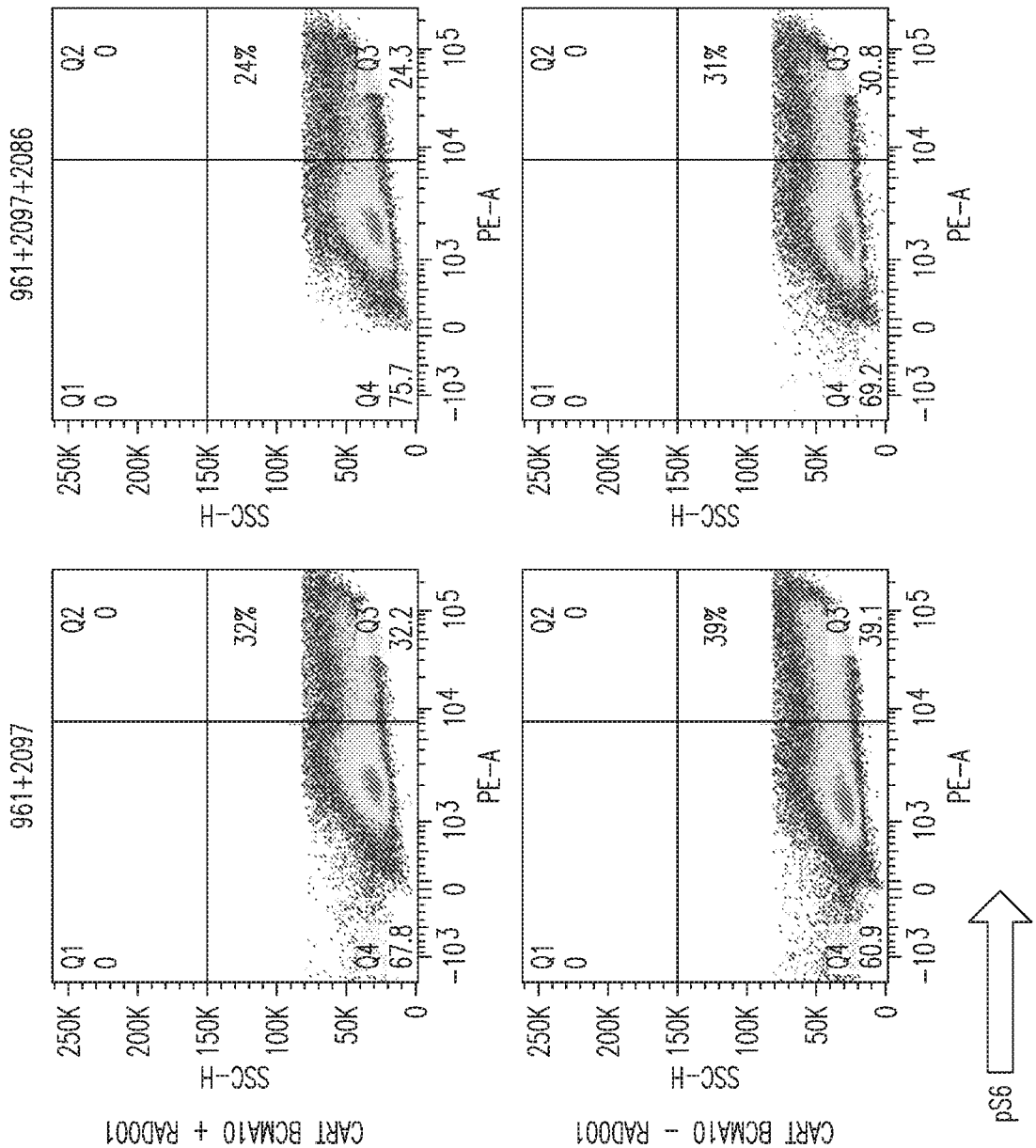

961+2097+2086
961+2097
CART BCMA10 + RAD001
CART BCMA10 - RAD001
SSC-H
PE-A
pS6
Q1
Q2
Q3
Q4
24%
32%
31%
39%
75.7
24.3
67.8
32.2
69.2
30.8
60.9
39.1

FIG.58A-2

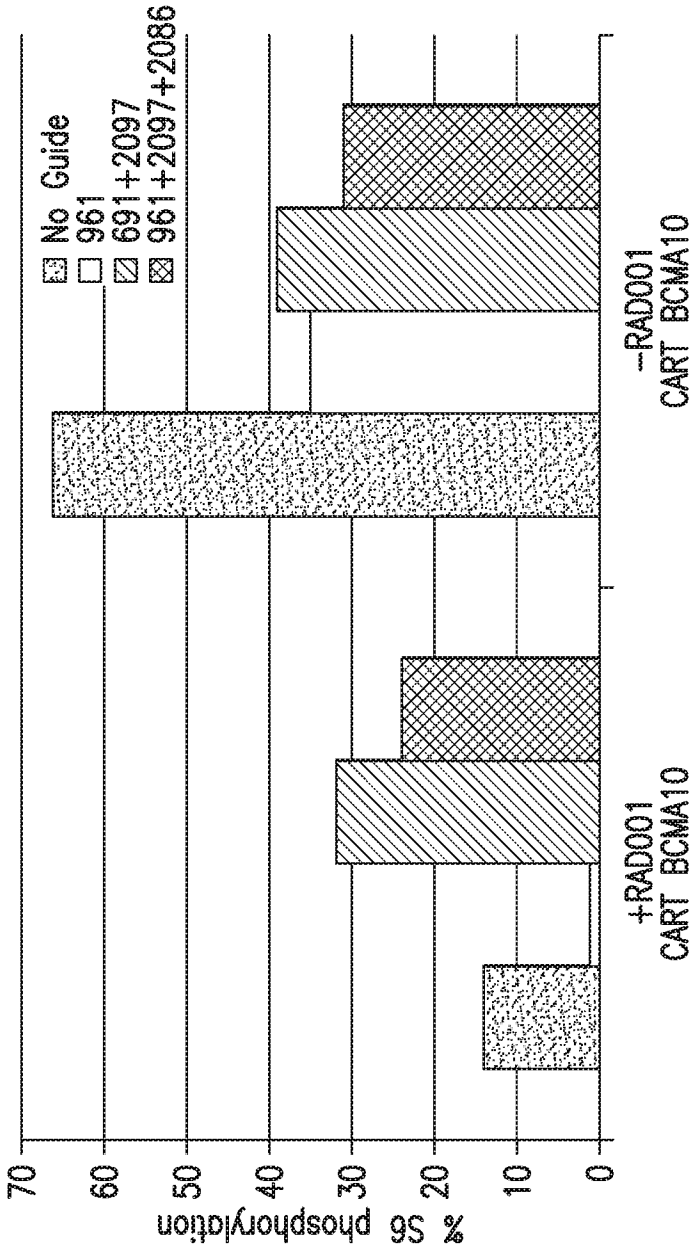

No Guide
961
691+2097
961+2097+2086
% S6 phosphorylation
0
10
20
30
40
50
60
70
+RAD001
CART BCMA10
-RAD001
CART BCMA10

FIG.58A-3

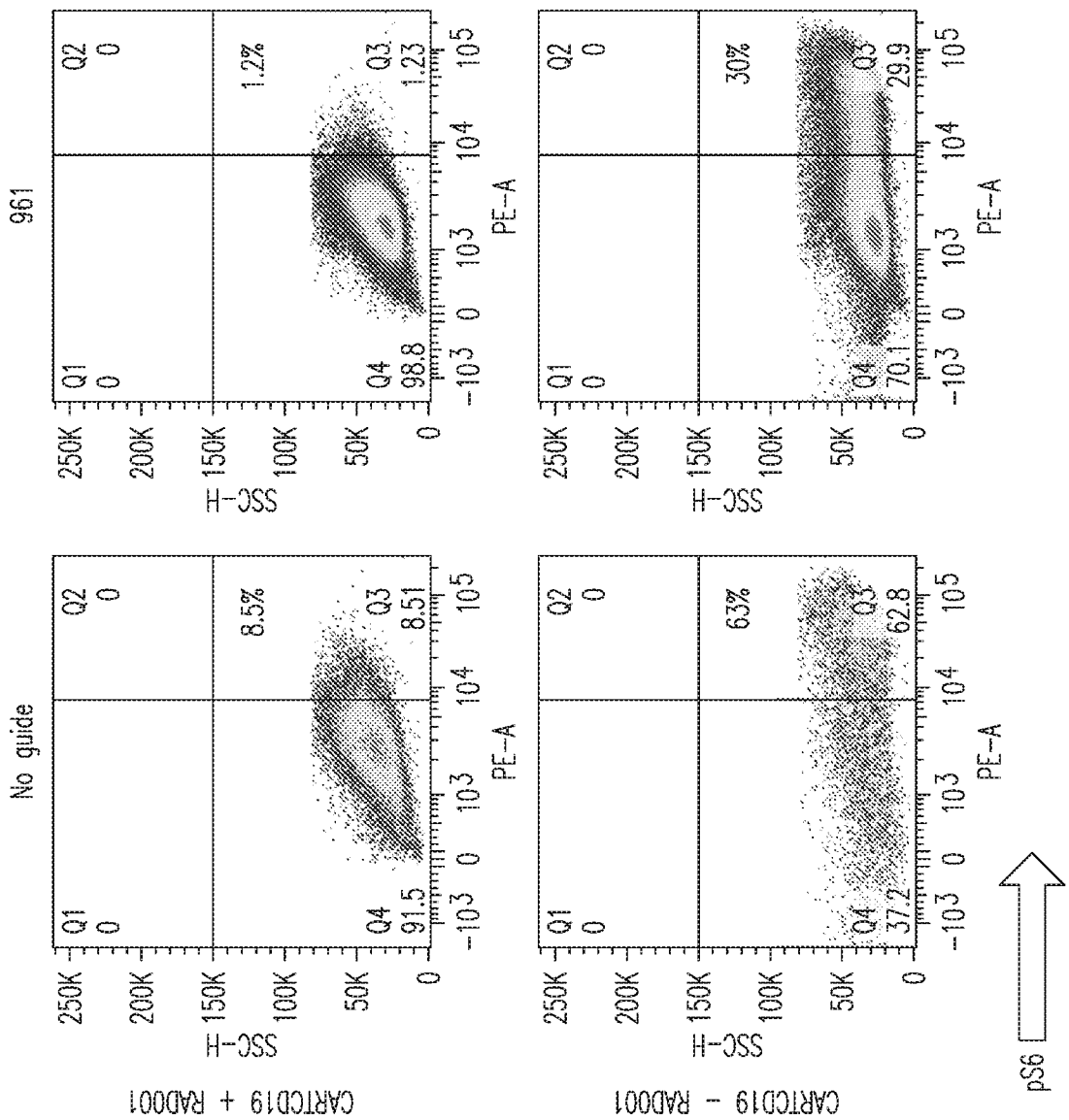

961
No guide
CART CD19 + RAD001
CART CD19 - RAD001
SSC-H
PE-A
pS6
Q1
Q2
Q3
Q4
1.2%
1.23
98.8
8.5%
8.51
91.5
30%
29.9
70.1
63%
62.8
37.2

FIG. 58B-1

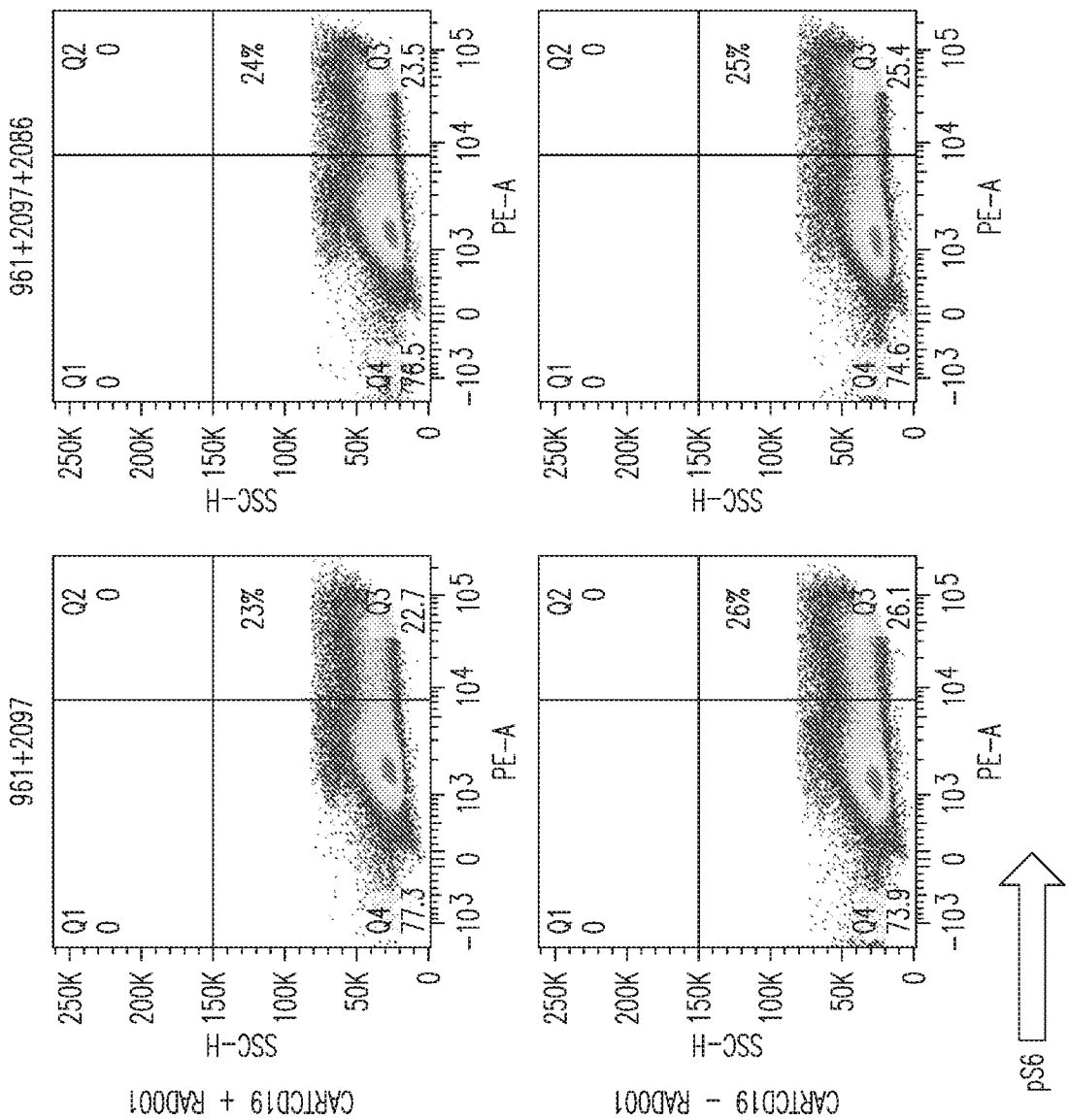

961+2097+2086
961+2097
CARTCD19 + RAD001
CARTCD19 - RAD001
SSC-H
PE-A
pS6
Q1
Q2
Q3
Q4
24%
23%
25%
26%
76.5
77.3
74.6
73.9
23.5
22.7
25.4
26.1

FIG.58B-2

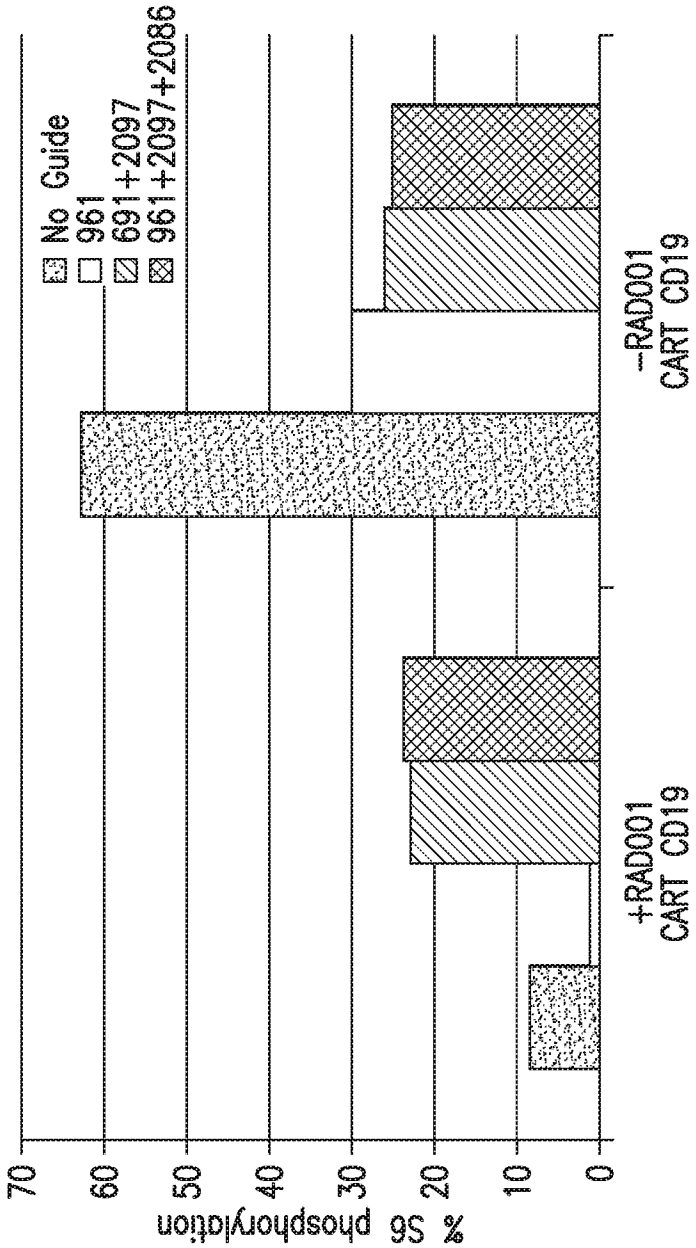

No Guide
961
691+2097
961+2097+2086
% S6 phosphorylation
70
60
50
40
30
20
10
0
+RAD001
CART CD19
-RAD001
CART CD19

FIG.58B-3

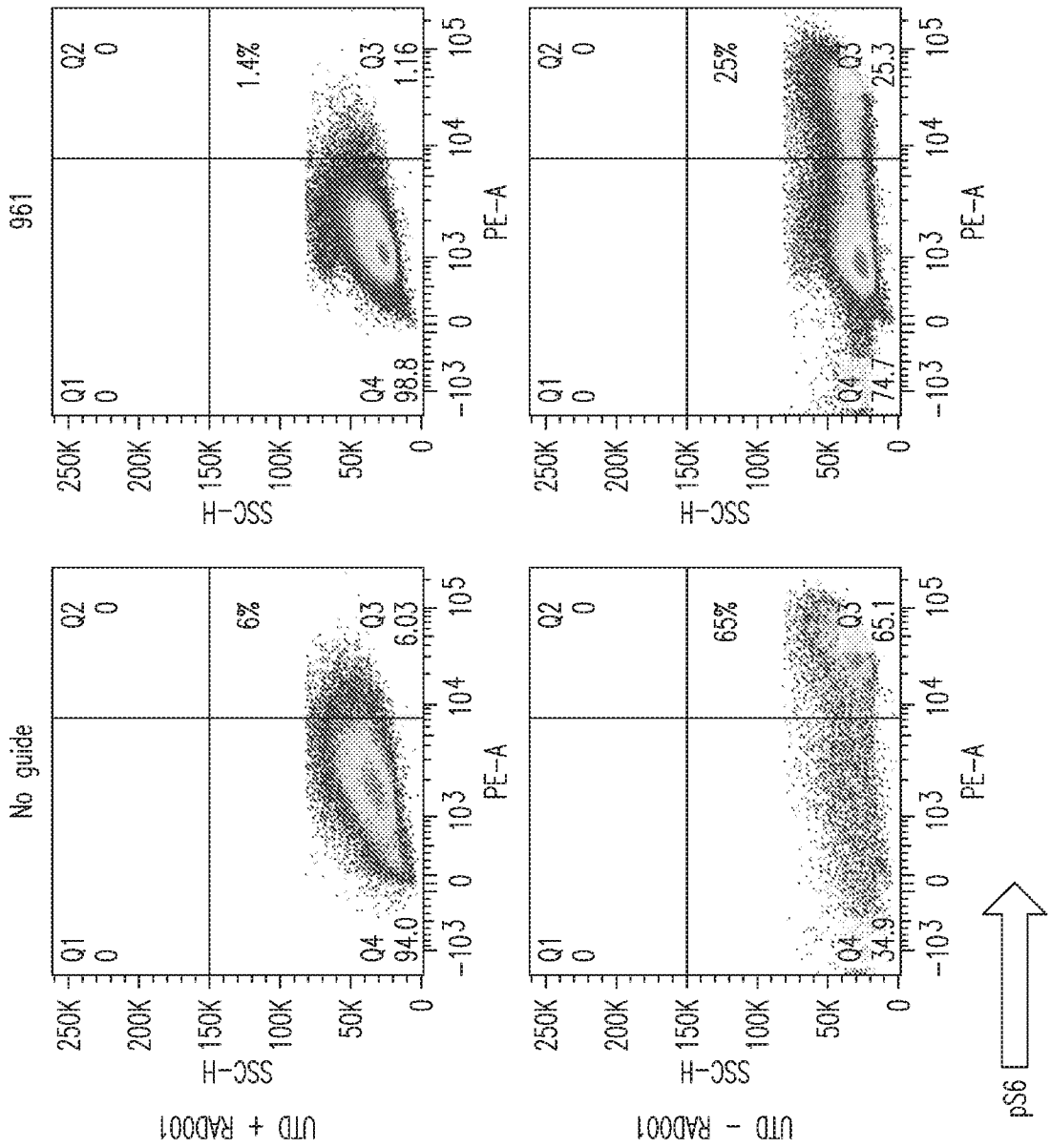

961
No guide
UTD + RAD001
UTD - RAD001
SSC-H
PE-A
Q1
Q2
Q3
Q4
1.4%
1.16
98.8
6%
6.03
94.0
25%
25.3
74.7
65%
65.1
34.9
250K
200K
150K
100K
50K
0
-10^3
0
10^3
10^4
10^5
pS6

FIG.58C-1

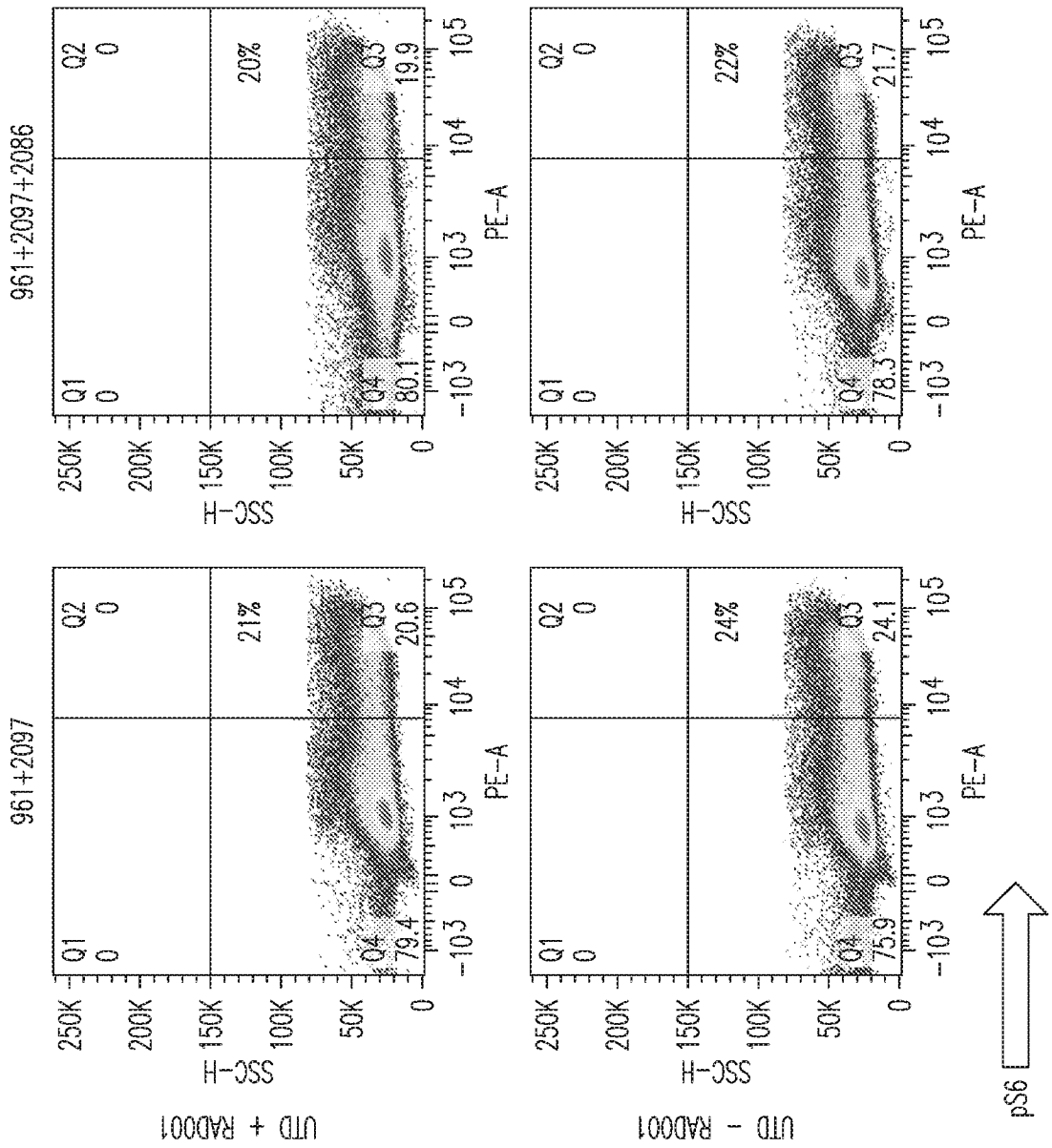

961+2097+2086
961+2097
UTD + RAD001
UTD - RAD001
SSC-H
PE-A
pS6
Q1
Q2
Q3
Q4
20%
19.9
80.1
21%
20.6
79.4
22%
21.7
78.3
24%
24.1
75.9

FIG.58C-2

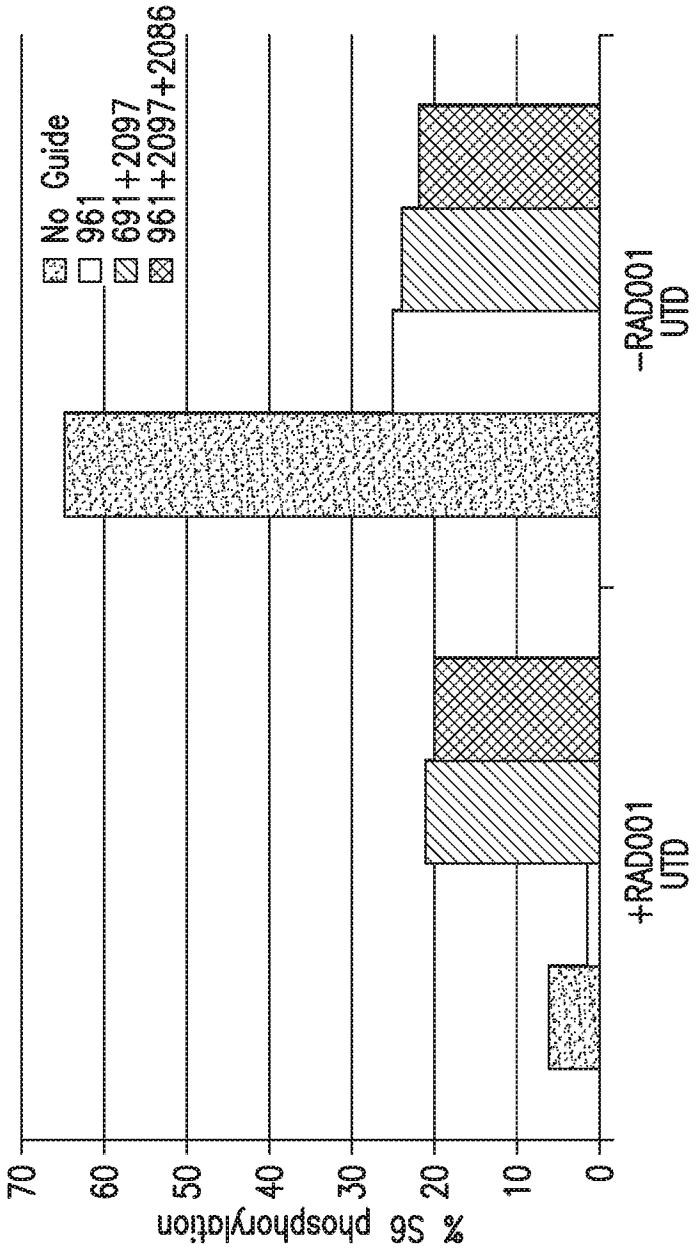

No Guide
961
691+2097
961+2097+2086
% S6 phosphorylation
70
60
50
40
30
20
10
0
+RAD001
UTD
-RAD001
UTD

FIG.58B-3

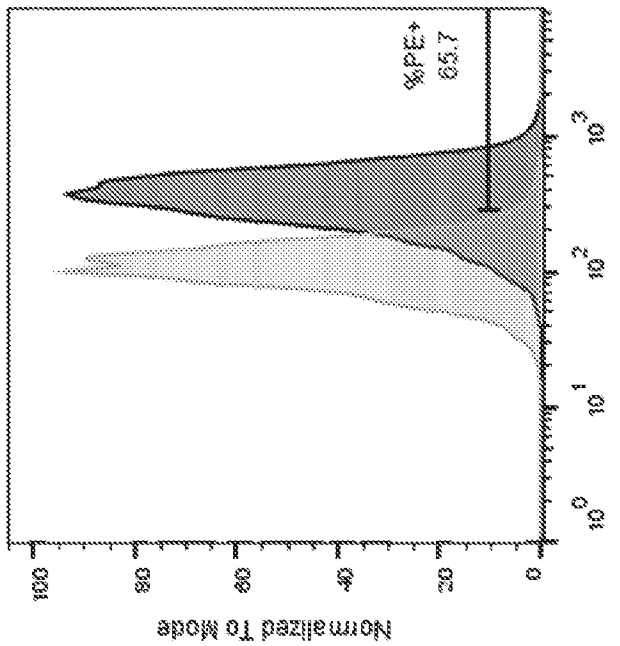


FIG. 59

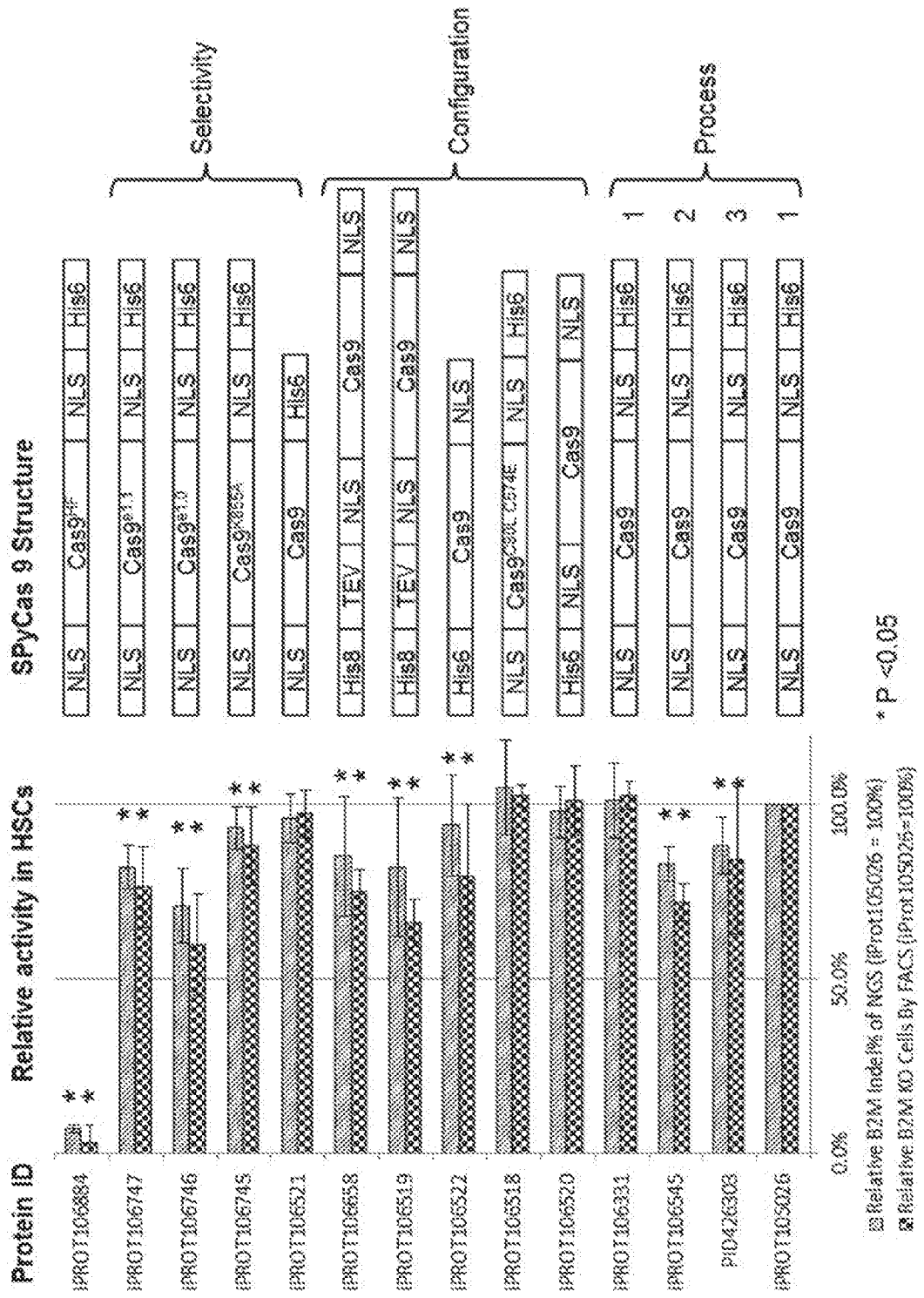

Protein ID
Relative activity in HSCs
SPyCas 9 Structure
Selectivity
Configuration
Process
#PROT106384
#PROT106747
#PROT106746
#PROT106745
#PROT106521
#PROT106658
#PROT106519
#PROT106522
#PROT106518
#PROT106520
#PROT106331
#PROT106545
PID426308
#PROT105026
NLS
Cas9
Cas9HF
Cas9ET1
Cas9ET2.0
Cas9VRER
Cas9VQR
Cas9EQR
Cas9VRQR
His6
His8
TEV
0.0%
50.0%
100.0%
Relative B2M Indel% of NGS (#Prot105026 = 100%)
Relative B2M KO Cells By FACS (#Prot105026=100%)
* P <0.05

FIG.60

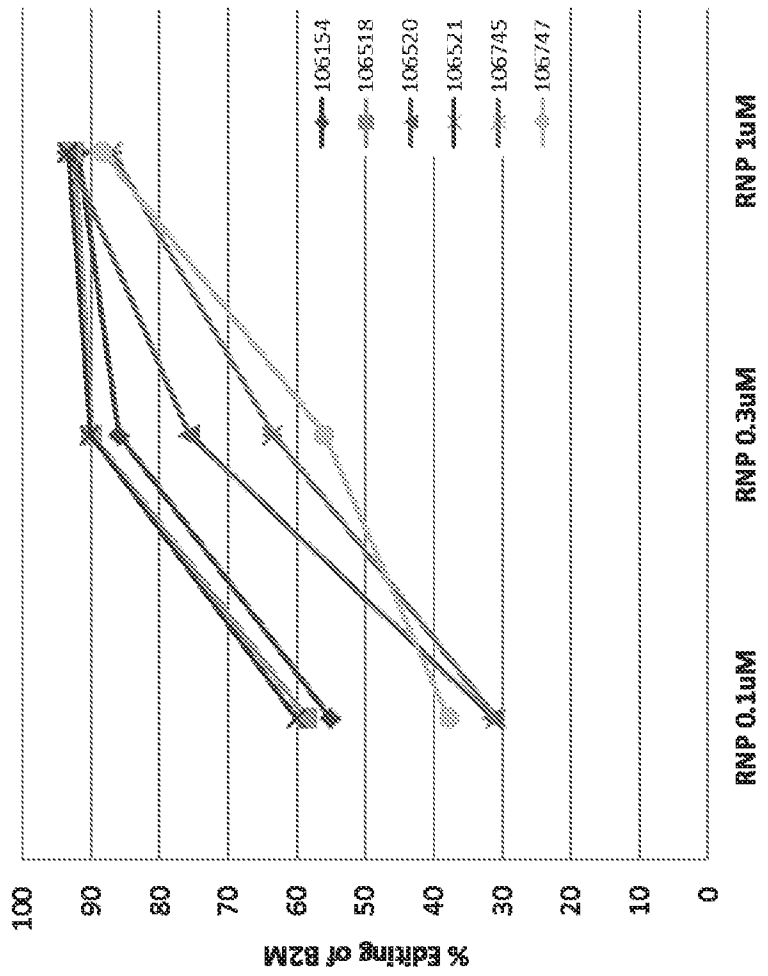

% editing of B2M
100
90
80
70
60
50
40
30
20
10
0
RNP 0.1uM
RNP 0.3uM
RNP 1uM
106154
106518
106520
106521
106745
106747

FIG.61

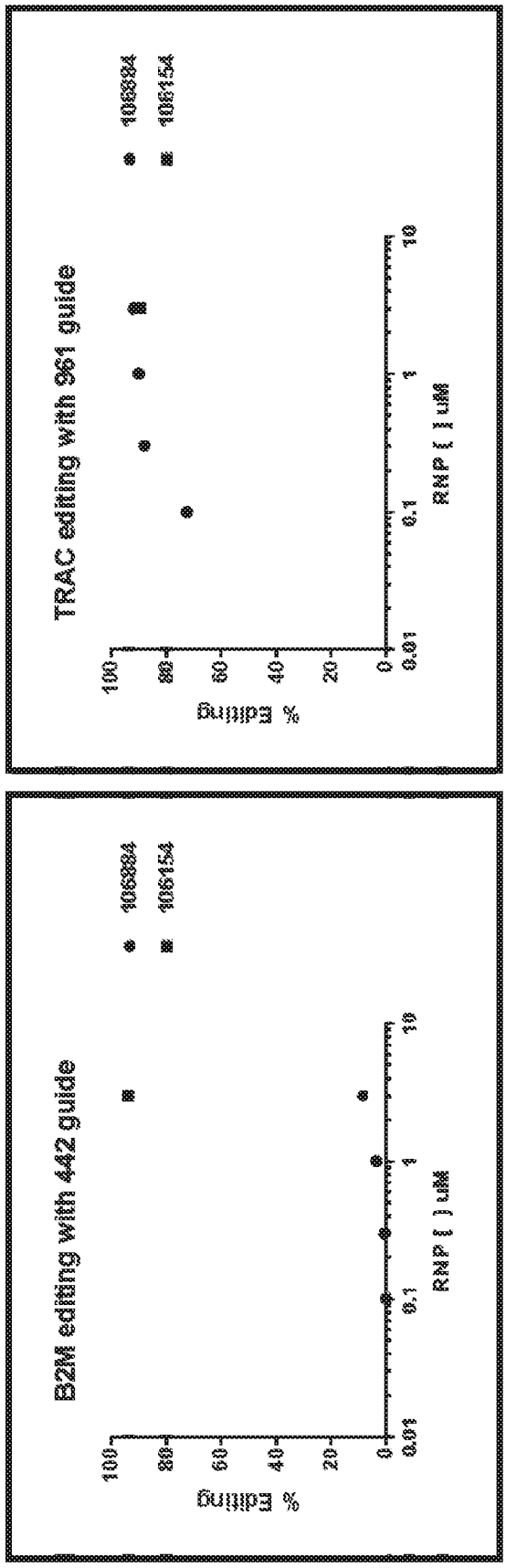
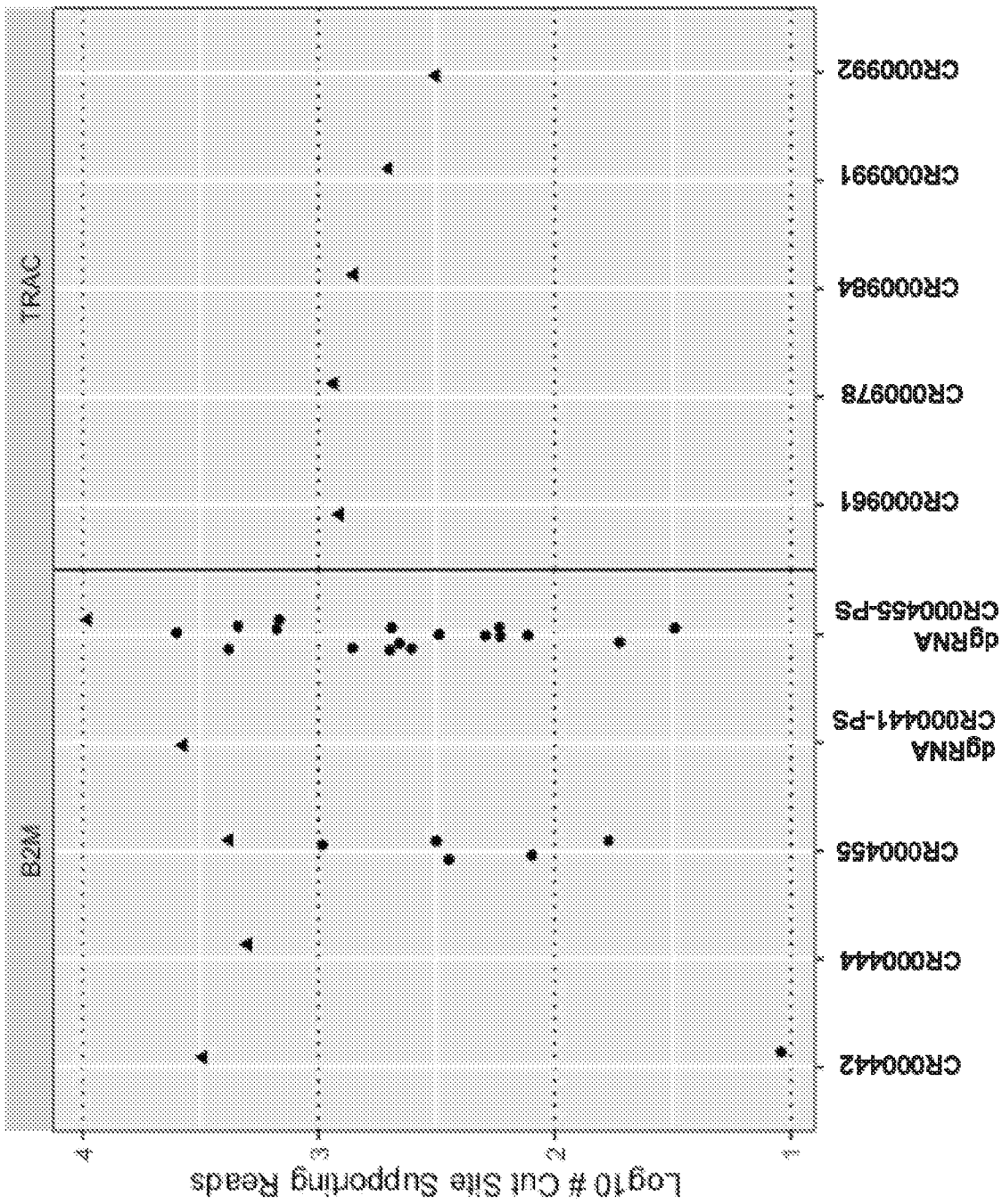

TRAC editing with 961 guide
1063884
1066154
% editing
RNP ( ) uM
B2M editing with 442 guide
1063884
1066154
% editing
RNP ( ) uM

FIG.62

FIG.63


TRAC
B2M
CR000992
CR000991
CR000984
CR000978
CR000961
dgRNA CR000455-PS
dgRNA CR000441-PS
CR000455
CR000444
CR000442
Log10 # Cut Site Supporting Reads

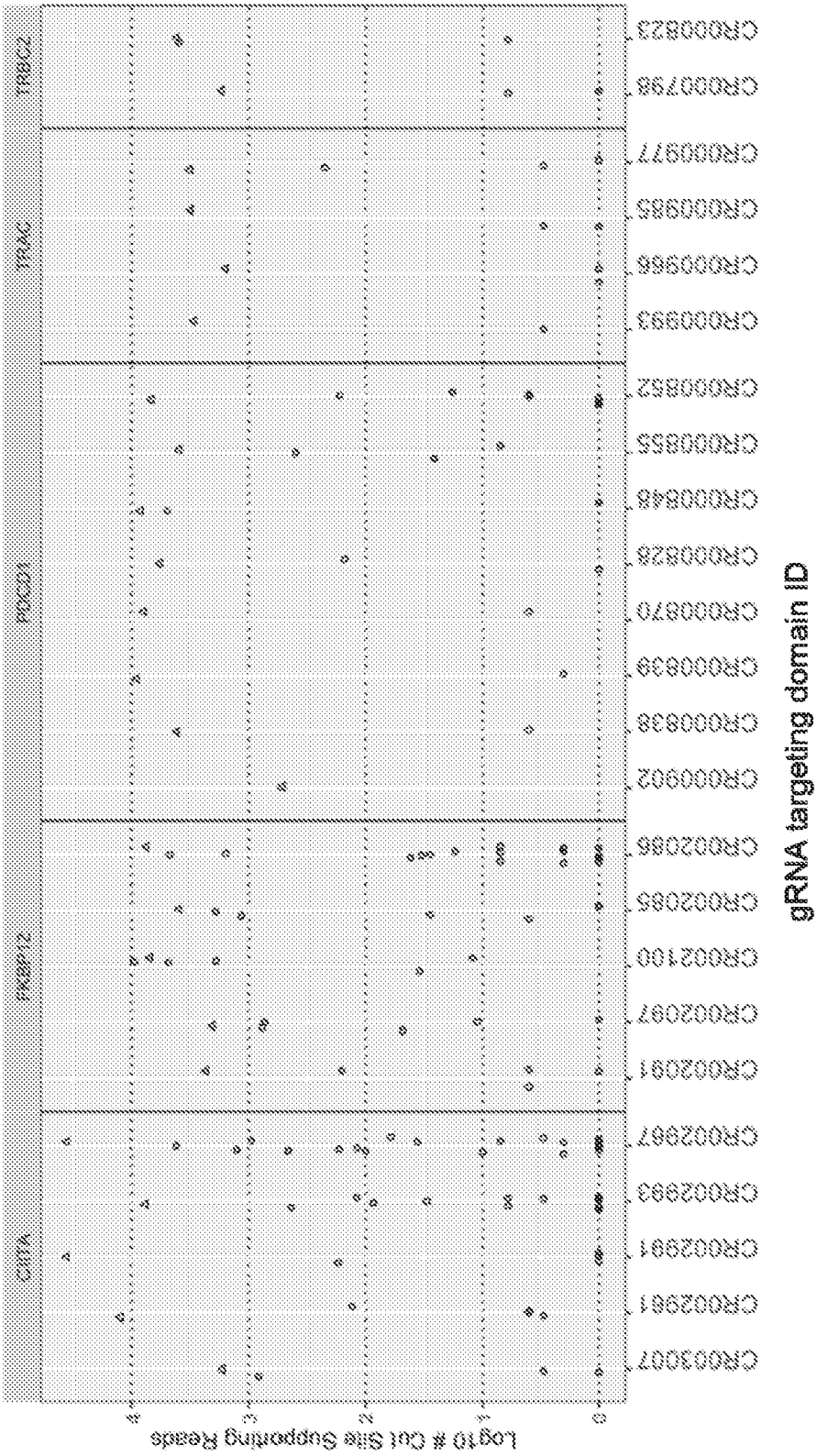

CR003007
CR002961
CR002991
CR002993
CR002987
CR002091
CR002097
CR002100
CR002085
CR002086
CR000902
CR000838
CR000839
CR000870
CR000828
CR000846
CR000855
CR000852
CR000893
CR000966
CR000985
CR000977
CR000798
CR000823
CIITA
FKBP12
PDCD1
TRAC
TRBC2
gRNA targeting domain ID
Log10 # Cut Site Supporting Reads
0
1
2
3

FIG.64

gRNA Targeting Domain ID	Target	Species	% CD3-negative cells (Mean)	SD
CR005334	CD3 delta	Human	98.8	0.4
CR005335	CD3 delta	Human	3.2	0.3
CR005336	CD3 delta	Human	4.3	0.4
CR005337	CD3 delta	Human	13.1	0.7
CR005338	CD3 delta	Human	2.8	0.3
CR005339	CD3 delta	Human	19.4	2.1
CR005340	CD3 delta	Human	1.9	0.1
CR005341	CD3 delta	Human	5.0	0.6
CR005342	CD3 delta	Human	6.5	1.0
CR005343	CD3 delta	Human	2.5	0.5
CR005344	CD3 delta	Human	23.2	1.0
CR005345	CD3 delta	Human	71.9	2.1
CR005346	CD3 delta	Human	3.1	0.6
CR005347	CD3 delta	Human	30.6	2.2
CR005348	CD3 delta	Human	6.3	0.8

FIG.65

gRNA Targeting Domain ID	Target	Species	% CD3-negative cells (Mean)	SD
CR005349	CD3 gamma	Human	3.1	0.4
CR005350	CD3 gamma	Human	2.6	0.6
CR005351	CD3 gamma	Human	9.8	0.3
CR005352	CD3 gamma	Human	3.6	0.6
CR005353	CD3 gamma	Human	2.3	0.1
CR005354	CD3 gamma	Human	8.8	0.2
CR005355	CD3 gamma	Human	2.7	0.6
CR005356	CD3 gamma	Human	27.9	2.9
CR005357	CD3 gamma	Human	2.6	0.5
CR005358	CD3 gamma	Human	2.2	0.2
CR005359	CD3 gamma	Human	3.0	0.4
CR005360	CD3 gamma	Human	2.5	0.7
CR005361	CD3 gamma	Human	2.5	0.5
CR005362	CD3 gamma	Human	17.7	0.8
CR005363	CD3 gamma	Human	11.9	0.7

FIG.66

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/057318

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/113 A61K35/17 A61P35/00 C12N15/09
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2015/136001 A1 (CELLECTIS [FR]) 17 September 2015 (2015-09-17)	1,2, 18-68, 76-79, 83-139, 155-162, 280-285
A	the whole document	6,7, 80-82

X	WO 2014/165825 A2 (HARVARD COLLEGE [US]; CHILDRENS MEDICAL CENTER [US]) 9 October 2014 (2014-10-09)	1,2, 18-68, 76-79, 83-139, 155-162, 280-285
A	the whole document	6,7, 80-82

	-/--	

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 February 2017	09/05/2017

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Spindler, Mark-Peter

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/057318

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J REN ET AL: "Multiplex Cripsr/Cas9 Genome Editing to Generate Potent Universal CART and PD1-Deficient Cells Against Leukemia", BLOOD, vol. 126, no. 23, 3 December 2015 (2015-12-03), page 4280, XP055348715,	1,2, 18-68, 76-79, 83-139, 155-162, 280-285
A	the whole document	6,7, 80-82

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A	the whole document	7,80-82

X	LUKE A. GILBERT ET AL: "Genome-Scale CRISPR-Mediated Control of Gene Repression and Activation", CELL, vol. 159, no. 3, 9 October 2014 (2014-10-09), pages 647-661, XP055247644, US ISSN: 0092-8674, DOI: 10.1016/j.cell.2014.09.029	1,2, 18-68, 93-105, 109-118, 125-137
A	the whole document -& LUKE A GILBERT: "Genome-Scale CRISPR-Mediated Control of Gene Repression and Activation; excerpt of sgRNA library", CELL, 9 October 2014 (2014-10-09), XP055348694, the whole document	6,7, 80-82

X	DATABASE WPI Week 201572 Thomson Scientific, London, GB; AN 2015-42037B XP002767532, -& CN 104 611 370 A (SHENZHEN KEHUIRUI BIOLOGICAL PHARM CO) 13 May 2015 (2015-05-13)	1,18-68, 76,77, 90,91, 93-105, 109-118, 125-137
A	abstract	2,6,7, 78-82

	-/--	

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/057318

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2014/191128 A1 (CELLECTIS [FR]) 4 December 2014 (2014-12-04) the whole document -----	1,2,6,7, 18-68, 76-139, 155-162, 280-285
A	WO 2015/161276 A2 (EDITAS MEDICINE INC [US]) 22 October 2015 (2015-10-22) the whole document -----	1,2,6,7, 18-68, 76-139, 155-162, 280-285
X,P	WO 2016/069282 A1 (UNIV PENNSYLVANIA [US]) 6 May 2016 (2016-05-06) the whole document -----	1,2,6, 18-68, 76-79, 83-139, 155-162, 280-285
A,P		7,80-82
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X,P	WO 2016/160721 A1 (HARVARD COLLEGE [US]) 6 October 2016 (2016-10-06) the whole document -----	1,2,6,7, 18-68, 76-139, 155-162, 280-285
X,P	WO 2016/183041 A2 (HARVARD COLLEGE [US]) 17 November 2016 (2016-11-17) the whole document -----	1,2,6,7, 18-68, 76-139, 155-162, 280-285

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2016/057318

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

6, 7(completely); 1, 2, 18-68, 76-139, 155-162, 280-285(partially)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 6, 7(completely); 1, 2, 18-68, 76-139, 155-162, 280-285(partially)

gRNA molecule targeting B2M; composition comprising said gRNA molecule; nucleic acid encoding said gRNA molecule; vector comprising said nucleic acid; method of altering a targeting sequence of a cell using said gRNA molecule; cell altered by said method; cell comprising said gRNA, said composition, said nucleic acid or said vector; method of providing an anti-tumor immunity using said cell; medical implementations of said gRNA, said composition, said nucleic acid, said vector or said cell

---

2-20. claims: 3-5, 8-13, 69-73, 140-154, 163-226(completely); 1, 2, 18-68, 76-139, 155-162, 280-285(partially)

gRNA molecule targeting CD247, CD3D, CD3E, CD3G, TRAC, TRBC1, TRBC2, HLA-A, HLA-B, HLA-C, DCK, CD52, FKBP1A, CIITA, NLRC5, RFXANK, RFX5, RFXAP, or NR3C1, respectively; implementations thereof as indicated for invention 1); exact claim numbers may vary

---

21-46. claims: 14-17, 74, 75(completely); 18-68, 76, 77, 93-137, 155-162, 280-285(partially)

gRNA molecule targeting CD274, HAVCR2, LAG3, PDCD1, PD-L2, CTLA4, CEACAM, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3, B7-H4, HVEM, KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, TGF beta, PTPN11 or a downstream effector thereof, respectively; implementations thereof as indicated for invention 1); exact claim numbers may vary

---

47. claims: 227-235(completely); 278-285(partially)

a modified cell having reduced or eliminated expression of a component of the T cell receptor, B2M and/or CIITA; a modified cell comprising an insertion or deletion of at least one base pair at or near a gene encoding a component of the T cell receptor, B2M and/or CIITA; population of said cells; implementations thereof

---

48. claims: 236-277(completely); 278-285(partially)

a cell comprising a nucleic acid sequence encoding a CAR and an indel at or near a gene encoding a component of a TCR; population of cells comprising said cells; implementations thereof

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2016/057318

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		WO 2016069283 A1	06-05-2016
WO 2016073955 A2	12-05-2016	NONE	
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		WO 2016160721 A1	06-10-2016
WO 2016183041 A2	17-11-2016	NONE	