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(54) Title: SOLUBLE VIRUS-SPECIFIC T-CELL RECEPTOR COMPOSITIONS

(57) Abstract: Compositions and methods for diagnosing a viral infection and methods of inhibiting such an infection are described. The methods are based on the identification of T-cell receptor gene sequences from cytotoxic T cell clones that are specific for HIV-I or HCV. Soluble T-cell receptor compositions that bind to HLA class I-restricted of HIV and HCV pathogens were identified and constructed.

SOLUBLE VIRUS-SPECIFIC T-CELL RECEPTOR COMPOSITIONS

Background of the Invention

Viral infections such as infection with human immunodeficiency virus (HIV) such as HIV-1 and infection with hepatitis C virus (HCV) are a significant public health problem. A number of drugs are currently used to treat individuals infected with such viral infections, e.g., anti-retroviral drugs include Reverse transcriptase (RT) inhibitors and Protease inhibitors (PI). Although these agents have been effective in treating HIV infection, development of drug resistant strains and cumulative drug toxicity of the virus is a concern.

Summary of the Invention

The invention features methods and compositions for diagnosis and treatment of viral infections. The methods are based on the identification of T-cell receptor gene sequences from cytotoxic T cell clones that are specific for HIV-1 or HCV. Accordingly, the invention includes isolated T cell receptor genes and polypeptides encoded by the genes, which encode soluble T cell receptor polypeptides or proteins that specifically bind to cytotoxic T cell epitopes in HIV-1 or HCV and polypeptides encoded by the genes.

The epitope comprises or consists of a short, 8 to 11-mer peptide that is associated with a class I major histocompatibility complex (MHC) antigen such as an HLA molecule on the surface of a cell. The epitope contains polypeptide sequence corresponding to or derived from a naturally-occurring HIV or HCV protein.

The T cell receptor genes encode for both the alpha chain of the T cell receptor and the beta chain of the T cell receptor. Both the TCR alpha chain and the TCR beta chain comprise or consist of a constant region (C region), a variable region (V region) and a complementary-determining 3 region (CDR3) region. The CDR3 regions mediate the interaction with the antigenic peptide/MHC class I complex and consist of a random sequence of 1-90 nucleotides that are generated by somatic recombination. These gene sequences are used to construct recombinant HIV-1 or HCV-specific soluble TCR receptor molecules, which are used for diagnostic *in vitro* use and therapeutic *in vivo* use. For instance, these soluble TCRs can be used as a staining reagent to detect HIV-1 or HCV cytotoxic T cell epitope presentation in patient-derived tissue or fluid samples *in vitro* assays. Optionally, the soluble T cell receptor

polypeptide can be associated with a detectable marker such as a fluorescent molecule. The detectable marker is linked to or conjugated to the receptor polypeptide to facilitate diagnostic methods. Moreover, a plurality of soluble single chain HLA class I-restricted T cell receptor polypeptides are immobilized on a solid support such as a chip or plate. For example, the TCRs are configured in a microarray format for identification and detection of processed viral epitopes. For therapeutic purposes, a cytotoxic molecule or cytokine is linked to or associated with the TCR.

Preferred soluble TCR constructs include the following sequences that correspond to TCR α, β chain pairs: Vb sequence CASSQGVTLLN (SEQ ID NO:4) and Va5 sequence CAETY (SEQ ID NO:6) . This soluble TCR has an epitope specificity of SEQ ID NO:5 (HIV-1 vpr) in the context of HLA class I molecule A2. Derivatives of the sequence of the TCR are also within the scope of the invention. Derivative TCRs are characterized by a higher binding affinity to the HLA class I restricted epitope shown in Table 1 below. For example, a derivative soluble TCR construct relative to the reference sequences SEQ ID NO:4 and 6 may include 1, 2, 3, 4 or more conservative or non-conservative amino amino acid substitutions and is characterized by a binding affinity for the epitope that is increased compared to a construct containing the original reference sequence. A preferred soluble TCR construct with an epitope binding specificity for HCV include sequences that correspond to TCR α, β chain pairs: Va sequence CAVNEYGQNFV (SEQ ID NO:27) and Vb sequence CAWSGGLNTEAF (SEQ ID NO:29). This soluble TCR construct has an epitope binding specificity of SEQ ID NO:28, an HCV peptide that is also presented in the context of HLA class I molecule A2. These and other TCR sequences as well as their binding specificities and HLA restriction are shown in Table 1.

By "substantially pure" is meant a nucleic acid, polypeptide, or other molecule that has been separated from the components that naturally accompany it. Typically, the polypeptide is substantially pure when it is at least 60%, 70%, 80%, 90%, 95%, or even 99%, by weight, free from the proteins and naturally-occurring organic molecules with which it is naturally associated. For example, a substantially pure polypeptide may be obtained by extraction from a natural source, by expression of a recombinant nucleic acid in a cell that does not normally express that protein, or by chemical synthesis. An isolated fragment of a protein means a peptide having a portion of the sequence of the reference protein which is less than the entire sequence, and does not contain the naturally occurring flanking regions. An isolated polypeptide lacks one or more

amino acids, which immediately flank the reference fragment in the naturally-occurring molecule.

Where a particular polypeptide or nucleic acid molecule is said to have a specific percent identity to a reference polypeptide or nucleic acid molecule of a defined length, the percent identity is relative to the reference polypeptide or nucleic acid molecule. Thus, a peptide that is 50% identical to a reference polypeptide that is 100 amino acids long can be a 50 amino acid polypeptide that is completely identical to a 50 amino acid long portion of the reference polypeptide. It might also be a 100 amino acid long polypeptide which is 50% identical to the reference polypeptide over its entire length. The same rule applies for nucleic acid molecules.

For polypeptides, the length of the reference polypeptide sequence will generally be at least 5 amino acids in length. For example, the peptide is 5, 6, 7, 8, 9, 10, 11, 12 amino acids in length. In some cases, the peptide is larger, e.g., 15, 20, 25 amino acids or more in length. For example, the peptide of a specific sequence, e.g., epitope sequence, is flanked by other amino acids that differ from those amino acids which flank the sequence in a naturally-occurring protein. For nucleic acids, the length of the reference nucleic acid sequence will generally be at least 15, 20, or 25 nucleotides in length. However, larger constructs, e.g., those that are at least 50 nucleotides, preferably at least 60 nucleotides, more preferably at least 75 nucleotides, and most preferably 100 nucleotides or 300 nucleotides.

The invention also encompasses derivative peptides corresponding to TCR sequences or epitope sequences. In the case of polypeptide sequences which are less than 100% identical to a reference sequence, the non-identical positions are preferably, but not necessarily, conservative substitutions for the reference sequence. Conservative substitutions typically include substitutions within the following groups: glycine and alanine; valine, isoleucine, and leucine; aspartic acid and glutamic acid; asparagine and glutamine; serine and threonine; lysine and arginine; and phenylalanine and tyrosine. In peptides in which amino acids substitutions are made relative to the reference sequence, the binding affinity of the T-cell receptor to its HLA-restricted epitope is increased. Alternatively, constructs containing derivative sequences have great stability, e.g., a longer half-life in a physiologically acceptable solution such as culture media or a bodily fluid such as blood, plasma, or serum. For example, the binding affinity and/or stability of such derivative peptides is at least 5%, 10%, 25%, 50%, 75%, 90%, 100%, 2-fold, 5-fold, 10-fold, 20-fold, or more relative to that of the reference peptide sequence. Optionally, derivative peptide sequences include additional amino acids that flank the reference

sequences on the amino-terminal and/or the carboxy-terminal end of the sequence. As is described above, such constructs, which contain non-naturally occurring flanking sequences are characterized as having increased epitope binding affinity and/or increased stability. Nucleic acid sequences that encode such derivative peptide sequences are encompassed by the invention.

An isolated or purified nucleic acid molecule is one that is separated from the 5' and 3' coding sequences or non-coding sequences with which it is immediately contiguous in the naturally occurring genome of an organism. Isolated nucleic acid molecules include nucleic acid molecules which are not naturally occurring, e.g., nucleic acid molecules created by recombinant DNA techniques. The nucleic acids identified herein include a sequence that are at least 85%, 90%, 95%, 98%, 99% identical to a reference sequence and degenerate variants of a reference nucleic acid sequence.

Other features and advantages of the invention will be apparent from the following description of the preferred embodiments thereof, and from the claims. The entire contents of references cited herein are hereby incorporated by reference.

Detailed Description of the Invention

HIV-1- or HCV-specific cells recognizing defined, MHC class I restricted cytotoxic T cell epitopes were isolated by limiting dilution cloning. Cloned cells were stained with MHC class I tetramers refolded with the respective epitopic peptide, and tetramer-binding cells were sorted using a FACS ARIA instrument. mRNA of sorted cells was extracted, reverse transcribed and cDNA of the TCR gene was amplified by nested PCR. PCR products were ligated into a cloning vector used to transform *E. coli*. After bacterial amplification, vector inserts were purified and sequenced according to standard procedures. The sequences of the following TCRs were identified.

Table 1: TCR sequences

TCR (α(a), β(b), chain pairs)	Epitope specificity	Restricting HLA class I type
Vb27-CASSLGQGLANYGYT-J1.2 SEQ ID NO:1 Va3-CAVRDLTGNQFY-J49 SEQ ID NO:3	FL8 (FLKEKGGL) SEQ ID NO:2 HIV-1 (nef)	B8
Vb14-CASSQGVTLLN- J2.1	AL9 (AIIRILQQL)	A2

SEQ ID NO:4 Va5-CAETY-J36 SEQ ID NO:6	SEQ ID NO:5 HIV-1 (vpr)	
Vb19-CASSIDGASNQPQH-J1.5 SEQ ID NO:7 Va13.2-CAENSDAGGTSYGKLT-J52 SEQ ID NO:9	SL9 (SLYNTVATL) SEQ ID NO:8 HIV-1 (gag)	A2
Vb15-CATSRGAGSNTGELF-J2.2 SEQ ID NO:10 Va12.2-CAVRGSGTYKYI-J40 SEQ ID NO:11	FL8 (FLKEKGGL) SEQ ID NO:2 HIV-1 (nef)	B8
Va19-CALSGNHSGGATNKLI-J32 SEQ ID NO:12 Vb4.3-CASSPWTGGGQPQH-J1.5 SEQ ID NO:14	TW10 (TSTLQEQIGW) SEQ ID NO:13 HIV-1 (gag)	B57
Va5-CAASGGYQKVTFGTGTKLQVIP SEQ ID NO:15 Vb19-CASTGTYGYT-J1.2 SEQ ID NO:16	KF11 (KAFSPEVIPMF) SEQ ID NO:17 HIV-1 (gag)	B57
Va12.3-CAMSAQQAGTALI-J15 SEQ ID NO:18 Vb11.2-CASSLVIMSEQY-J2.7 SEQ ID NO:20	SL9 (SEGATPQDL) SEQ ID NO:19 HIV-1 (gag)	B60
Va13.1-CAATSGYALN-J41 SEQ ID NO:21 Vb9-CASSVQGEFREKLF-J1.4 SEQ ID NO:23	EI8 (EIYKRWII) SEQ ID NO:22 HIV-1 (gag)	B8
Va27-CAGRDYKLS-J20 SEQ ID NO:24 Vb20.1-CSARGDNPNTEAF—J1.1 SEQ ID NO:26	KL9 (KEKGGLEGL) SEQ ID NO:25 HIV-1 (nef)	B60
Va8.1-CAVNEYGQNFV-J26 SEQ ID NO:27 Vb30-CAWSGGLNTEAF-J1.1 SEQ ID NO:29	AL9 (ALYDVVTKL) SEQ ID NO:28 (HCV)	A2
Vb27- CASSVRTGELF-J2.2 SEQ ID NO:30 Va29- CAASFTQNGLT-J45 SEQ ID NO:32	QK10 (QVPLRPMTYK) SEQ ID NO:31 HIV-1 (nef)_	A3 and A11
Vb9- CASSERDSQYQETQY-J2.5 SEQ ID NO:33 Va29- CAASFTQNGLT-J45 SEQ ID NO:34	QK10 (QVPLRPMTYK) SEQ ID NO:31 HIV-1 (nef)	A3 and A11
Vb14-CASSPVLYEQY-J2.7 SEQ ID NO:35 Va39-CAVVAQGGSEKLV-J57 SEQ ID NO:36	QK10 (QVPLRPMTYK SEQ ID NO:31 HIV-1 (nef)	A3 and A11

Vb9-CASSARAFPEGNQPQH-J1.5 SEQ ID NO:37 Va39-CAVVAQGGSEKLV-J57 SEQ ID NO:38	QK10 (QVPLRPMTYK) SEQ ID NO:31 HIV-1 (nef)	A3 and A11
Vb10.2-CASSETNRVMEAF-J1.1 SEQ ID NO:39 Va8.6-CAVSDPGFKTI-J9 SEQ ID NO:40	QK10 (QVPLRPMTYK) SEQ ID NO:31 HIV-1 (nef)	A3
Vb24-CATSAGRQRDTGELF-J2.2 SEQ ID NO:41 Va8.6-CAVSDPGFKTI-J9 SEQ ID NO:42	QK10 (QVPLRPMTYK) SEQ ID NO:31 HIV-1 (nef)	A3
Vb25.1-CASSNGYEQY-J2.7 SEQ ID NO:43 Va38.2-CAYRSDNDMR-J43 SEQ ID NO:44	KV10 (KLVALGINAV) SEQ ID NO:45 (HCV)	A2
Vb24.1-CATSSQDGQVYEQY-J2.7 SEQ ID NO:46 Va24-CASYKAAGNKLT-J17 SEQ ID NO:47	GT9 (GPRLGVRAT) SEQ ID NO:48 (HCV)	B7
Vb7.9-CASSSPKDPSNQPQH-J1.5 SEQ ID NO: 82 Va5-CAEDPTSSSGYALN-J4 SEQ ID NO: 84	KK10 (KRWIILGLNK) SEQ ID NO: 83 (HIV-1 gag)	B27

Table 2: Nucleotide sequences encoding TCRs

HCV-A2-KV10 (KLVALGINAV)

Vb25.1-CASSNGYEQY-J2.7 (SEQ ID NO:43)

NNNNNNNNGNNNNNNNTCGCCCTTNNCAGTGGTTCAACGCAGAGTACGCGGGGGG
GAGACATCCTCTCTAGCCCCAACTGTGCCATGACTATCAGGCTCCTCTGCTACATGG
GCTTTTATTTTCTGGGGGCAGGCCTCATGGAAGCTGACATCTACCAGACCCCAAGAT
ACCTTGTTATAGGGACAGGAAAGAAGATCACTCTGGAATGTTCTCAAACCATGGGC
CATGACAAAATGTACTGGTATCAACAAGATCCAGGAATGGAACTACACCTCATCCA
CTATTCCTATGGAGTTAATTCCACAGAGAAGGGAGATCTTTCCTCTGAGTCAACAGT
CTCCAGAATAAGGACGGAGCATTTTCCCCTGACCCTGGAGTCTGCCAGGCCCTCACA
TACCTCTCAGTACCTCTGTGCCAGCAGTAATGGATACGAGCAGTACTTCGGGCCGGG
CACCAGGCTCACGGTCACAGAGGACCTGAAAAACGTGTTCCCACCCGAGGTCGCTG
TGTTTGAGCCATCAGAAGCAGAGATCTCCCACACCAAGGGCGAATTCGTTTAAACCT
GCAGGACTAGTCCCTTTAGTGAGGGTTAATTCTGAGCTTGGCGTAATCATGGTCATA
GNNNNTTTCCTNN (SEQ ID NO:49)

Va38.2-CAYRSDNDMR-J43 (SEQ ID NO:44)

NNNNNNNGGNNNNNNNANTCGCCCTTNNNAGTGGTATCAACGCAGAGTACGCGGG
GAGAAGAGGAGGCTTCTCACCCTGCAGCAGGGACCTGTGAGCATGGCATGCCCTGG
CTTCCTGTGGGCACTTGTGATCTCCACCTGTCTTGAATTTAGCATGGCTCAGACAGTC
ACTCAGTCTCAACCAGAGATGTCTGTGCAGGGGGCAGAGACCGTGACCCTGAGCTG
CACATATGACACCAGTGAGAGTGATTATTATTTATTCTGGTACAAGCAGCCTCCCAG
CAGGCAGATGATTCTCGTTATTCGCCAAGAAGCTTATAAGCAACAGAATGCAACAG
AGAATCGTTTCTCTGTGAACTTCCAGAAAGCAGCCAAATCCTTCAGTCTCAAGATCT
CAGACTCACAGCTGGGGGATGCCGCGATGTATTTCTGTGCTTATAGGAGCGACAATG
ACATGCGCTTTGGAGCAGGGACCAGACTGACAGTAAAACCAAATATCCAGAACCCT
GACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTCTGTCTGCCTA
TTCACCGATTTTGATTCTCAAACAAATGTGTCACAAAGTAAGGATTCTGATGTGTAT
AAGGGCGAATTCGTTTAAACCTGCAGGACTAGTCCCTTTAGTGAGGGTTAATTCTGA
GCTTGGCGTANTCATGGTCATAGNNNNNTTTCNNNN (SEQ ID NO:50)

HCV-B7-GT9 (GPRLGVRAT) (SEQ ID NO:48)

Vb24.1-CATSSQDGQVYEQY-J2.7 (SEQ ID NO:46)

NNNNNNNNNNNNNNCNNNTCGCCCTTAAGCAGTGGTATCAACGCAGAGTACGCGG
GGAGAGCTGGAAACACCTCCATCCTGCCTCTTCATGCCATGGCCTCCCTGCTCTTCTT
CTGTGGGGCCTTTTATCTCCTGGGAACAGGGTCCATGGATGCTGATGTTACCCAGAC
CCCAAGGAATAGGATCACAAAGACAGGAAAGAGGATTATGCTGGAATGTTCTCAGA
CTAAGGGTCATGATAGAATGTACTGGTATCGACAAGACCCAGGACTGGGCCTACGG
TTGATCTATTACTCCTTTGATGTCAAAGATATAAACAAAGGAGAGATCTCTGATGGA
TACAGTGTCTCTCGACAGGCACAGGCTAAATTCTCCCTGTCCCTAGAGTCTGCCATC
CCCAACCAGACAGCTCTTTACTTCTGTGCCACCAGTTCCCAGGACGGGCAAGTCTAC
GAGCAGTACTTCGGGCCGGGCACCAGGCTCACGGTCACAGAGGACCTGAAAAACGT
GTTCCCACCCGAGGTCGCTGTGTTTGAGCCATCAGAAGCAGAGATCTCCCACACCAA
GGGCGAATTCGTTTAAACCTGCAGGACTAGTCCCTTTAGTGAGGGTTAATTCTGAGC
TTGGCGTAATCATGGTCATAGCTNNNTTNNNNGNN (SEQ ID NO:51)

Va24-CASYKAAGNKLT-J17 (SEQ ID NO:47)

NNNNNNNNNNNNNCNNCNAATTCGCCCTTANGCAGTGGTATCAACGCAGAGTACGC
GGGGGTTTTTCTGCTGTGGGTACGTGAGCAGGAAACATGGAGAAGAATCCTTTGGC
AGCCCCATTACTAATCCTCTGGTTTCATCTTGACTGCGTGAGCAGCATACTGAACGT
GGAACAAAGTCCTCAGTCACTGCATGTTCAGGAGGGAGACAGCACCAATTTCACCT
GCAGCTTCCCTTCCAGCAATTTTTATGCCTTACACTGGTACAGATGGGAAACTGCAA
AAAGCCCCGAGGCCTTGTTTGTAATGACTTTAAATGGGGATGAAAAGAAGAAAGGA
CGAATAAGTGCCACTCTTAATACCAAGGAGGGTTACAGCTATTTGTACATCAAAGGA
TCCCAGCCTGAAGACTCAGCCACATACCTCTGTGCCTCCTACAAAGCTGCAGGCAAC
AAGCTAACTTTTGGAGGAGGAACCAGGGTGCTAGTTAAACCAAATATCCAGAACCC
TGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTCTGTCTGCCT
ATTCACCGATTTTGATTCTCAAACAAATGTGTCACAAAGTAAGGATTCTGATGTGTA

TAAGGGCGAATTCGTTTAAACCTGCAGGACTAGTCCCTTTAGTGAGGGTTAATTCTG
AGCTTGGCGTAATCATGGTCNTANNNTNNTNNNNNN (SEQ ID NO:52)

HCV A2-AL9
Va8.1-CAVNEYGQNFV-J26 (SEQ ID NO:27)

NNNNNNNNNNGNNNNCNNNTCNCCCTTATACNCATCAGAATCCTTACTTTGTGACA
CATTTGTTTGAGAATCAAAATCGGTGACTAGGCAGACAGACTTGTCACTGGATTTAG
AGTCTCTCAGCTGGTACACGGCAGGGTCAGGGTTCTGGATATAGGGCAGCACGGAC
AATCTGGTTCCGGGACCAAAGACAAAATTCTGACCATACTCATTCACGGCACAGAA
GTACTCAGCTGTGTCACTCCACTGCACAGAGGGTTTCCTCAGATTAAAGGAGAATTT
ACTCTTTATAAATTCAGCCTCAAAGCCCTTGATGCCTTTAACCAGTGGATCCCCTGA
AAAGTACTTGAGGAGAAGCTGAAGGTGTTGACCAGGGTACTGGACATACCAGAAGA
GATTAACAGTTCCACCGTAGGAATAGTTGCATCCCAACTCCAGTGAGGCTGCTTCAG
AGAGAATTACGTGGTGGTTATGCTGGCTCACAGACTGGGCTCTGGCATCTCTCAGGG
CAAAAATCATCCCCAGCACTGGTATGAGCAACAGGAGCATGGCTGAGCTGTGGAAA
CACTGCAAGCGTCTCTTTGGAAATTCTCCTCGGGGCCAGTAGGAAAGTGGCTGGAAC
CCAGGTCTTGAGAATAGCGAGCGTGAGGAAGGTTGGGCTAGGCAAGTCTCTTGTTTT
GGTAAGAATCCCCGCGTACTCTGCGTTGATACCACTGCTTAANGGCGAATTCGTTTA
AACCTGCNNNACTAGTCCCTTTAGTGAGGGTTAATTCTGAGCTTGGNGTAATCATGG
TCNNNNNNTGTTTTCCNGN (SEQ ID NO:53)

HCV A2-AL9
Vb30-CAWSGGLNTEAF-J1.1 (SEQ ID NO:29)

NNNNNNNNNNNNNNNTCGCCCTTGGTGTGGGANNNCTCTGCTTCTGATGGCTCAAA
CACAGCGACCTCGGGTGGGAACACCTTGTTCAGGTCCTCTACAACTGTGAGTCTGGT
GCCTTGTCCAAAGAAAGCTTCAGTGTTCAGGCCTCCCGACCAGGCACAGAGATAGA
AGCCAGAGTCACTGAGAAGGAGCTTCTTAGAACTCAGGATGAACTGCCGGTCCTGG
GGTCTGGAGGCTGAGAGATTCTGGGGCACCTCAGAGCTGATCTGGCCAATACCAAC
GGAGTAGAAGAGCAGCTGGAGGCCCCTGCCTGCAGCCTGTCGGTACCAGTATAGGT
TGGGGTTTGATGTTCCCTCCACAGTGCACTCCAGAGAGAGCGGGCTGCCCACAGGCT
GCACCAGGGTCGCTGGCCATTGATGAATAGTCTGAGATCTGACCCCAAAGAAAGTG
CCCAGGAGAAGGGCAAGGAGAGAGCAGAGCATCATCCAAGCCAGCCTTTCCTTCAG
CTAGTCTGGGGGACAGACGCCTCCTCTTCTGGGCCAGTGATGTGGCCAGGCACACCA
GTGTGGCCCGCGTACTCTGCGTTGATACCACTGCTTAAGGGCGAATTCGCGGCCGCT
AAATTCAATTCGCCCTATAGTGAGTCGTATTACAATTCACTGGCNNNNCNNTTTTAN
(SEQ ID NO:54)

B8-EI8
Va13.1-CAATSGYALN-J41 (SEQ ID NO:21)

NNNNNNNNNNNNNCGCCCTTATACACATCAGAATCCTTACTTTGTGACACATTTGTT
TGAGAATCAAAATCGGTGAATAGGCAGACAGACTTGTCACTGGATTTAGAGTCTCTC
AGCTGGTACACGGCAGGGTCAGGGTTCTGGATATGGGGTGTGACCAACAGCGAGGT
GCCTTTGCCGAAGTTGAGTGCATACCCGGACGTTGCTGCACAGAAGTAGACAGCCG
AGTCTTCAGGTTGGGTCTCTGTGATGTGCAGGGAGAAATGTTTGGCTGTCTTGTTCA

ATGTAACAGCAATTCGTTGGTCTTTCTTTTCGCCCACATTTGAACGAATGTCTATAAT
AAGCTGAGGTCTTTTTCCAAGTTCTTGCTTATACCAAGGGAAGTAGTTTGAGGCACT
GTCTGAATAAGTACACTTGATAACAGCGCTGTCTCCCTCCTGGACACTCAGGGTTGA
AGGATGCTGCTCCACATTCTCTCCATTCACCAAGTCCAGCTGCAGCCACAGGAATAT
AAATACAGCTCGAATGGATGTCATCCTTGTTCTTCCCAATTAAGATCAGTCATTGAC
CTGCAACCTCCAGTTATCCCCGCGTACTCTGCGTTGATACCACTGCTTAAGGGCGAA
TTCGCGGCCGCTAAATTCAATTCGCCCTATAGTGAGTCGTATTACAATTCACTGGCN
TNCCNTTTTTAN (SEQ ID NO:55)

B8-EI8
Vb9-CASSVQGEFREKLF-J1.4 (SEQ ID NO:23)

NNNNNNNNNNNNNNNCGCCCTTGGTGTGGGANANCTCTGCTTCTGATGGCTCAAA
CACAGCGACCTCGGGTGGGAACACCTTGTTCAGGTCCTCCAAGACAGAGAGCTGGG
TTCCACTGCCAAAAAACAGTTTTTCTCTAAACTCCCCCTGTACGCTGCTGGCACAGA
AATACAAAGCTGAGTCCCCCAGCTCCAGAGAGCTCAGGTTTAGTTCAGAGTGCAAG
TCAGGGAACTGTTGTGCGGAGAATCGTTCAAGAATGTTTCCTTTTGCTCTCTCTTCTC
CATTATAATACTGAATGAGGAACTGGAGGCCCTGGTCCAGGCTCTGTTGGTACCAGT
ACACAGAGAGGTCTCCAGACCTAGGGGAGCATCTCAGCGTCACTCGCTGTCCAGTT
GCTGTGATCAGGTGCTTTGGGGTTTGTGTGACTCCAGAATCCACTGGGCCTGCTCCC
AGGAGACAAAAGGCCACACAGCAGAGGAGCCTGAAGCCCATGGCAGGATCTCCTA
GCTTGGGGCTGGTGTCTCTGTAGTAAGCATTCTCCCCGCGTACTCTGCGTTGATACCA
CTGCTTAAGGGCGAATTCGCGGCCGCTAAATTCAATTCGCCCTATAGTGAGTCGTAT
TACAATTCACTGGCCNNNNNTTTTTACANNNN (SEQ ID NO:56)

B60-KL9
Va27-CAGRDYKLS-J20 (SEQ ID NO:24)

NNNNNNNNNNNNNCGCCCTTATACACATCAGAATCCTTACTTTGTGACACATTTGTT
TGAGAATCAAAATCGGTGAATAGGCAGACAGACTTGTCACTGGATTTAGAGTCTCTC
AGCTGGTACACGGCAGGGTCAGGGTTCTGGATATTTGCTCTTACAGTTACTGTGGTT
CCGGCTCCAAAGCTGAGCTTGTAGTCGCGTCCTGCACAGAGGTAGAGGCCTGTATCA
CCAGGCTGGGCCGCAGTGATGTGGAGAGAACTGTCCTTTCTTGCATCACCAAACTGA
AAGGTTAGTCTCTTCAGCTTCTTCACTTCTCCACCCGTAACTACTGTCACCAGGAGGA
CAGGACCTTCCCCAGGCTCCTGTCTGTACCATTGTAAGCTGGAAAAAACACTTGAGG
AGTTGCAGTACACAGTGAGATTTTCTCCCTCTTGGATGCTTAGAAACTGAGGGCTCT
GCTCCAGCAGCTGGGTGCTCACCCATGCCAACTGAATCCAAAGAATGGACACGGAG
AATTTCAGGACCATCTTGTCTTTCTATCACATGGTGGACATGGCCCCTGACTTTAGCT
GCTCCTGAAAGAGCCCGTCCTGGAACANACTTCTCTGNNCTANAANANTGCTTGCTG
CCACCCACTTTGAGTTCCATANAAAGCCCCCCCGCGACTCTGCGTTGATACCACTGCT
TNAGGGCGANNTCNCGNNCNNTAAATTCAATTCGCCCTATAGTGAGTCGTANTACA
ATTCACTGGCNNNNNNNTTTTANN (SEQ ID NO:57)

B60-KL9
VB20.1-CSARGDNPNTEAF-J1.1 (SEQ ID NO:26)

NNNNNNNGGNNNCNNANTCGCCCTTANGCAGTGGTATCAACGCAGAGTACGCGGTA
AGCAGTGGTATCAACGCAGAGTACGCGGGAGAGAAGGTGGTGTGAGGCCATCACGG

AAGATGCTGCTGCTTCTGCTGCTTCTGGGGCCAGGCTCCGGGCTTGGTGCTGTCGTCT
CTCAACATCCGAGCTGGGTTATCTGTAAGAGTGGAACCTCTGTGAAGATCGAGTGCC
GTTCCCTGGACTTTCAGGCCACAACTATGTTTTGGTATCGTCAGTTCCCGAAACAGA
GTCTCATGCTGATGGCAACTTCCAATGAGGGCTCCAAGGCCACATACGAGCAAGGC
GTCGAGAAGGACAAGTTTCTCATCAACCATGCAAGCCTGACCTTGTCCACTCTGACA
GTGACCAGTGCCCATCCTGAAGACAGCAGCTTCTACATCTGCAGTGCTAGAGGGGA
CAACCCGAACACTGAAGCTTTCTTTGGACAAGGCACCAGACTCACAGTTGTAGAGG
ACCTGAACAAGGTGTTCCCACCCGAGGTCGCTGTGTTTGAGCCATCAGAAGCAGAG
ATCTCCCACACCAAGGGCGAATTCGTTTAAACCTGCAGGACTAGTCCCTTTAGTGAG
GGTTAATTCTGAGCTTGGCGTAATCATGGTCATANNNNNNTTTCCTNN (SEQ ID NO:58)

A2-AL9 alpha chain:
Va5-CAETY-J36 (SEQ ID NO:6)

NNNNNNNNNNNNCGCCCTTATACACATCAGAATCCTTACTTTGTGACACATTTGTTT
GAGAATCAAAATCGGTGAATAGGCAGACAGACTTGTCACTGGATTTAGAGTCTCTC
AGCTGGTACACGGCAGGGTCAGGCTTCTGGATATAGGGAATAACGGTGAGTCTCGT
TCCAGTCCCAAAGAAGAGGTTGTTTGCCCCAGTTTGATAAGTCTCTGCACAGAAGTA
GATAGCTGAGTCCCCAGTCTGGGTGTCTGCAATGCGCAGAGACAGATGTTTATCCTT
TTTATTCAATAGAACAGTGAGTCTTTGGTCTTGTTTCATGTCCATATTTGAGAAAATA
TACGTCAGCAACTGGAGACCTGCTCCAGATTCTTGCTTATACCAGTATAAGTAGGTG
GAGGAGCTGTCTGTGTAAGTGCAGTTTATAACGGAGCTGTCTCCCTCTCGGACACTC
AGGAAAAGACTCTGCTCCACATCCTCTCCTCTACTCATACAGTCCAGCTGCAGCCAC
AAAAACAGGAACGAAAATCCAGCAAATGTCTTCATTGTTCTCCCCACTGGGACCTGC
CCCGCGTACTCTGCGTTGATACCACTGCTTAAGGGCGAATTCGCGGCCGCTAAATTC
AATTCGCCCTATAGTGAGTCGTATTACAATTCACTGNNNNNNNNTTTNNNNN (SEQ ID NO:59)

A2-AL9 beta chain: Vb14-CASSQGVTLLN-J2.1 (SEQ ID NO:4)

NNNNNNNNNNNNNNCGCCCTTGGTGTGGGAGANCTCTGCTTCTGATGGCTCAAAC
ACAGCGACCTCGGGTGGGAACACGTTTTTCAGGTCCTCTAGCACGGTGAGCCGTGTC
CCTGGCCCGAAGAACTGCTCATTCAACAAAGTCACCCCTTGGCTGCTGGCACAGAA
ATAAACTCCAGAATCCTCCAGTTCTGCAGGCTGCACCTTCAGAGTAGAATACGTCCC
TCCAGTCCTTTCAGCTAAGAATCGATTGTTGGGCATACCGGACTCATCCTGTTTAGA
CTCTTTCACAAAATGTAACAGAAATTTTATTTCTTTTCCCATAACACGTCGATACCAA
TAAAGATTATCATGTCCAGAAATTGGGTCACATCTCAGAGTCACAGTCTGGCCCTTC
TCTATTACGCTGTGGCTGGGGAACTGAGTAACTCCAGCTTCTATGTGCTAAGCATGA
GAAAAAGGAAAGCAAATCTGTCTCTTGGCCCTGTAAGATGTGGCCTCCAGTGACATC
AGTATATTAGCCAATGTCCACAGTCTCAGGAGCTCCCTCTACCCCGCGTACTCTGCG
TTGATACCACTGCTTAAGGGCGAATTCGCGGCCGCTAAATTCAATTCGCCCTATAGT
GAGTCGTATTACAATTCACTGGCN (SEQ ID NO:60)

B8-FL8 alpha chain: Va12.2-CAVRGSGTYKYI-J40 (SEQ ID NO:11)

NNNNGNNCNNANTCGCCCTTNAGCAGTGGTATCAACGCAGAGTACGCGGGGAAGA
ATGATGAAATCCTTGAGAGTTTTACTAGTGATCCTGTGGCTTCAGTTGAGCTGGGTTT
GGAGCCAACAGAAGGAGGTGGAGCAGAATTCTGGACCCCTCAGTGTTCCAGAGGGA
GCCATTGCCTCTCTCAACTGCACTTACAGTGACCGAGTTTCCCAGTCCTTCTTCTGGT
ACAGACAATATTCTGGGAAAAGCCCTGAGTTGATAATGTCCATATACTCCAATGGTG
ACAAAGAAGATGGAAGGTTTACAGCACAGCTCAATAAAGCCAGCCAGTATGTTTCT
CTGCTCATCAGAGACTCCCAGCCCAGTGATTCAGCCACCTACCTCTGTGCCGTGCGA
GGCTCAGGAACCTACAAATACATCTTTGGAACAGGCACCAGGCTGAAGGTTTTAGC
AAATATCCNGAACCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTG
ACAAGTCTGTCTGCCTATTCACCGATTTTGATTCTCAAACAAATGTGTCACAAAGTA
AGGATTCTGATGTGTATAANGGCGAATTCGTTTAAACCTGCAGGACTAGTCCCTTTA
GTGAGGGTTAATTCTGANCTTGGCGTANTCATGGNNNNNNNNNNNNTTNNNNNNN
(SEQ ID NO:61)

B8-FL8 beta chain: Vb15-CATSRGAGSNTGELF-J2.2 (SEQ ID NO:10)

NNNNNNNNCNNNNTCGCCCTTANGCAGTGGTATCACGCAGAGTCGCGGGGGAGACA
GACAGATGCTTCATTCCTGCATGGGGTGGTATTCCTGCCATGGGTCCTGGGCTTCTCC
ACTGGATGGCCCTTTGTCTCCTTGGAACAGGTCACGGGGATGCCATGGTCATCCAGA
ACCCAAGATACCAGGTTACCCAGTTTGGAAAGCCAGTGACCCTGAGTTGTTCTCAGA
CTTTGAACCATAACGTCATGTACTGGTACCAGCAGAAGTCAAGTCAGGCCCCAAAG
CTGCTGTTCCACTACTATGACAAAGATTTTAACAATGAAGCAGACACCCCTGATAAC
TTCCAATCCAGGAGGCCGAACACTTCTTTCTGCTTTCTTGACATCCGCTCACCAGGCC
TGGGGGACGCAGCCATGTACCTGTGTGCCACCAGCAGAGGGGCAGGATCGAACACC
GGGGAGCTGTTTTTTGGAGAAGGCTCTAGGCTGACCGTACTGGAGGACCTGAAAAA
CGTGTTCCCACCCGAGGTCGCTGTGTTTGAGCCATCAGAAGCAGAGATCTCCCACAC
CAAGGGCGAATTCGTTTAAACCTGCAGGACTAGTCCCTTTAGTGAGGGTTAATTCTG
AGCTTGGCGTANTCATGGNNNNNNNNNTNTTTNCNNGN (SEQ ID NO:62)

A2-SL9: Va13.2-CAENSDAGGTSYGKLT-J52 (SEQ ID NO:9)

NNNNNNNGNNNCNNANTCGCCCTNNAGCAGTGGTATCAACGCAGAGTACGCGGGG
ATGGCTGGAGATTGCAGGTTTATGACTGATCCTATTTGGGAAGAACAATGATGGCAG
GCATTCGAGCTTTATTTATGTACTTGTGGCTGCAGCTGGACTGGGTGAGCAGAGGAG
AGAGTGTGGGGCTGCATCTTCCTACCCTGAGTGTCCAGGAGGGTGACAACTCTATTA
TCAACTGTGCTTATTCAAACAGCGCCTCANACTACTTCATTTGGTACAAGCAAGAAT
CTGGAAAAGATCCTCAATTCATTATAGACATTCGTTCAAATATGGACAAAAGGCAA
GGCCAAAGAGTCACCGTTTTATTGAATAAGACAGTGAAACATCTCTCTCTGCAAATT
GCAGCTACTCAACCTGGAGACTCAGCTGTCTACTTTTGTGCAGAGAATTCTGATGCT
GGTGGTACTAGCTATGGAAAGCTGACATTTGGACAAGGGACCATCTTGACTGTCCAT
CCNAATATCCAGAAGCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGT
GACAAGTCTGTCTGCCTATTCACCGATTTTGATTCTCAAACAAATGTGTCACAAAGT
AAGGATTCTGATGTGTATAAGGGCGAATTCGTTTAAACCTGCAGGACTAGTCCCTTT
AGTGAGGGTTAATTCTGAGCTTGGCGTATCATGTNNNNNN (SEQ ID NO:63)
(SEQ ID NO:63)

A2-SL9: Vb19-CASSIDGASNQPQH-J1.5 (SEQ ID NO: 7)

NNNNNNNNGNNNNCNANTTCGCCCTTCCCTTTGCACTATGAGCAACATTTGTTTCCT
GGGAGCAAACACCGTGGATGGTGGAATCACTCAGTCCCCGAAGTACCTGTTCAGAA
AGGAAGGACAGAATGTGACCCTGAGTTGTGAACAGAATTTGAACCACGATGCCATG
TACTGGTACCGACAGGACCCAGGGCAAGGGCTGAGATTGATCTACTACTCACAGAT
AGTAAATGACTTTCAGAAAGGAGGTATAGCTGAAGGGTACAGCGTCTCTCGGGAGA
AGAAGGAATCCTTTCCTCTCACTGTGACATCGGCCCAAAAGAACCCGACAGCTTTCT
ATCTCTGTGCCAGTAGTATAGATGGCGCTAGCAATCAGCCCCAGCATTTTGGTGATG
GGACTCGACTCTCCATCCTAGAGGACCTGAACAAGGTGTTCCCACCCGAGGTCGCTG
TGTTTGAGCCATCAGAAGCAGAGATCTCCCACACCAAGGGCGAATTCGTTTAAACCT
GCAGGACTAGTCCCTTTAGTGAGGGTTAATTCTGAGCTTGGCGTAATCATGGTCATA
NNNNNTTNNNNN (SEQ ID NO:64)

B8-FL8: Vb27-CASSLGQGLANYGYT-J1.2 (SEQ ID NO: 1)

NNNNNNNNNNNNTNNNNNNGTCCTCTACNACGGTTAACCTGGTCCCCGAACCGAAG
GTGTAGCCATAGTTAGCTAAGCCCTGCCCTAAACTGCTGGCACAGAAGTACGGAGA
GGTCTGGTTGGGGCTGGGCGACTCCAGGATCAGGGGGAAATTCCTCTTCTCTTTTCG
AGAGACTTTGTACCCTTCAGGAACACCTCCCTTATCAGTCACCTCAACATTCATTGA
ATAGTAGATCTGCCTTAAGCCCAGCCCTGGGTCTTGTCGATACCAGGACATATACTC
ATGGTTCATATTCTGAGAACAAGTCACTGTTAACTTCTTTCCAGTCACTGTGATGAG
GTATCTTGGGTTCTGGGTCACTTGGGCTTCCAGGGGGCCTGCTCCTAGAAGGCAAAG
GACCACATAGCCAAGGAGCTGGGGGCCCATGGCAGCATCAGGCAGGTGTCTGCCAG
TTCTGGGGGCTCCAGGTGGTTTCTGTAACGTCTCCACCTCTTCCCCCGCGTACTCTGC
GTTGATACCACTGCNNNCNCTGCGTTGANACNNCTGNNN (SEQ ID NO:65)

B8-FL8: Va3-CAVRDLTGNQFY-J49 (SEQ ID NO: 3)

GACCCCCCNNNNNNCGCCCGCCGNGAGCTTANNTGGAGCCATGGCCTCTGCACCCA
TCTCGATGCTTGCGATGCTCTTCACATTGAGTGGGCTGAGAGCTCAGTCAGTGGCTC
AGCCGGAAGATCAGGTCAACGTTGCTGAAGGGAATCCTCTGACTGTGAAATGCACC
TATTCAGTCTCTGGAAACCCTTATCTTTTTTGGTATGTTCAATACCCCAACCGAGGCC
TCCAGTTCCTTCTGAAATACATCACAGGGGATAACCTGGTTAAAGGCAGCTATGGCT
TTGAAGCTGAATTTAACAAGAGCCAAACCTCCTTCCACCTGAANAAACCATCTGCCC
TTGTGAGCGACTCCGCTTTGTACTTCTGTGCTGTGAGAGACCTCACCGGTAACCAGT
TCTATTTTGGGACAGGGACAAGTTTGACGGTCATTCCAAATATCCAGAACCCTGACC
CTGCCGTGTACCAGCTGANAGACTCTAAATCCAGTGACAAGTCTGTCTGCCTATTCA
CCGATTTTGATTCTCAAACAAATGTGTCACAAANNNNN (SEQ ID NO:66)

B57-TW10
Va19-CALSGNHSGGATNKLI-J32 (SEQ ID NO:12)

NNNGGNCGCNNATTCGCCCTTAAGCAGTGGTATCAACGCAGAGTACGCGGGGCAGT
AACTTTGCTAGTACCTCTTGAGTGCAAGGTGGAGAATTAAGATCTGGATTTGAGACG
GAGCACGGAACATTTCACTCAGGGGAAGAGCTATGAACATGCTGACTGCCAGCCTG
TTGAGGGCAGTCATAGCCTCCATCTGTGTTGTATCCAGCATGGCTCAGAAGGTAACT
CAAGCGCAGACTGAAATTTCTGTGGTGGAGAAGGAGGATGTGACCTTGGACTGTGT
GTATGAAACCCGTGATACTACTTATTACTTATTCTGGTACAAGCAACCACCAAGTGG
AGAATTGGTTTTCCTTATTCGTCGGAACTCTTTTGATGAGCAAAATGAAATAAGTGG
TCGGTATTCTTGGAACTTCCAGAAATCCACCAGTTCCTTCAACTTCACCATCACAGC
CTCACAAGTCGTGGACTCAGCAGTATACTTCTGTGCTCTGAGTGGAAATCACTCAGG
TGGTGCTACAAACAAGCTCATCTTTGGAACTGGCACTCTGCTTGCTGTCCGGCCAAA
TATCCAGAACCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGACAA
GTCTGTCTGCCTATTCACCGATTTTGATTCTCAAACAAATGTGTCACAAAGTAAGGA
TTCTGATGTGTATAANGGCGAATTCGTTTAAACCTGCANGGACTAGTCCCTTTAGTG
AGGGNTAATTCTGANCTNGNCGNNATCNNNNNNNNNNNNNNNNTNNNNNNNN
(SEQ ID NO:67)

B57-TW10
Vb4.3-CASSPWTGGGQPQH-J1.5 (SEQ ID NO:14)

NNNNNNNGNNNNCNNNTTCGCCCTTANGCAGTGTATCAACGCAGAGTACGCGGGAA
GCAGTGGTATCAACGCAGAGTACGCGGGAAGCAGTGGTATCAACGCAGAGTACGCG
GGAAGCAGTGGTATCAACGCAGAGTACGCGGGAAGCAGTGGTATCAACGCAGAGTA
CGCGGGAAGCAGTGGTATCAACGCAGAGTACGCGGGGGTCATAACGCTATGTATTG
GTACAAGCAAAGTGCTAAGAAGCCACTGGAGCTCATGTTTGTCTACAGTCTTGAAGA
ACGGGTTGAAAACAACAGTGTGCCAAGTCGCTTCTCACCTGAATGCCCCAACAGCTC
TCACTTATTCCTTCACCTACACACCCTGCAGCCAGAAGACTCGGCCCTGTATCTCTGC
GCCAGCAGCCCGTGGACAGGGGGCGGCCAGCCCCAGCATTTTGGTGATGGGACTCG
ACTCTCCATCCTAGAGGACCTGAACAAGGTGTTCCCACCCGAGGTCGCTGTGGTTGA
GCCATCAGAAGCGAGATCTCCCACACCAAGGGCGAATTCGTTTAAACCTGCAGGAC
TAGTCCCTTTAGTGAGGGTTAATTCTGAGCTTGGCGTAATCATGGTCNTAGNNNNGT
TTCCNGA (SEQ ID NO:68)

B57-KF11
Va5-CAASGGYQKVTFGTGTKLQVIP (SEQ ID NO:15)

NNNNNNNNNNNNNNTCNCCCTTNNNCNGNGGTNNCNNCGCNNAGNANNCGGGGGA
AGANATACTTGNNNNTATNGCTCTCTTGGCTGGAGATTGCAGGTCCCAGTGGGGAG
AACAATGAAGACATTTGCTGGATTTTCGTTCCTGTTTTTGTGGCTGCAGCTGGACTGT
ATGAGTAGAGGAGAGGATGTGGAGCAGAGTCTTTTCCTGAGTGTCCGAGAGGGAGA
CAGCTCCGTTATAAACTGCACTTACACAGACAGCTCCTCCACCTACTTATACTGGTA
TAAGCAAGAACCTGGAGCAGGTCTCCAGTTGCTGACGTATATTTTTTCAAATATGGA
CATGAAACAAGACCAAAGACTCACTGTTCTATTGAATAAAAAGGATAAACATCTGT
CTCTGCGCATTGCAGACACCCAGACTGGGGACTCAGCTATCTACTTCTGTGCAGCTT
CTGGGGGTTACCAGAAAGTTACCTTTGGAACTGGAACAAAGCTCCAAGTCATCCCA
AATATCCAGAAGCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGA
CAAGTCTGTCTGCCTATTCACCGATTTTGATTCTCAAACAAATGTGTCACAAAGTAA
GGATTCTGATGTGTATATCACAGACAAAACTGTCCATAGACCTCATGTCTAGCACAG
TTTTGTCTGTGATCCCGCGTACTCTGCGTTGATACCACTGCTTANNNGNCGAATTCGT
TTAAACCTGCNNNACTAGTCCCTTTANTGAGGGTTAATTCTGANCTTGNNGTAATCN
TGGNNNNNNCNNNNNNTTTNCCNGNNNNN (SEQ ID NO:69)

B57-KF11
Vb19-CASTGTYGYT-J1.2 (SEQ ID NO:16)

NNNNNNNNNCNCNNANTCGCCCTTAAGCAGTGGTATCAACGCAGAGTACGCGGGGA
CATTAGGCCAGGAGAAGCCCCCGAGCCAAGTCTCTTTTCTCATTCTCTTCCAACAAG
TGCTTGGAGCTCCAAGAAGGCCCCCTTTGCACTATGAGCAACCAGGTGCTCTGCTGT
GTGGTCCTTTGTCTCCTGGGAGCAAACACCGTGGATGGTGGAATCACTCAGTCCCCA
AAGTACCTGTTCAGAAAGGAAGGACAGAATGTGACCCTGAGTTGTGAACAGAATTT
GAACCACGATGCCATGTACTGGTACCGACAGGACCCAGGGCAAGGGCTGAGATCGA
TCTACTACTCACAGATAGTAAATGACTTTCAGAAAGGAGATATAGCTGAAGGGTAC
AGCGTCTCTCGGGAGAAGAAGGAATCCTTTCCTCTCACTGTGACATCGGCCCAAAAG
AACCCGACAGCTTTCTATCTCTGTGCCAGTACCGGGACTTATGGCTACACCTTCGGTT
CGGGGACCAGGTTAACCGTTGTAGAGGACCTGAACAAGGTGTTCCCACCCGAGGTC
GCTGTGTTTGAGCCATCAGAAGCAGAGATCTCCCACACCAAGGGCGAATTCGTTTAA
ACCTGCAGGACTAGTCCCTTTAGTGAGGGTTAATTCTGAGCTTGGCGTANTCATGGT
CNNNNNNTNNNTTNCCNGNN (SEQ ID NO:70)

B60-SL9
Va12.3-CAMSAQQAGTALI-J15 (SEQ ID NO:18)

NNNNNNNGNNNNCNNNTCGCCCTTNAGCAGTGGTATCAACGCAGAGTACGCGGGG
AGGACAGATTTCTTTTATGATTCCTACAGCAGAAAAATGAGAAACGTTTGTTATTAT
TTTTTTTTCGTGTTTAAAGTTTGAATCCTCAGTGAACCAGGGCAGAAAAGAATGATG
AAATCCTTGAGAGTTTTACTGGTGATCCTGTGGCTTCAGTTAAGCTGGGTTTGGAGC
CAACAGAAGGAGGTGGAGCAGGATCCTGGACCACTCAGTGTTCCAGAGGGAGCCAT
TGTTTCTCTCAACTGCACTTACAGCAACAGTGCTTTTCAATACTTCATGTGGTACAGA
CAGTATTCCAGAAAAGGCCCTGAGTTGCTGATGTACACATACTCCAGTGGTAACAAA
GAAGATGGAAGGTTTACAGCACAGGTCGATAAATCCAGCAAGTATATCTCCTTGTTC
ATCAGAGACTCACAGCCCAGTGATTCAGCCACCTACCTCTGTGCAATGAGCGCGCA

ACAGGCAGGAACTGCTCTGATCTTTGGGAAGGGAACCACCTTATCAGTGAGTTCCAA
TATCCAGAACCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGACAA
GTCTGTCTGCCTATTCACCGATTTTGANTCTCAAACAAATGTGTCACAAAGTAAGGA
TTCTGATGTGTATAANGGCGAATTCGTTTAAACCTGCAGGACTAGTCCCTTTAGTGA
GGGTTAATTCTGAGCTTGGCGNNATCNNNNNNAANNNTNTTTTNNNNNNNNN (SEQ ID NO:71)

B60-SL9 Vb11.2
Vb11.2-CASSLVIMSEQY-J2.7 (SEQ ID NO:20)

NNNNNNNNGNNNCNNNTCGCCCTTGGTGTGGGAGANCTCTGCTTCTGATGGCTCAA
ACACAGCGACCTCGGGTGGGAACACGTTTTTCAGGTCCTCTGTGACCGTGAGCCTGG
TGCCCGGCCCGAAGTACTGCTCGCTCATGGTGACTAAGCTGCTGGCACAGAGATAC
ACGGCCGAGTCCTCAAGCTTTGCAGGCTGGATCTTGAGAGTGGAGTCTACTCCTTTG
AGCCTCTCTGCAGAAAATCGATCCTTAGGCAACTGTGAATCATCCACTACACCGTTA
TTCTGAAACTGAATCAGAAGCTTTGGGCCCTGTCCCAGGATCTGCTGGTACCAGTAA
AGGGTAGCATGGCCAGATATAGGATTGCACCAAAAAGCCACACTCTGCCTTTTCTCT
ATAATCTTATATCTGGGAGACTGGGCAACTCCAGCTTCTGTGAGTTCTGCTCCCAGG
AGACAGAGGGCCGCCCAGCAGAGGAGCCTGGTGCCCATGGCAGGGTCAGGGAAGG
ATGGGAGCTTTGCCCAATCAAGGTCACTGTGAGCAACAGCCCCCGCGTACTCTGCGT
TGATACCACTGCTTAAGGGCGAATTCGTTTAAACCTGCAGGACTAGTCCCTTTAGTG
AGGGTTAATTCTGAGCTTGGCGTNNTCATGGTNNNNNNNNNTTTNCCNNNN (SEQ ID NO:72)

A3/A11 QK10

Vb27-CASSVRTGELF-J2.2 (SEQ ID NO:30)
NNNNNNNNNNNANTCGCCCTTGGTGTGGGAGANCTCTGCTTCTGATGGCTCAAACA
CAGCGACCTCGGGTGGGAACACGTTTTTCAGGTCCTCCAGTACGGTCAGCCTAGAGC
CTTCTCCAAAAAACAGCTCCCCGGTCCGTACGCTGCTGGCACAGAAGTACAGAGAG
GTCTGGTTGGGGCTCGGCGACTCCAGGATCAGGGGGAAATTCCTCTTCTCTTTTCGA
GAGACTTTGTACCCTTCAGGAACATCTCCCTTATCAGTCACCTCAACATTCATTGAAT
AGTAGATCTGCCTTAAGCCCAGCCCTGGGTCTTGNTGNNACCAGAACAGAATTCGA
GAAGGGCGAATTCGCGGCCGCTAAATTCAATTCGCCCTATAGTGAGTCGTATTACAA
TTCACTGGCCGNNNTTTTANNN (SEQ ID NO:73)

Vb9-CASSERDSQYQETQY-J2.5 (SEQ ID NO:33)
NNNNNNNNNNNNNTCGCCCTTGGTGTGGGAGANCTCTGCTTCTGATGGCTCAAACA
CAGCGACCTCGGGTGGGAACACGTTTTTCAGGTCCTCGAGCACCAGGAGCCGCGTG
CCTGGCCCGAAGTACTGGGTCTCTTGGTACTGACTGTCCCTCTCGCTGCTGGCACAG
AAATACAAAGCTGAGTCCCCCAGCTCCAGAGAGCTCAGGTTTAGTTCAGAGTGCAA
GTCAGGGAACTGTTGTGCGGAGAATCGTTCAAGAATGTTTCCTTTTGCTCTCTCTTCT
CCATTATAATACTGAATGAGGAACTGGAGGCCCTGGTCCAGGCTCTGATGGTACCAN
NACAGAATTCGAGAAGGGCGAATTCGCGGCCGCTAAATTCAATTCGCCCTATAGTG
AGTCGTATTACAATTCACTGGCCGNNCGTTTTANAN (SEQ ID NO:74)

Va29-CAASFTQNGLT-J45 (SEQ ID NO:34)

NNNNNNNNNNNNANTCGCCCTTANCAGTGGTATCAACGCAGAGTACGCGGGGGGA
CATGAATAAAGCACAGGAGGTTGAAGTCAGATTTGCAGCTTTCTAGGCGGGAGACA
AGACAATCTGCATCTTCACAGGGGGGATGGCCATGCTCCTGGGGGCATCAGTGCTG
ATTCTGTGGCTTCAGCCAGACTGGGTAAACAGTCAACAGAAGAATGATGACCAGCA
AGTTAAGCAAAATTCACCATCCCTGAGCGTCCAGGAAGGAAGAATTTCTATTCTGAA
CTGTGACTATACTAACAGCATGTTTGATTATTTCCTATGGTACAAAAAATACCCTGCT
GAAGGTCCTACATTCCTGATATCTATAAGTTCCATTGAGGATAAAAATGAAGATGGA
AGATTCACTGTCTTCTTAAACAAAAGTGCCAAGCACCTCTCTCTGCACATTGTGCCCT
CCCAGCCTGGAGACTCTGCAGTGTACTTCTGTGCAGCAAGCTTCACGCAGAACGGAC
TCACCTTTGGCAAAGGGACTCATCTAATCATCCAGCCCTATATCCAGAACCCTGACC
CTGCCGTGTACCAGCTGAGAGACTCTAACTCCAGTGACAAGTCTGTCTGCCTATTCA
CCGATTTTGATTCTCAAACAAATGTGTCACAAAGTAAGGATTCTGATGTGTATAANG
NCGAATTCGCGGCCGCTAAATTCAATTCGCCCTATAGTGAGTCGTATTACAATTCAC
TGNNNNNCNNNNTTTNN (SEQ ID NO:75)

A3/A11 QK10

Vb14-CASSPVLYEQY-J2.7 (SEQ ID NO:35)
NNNNNNNNNNNNNCGCCCTTGGTGTGGGANANCTCTGCTTCTGATGGCTCAAACAC
AGCGACCTCGGGTGGGAACACGTTTTTCAGGTCCTCTGTGACCGTGAGCCTGGTGCC
CGGCCCGAAGTACTGCTCGTATAGAACGGGGCTGCTGGCACAGAAATAAACTCCAG
AATCCTCCAGTTCTGCAGGCTGCACCTTCAGAGTAGAATACGTCCCTCCAGTCCTTT
CAGCTAAGAATCGATTGTTGGGCATACCGGACTCATCCTGTTTAGACTCTTTCACAA
AATGTAACAGAAATTTTATTTCTTTTCCCATAACATGTCGATACCAGTACAGAATTC
GAGAAGGGCGAATTCGCGGCCGCTAAATTCAATTCGCCCTATAGTGAGTCGTATTAC
AATTCACTGGCCGNCGTTTTNNNN (SEQ ID NO:76)

Vb9-CASSARAFPEGNQPQH-J1.5 (SEQ ID NO:37)
NNNNNTNNNNNNNNATTCGCCCTTGGTGTGGGANANCTCTGCTTCTGANGGCTCAAA
CACAGCGACCTCGGGTGGGAACACCTTGTTCAGGTCCTCTAGGATGGAGAGTCGAG
TCCCATCACCAAAATGCTGGGGCTGATTGCCCTCTGGGAAGGCCCGGGCGCTGCTGG
CACAGAAATACAAAGCTGAGTCCCCCAGCTCCAGAGAGCTCAGGTTTAGTTCAGAG
TGCAAGTCAGGGAACTGTTGTGCGGAGAATCGTTCAAGAATGTTTCCTTTTGCTCTC
TCTTCTCCATTATAATAGTGAATGAGGAACTGGAGGCCCTGGTCCAGGCTCTGACGG
TACCAGTACAGAATTCGAGAAGGGCGAATTCGCGGCCGCTAAATTCAATTCGCCCTA
TAGTGAGTCGTATTACAATTCACTGGCCGTCGTTTTANAN (SEQ ID NO:77)

Va39-CAVVAQGGSEKLV-J57 (SEQ ID NO:38)
NNNNNTNNNNNNNNATTCGCCCTTGGTGTGGGANANCTCTGCTTCTGANGGCTCAAA
CACAGCGACCTCGGGTGGGAACACCTTGTTCAGGTCCTCTAGGATGGAGAGTCGAG
TCCCATCACCAAAATGCTGGGGCTGATTGCCCTCTGGGAAGGCCCGGGCGCTGCTGG
CACAGAAATACAAAGCTGAGTCCCCCAGCTCCAGAGAGCTCAGGTTTAGTTCAGAG
TGCAAGTCAGGGAACTGTTGTGCGGAGAATCGTTCAAGAATGTTTCCTTTTGCTCTC
TCTTCTCCATTATAATAGTGAATGAGGAACTGGAGGCCCTGGTCCAGGCTCTGACGG
TACCAGTACAGAATTCGAGAAGGGCGAATTCGCGGCCGCTAAATTCAATTCGCCCTA
TAGTGAGTCGTATTACAATTCACTGGCCGTCGTTTTANAN (SEQ ID NO:78)

A3 QK10

Vb10.2-CASSETNRVMEAF-J1.1 (SEQ ID NO:39)
NNNNNNNNANNNNTTCGCCCTTGGTGTGGGAGNNCTCTGCTTCTGATGGCTCAAAC
ACAGCGACCTCGGGTGGGAACACCTTGTTCAGGTCCTCTACAACTGTGAGTCTGGTG
CCTTGTCCAAAGAAAGCTTCCATTACCCTGTTTGTTTCACTGCTGGCGCAGAAATAC
ACAGATGTCTGGGAGCGGGTAGCTGACTCCAGAGTGAGGGGGAAATTCTCTGTCTT
GGATCTGGAGACAACATAGCCATCGGGGACTTCTCCTTTATCTGTAATATCAGCAGC
TGCTGAGTAATAGATCAGCCTCAGCCCATGTCCCAGGTCTTGACGGTACCAGAACAG
AATTCGAGAAGGGCGAATTCGCGGCCGCTAAATTCAATTCGCCCTATAGTGAGTCGT
ATTACAATTCACTGGCCGTCGTTTTACN (SEQ ID NO:79)

Vb24-CATSAGRQRDTGELF-J2.2 (SEQ ID NO:41)
NNNNNNNNNNNNTCGCCCTTGGTGTGGGANNNCTCTGCTTCTGATGGCTCAAACAC
AGCGACCTCGGGTGGGAACACGTTTTTCAGGTCCTCCAGTACGGTCAGCCTAGAGCC
TTCTCCAAAAAACAGCTCCCCGGTGTCTCGCTGCCTCCCGGCACTGGTGGCACAGAA
GTAAAGAGCTGTCTGGTTGGGGATGGCAGACTCTAGGGACAGGGAGAATTTAGCCT
GTGCCTGTCGAGAGACACTGTATCCATCAGAGATCTCTCCTTTGTTTATATCTTTGAC
ATCAAAGGAGTAATAGATCAACTGTAGGCCCAGTCCTGGGTCTTGATGGTACCAATA
CAGAATTCGAGAAGGGCGAATTCGCGGCCGCTAAATTCAATTCGCCCTATAGTGAGT
CGTATTACAATTCACTGGCCGTCGTTTTANNN (SEQ ID NO:80)

Va8.6-CAVSDPGFKTI-J9 (SEQ ID NO:40)
NNNNNNNNNNNNNANNNTCGCCCTTATACNCATCAGAATCCTTACTTTGTGACACA
TTTGTTTGAGAATCAAAATCGGTGAATAGGCAGACAGACTTGTCACTGGATTTAGAG
TCTCTCAGCTGGTACACGGCAGGGTCAGGGTTCTGGATATTTGCTTTAACAAATAGT
CTTGTTCCTGCTCCAAAGATAGTTTTGAAGCCTGGATCACTCACAGCACAGAAGTAC
TCAGCCGTGTCGCTTATATGGACTGAGGGTTTCCTCAAGTGGAAGGAAGTTTGACTC
TTGTTAAATTCAGCCTCAAAACCGTTGATGCCTTTAACCAGGGTGGATCCTGATAAA
TACTTCAGGAGAAGCTGGAGTCCTTGGTTGGGGTATTGCACATACCAGAAGAGATA
CACTGAAACAGACGATGAGTAGTTGCACCTCAGCACCACAGGGGCTTCTTCAAAGA
CAGGGACTTGGCTGTCAAGCTGGGTCACAGGCTGGGCTCTGGTTCCTCCCCGGGTAA
AAATCACCTGGAACGCTGGGACGAGCAGCAGGAGCATGGCTGAGCAGTGGCAATGC
TGCAGGACCTTGAGCTGGGCGGACAGAAGCCAAGGGCGCTGAGCCTCAGGAGCTAG
GAACTGTGAGGAGGTTGGATTGGACAAGTCCCTGGCTTTGAAAAGTTTCAGAAACA
GCCCCGCGTACTCCCCGCGTACTCTGCGTTGATACCACTGCTTAAGGGCGAATTCGC
GGCCGCTAAATTCAATTCGCCCTATAGTGAGTCNNATTACAATTCACTGGCNN (SEQ
ID NO:81)

B27-KK10
Va5-CAEDPTSSSGYALN-J4 (SEQ ID NO: 84)

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CAGCTGAGAGACTCTAAATCCAGTGACAAGTCTGTCTGCCTATTCACCGATTTTGAT
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TAAACCTGCAGGACTAGTCCCTTTAGTGAGGGTTAATTCTGAGCTTGGCGTAATCNT
NNNNNNNNNNNTTTTNNNNNNN (SEQ ID NO:85)

Vb7.9-CASSSPKDPSNQPQH-J1.5 (SEQ ID NO: 82)

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GGATCTGGTAAAGCTCCCATCCTGCCCTGACCCTGCCATGGGCACCAGCCTCCTCTG
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AAGGTGTTCCCACCCGAGGTCGCTGTGTTTGAGCCATCAGAAGCAGAGATCTCCCAC
ACCAAGGGCGAATTCGTTTAAACCTGCAGGACTAGTCCCTTTAGTGAGGGTTAATTC
TGAGCTTGGCGTAATCNNNNNNNNNNNNTTTTTNNNNNNNN (SEQ ID NO:86)

Pathogen-specific soluble TCR constructs

Molecular compounds that specifically recognize HIV-1 cytotoxic T cell epitopes bound to MHC class I molecules on the surface of HIV-1 infected cells are powerful tools for the direct targeting of infected cells for *in vivo* immunotherapeutic approaches. Moreover, these compounds are used for the diagnostic *ex vivo* assessment of HIV-1 antigen presented on lymphocytes or professional antigen presenting cells during natural infection. Soluble, single chain α/β T cell receptor constructs that specifically bind to cognate MHC complexes represent the most promising molecules for the direct *ex vivo* or *in vivo* targeting of HIV-1 infected cells. The amino acid sequences of soluble TCRs recognizing a specific pathogen is based on the sequences of naturally-occurring TCRs. Prior to this disclosure, only very limited information was available on the TCR sequences of naturally occurring TCRs specific for HIV-1 or HCV epitopes. The data described herein elucidates sequences for HIV-1 or HCV-specific TCR genes that are used for the construction of soluble TCRs for diagnostic and therapeutic use.

Presently, recombinant HIV-1-specific antibodies are available for the direct targeting of HIV-1 infected cells. One drawback of the antibody approach is that only the envelope of the

HIV-1 virus is accessible for HIV-1 antibodies, while the functionally most important HIV proteins are hidden inside the envelope and only accessible to the immune system after intracellular processing and presentation by MHC class I or II molecules. Once presented by MHC molecules, these HIV gene products are recognized by TCRs, but not by antibodies. HIV-1 antibodies therefore only allow for a very limited targeting of HIV-1 infected cells. The compositions described herein provide a solution to this problem.

The soluble TCRs, which are specific for HIV1 or HCV have significant advantages over existing approaches

The complete sequences of TCR alpha and beta chains of naturally-occurring HIV-1-specific CD8+ T cell clones have been identified. These TCR sequences of HIV-1 or HCV-specific CD8+ T cells have been identified to date.

The TCR sequences are useful for the production of recombinant single chain TCR that are able to specifically recognize HIV-1 infected cells. These recombinant TCR are practically used for (i) the *in vivo* targeting of HIV-1 infected cells in immunotherapeutic approaches, (ii) the *ex vivo* assessment of HIV-1 antigen expression on lymphocytes or professional antigen presenting cells. The quantitative analysis of HIV-1 antigen expression is important in studies on HIV-1 immunopathogenesis and are useful for the *ex vivo* monitoring of immunotherapeutic treatment approaches.

Currently, treatment of HIV-1 infected patients is based on the use of antiretroviral drugs. These drugs are very effective, but have cumulative toxicity, are associated with high pill burdens and can lead to viral resistance. Therefore, there is a continuing need for other treatment options for these patients. Immunotherapeutic treatment approaches with soluble TCRs represent an alternative treatment option for the HIV-1 or HCV infected patient population. In addition, the TCR are used for the *ex vivo* assessment of HIV-1 antigen expression.

Methods of Diagnosis

Soluble TCRs are used to analyze HLA class I-mediated presentation of cytotoxic T cell epitope presentation on professional antigen presenting cells. For example, a sample of bodily fluid, e.g., blood, or bodily tissue, e.g., lymph node, is obtained from a subject. Leukocytes from the sample are contacted with single chain TCRs described herein. To increase sensitivity, four single chain TCR constructs linked together, e.g., with a central streptavidin to form a tetrameric complex. The construct is linked to a detectable marker, e.g., it is labeled with a fluorescence fluorophore. Detectable markers include fluorochromes such as Phycoerythrin (PE), Fluorescein isothiocyanate (FITC), and Allophycocyanin (APC). Detection is carried out by flow cytometry and/or tissue staining (immunohistochemistry). In another example, a plurality of TCR constructs are immobilized in a microarray, e.g., a chip or plate, and a patient-derived sample is allowed to contact the array, the array is washed, and bound cells detected. In this manner, the peptide expressed or presented on the antigen presenting cell of a patient is determined. Thus, soluble TCRs are also useful as a research tool for the *ex vivo* assessment and quantification of HIV-1 or HCV CTL epitope presentation. They are useful tools for identifying patients who express specific HIV-1 or HCV CTL epitopes, and are therefore promising candidates for immunotherapeutic interventions described herein.

Methods of Therapy

To treat patients infected with HCV or HIV, one or a mixture of soluble single chain TCR constructs are administered. The TCRs are conjugated to a second composition such as a cytokine, such as interleukin-2, interferon-gamma, interferon-alpha or cytotoxic reagents, such as perforin, granzyme or specific drugs. For treatment of HCV, the soluble single chain HCV-specific TCR is optionally conjugated or linked to an interferon such as interferon-alpha. One advantage of such a construct is increased half-life and the antigen-specific delivery of these reagents directly to infected cells. This therapeutic strategy reduces the overall drug dose, the dosing frequency, and the treatment-associated side effects.

A TCR construct is selected based on the genetic characteristics (e.g., prevalence of particular HLA type) of the target population. For example, a pool of soluble TCRs are used that recognize a repertoire of cytotoxic T cell epitopes that a restricted by the most frequently-occurring HLA class I molecules in a specific population. Alternatively, the HLA type of one

particular patient is determined and one or more HLA specific TCRs are selected for administration based on the HLA type of the patient.

Parenteral administration, such as intravenous, subcutaneous, intramuscular, and intraperitoneal delivery routes, may be used to deliver soluble TCR constructs. For instance, soluble TCR have been intravenously injected into mice at a dose of 32μg per animal. Determination of patient doses is carried using methods wells known in the art.

The compositions are administered to inhibit a viral pathogen. Determination of the proper dosage and administration regime for a particular situation is within the skill of the art. An effective amount of a therapeutic compound is preferably from about 0.1 mg/kg to about 150 mg/kg. Effective doses vary, as recognized by those skilled in the art, depending on route of administration, excipient usage, and coadministration with other therapeutic treatments including use of other agents or therapeutic agents. A therapeutic regimen is carried out by identifying a mammal, e.g., a human patient suffering from (or at risk of developing) infection by a viral pathogen, using standard methods. The pharmaceutical compound is administered to such an individual using methods known in the art. Preferably, the compound is administered orally, rectally, nasally, topically or parenterally, e.g., subcutaneously, intraperitoneally, intrathecally, intramuscularly, and intravenously.

Other Embodiments

While the invention has been described in conjunction with the detailed description thereof, the foregoing description is intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended claims. Other aspects, advantages, and modifications are within the scope of the following claims.

What is claimed is:

1. A composition comprising an isolated nucleic acid encoding a soluble HLA class I-restricted T cell receptor (TCR) polypeptide, which polypeptide specifically binds to an HIV or HCV epitope.

2. The composition of claim 1, wherein said nucleic acid encode an isolated TCR polypeptide comprising SEQ ID NO:4.

3. The composition of claim 1, wherein said nucleic acid encode an isolated TCR polypeptide comprising SEQ ID NO:6.

4. The composition of claim 1, wherein said nucleic acid encode an isolated TCR polypeptide comprising SEQ ID NO:4 and SEQ ID NO:6

5. The composition of claim 1, wherein said nucleic acid encode an isolated TCR polypeptide comprising SEQ ID NO:27.

6. The composition of claim 1, wherein said nucleic acid encode an isolated TCR polypeptide comprising SEQ ID NO:29.

7. The composition of claim 1, wherein said nucleic acid encode an isolated TCR polypeptide comprising SEQ ID NO:27 and SEQ ID NO: 29.

8. A composition comprising an isolated TCR polypeptide, which binds specifically to a HIV or HCV epitope.

9. The composition of claim 8, wherein said isolated TCR polypeptide comprises SEQ ID NO:4.

10. The composition of claim 8, wherein said isolated TCR polypeptide comprises SEQ ID NO:6.

11. The composition of claim 8, wherein said isolated TCR polypeptide comprises SEQ ID NO:4 and SEQ ID NO:6

12. The composition of claim 8, wherein said isolated TCR polypeptide comprises SEQ ID NO:27.

13. The composition of claim 8, wherein said isolated TCR polypeptide comprises SEQ ID NO:29.

14. The composition of claim 8, wherein said isolated TCR polypeptide comprises SEQ ID NO:27 and SEQ ID NO: 29.

15. The composition of claim 1 or 8, wherein said TCR polypeptide binds to an HIV-1 epitope.

16. The composition of claim 1 or 8, wherein said TCR polypeptide binds to an HCV epitope.

17. The nucleic acid of claim 1, wherein said nucleic acid comprises an alpha chain T cell receptor sequence and a beta chain receptor sequence.

18. The composition of claim 8, wherein said TCR polypeptide further comprises a detectable marker.

19. The TCR polypeptide of claim 18, wherein said detectable marker is a fluorochrome.

20. The TCR polypeptide of claim 8, wherein said TCR polypeptide further comprises a cytotoxic composition.

21. The TCR polypeptide of claim 8, wherein said TCR polypeptide further comprises a cytokine.

22. A composition comprising a plurality of soluble single chain HLA class I-restricted T cell receptor polypeptides of claim 8 immobilized on a solid support, wherein each of said plurality bind to different viral epitope

23. The composition of claim 8, wherein said TCR polypeptide comprises an alpha chain sequence and a beta chain sequence, each of said alpha and beta chain sequences being at least 8 residues in length.

24. The composition of claim 8, wherein each of said alpha and beta chain sequences are between 8 and 20 residues in length.

25. The composition of claim 8, wherein said polypeptide comprises an α chain sequence and a β chain sequence pair in Table 1.

26. The composition of claim 8, wherein said polypeptide comprises an alpha chain sequence selected from those listed in Table 1.

27. The composition of claim 8, wherein said polypeptide comprises a beta chain sequence selected from those listed in Table 1.

28. The composition of claim 1, wherein said nucleic acid comprises an alpha-chain encoding sequence selected from those listed in Table 2.

29. The composition of claim 2, wherein said nucleic acid comprises a beta chain encoding sequence is selected from those listed in Table 2.

30. A method of diagnosing a viral infection, comprising contacting an isolated virus-specific soluble T-cell receptor construct with a sample of a bodily fluid or tissue from a test subject and detecting binding to a T-cell receptor construct, wherein said binding indicates a viral infection.

31. A method of inhibiting a viral infection comprising administering to a subject an isolated single chain soluble virus specific T cell receptor, said receptor comprising a cytotoxic agent.

32. The method of claim 31, wherein said receptor specifically binds to an HIV or HCV epitope.