



(12) **DEMANDE DE BREVET CANADIEN**
CANADIAN PATENT APPLICATION

(13) **A1**

(86) **Date de dépôt PCT/PCT Filing Date:** 2022/09/16
(87) **Date publication PCT/PCT Publication Date:** 2023/03/23
(85) **Entrée phase nationale/National Entry:** 2024/03/15
(86) **N° demande PCT/PCT Application No.:** US 2022/076618
(87) **N° publication PCT/PCT Publication No.:** 2023/044461
(30) **Priorité/Priority:** 2021/09/17 (US63/245,661)

(51) **Cl.Int./Int.Cl. C12N 15/62** (2006.01),
A61K 35/17 (2015.01), **A61K 38/00** (2006.01),
A61P 35/00 (2006.01), **C07K 14/705** (2006.01),
C07K 14/71 (2006.01), **C07K 14/715** (2006.01),
C07K 19/00 (2006.01), **C12N 15/63** (2006.01),
C12N 5/0781 (2010.01), **C12N 5/0783** (2010.01),
C12N 5/0784 (2010.01), **C12N 5/10** (2006.01)

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(54) **Titre : RECEPTEURS DE COMMUTATION UTILISANT DES DOMAINES DE SIGNALISATION D'IL-9**

(54) **Title: SWITCH RECEPTORS USING IL-9 SIGNALING DOMAINS**

(57) **Abstrégé/Abstract:**

The present disclosure generally relates to, inter alia, a class of chimeric switch receptors containing an endodomain of an IL-9 receptor, engineered to modulate transcriptional regulation in a ligand-dependent manner. The disclosure also provides compositions and methods useful for producing such receptors, nucleic acids encoding same, host cells genetically modified with the nucleic acids, as well as methods for modulating gene expression, modulating an activity of a cell, and/or for the treatment of various health conditions or diseases.



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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property

Organization

International Bureau

(43) International Publication Date

23 March 2023 (23.03.2023)



(10) International Publication Number

WO 2023/044461 A3

(51) International Patent Classification:

C07K 14/71 (2006.01) **C12N 5/0784** (2010.01)
C07K 14/715 (2006.01) **A61K 35/17** (2015.01)
C07K 14/705 (2006.01) **A61P 35/00** (2006.01)
C07K 19/00 (2006.01) **A61K 38/00** (2006.01)
C12N 5/0781 (2010.01) **A61K 39/00** (2006.01)
C12N 5/0783 (2010.01)

(21) International Application Number:

PCT/US2022/076618

(22) International Filing Date:

16 September 2022 (16.09.2022)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/245,661 17 September 2021 (17.09.2021) US

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(81) **Designated States** (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available):

ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:

11 May 2023 (11.05.2023)

(54) **Title:** SWITCH RECEPTORS USING IL-9 SIGNALING DOMAINS

(57) **Abstract:** The present disclosure generally relates to, *inter alia*, a class of chimeric switch receptors containing an endodomain of an IL-9 receptor, engineered to modulate transcriptional regulation in a ligand-dependent manner. The disclosure also provides compositions and methods useful for producing such receptors, nucleic acids encoding same, host cells genetically modified with the nucleic acids, as well as methods for modulating gene expression, modulating an activity of a cell, and/or for the treatment of various health conditions or diseases.

WO 2023/044461 A3

SWITCH RECEPTORS USING IL-9 SIGNALING DOMAINS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/245,661, filed September 17, 2021, which is incorporated herein by reference in its entirety.

FIELD

[0002] The present disclosure relates generally to synthetic cellular receptors that bind extracellular ligands and have IL-9 endodomains. The disclosure also provides compositions and methods useful for producing such receptors, nucleic acids encoding same, host cells genetically modified with the nucleic acids, as well as methods for modulating gene expression, modulating an activity of a cell, and/or for the treatment of various health conditions or diseases.

BACKGROUND

[0003] The manipulation of cells, particularly immune cells, to differentiate, develop specialized functions and expand in numbers is of great clinical interest. Many protein factors that affect these activities are known in the art, including in particular cytokines and chemokines. However, these signaling molecules also have pleiotropic effects on cells not targeted for manipulation, and thus methods of selectively activating signaling in a targeted cell population are desirable. The ability to engineer immune cells to carry out controlled behaviors is of interest in the field. For example, in adoptive immunotherapy T cells are isolated from blood, processed *ex vivo*, and re-infused into patients. Such T cells have been developed for use in therapeutic applications such as the treatment of cancer, infection, and autoimmune diseases.

[0004] A critical challenge in cell based therapies is the ability to engineer receptors that respond to native molecules while also allowing the selective manipulation of immune cells. Some groups have manipulated proteins to bind and respond to modified ligands in a manner independent, or orthogonal, from the influence of the native proteins or ligands. This technology relies on the engineering of both an orthogonal cytokine and an orthogonal receptor, and, relies on the premise that native molecules will not recognize the orthogonal receptor. One of the challenges associated with generating orthogonal ligand-receptor pairs is finding mutations that efficiently prevent activation by the endogenous molecule without otherwise compromising the

receptor's structure or intrinsic ability to activate gene transcription. In alternative methods, to modulate signaling in immune cells, the only approach to prevent negative signals delivered by molecules such as PD-1, is to give patients systemic treatment of antagonistic antibodies that bind to PD-1. This approach has the limitation that systemic treatment prevents T cells that are present in the tumor microenvironment and the entire immune system from being inactivated, which in some patients can result in autoimmunity or systemic inflammatory syndrome (Beck et al., 2006, J Clin Oncol 24: 2283-9; Blansfield et al., 2005, J Immunother 28: 593- 8; Dougan et al., 2009, Annual Review of Immunology 27: 83-117).

[0005] The disclosure provided here provides solutions to the problems existing with previous attempts to manipulate immune cells and potentially offer improved methods for treatments involving cell transfer.

SUMMARY

[0006] The present disclosure generally relates to, among other things, chimeric switch receptors containing an endodomain of an IL-9 receptor, engineered to modulate transcriptional regulation in a ligand-dependent manner. The activity of these switch receptors can be controlled by the presence of an extracellular ligand, allowing for spatial and temporal control of specific gene expression in mammalian cells, as well as for use in modulating cell activities or in treating various health conditions, such as diseases.

[0007] In one aspect, provided herein are recombinant nucleic acid molecules encoding chimeric receptors that comprise an extracellular portion comprising a binding domain of an endogenous cytokine receptor, an intracellular portion comprising an endodomain of an IL-9 receptor, and a transmembrane domain that joins the extracellular portion and intracellular portion.

[0008] In some embodiments, the recombinant nucleic acid molecule further comprises one or more linkers.

[0009] In some embodiments, the endogenous cytokine receptor is selected from IL-2rb, IL-2ra, IL-4r, IL-7ra, IL-15ra, and IL-21ra.

[0010] In some embodiments, the endogenous cytokine receptor comprises an amino acid sequence having at least 80% sequence identity to an amino acid sequence selected from SEQ ID Nos: 1-6.

[0011] In some embodiments, the transmembrane domain is selected from the transmembrane domain of IL-9, IL-7ra, IL-2rb, and TNFR1. In some embodiments, the transmembrane domain comprises an amino acid sequence selected from SEQ ID Nos: 53-56.

[0012] In some embodiments, the chimeric receptor comprises an amino acid sequence having at least 80% sequence identity to an amino acid sequence selected from SEQ ID Nos: 63-80.

[0013] In one embodiment, the chimeric receptor comprises the amino acid sequence selected from SEQ ID Nos: 63 and 72.

[0014] In one embodiment, the recombinant nucleic acid molecule is incorporated into a vector.

[0015] In one embodiment, the recombinant nucleic acid molecule further comprises a signal sequence. In one embodiment, the signal sequence comprises the amino acid sequence of MAAPALSWRLPLLILLPLATSWASA (SEQ ID NO: 62).

[0016] In one embodiment, the recombinant nucleic acid molecule further comprises a 2A linker.

[0017] In one embodiment, the recombinant nucleic acid molecule further comprises a nucleic acid sequence encoding a chimeric antigen receptor.

[0018] Another aspect provides recombinant nucleic acid molecules encoding chimeric receptors comprising an extracellular portion comprising a binding domain of an endogenous inhibitory receptor an intracellular portion comprising an endodomain of an IL-9 receptor linked to a BOX1/2 common gamma chain domain; and a transmembrane domain that joins the extracellular portion and the intracellular portion.

[0019] In some embodiments, the recombinant nucleic acid molecule further comprises one or more linkers.

[0020] In some embodiments, the endogenous inhibitory receptor is selected from TGF-beta R1, TGF-beta R2, IL-10ra, FAS, CTLA4, LAG3, TIM3, PD1, ILT2, ILT3, ILT4, ILT5, and VEGF.

[0021] In some embodiments, the endogenous inhibitory receptor comprises an amino acid sequence having at least 80% sequence identity to an amino acid sequence selected from SEQ ID Nos: 7-52.

[0022] In some embodiments, the transmembrane domain is selected from the transmembrane domain of IL-9, IL-7ra, IL-2rb, and TNFR1.

[0023] In some embodiments, the transmembrane domain is selected from the transmembrane domain of IL-9, IL-7ra, IL-2rb, and TNFR1.

[0024] In some embodiments, the chimeric receptor comprises an amino acid sequence having at least 80% sequence identity to an amino acid sequence selected from SEQ ID Nos: 81-203.

[0025] Another aspect provides recombinant nucleic acid molecules encoding chimeric receptors comprising an extracellular portion comprising a binding domain of an endogenous inhibitory receptor linked to an agent specific for the common gamma chain; an intracellular portion comprising an endodomain of an IL-9 receptor; and a transmembrane domain that joins the extracellular portion and the intracellular portion.

[0026] In some embodiments, the recombinant nucleic acid molecule further comprises one or more linkers.

[0027] In some embodiments, the endogenous inhibitory receptor is selected from TGF-beta R1, TGF-beta R2, IL-10ra, FAS, CTLA4, LAG3, TIM3, PD1, ILT2, ILT3, ILT4, ILT5, and VEGF.

[0028] In some embodiments, the endogenous inhibitory receptor comprises an amino acid sequence having at least 80% sequence identity to an amino acid sequence selected from SEQ ID Nos: 7-52.

[0029] In some embodiments, the transmembrane domain is selected from the transmembrane domain of IL-9, IL-7ra, IL-2rb, and TNFR1. In some embodiments, the transmembrane domain comprises an amino acid sequence selected from SEQ ID Nos: 53-56.

[0030] In some embodiments, the agent specific for the common gamma chain comprises a nanobody, a darpin, IL-2, IL-4, IL-7, and scFV.

[0031] Another aspect relates to an expression vector comprising the recombinant nucleic acid molecules of the disclosure.

[0032] Another aspect relates to a recombinant host cell comprising the recombinant nucleic acid of the present disclosure or expression vector of the present disclosure. In some embodiments, the recombinant host cell is a eukaryotic cell. In some embodiments, the recombinant host cell is an animal cell. In some embodiments, the recombinant host cell is a mammalian cell. In some embodiments, the host cell is an immune cell, a neuron, an epithelial cell, and endothelial cell, or a stem cell. In some embodiments, the immune cell is a B cell, a

monocyte, a natural killer (NK) cell, a basophil, an eosinophil, a neutrophil, a dendritic cell, a macrophage, a regulatory T cell, a helper T cell (T_H), a cytotoxic T cell (T_{CTL}), or other T cell.

[0033] Another aspect provides a composition comprising a recombinant nucleic acid of the present disclosure.

[0034] Another aspect provides a composition of cells comprising the expression vector of the present disclosure.

[0035] Another aspect provides a polypeptide encoded by the recombinant nucleic acid the present disclosure.

[0036] Another aspect provides a composition of one or more polypeptides encoded by one or more recombinant nucleic acids of the present disclosure. In one embodiment, the polypeptide comprises an amino acid sequence having at least 80% sequence identity to an amino acid sequence selected from SEQ ID Nos: 1-6. In one embodiment, the polypeptide comprises an amino acid sequence selected from SEQ ID Nos: 53-56. In one embodiment, the polypeptide comprises an amino acid sequence having at least 80% sequence identity to an amino acid sequence selected from SEQ ID Nos: 63-80.

[0037] Another aspect provides a composition of cells capable of expressing the chimeric receptor encoded by the recombinant nucleic acid of the present disclosure.

[0038] Another aspect provides a composition of cells comprising a chimeric receptor comprising an amino acid sequence selected from SEQ ID Nos: 63-203.

[0039] Another aspect relates to a method for modulating the activity of an immune cell comprising administering, to an immune cell, the recombinant nucleic acid of the present disclosure.

[0040] In one embodiment, the immune cell is a B cell, a monocyte, a natural killer (NK) cell, a basophil, an eosinophil, a neutrophil, a dendritic cell, a macrophage, a regulatory T cell, a helper T cell (T_H), a cytotoxic T cell (T_{CTL}), or other T cell. In one embodiment, the immune cell is a T cell. In one embodiment, the T cell is a CAR-T cell.

[0041] Another aspect relates to a method of treating a subject that involves administering, to the subject, a cell expressing the recombinant nucleic acid of the present disclosure.

[0042] In some embodiments, the subject is treated for cancer.

[0043] In some embodiments, the subject is treated for autoimmune disease.

[0044] In some embodiments, the subject is treated for infection.

[0045] The foregoing summary is illustrative only and is not intended to be in any way limiting. In addition to the illustrative embodiments and features described herein, further aspects, embodiments, objects and features of the disclosure will become fully apparent from the drawings and the detailed description and the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0046] FIG. 1 shows the pSTAT expression profile in either stimulated or unstimulated primary human T cells transduced with a lentiviral vector encoding switch receptors of SEQ ID NO:63+CAR+ (IL21R ECD + IL9R TM + IL9R ICD and CAR 4D5), SEQ ID NO:66 (IL15Ra + IL9R TM + IL9R ICD), SEQ ID NO:72+CAR+ (IL4R ECD + IL9R TM + IL9R ICD and CAR 4D5), or SEQ ID NO:153+CAR+ (IL10Ra ECD + IL9R TM + IL9R ICD and CAR 4D5).

[0047] FIG. 2 shows a real-time cytotoxicity assay (RTCA) with T cells co-expressing switch receptor SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) against SKOV-3 human ovarian adenocarcinoma cells expressing HER2. Double-positive T cells (SEQ63+CAR+) were left unstimulated (“no stim”) before being added on SKOV-3 tumor cells at a 1:8 effector-to-target ratio, or preconditioned for 48 hours with IL21 before addition to the plate with continued ligand stimulation (“preconditioned + IL21”). Untransduced T cells (UTD) served as control and were added on tumor cells with continued IL21 stimulation (“UTD + IL21”).

[0048] FIG. 3 shows a real-time cytotoxicity assay (RTCA) with T cells co-expressing switch receptor SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) against SKOV-3 human ovarian adenocarcinoma cells expressing HER2. Double-positive T cells (SEQ72+CAR+) were left unstimulated (“no stim”) before being added on SKOV-3 tumor cells at a 1:8 effector-to-target ratio, or preconditioned for 48 hours with IL4 before addition to the plate with continued ligand stimulation (“preconditioned + IL4”). Untransduced T cells (UTD) served as control and were added on tumor cells with continued IL4 stimulation (“UTD + IL4”).

[0049] FIG. 4 shows a real-time cytotoxicity assay (RTCA) with T cells co-expressing switch receptor SEQ113 (Fas ECD + IL9R TM + IL9R ICD) and CAR (4D5) against SKOV-3 human ovarian adenocarcinoma cells expressing HER2. Double-positive T cells (SEQ113+CAR+) were left unstimulated (“no stim”) before being added on SKOV-3 tumor cells at a 1:4 effector-to-target ratio, or preconditioned for 48 hours with FasL before addition to the plate

(“preconditioned + no stim”). Untransduced T cells (UTD) served as control and were added on tumor cells unstimulated (“UTD + no stim”).

[0050] FIG. 5 shows hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptor SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) and cocultured with IL-21 (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graph depicts fold change over unstimulated.

[0051] FIG. 6 shows hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptor SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) and cocultured with IL-4 (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graph depicts fold change over unstimulated.

[0052] FIG. 7 shows hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptor SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) and cocultured with IL-4 (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of EGF in pg/mL.

[0053] FIGs. 8A-8B show hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptors SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 8A) and SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 8B) and cocultured with their respective ligands (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of FGF-2 in pg/mL.

[0054] FIGs. 9A-9B show hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptors SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 9A) and SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 9B) and cocultured with their respective ligands

(i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of GM-CSF in pg/mL.

[0055] FIG. 10 shows hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptor SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) and cocultured with its respective ligand (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of IFN α 2 in pg/mL.

[0056] FIGs. 11A-11B show hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptors SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 11A) and SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 11B) and cocultured with their respective ligands (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of IFN γ in pg/mL.

[0057] FIG. 12 shows hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptor SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) and cocultured with its respective ligand (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of IL-10 in pg/mL.

[0058] FIGs. 13A-13B show hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptors SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 13A) and SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 13B) and cocultured with their respective ligands (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of IL-1 α in pg/mL.

[0059] FIG. 14 shows hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptor SEQ72

(IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) and cocultured with its respective ligand (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of IL-2 in pg/mL.

[0060] FIGs. 15A-15B show hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptors SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 15A) and SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 15B) and cocultured with their respective ligands (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of IL-3 in pg/mL.

[0061] FIGs. 16A-16B show hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptors SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 16A) and SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 16B) and cocultured with their respective ligands (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of IL-6 in pg/mL.

[0062] FIGs. 17A-17B show hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptors SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 17A) and SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 17B) and cocultured with their respective ligands (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of IP-10 in pg/mL.

[0063] FIGs. 18A-18B show hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptors SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 18A) and SEQ72 (IL4R ECD + IL9R TM + IL9R ICD) and CAR (4D5) (FIG. 18B) and cocultured with their respective ligands (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture

supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of MIP-1a in pg/mL.

[0064] FIG. 19 shows hybrid cytokine receptors induce functional activation of T cells in response to ligand stimulation. T cells were transduced with hybrid cytokine receptor SEQ63 (IL21R ECD + IL9R TM + IL9R ICD) and CAR (4D5) and cocultured with its respective ligand (i) before, (ii) during, or (iii) before + during, co-culture with target cells for 160hrs. Cell culture supernatants were collected and the concentrations of effector cytokines measured by Luminex assay. The graphs shows concentration of RANTES in pg/mL.

DETAILED DESCRIPTION OF THE DISCLOSURE

[0065] The present disclosure generally relates to, among other things, chimeric switch receptors containing an endodomain of an IL-9 receptor and a binding domain of an endogenous receptor, where the chimeric switch receptor is engineered to modulate transcriptional regulation in a ligand-dependent manner. The activity of these switch receptors can be controlled by the presence of an extracellular ligand, allowing for spatial and temporal control of specific gene expression in mammalian cells, as well as for use in modulating cell activities, immune system responses, or in treating various health conditions, such as diseases. Particularly, the chimeric switch receptor (termed “IL-9 switch receptor”), even though containing the endodomain of an IL-9 receptor, does not require IL-9 for activation and can be tailored to be activated by ligands specific for the binding domains of the endogenous receptors, such as normally inhibitory ligands. This class of chimeric switch receptors is synthetic and recombinant, and does not occur in nature. As described below, the chimeric switch receptors disclosed herein can be synthetic polypeptides, and can be engineered, designed, or modified so as to provide desired and/or improved properties, *e.g.*, modulating transcription. The disclosure also provides compositions and methods useful for producing such receptors, nucleic acids encoding same, cells genetically modified with the nucleic acids, as well as methods for modulating an activity of a cell, modulating immune system, and/or for the treatment of various diseases.

[0066] In the following detailed description, the illustrative alternatives described in the detailed description and claims are not meant to be limiting. Other alternatives may be used and other changes may be made without departing from the spirit or scope of the subject matter

presented here. It will be readily understood that the aspects, as generally described herein, can be arranged, substituted, combined, and designed in a wide variety of different configurations, all of which are explicitly contemplated and make part of this application.

DEFINITIONS

[0067] The singular form “a”, “an”, and “the” include plural references unless the context clearly dictates otherwise. For example, the term “a cell” includes one or more cells, including mixtures thereof. “A and/or B” is used herein to include all of the following alternatives: “A”, “B”, “A or B”, and “A and B.”

[0068] The terms “administration” and “administering”, as used herein, refer to the delivery of a composition or formulation as disclosed herein by an administration route including, but not limited to, intravenous, intra-arterial, intracranial, intramuscular, intraperitoneal, subcutaneous, intramuscular, or combinations thereof. The term includes, but is not limited to, administration by a medical professional and self-administration.

[0069] “Cancer” refers to the presence of cells possessing several characteristics typical of cancer-causing cells, such as uncontrolled proliferation, immortality, metastatic potential, rapid growth and proliferation rate, and certain characteristic morphological features. Cancer cells can aggregate into a mass, such as a tumor, or can exist alone within a subject. A tumor can be a solid tumor, a soft tissue tumor, or a metastatic lesion. As used herein, the term “cancer” also encompasses other types of non-tumor cancers. Non-limiting examples include blood cancers or hematological cancers, such as leukemia. Cancer can include premalignant, as well as malignant cancers.

[0070] The terms “cell”, “cell culture”, and “cell line” refer not only to the particular subject cell or cell line but also to the progeny or potential progeny of such a cell, cell culture, or cell line, without regard to the number of transfers or passages in culture. It should be understood that not all progeny are exactly identical to the parental cell. This is because certain modifications may occur in succeeding generations due to either mutations (*e.g.*, deliberate or inadvertent mutations) or environmental influences (*e.g.*, methylation or other epigenetic modifications), such that progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein, so long as the progeny retain the same functionality as that of the original cell, cell culture, or cell line.

[0071] As used herein “endogenous” refers to any material from or produced inside an organism, cell, tissue or system (e.g., as it would occur in nature or naturally produced).

[0072] The term “percent identity”, as used herein in the context of two or more nucleic acids or proteins, refers to two or more sequences or subsequences that are the same or have a specified percentage of nucleotides or amino acids that are the same (e.g., about 60% sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity over a specified region, when compared and aligned for maximum correspondence over a comparison window or designated region) as measured using a BLAST or BLAST 2.0 sequence comparison algorithms with default parameters described below, or by manual alignment and visual inspection. See e.g., the NCBI web site at ncbi.nlm.nih.gov/BLAST. Such sequences are then said to be “substantially identical.” This definition also refers to, or may be applied to, the complement of a sequence. This definition also includes sequences that have deletions and/or additions, as well as those that have substitutions. Sequence identity can be calculated over a region that is at least about 20 amino acids or nucleotides in length, or over a region that is 10-100 amino acids or nucleotides in length, or over the entire length of a given sequence. Sequence identity can be calculated using published techniques and widely available computer programs, such as the GCS program package (Devereux et al, *Nucleic Acids Res.* 12:387, 1984), BLASTP, BLASTN, FASTA (Atschul *et al.*, *J Mol Biol* **215**:403, 1990). Sequence identity can be measured using sequence analysis software such as the Sequence Analysis Software Package of the Genetics Computer Group at the University of Wisconsin Biotechnology Center (1710 University Avenue, Madison, Wis. 53705), with the default parameters thereof.

[0073] As used herein, a “subject” or an “individual” includes animals, such as human (e.g., human subject) and non-human animals. In some embodiments, a “subject” or “individual” is a patient under the care of a physician. Thus, the subject can be a human patient or a subject who has, is at risk of having, or is suspected of having a disease of interest (e.g., cancer) and/or one or more symptoms of the disease. The subject can also be a subject who is diagnosed with a risk of the condition of interest at the time of diagnosis or later. The term “non-human animals” includes all vertebrates, e.g., mammals, e.g., rodents, e.g., mice, non-human primates, and other mammals, such as e.g., sheep, dogs, cows, chickens, and non-mammals, such as amphibians, reptiles, *etc.*

[0074] Where a range of values is provided, it is understood that each intervening value, to the tenth of the unit of the lower limit unless the context clearly dictates otherwise, between the upper and lower limit of that range and any other stated or intervening value in that stated range, is encompassed within the disclosure. The upper and lower limits of these smaller ranges may independently be included in the smaller ranges, and are also encompassed within the disclosure, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the disclosure.

[0075] All ranges disclosed herein also encompass any and all possible sub-ranges and combinations of sub-ranges thereof. Any listed range can be recognized as sufficiently describing and enabling the same range being broken down into at least equal halves, thirds, quarters, fifths, tenths, *etc.* As a non-limiting example, each range discussed herein can be readily broken down into a lower third, middle third and upper third, and so forth. As will also be understood by one skilled in the art all language such as “up to”, “at least”, “greater than”, “less than”, and the like include the number recited and refer to ranges which can be subsequently broken down into sub-ranges as discussed above. Finally, as will be understood by one skilled in the art, a range includes each individual member. Thus, for example, a group having 1-3 articles refers to groups having 1, 2, or 3 articles. Similarly, a group having 1-5 articles refers to groups having 1, 2, 3, 4, or 5 articles, and so forth.

[0076] It is appreciated that certain features of the disclosure, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the disclosure, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable sub-combination. All combinations of the embodiments pertaining to the disclosure are specifically embraced by the present disclosure and are disclosed herein just as if each and every combination was individually and explicitly disclosed. In addition, all sub-combinations of the various embodiments and elements thereof are also specifically embraced by the present disclosure and are disclosed herein just as if each and every such sub-combination was individually and explicitly disclosed herein.

IL-9 AND COMMON GAMMA CHAIN RECEPTORS

[0077] Interleukin-9 (IL-9) is a member of a group of cytokines referred to as the common γ chain cytokines. Common γ chain cytokines exert numerous functions on immune cell survival, function and proliferation. The γ c family consists of six members—IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21—which all have unique receptors. Upon receptor ligation, γ c cytokines through JAK1 and JAK3 activate various developmental pathways including STAT1, STAT3, STAT5, MAPK, and PI3K/AKT pathways.

[0078] An important aspect of γ c receptor signaling is positive and negative regulation of pathways to either enhance or repress signaling. Some of the γ c cytokines can mediate similar signaling pathways and transcriptional programs (Kovanen PE, Rosenwald A, Fu J, Hurt EM, Lam LT, Giltneane JM, et al. Analysis of Gamma C-Family Cytokine Target Genes. Identification of Dual-Specificity Phosphatase 5 (DUSP5) as a Regulator of Mitogen-Activated Protein Kinase Activity in Interleukin-2 Signaling. *J Biol Chem* (2003) 278(7):5205–13; Osinalde N, Sanchez-Quiles V, Akimov V, Guerra B, Blagoev B, Kratchmarova I. Simultaneous Dissection and Comparison of IL-2 and IL-15 Signaling Pathways by Global Quantitative Phosphoproteomics. *Proteomics* (2015) 15(2-3):520–31), however, physiological differences in cytokine signaling are mediated by competition for γ c between the different receptors (Gonnord P, Angermann BR, Sadtler K, Gombos E, Chappert P, Meier-Schellersheim M, et al. A Hierarchy of Affinities Between Cytokine Receptors and the Common Gamma Chain Leads to Pathway Cross-Talk. *Sci Signal* (2018) 11(524)), variability in receptor expression on T cell subsets, a bias for signaling through different STAT molecules, and differences in activation of the MAPK and PI3K pathways (Zeng R, Spolski R, Casas E, Zhu W, Levy DE, Leonard WJ. The Molecular Basis of IL-21-Mediated Proliferation. *Blood* (2007) 109(10):4135–42; Gadina M, Sudarshan C, Visconti R, Zhou YJ, Gu H, Neel BG, et al. The Docking Molecule Gab2 is Induced by Lymphocyte Activation and is Involved in Signaling by Interleukin-2 and Interleukin-15 But Not Other Common Gamma Chain-Using Cytokines. *J Biol Chem* (2000) 275(35):26959–66).

[0079] The IL-9 receptor alpha (IL-9R α), a member of the type I hematopoietin receptor superfamily, has high affinity (K_d of approximately 100 pM) for IL-9. This 64-kDa glycoprotein is reported on a variety of hematopoietic cells, particularly T cells. Similar to the other members of the IL-2 receptor family, IL-9R α also forms a heterotypic receptor complex with the common gamma (γ c) chain. In the IL-9R heterocomplex, the IL-9R α chain is the ligand binding domain

and γ chain serves as the signaling subunit. The IL-9R α subunit is characterized by four extracellular cysteines and the conserved WSXWS motif, while the intracellular domain contains a BOX1 consensus sequence and a serine rich region. IL-9R α is found in both membrane bound and soluble forms, whereas the γ c subunit is observed only in a membrane bound form.

[0080] IL-9 binding to IL-9R α results in the formation the IL-9R heterocomplex. A hallmark of the IL-9R heterocomplex is the absence of any intracellular enzymatic activity, and, therefore, Janus kinases (JAK) need to mediate the phosphorylation of the receptor (Knoops L., Renauld J.C. IL-9 and its receptor: From signal transduction to tumorigenesis. *Growth Factors*. 2004;22:207–215). Upon IL-9 binding to the receptor, a conformational change occurs in the IL-9R heterocomplex, which allows JAK molecules to bind to the proline rich BOX1 motif in the membrane-proximal region of IL-9R α . JAK1 associates with IL-9R α , whereas JAK3 binds to γ c. Phosphorylated JAK1 and JAK3 then mediate the phosphorylation of receptor tyrosine residues. Phosphorylated tyrosine residues act as docking sites for the downstream Src homology 2 (SH2) domain containing signaling molecules such as Signal Transducer and Activator of Transcription (STAT) transcription factors, insulin receptor substrate (IRS), and the adaptors of the Mitogen-Activated Protein Kinase (MAPK) pathways.

COMPOSITIONS OF THE DISCLOSURE

[0081] As described in greater detail below, one aspect of the present disclosure relates to recombinant nucleic acids encoding chimeric switch receptors that include an extracellular portion comprising a binding domain of an endogenous cytokine receptor or endogenous inhibitory receptor, an intracellular portion comprising an endodomain of an IL-9 receptor, and transmembrane domain that joins the extracellular portion and the intracellular portion. Such receptors are engineered to modulate transcriptional regulation in a ligand-dependent manner with various advantages including the ability to convert an otherwise negative signal into a positive signal in the cell. Thus, the present disclosure also encompasses switch receptors that are able to switch negative signals to positive signals for enhancement of an immune response. The present disclosure also encompasses receptors that are able to bind to an endogenous or exogenously given ligand (e.g. a cytokine) and, regardless of the cytokine, result in activation of STAT5, for example, via the common gamma chain and IL-9 endodomain.

[0082] As described in the Examples, certain recombinant nucleic acids encoding chimeric receptors can be tested and validated in T cells. These chimeric receptors are expected to show

similar performance in mouse models as well as models in other suitable animals or *in vitro* systems. The receptors disclosed herein may be engineered into various immune cell types for enhanced discrimination and elimination of tumors, or in recombinant host cells for control of autoimmunity and infection. Accordingly, recombinant host cells and compositions of cells, such as immune cells capable of expressing one or more of the chimeric receptors disclosed herein, are also within the scope of the disclosure. In some embodiments, a composition of cells expresses the chimeric receptor encoded by the recombinant nucleic acid described herein.

Switch Receptors

[0083] The present disclosure is based, *inter alia*, on recombinant nucleic acid molecules encoding chimeric receptors which comprise an endodomain of an IL-9 receptor, thus creating chimeric receptors that can respond to various extracellular ligands while maintaining the ability to initiate intracellular signaling through the IL-9 receptor endodomain. Immune cells expressing these chimeric receptors may be useful in the context of modulating immune cell activity. In some embodiments, the ligand can be added exogenously and not be limited to production within the cell.

[0084] As outlined above, some embodiments of the present disclosure relate to recombinant nucleic acid molecules encoding chimeric receptors containing the endodomain of an IL-9 receptor. In particular, the chimeric receptors, even though containing an IL-9 endodomain, do not require binding of IL-9 for the functioning of the receptors. Generally, the chimeric receptors comprise an extracellular portion, an intracellular portion comprising an endodomain of an IL-9 receptor, and a transmembrane domain that joins the extracellular portion and the intracellular portion. In some embodiments, extracellular portion comprises a binding domain of an endogenous cytokine receptor. In some embodiments, the extracellular portion comprises a binding domain of an endogenous inhibitory receptor.

[0085] In some embodiments, provided herein is a recombinant nucleic acid encoding a chimeric polypeptide including: (a) an extracellular portion comprising a binding domain of an endogenous cytokine receptor; (b) an intracellular portion comprising an endodomain of an IL-9 receptor; (c) a transmembrane domain that joins the extracellular portion and the intracellular portion.

[0086] In some embodiments, provided herein is a recombinant nucleic acid encoding a chimeric polypeptide including: (a) an extracellular portion comprising a binding domain of an

endogenous inhibitory receptor; (b) an intracellular portion comprising an endodomain of an IL-9 receptor linked to a BOX1/2 common gamma chain domain; (c) a transmembrane domain that joins the extracellular portion and the intracellular portion.

[0087] In some embodiments, provided herein is a recombinant nucleic acid encoding a chimeric polypeptide including: (a) an extracellular portion comprising a binding domain of an endogenous inhibitory receptor linked to an agent specific for the common gamma chain; (b) an intracellular portion comprising an endodomain of an IL-9 receptor; (c) a transmembrane domain that joins the extracellular portion and the intracellular portion.

Extracellular Portions

[0088] As outlined above, the extracellular portions of the chimeric receptors (*e.g.*, switch receptors) in some embodiments of the disclosure have a binding domain of an endogenous cytokine receptor or an endogenous inhibitory receptor. A binding domain of an endogenous cytokine receptor can be an extracellular portion of an endogenous cytokine receptor, or a fragment or truncation thereof that can bind a cytokine polypeptide sequence. In some embodiments, the endogenous cytokine receptor is a member of the common gamma chain receptor family. Members of the common gamma chain receptor family are known in the art and are discussed *supra*. In some embodiments, the endogenous cytokine receptor is selected from IL-2rb, IL-2ra, IL-4r, IL-7ra, IL-15ra, and IL-21ra. As described *supra*, IL-2rb, IL-2ra, IL-4r, IL-7ra, IL-15ra, and IL-21ra are all part of the common gamma chain family. Therefore, these receptors are capable of recruiting the common gamma chain, upon ligand binding, and signaling can proceed through the IL-9 endodomain.

[0089] In one embodiment, the endogenous cytokine receptor comprises the amino acid sequence of IL-2rb (SEQ ID NO:1) below:

AVNGTSQFTCFYNSRANISCVWSQDGALQDTSCQVHAWPDRRRWNQTCELLPVSQAS
WACNLILGAPDSQKLTTVDIVTLRVLCREGVRWRVMAIQDFKPFENLRLMAPISLQVVH
VETHRCNISWEISQASHYFERHLEFEARTLSPGHTWEEAPLLTLKQKQEWICLETLPDT
QYEFQVRVKPLQGEFTTWSPWSQPLAFRTKPAALGKDT

[0090] In one embodiment, the endogenous cytokine receptor comprises the amino acid sequence of IL-2ra (SEQ ID NO:2) below:

ELCDDDPPEIPHATFKAMAYKEGTMLNCECKRGFRRIKSGSLYMLCTGNSSHSSWDNQ
CQCTSSATRNTTKQVTPQPEEQKERKTTEMQSPMQPVDQASLPGHCREPPPWENEATER

IYHFVVGQMVYYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTGEMETSQFPG
EEKPQASPEGRPESETSCLVTTTDFQIQTEMAATMETSIFTTEYQ

[0091] In one embodiment, the endogenous cytokine receptor comprises the amino acid sequence of IL-4 (SEQ ID NO:3) below:

MKVLQEPTCVSDYMSISTCEWKMNPTNCSTELRLLYQLVFLSEAHTCIPENNGGAGC
VCHLLMDDVVSADNYTLDLWAGQQLLWKGSEHKPSEHVKPRAPGNLTVHTNVSDTLLL
TWSNPYPDPNYLYNHLTYAVNIWSENDPADFRIYNVTYLEPSLRIAASTLKSGISYRARV
RAWAQCYNNTWSEWSPSTKWHNSYREPFEQH

[0092] In one embodiment, the endogenous cytokine receptor comprises the amino acid sequence of IL-7ra (SEQ ID NO:4) below:

ESGYAQNGDLEDAELDDYSFSCYSQLEVNGSQHSLTCAFEDPDVNITNLEFEICGALVEV
KCLNFRKLQEIYFIETKKFLLIGKSNICVKVGEKSLTCKKIDLTIVKPEAPFDLSVVYR
EGANDFVVTFTNTSHLQKKYVKVLMHDVAYRQEKDENKWTHVNLSSSTKLTLQKRLQP
AAMYIEIKVRSIPDHYFKGFWSEWSPSYFRTPEINNSSGEMD

[0093] In one embodiment, the endogenous cytokine receptor comprises the amino acid sequence of IL-15ra (SEQ ID NO:5) below:

ITCPPPMMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTPS
LKCIRDPALVHQRPAAPPSTVTTAGVTPQPESLSPSGKEPAASSPSSNNTAATTAAIVPGSQ
LMPSKSPSTGTTEISSHESSHGTPSQTTAKNWELTASASHQPPGVYPQGHSDTT

[0094] In one embodiment, the endogenous cytokine receptor comprises the amino acid sequence of IL-21ra (SEQ ID NO:6) below:

CPDLVCYTDYLQTVICILEMWNLHPSTLTLTWQDQYEELKDEATSCSLHRSAHNATHAT
YTCHMDVFHFMADDIFSVNITDQSGNYSQECGSFLLAESIKPAPPFNVTVTFSGQYNISW
RSDYEDPAFYMLKGKLQYELQYRNRGDPWAVSPRRKLISVDSRSVSLPLEFRKDSSYE
LQVRAGPMPGSSYQGTWSEWSDPVIFQTQSEELKE

[0095] In some embodiments, the extracellular portions of the chimeric polypeptides disclosed herein (*e.g.*, IL-9 switch receptors) having at least 80% sequence identity, such as, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or 99% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 1-6 in the Sequence Listing. In some embodiments, the extracellular portion includes an amino acid

sequence having at least 90% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 1-6. In some embodiments, the extracellular portion includes an amino acid sequence having at least 95% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 1-6. In some embodiments, the extracellular portion includes an amino acid sequence having about 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 1-6. In some embodiments, the extracellular portion includes an amino acid sequence having a sequence selected from the group consisting of SEQ ID NOS: 1-6, wherein one, two, three, four, or five of the amino acid residues in any one of the SEQ ID NOS: 1-6 is substituted by a different amino acid residue.

[0096] In another aspect of the present disclosure, the extracellular portion of the chimeric receptor of the disclosure can also comprise a binding domain of an endogenous inhibitory receptor. Specifically, as described *supra*, in some embodiments, provided herein is a recombinant nucleic acid encoding a chimeric polypeptide including: (a) an extracellular portion comprising a binding domain of an endogenous inhibitory receptor linked to an agent specific for the common gamma chain; (b) an intracellular portion comprising an endodomain of an IL-9 receptor; (c) a transmembrane domain that joins the extracellular portion and the intracellular portion.

[0097] As described *supra*, signaling through the IL-9 endodomain requires recruitment of the common gamma chain. In some embodiments, the binding domains of the extracellular portion of the inhibitory receptors described herein are not able to naturally recruit the common gamma chain in order to elicit signaling through the IL-9 endodomain of the chimeric receptor.

Accordingly, in these embodiments, the binding domain of the endogenous inhibitory receptor is linked to an agent specific for the common gamma chain. The binding domain of the inhibitory receptor is linked to the agent specific for the common gamma chain such that both components are able to function in their intended way (e.g., the binding domain is able to bind a ligand and the agent specific for the common gamma chain is able to bind the common gamma chain).

[0098] In some embodiments, the agent specific for the common gamma chain comprises agent specific for the common gamma chain comprises a nanobody, a darpin, IL-2, IL-4, IL-7, or an scFv.

[0099] In some embodiments, an scFv directed to the common gamma chain is cloned in frame with the extracellular portion of the chimeric receptor, with suitable linker sequences inserted

between these components. The binding of the common gamma chain to the scFv will be sufficient to induce chimeric receptor dimerization.

[0100] scFVs directed to the common gamma chain as well as their sequences are known in the art and described in WO 2017/021540. However, the use of scFVs directed to the common gamma chain with respect to switch receptors is not disclosed therein.

[0101] A binding domain of an endogenous inhibitory receptor can be an extracellular portion of an endogenous inhibitory receptor, or a fragment or truncation thereof that can bind a cytokine polypeptide sequence and subsequently decrease immune activity. For example, a natural inhibitory receptor can reduce T cell proliferation, T cell survival, cytokine release, or immune cell lytic activity upon binding of a natural agonist.

[0102] Endogenous inhibitory receptors are well known in the art and are contemplated for use in the compositions described herein (Turnis et al., “Inhibitory Receptors as Targets for Cancer Immunotherapy,” *Eur J Immunol* 2015 45(7):1892-1905).

[0103] In some embodiments, the endogenous inhibitory receptor signals through trimerization. In some embodiments, the endogenous inhibitory receptor is a member of the TNF receptor superfamily.

[0104] In some embodiments, the endogenous inhibitory receptor signals as functional dimers of dimers. In some embodiments, the endogenous inhibitory receptor is a member of the TGF beta superfamily of receptors. Receptors in this family include, for example, Type I, Type II, and Type III receptors. Exemplary members of the Type I receptor family include, without limitation, ACVRL1, ACVR1A, BMPR1A, ACVR1B, TGF β R1, BMPR1B, and ACVR1C. Exemplary members of the Type II receptor family include, without limitation, TGFBR2, BMPR2, ACVR2A, ACVR2B, and AMHR2. TGF β R3 is a member of the Type III family of receptors.

[0105] In some embodiments, the endogenous inhibitory receptor signal as dimers. In some embodiments, the endogenous inhibitory receptor is a member of the VEGF family of receptors. Receptors in this family include, for example, VEGFR1, VEGFR2, and VEGFR3.

[0106] In some embodiments, the endogenous inhibitory receptor is selected from TGF-beta R1, TGF-beta R2, IL-10ra, FAS, CTLA4, LAG3, TIM3, PD1, ILT2, ILT3, ILT4, ILT5, and VEGF. Thus, in some embodiments, the extracellular portion of the chimeric receptor of the disclosure can be a binding domain of TGF-beta R1, TGF-beta R2, IL-10ra, FAS, CTLA4, LAG3, TIM3, PD1, ILT2, ILT3, ILT4, ILT5, and VEGF.

[0107] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of TGFBR1 (SEQ ID NO:7) below:

LQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPDRPFVCAPSSKTGS
VTTYCCNQDHCNKIELPTTVKSSPGLGPVEL

[0108] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of TGFBR2 (SEQ ID NO:8) below:

TIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQE
VCVAVWRKNDENITLETVCHDPKLPYHDFILEDAAAPKCIMKEKKKPGETFFMCSCSSD
ECNDNIIFSEEYNTSNPDLLLIVIFQ

[0109] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of IL-10ra (SEQ ID NO:9) below:

HGTELPSPPSVWFEEFFHHILHWTPIPNQSESTCYEVALLRYGIESWNSISNCSQTLSDYD
LTAVTLDLYHSNGYRARRVRAVDGSRHSNWTVTNTRFSVDEVTLTVGSVNLEIHNGFILG
KIQLPRPKMAPANDTYESIFSHFREYEIAIRKVPGNFTFTHKKVKHENFSLTSGEVGEFC
VQVKPSVASRSNKGMSKEECISLTRQYFTVTN

[0110] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of FAS (SEQ ID NO:10) below:

QVTDINSKGLELRKTVTTVETQNLEGLHHDGQFCHKPCPPGERKARDCTVNGDEPDCV
PCQEGKEYTDKAHFSSKCRRCRLCDEGHGLEVEINCTRTQNTKCRCKPNFFCNSTVCEH
CDPCTKCEHGIKECTLTSNTKCKEEGSRSN

[0111] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of CTLA4 (SEQ ID NO:11) below:

KAMHVAQPAVVLAASSRGIAFVCEYASPGKATEVRVTVLRQADSQVTEVCAATYMMG
NELTFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELMYPPPYLIGINGTQIYVI
DPEPCPDS

[0112] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of LAG3 (SEQ ID NO:12) below:

LQPGAIEVPVWVAQEGAPALPCSPITPLQDLSLLRRAGVTWQHQPDSGPPAAAPGHPLA
PGPHPAAPSSWGPRPRRYTVLSVGPGLRSGRLPLQPRVQLDERGRQRGDFSLWLRPAR
RADAGEYRAAVHLRDRALSCRLRLRLGQASMTASPPGSLRASDWVILNCSFSRPDRPAS

VHWFRNRGQGRVPVRESPHHHLAESFLFLPQVSPMDSGPWGCILTYRDGFNVSIMYNLT
VLGLEPPTPLTVYAGAGSRVGLPCRLPAGVGTRSFLLAKWTTPPGGGPDLLVTGDNGDFT
LRLEDVVSQAQAGTYTCHIHLLQEQLNATVTLAIITVTPKSFGSPGSLGKLLCEVTPVSGQ
ERFVWSSLDTPSQRFSFGPWLEAQEAQLLSQPWQCQLYQGERLLGAAVYFTELSSPGAQ
RSGRAPGALPAGHL

[0113] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of TIM3 (SEQ ID NO:13) below:

SEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWKGACPVFECGNVVLRTDERDVNYW
TSRYWLNGDFRKGDVSLTIENVTLADSGIYCCRIQIPGIMNDEKFNLLKLVKPAKVTPAPT
RQRDFTAAFPRLTTRGHGPAETQTLGSLPDINLTQISTLANELRDSRLANDLRDSGATI
RIG

[0114] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of PD1 (SEQ ID NO:14) below:

FTVTVPKDLVVEYGSNMTIECKFPVEKQLDLAALIVYWEMEDKNIIQFVHGEEDLKVQ
HSSYRQRARLLKDQLSLGNAALQITDVKLQDAGVYRCMISYGGADYKRITVKVNAPYN
KINQRILVVDVPTSEHELTCQAEGYPKAEVIWTSSDHQVLSGKTTTTNSKREEKLFNVTS
TLRINTTTNEIFYCTFRRLDPEENHTAELVIPELPLAHPNER

[0115] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of ILT2 (SEQ ID NO:15) below:

GHLPKPTLWAEPGSVITQGSPVTLRCQGGQETQEYRLYREKKTALWITRIPQELVKKGQ
FPIPSITWEHAGRYRCYYGSDTAGRSESSDPLELVVTGAYIKPTLSAQSPSPVNSGGNVIL
QCDSQVAFDGFSLCKEGEDEHPQCLNSQPHARGSSRAIFSVGPVSPSRWWYRCYAYDS
NSPYEWSLPSDLLELLVLGVSKKPSLSVQPGPIVAPEETLTLQCGSDAGYNRFVLYKDGE
RDFLQLAGAQPQAGLSQANFTLGPVSRSYGGQYRCYGAHNLSSEWSAPSDPLDILIAGQ
FYDRVLSLVQPGPTVASGENVTLLCQSQGWMTFLLTKEGAADDPWRLRSTYQSQKY
QAEFPMGPVTSAHAGTYRCYGSQSSKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSG
PEDQPLTPTGSDPQSGGLGRHLGV

[0116] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of ILT3 (SEQ ID NO:16) below:

QAGPLPKPTLWAEPGSVISWGNSTIWCQGTLEAREYRLDKEESPAPWDRQNPLEPKNK
ARFSIPSMTEYAGRYRCYYRSPVGWSQPSDPLELVMTGAYSKPTLSALPSPLVTSGKS

VTLLCQSRSPMDTFLLIKERA AHPLLHLRSEHGAQQHQA EFPMSPVTSVHGGTYRCFSS
HGF SHYLLSHPSDPLELIVSGSLEDPRPSPTRSVSTAAGPEDQPLMPTGSPHSGLRRHWE

[0117] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of ILT4 (SEQ ID NO:17) below:

QTGTIPKPTLWAE PDSVITQGSPVTLSCQGSLEAQEYRLYREKK SASWITRIRPELVKNG
QFHIPSITWEHTGRYGCQYYSRARWSELS DPLVLVMTGAYPKPTLSAQPSPVVTS GGRV
TLQCESQVAFGGFILCKEGEEHPQCLNSQPHARGSSRAIFSVGPVSPNRRWSHRCYGYD
LNSPYVWSSPSDLELLVPGVSKKPSLSVQPGPVVAPGESLTLQCVSDVGYDRFVLYKE
GERDLRQLPGRQPQAGLSQANFTLGPVSRSYGGQYRCYGAHNLSSECSAPSDPLDILITG
QIRGTPFISVQPGPTVASGENVTLLCQSWRQFHTFLLTKAGAADAPLRLRSIHEY PKYQA
EFPMSPV TSAHAGTYRCYGS LNSDPYLLSHPSEPLELVVSGPSMGSSPPPTGP ISTPAGPE
DQPLTPTGSDPQSG LGRHLGV

[0118] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of ILT5 (SEQ ID NO:18) below:

GPFPKPTLWAE PGSVISW GSPVTIWCQGSQEAQEYRLHKEGSPEPLDRNNPLEPKNKAR
FSIPSMTEHHAGRYRCHYYSSAGWSEPSDPLEMVM TGAYSKPTLSALPSPVVASGGNM
TLRCGSQKGYHHFVLMKEGEHQLPRTLDSQQLHSRGFQALFPVGPVTPSHRWRFTCY Y
YYTNTPWVWSHPSDPLEILPSGVSRKPSLLTLQGPVLAPGQSLTLQCGSDVGYNRFVLY
KEGERDFLQRP GQQPQAGLSQANFTLGPVSPSNGGQYRCYGAHNLSSEWSAPSDPLNIL
MAGQIYDTVSLSAQPGPTVASGENVTLLCQSWWQFD TFLLTKEGA AHPLRLRSMYGA
HKYQA EFPMSPV TSAHAGTYRCYGSYSSNPHLLSHPSEPLELVVSGHSGGSSLPPTGPPS
TPGLGRYLE

[0119] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of VEGFR1 (SEQ ID NO:19) below:

SKLKDPELSLKGTQHIMQAGQTLHLQCRGEAAHKWSLP EMVSKESERLSITKSACGRNG
KQFCSTLTLNTAQANHTGFYSCKYLA VPTSKKKETESA IYIFISDTGRPFVEMYSEIPEIIH
MTEGRELVIPCRVTSPNITVT LKKFPLDTLIPDGKR IIWDSRKGFII SNATYKEIGLLTCEAT
VNGHLYK TNYLTHRQTNTIIDVQISTPRPVKLLRGHTLVLNCTATTPLNTRVQMTWSYP
DEKNKRASVRRRIDQSN SHANIFYSVLTIDKMQNKDKGLYTCRVRSGPSFKSVNTSVHI
YDKAFITVKHRKQQVLETVAGKRSYRLSMKVKAFPSPEVVWLKDGLPATEKSARYLTR
GYSIIKDVTEEDAGNYTILLSIKQSNVFKNL TATLIVNVKPQIYEKAVSSFPDPALYPLGS
RQILTCTAYGIPQPTIKWFWHPCNHNHSEARCD FCSNNEESFILDADSNMGNRIESITQR
MAIIEGKNKMASTLVVADSRISGIYICIASNKVGTVGRN ISFYITDVPNGFHV NLEKMPTE

GEDLKL SCTV NKFLYRDVTWILLRTVNNRTMHYSISKQKMAITKEHSITLNLTIMNVSLQ
 DSGTYACRARNVYTGEELQKKEITIRDQEAPYLLRNLS DHTVAISSSTL DCHANGVPE
 PQITWFKNNHKIQQEPGILGPSSTLFIERVTEEDEGVYHCKATNQKGSVESSAYLTVQG
 TSDKSNLE

[0120] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of VEGFR2 (SEQ ID NO:20) below:

ASVGLPSVSLDLPRLSIQKDILT IKANTTLQITCRGQRDL D WLWPNNQSGSEQRVEVTEC
 SDGLFCKTLTIPKVIGNDTGAYKCFYRETDLASVIYVYVQDYRSPFIASVSDQHGVVYIT
 ENKNKTVVIPCLGSISNLNVSLCARYPEKRFVPDGNRISWDSKKGFTIPSYMISYAGMVF
 CEAKINDESYQSIMYIVVVVGYRIYDVVLSPSHGIELSVGEKLV LNCTARTELVN GIDFN
 WEYPSSKHQHKKLVNRDLKTQSGSEMKKFLSTLTIDGVTRSDQGLYTCAASSGLMTKK
 NSTFVRVHEKPFVAFSGMESLVEATVGERVRIPAKYLGYPPEIKWYKNGIPLESNHTI
 KAGHVLTIMEVSRDTGNYTVILTNPISKEKQSHVVSLV VYVPPQIGEKSLISP VDSYQY
 GTTQTLTCTVYAIPPPHHIHWYWQLEEECANEPSQAVSVTNPYPCEEWRSVEDFQGGNK
 IEVNKNQFALIEGKNKTVSTLVIQAANVSALYKCEAVNKVGRGERVISFHVTRGPEITLQ
 PDMQPTEQESVSLWCTADRSTFENLTWYKLG PQPLPIHV GELPTPVCKNLDTLWKL NAT
 MFSNSTNDILIMELKNASLQDQGDYVCLAQDRKTKKRHC VVRQLTVLERVAPTITGNLE
 NQTTSIGESIEVSCTASGNPPPQIMWFKDNETLVEDSGIVLKDGNRNL TIRRV RKEDEGL
 YTCQACSVLGCAKVEAFFIIEGAQEKTNLE

[0121] In one embodiment, the endogenous inhibitory receptor comprises the amino acid sequence of VEGFR3 (SEQ ID NO:21) below:

YSMTPTL NITEESHVIDTGDSLSISCRGQHPLEWAWPGAQEAPATGDKDSED TG VVRD
 CEGTDARPYCKVLLLHEVHANDTGSYVCYYKYIKARIEGT TAASSYVFVRDFEQPFINK
 PDTLLVNRKDAMWVPCLVSIPGLNVTLRSQSSVLWPDGQEVVWDDRRGMLVSTPLLH
 DALYLQCETTWDQDQDFLSNPFLVHITGNELYDIQLLPRKSLELLVGEKLV LNCTVWAEF
 NSGVTFDWDYPGKQAERGKWVPERRSQQTHTELSSILTIHNVSQHDLGSYVCKANNGI
 QRFRESTEVIVHENPFISVEWLKGPILEATAGDELVKLPVKLAAYPPPEFQWYKD GKALS
 GRHSPHALVLKEVTEASTGTYTLALWNSAAGLRRNISLELVVNVPPQIHEKEASSPSIYS
 RHSRQALTCTAYGVPLPLSIQWHWRPWTPCKMFAQRSLRRRQQQDLMPQCRDWRAVT
 TQDAVNPIESLDTWTEFVEGKNKTVSKLVIQANVVSAMYKCVVSNKVGQDERLIYFYV
 TTIPDGFTIESKPSEELLEGQPVLLSCQADSYKYEHLRWYRLNLSTLHDAHGNPLLLDCK
 NVHLFATPLAASLEEVAPGARHATLSLSIPRVAPEHEGHYVCEVQDRRSHDKHCHKKYL
 SVQALEAPRLTQNLTDLLVNVSDSLEMQLVAGAHAPSIVWYKDERLLEEKSGVDLAD
 SNQKLSIQRVREEDAGRYLCSVCNAKGCVNSSASVAVEGSEDKGSME

[0122] A number of other receptor sequences are contemplated for use in the extracellular portions of the chimeric receptors described herein. Such sequences may be used to switch the natural biology of the receptor ligand or provide for localized stimulation of a cell population. Exemplary sequences of the extracellular portions of such receptors are shown in Table 1 below.

Receptor Extracellular Portion	Amino Acid Sequence	SEQ ID NO
OPG	ETFPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKTVCA APCPDHYTDSWHTSDECLYCSPVCKELQYVKQECNRTHNR VCECKEGRYLEIEFCLKHRSCPPGFGVVQAGTPERNVT CKRCPDGFFSNETSSKAPCRKHTNCSVFGLLLTQKGNATHD NICSGNSESTQKCGIDVTLCCEEAFFRFAVPTKFTPNWLSVLVD NLPGTKVNAESVERIKRQHSSQEQTQQLKLWKHQN KDQDIVKKIHDIDLCENSVQRHIGHANLTFEQLRSLMESLPG KKVGAEDIEKTIKACKPSDQILKLLSLWRIKNGDQDTLKGLM HALKHSKTYHFPKTVTQSLKKTIRFLHSFTMYKLYQKLFLEM IGNQVQSVKISCL	22
TACI	MSGLGRSRRGGRSRVDQEERFPQGLWTGVAMRSCPEEQYW DPLLGTGCMSCKTICNHQSQRCAAFCSRSLSCRKEQGKFYDHL LRDCISCASICGQHPKQCA YFCENKL RSPVNLPPELRRQRSGE VENNSDNSGRYQGLEHRGSEASPALPGLKLSADQVALVYS	23
BCMA	MLQMAGQCSQNEYFDSLLHACIPCQLRCSSTPPLTCQRYC NASVTNSVKGTNA	24
NGFR	KEACPTGLYTHSGECKACNLGEGVAQPCGANQTVCEPCLD SVTFSDVVSATEPCKPCTECVGLQSMSAPCVEADDAVCRCA YGYQDETTGRCEACRVCEAGSLVFSCQDKQNTVCEE CPDGTYSDEANHVDPCLPCTVCEDTERQLRECTRWADAECE EIPGRWITRSTPPEGSDSTAPSTQEPEAPPEQDLIASTVAGVVT TVMGSSQPVVTRGTTDN	25
EDAR	EYSNCGENEYYNQTTGLCQECPPCGPGEEPYLSCGYGKDE DYGCVPKPAEKFSKGGYQICRRHKDCEGFFRATVLTPGDME NDAECGPCLPGYYMLENRPRNIYGMVCYSCLLAPPNTKECV GATSGASANFPGTSGSSTLSPFQHAHKELSGQGHATA	26
DCR2 (TNFRSF10 D)	ATIPRQDEVPPQTVAPQQQRSLKEECPAGSHRSEYTGACN PCTEGVDYTIASNNLPSCLLCTVCKSGQTNKSSCTTTRDTVC QCEKGSFQDKNSPEMCRCTCRTGCPRGMVKVSNCTPRSDIKC KNESAASSTGKTPAAEETVTTLGMLASPYH	27
DCR1 (TNFRSF10 C)	ATTARQEEVPQQTVAPQQQRHSFKGEECPAGSHRSEHTGAC NPCTEGVDYTNASNNPSCFPCTVCKSDQKHKSSCTMTRDT VCQCKEGTFRNENSPEMCRKCSRCPGSEVQVSNCTSWDDIQ CVEEFGANATVETPAAEETMNTSPGTPAPAAEETMNTSPGTP APAAEETMTTSPGTPAPAAEETMTTSPGTPAPAAEETMITSPG TPA	28

CD40	EPPTACREKQYLINSQCCSLCQPGQKLVSDCTEFTETETECLPCG ESEFLDTWNRETHCHQHXYCDPNLGLRVQQKGTSETDTICT CEEGWHCTSEACESCVLHRSCSPGFGVKQIATGVSDTICEPCP VGFFSNVSSAFEKCHPWTSCETKDLVVQQAGTNKTDVVCGP QDRLR	29
DR4	ASGTEAAAATPSKVWGSSAGRIEPRGGGRGALPTSMGQHGP SARARAGRAPGPRPAREASPRLRVHKTFKFVVVGVLQVVP SSAATIKLHDQSIGTQQWEHSPLGELCPPGSHRSEHPGACNR CTEGVGYTNASNNLFACLPCTACKSDEEERSPCTTTRNTACQ CKPGTFRNDNSAEMCRKCSRGCPRGMVKVKDCTPWSDIEC VHKESGNHGN	30
DR6	QPEQKASNIGTYRHVDRAATGQVLTCDKCPAGTYVSEHCTN TSLRVCSSCPVGTFRHENGIEKCHDCSQPCPWPMIEKLPCA ALTDRECTCPPGMFQSNATCAPHTVCPVGWGVRRKKGTETED VRCKQCARGTFSDVPSSVMKCKAYTDCLSQNLVVIKPGTKE TDNVCGLTLPFSSTSPSPGTAIFRPEHMETHEVPSSTYVPKG MNSTESNSSASVRPKVLSSIQEGTVPDNTSSARGKEDVNKTL PNLQVVNHQQGPHRHILKLLPSMEATGGEKSSTPIKGPGRG HPRQNLHKHFDINEH	31
DR5	ITQQDLAPQQRAPQQKRSSPSEGLCPPGHHISEDGRDCISCK YGQDYSTHWNDLLFCLRCTRCDSGEVELSPCTTTRNTVCQC EEGTFREEDSPEMCRKCRGTGCPRGMVKVGDCTPWSDIECVH KESGTKHSGEVPAVEETVTSSPGTPASPCS	32
DR3	QGGTRSPRCDCAGDFHKKIGLFCCRGCAPAGHYLKAPCTEPC GNSTCLVCPQDTFLAWENHHNSECARCQACDEQASQVALE NCSAVADTRCGCKPGWFVECVSQCVSSSPFYCQPCLDCGA LHRHTRLLCSRRDTCGTCLPGFYEHDGCVSCPTSTLGSCP ERCAAVCGWRQ	33
TNFRSF1B	LPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHA KVFCCTKTSDTVCDSCEDSTYTQLWNWVPECLSCGSRSSDQ VETQACTREQNRICTRPGWYCALSKQEGCRLCAPLRKCRP GFGVARPGTETSDVVCKPCAPGTFSNTTSSTDICRPHQICNVV AIPGNASMDAVCTSTSPTRSMAPGAVHLPQPVSTRSQHTQPT PEPSTAPSTSFLPMGPSPPAEGSTGD	34
TNFRSF1	LVPHLGDREKRDSVCPQGYIHPQNNISICCTKCHKGTLYN DCPGPGQDTCRECESGSFTAENHLRHCLSCSKCRKEMGQ VEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCLNG TVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKL CLPQIENVKGTEDSGTT	35
BMPR1B	KKEDGEAPTTPRPKVLRCCKCHHCPEDSVNNICSTDGYCFT MIEEDDSGLPVVTSGCLGLEGSDFQCRDTPIPHQRRSIECCTE RNECNKDLHPTLPPLKNRDFVDGPIHHR	36
BMPR1A	QNLD SMLHGTGMKSDSDQKKSENGVTLAPEDTLPFLKCYCS GHCPDDAINNTCITNGHCFAIIEEDDQGETTLASGCMKYEGS DFQCKDSPKAQLRRTIECCRTNLCNQYLQPTLPPVVIGPFFDG SIR	37

BMPR2	SQNQERLC AFKDPYQQDLGIGESRISHENG TILCSKGSTCYGL WEKSKGDINLVKQGCWSHIGDPQECHYECCVTTTPPSIQNG TYRFCCCSTDLCNVNFTENFPPDTPPLSPPHSFNDET	38
CSF3R	ECGHISVS APIVHLGDPITASCIKQNC SHLDPEPQILWRLGAE LQPGGRQQR LSGDTQESIITLPHLNHTQAFLSCCLNWGNSLQI LDQVELRAGYPPAIPHNLSCLMNLTTSSLICQWEPGPETHLPT SFTLKSFKSRGNCQTQGDSILDCVPKDGQSHCCIPRKHLLLY QNMGIWVQAENALGTSMSPQLCLDPM DVVKLEPPMLRTMD PSPEAAPPAQAGCLQLCWEPWQPGLHINQKCELRHKPQGEA SWALVGPLPLEALQYELCGLLPATAYTLQIRCIRWPLPGHWS DWSPSLELR TTERAPT VRLDTWWRQRQLDPRTVQLFWKPVP LEEDSGRIQGYV VSWRPSGQAGAILPLCNTTEL SCTFHLPSEA QEVALVA YNSAGTSRPTPVVFSESRGPALTRLHAMARDPHS LWVGWEPPNPWPQGYVIEWGLGPPSASNSNKTWRMEQNGR ATGFLLENIRPFQLYEIIVTPLYQDTMGPSQHVYAYSQEMA PSHAPELHLKHIGKTWAQLEWVPEPPELGKSPLTHYTIFWTN AQNQSFSAILNASSRGFVLHGLEPASLYHIHLMAASQAGATN STVLTMLTLTPEGSELH	39
CSF1R	IPVIEPSVPELVVKPGATVTLRCVGN GSVIEWDGPPSPHWTLY SDGSSSILSTNNATFQNTGTYRCTEPGDPLGGSAAIHLVVKDP ARPWNVLAQE VVVFEDQDALLPCLLTDPVLEAGVSLVRVRG RPLMRHTNYSFSPWHGFTIHRAKFIQSQDYQCSALMGGRKV MSISIRLKVQKVIPGPPALTLVPAELVRIRGEAAQIVCSASSVD VNFDVFLQHNNTKLAIPQQSDFHNNRYQKVLTLNLDQVDFQ HAGNYSCVASNVQGKHSTSMFFRVVESAYLNLSSSEQNLIQE VTVGEGNLKVMVEAYPGLOGFNWTYLGPFSDHQPEPKLA NATTKD TYRHTFTLSLPR LKPSEAGRYSFLARNPGGW RALTF ELTLRYPPEVS VIWTFINGSGTLLCAASGYQPQNVTLWQCSG HTDRCDEA QVLQVWDDPYPEVLSQEPFHKVTVQSLLTVELT EHNQTYECRAHNSVGSGSWAFIPISAGAHTHPPDEF LFTP	40
Activin R1A	MEDEKPKVNP KLYMCVCEGLSCGNEDHCEGQQCFSSLSIND GFHVYQKGCFQVYEQGKMTCKTPPSPGQAVECCQGDWCNR NITAQLPTKGKSFPGTQNFHLE	41
Activin R1B	SGPRGVQALLCACTSCLQANYTCETDGACMVSI FNLDGMEH HVRTCIPKVELVPAGKPFYCLSSEDLRNTHCCYTDYCNRIDL RVPSGHLKEPEHPSMWGPVE	42
Activin R1C	LSPGLKCVCLLCDSSNFTCQTEGACWASVMLTNGKEQVIKS CVSLPELNAQVFC HSSNNVTKTECCFTDFCNNITLHLPTASP APKLG PME	43
Activin R2B	SGRGEAETRECIYYNANWELERTNQSGLERCEGEQDKRLHC YASWRNSSGTIELVKKGCWLDDFNCYDRQECVATEENPQV YFCCCEGNFCNERFTHLPEAGGPEVTYEPPTAPTLLT	44
Activin R2A	AILGRSETQECLFFNANWEKDRTNQTGVEPCYGD KDKRRHC FATWKNISGSIEIVKQGCWLDDINCYDR TDCVEKKDSPEVYF CCCEGNMCNEKFSYFPEMEVTQPTSNPVT PKPP	45
TIGIT	MMTGTIETTGNISA EKGGSIILQCHLSSTTAQVTQVNWEQQD	46

	QLLAICNADLGWHISPSFKDRVAPGPGLGLTLQSLTVNDTGE YFCIYHTYPDGTYTGRIFLEVLESSVAEHGARFQIP	
FCGR2B	TPAAPPKAVLKLEPQWINVLQEDSVTLTCRGTHSPESDSIQW FHNGNLIPHTHTQPSYRFKANNDSDGEYTCQTGQTSLSDPVHL TVLSEWLVLQTPHLEFQEGETIVLRCHSWKDKPLVKVTFFQN GKSKKFSRSDPNFSIPQANHSHSGDYHCTGNIGYTLYSSKPVT ITVQAP	47
FCGR1	QVDTTKAVITLQPPWVSFQEETVTLHCEVLHLPGSSSTQWF LNGTATQTSTPSYRITSASVNDSDGEYRCQRGLSGRSDPIQLEI HRGWLLQVSSRVFTEGEPLALRCHAWKDKLVYNVLYYRN GKAFKFFHWNSNLTKTNISHNGTYHCSGMGKHRYTSAGIS VTVKELFPAPVLNASVTSPLLEGNLVTLSCETKLLQRPGLQ LYFSFYMGSKTLRGRNTSSEYQILTARREDSGLYWCEAATED GNVLKRSPELELQVLGLQLPTPVWFH	48
2B4	CQGSADHVVSISGVPLQLQPNISQTKVDSIAWKKLLPSQNGF HHILKWENGSLPSNTSNDRFSEIVKNLSLLIKAAQQQDSGLY CLEVTSISGKVQTATFQVFVFESLLPDKVEKPRLQGQGKILDR GRCQVALSCLVSRDGNVSYAWYRGSKLIQTAGNLTYLDEEV DINGHTYTCNVSNPVSWEHTLNLTDQCQNAHQEFRRWP	49
LAIR1	QEEDLPRPSISAEPTGTVIPLGSHVTFVCRGPVGVQTFRLERES RSTYNDTEDVSQASPESEARFRIDSVSEGNAGPYRCIYYKPP KWSEQSDYLELLVKETSGGPDSPDTEPGSSAGPTQRPSDNSH NEHAPASQGLKAEHLY	50
CD5	RLSWYDPDFQARLTRNSKCGQGLEVYLKDGWHMVCSSQ WGRSSKQWEDPSQASKVCQRLNCGVPLSLGPFLVTYTPQSSI ICYGQLGSFSNCSHSRNDMCHSLGLTCLEPQKTTTPPTTRPPPT TTPEPTAPPRLQLVAQSGGQHCAGVVEFYSGSLGGTISYEAQ DKTQDLENFLCNNLQCGSFLKHLPETEAGRAQDPGEPREHQ PLPIQWKIQNSSCTSLEHCFRKIKPKSGRVLALLCSGFQPKV QSRLVGGSSICEGTVEVRQGAQWAALCDSSSARSSLRWEEV CREQQCGSVNSYRVLDAGDPTSRGLFCPHQKLSQCHELWER NSYCKKVFTVCQDPNP	51
TWEAKR	EQAPGTAPCSRGSWSADLDKCMDCASCRARPHSDFCLGCA AAPPAPFRLLWP	52

[0123] In some embodiments, the extracellular portions of the chimeric polypeptides disclosed herein (*e.g.*, IL-9 switch receptors) having at least 80% sequence identity, such as, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or 99% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 7-52 in the Sequence Listing. In some embodiments, the extracellular portion includes an amino acid sequence having at least 90% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 7-52. In some embodiments, the extracellular portion includes an amino acid

sequence having at least 95% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 7-52. In some embodiments, the extracellular portion includes an amino acid sequence having about 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 7-52. In some embodiments, the extracellular portion includes an amino acid sequence having a sequence selected from the group consisting of SEQ ID NOS: 7-52, wherein one, two, three, four, or five of the amino acid residues in any one of the SEQ ID NOS: 7-52 is substituted by a different amino acid residue.

Transmembrane domain (TMD)

[0124] As outlined above, the chimeric switch receptors of the disclosure also include a transmembrane domain that joins the extracellular portion and the intracellular portion of the chimeric receptor.

[0125] The transmembrane domain is a region, which can be generally hydrophobic, and crosses the cell membrane. This domain can be positioned such that it directly or indirectly connects, or joins, the extracellular portion of the chimeric switch receptor to the intracellular portion of the chimeric switch receptor. This includes, but is not limited to recombinant fusions, covalent bonds, disulfide bonds, ionic bonds, hydrogen bonds, electrostatic bonds, and the like. Transmembrane domains may be a hydrophobic alpha helix that spans the cell membrane. The transmembrane domain associated with the endodomain is commonly used. However, in some embodiments, the transmembrane domain of TNFR1 is used in combination with extracellular portions from the TNF superfamily (e.g., DCR2, TNFRSF1, etc.) to stabilize the receptor structure.

[0126] The transmembrane domain can have any length. In some embodiments, the transmembrane domain includes 1 amino acid or 10 amino acids or 20 amino acids or 50 amino acids or 60 amino acids or 70 amino acids or 80 amino acids or 100 amino acids or 120 amino acids or 140 amino acids or 160 amino acids or 180 amino acids or 200 amino acids or 250 amino acids or 300 amino acids or any number therebetween.

[0127] In some embodiments, the transmembrane domain is selected from the transmembrane domain of IL-9, IL-7ra, IL-2rb, and TNFR1. Exemplary amino sequences of transmembrane domains for use herein are shown in Table 2.

Table 2. Transmembrane domain sequences.

Transmembrane domain	Amino acid sequence	SEQ ID NO
IL-9	LIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPR	53
IL-7ra	PILLTISILSFFSVALLVILACVLW	54
IL-2rb	IPWLGHLLVGLSGAFGFILVYLLI	55
TNFR1	VLLPLVIFFGLCLLSLLFIGLMY	56

[0128] In some embodiments, the transmembrane domain comprises the transmembrane domain of IL-9. In some embodiments, the transmembrane domain comprises the amino acid sequence of LIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPR (SEQ ID NO: 53).

[0129] In some embodiments, the transmembrane domain comprises the transmembrane domain of TNFR1. In some embodiments, the transmembrane domain comprises the amino acid sequence of VLLPLVIFFGLCLLSLLFIGLMY (SEQ ID NO: 56).

[0130] In some embodiments, the transmembrane domain includes an amino acid sequence exhibiting at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% sequence identity to one or more of SEQ ID NOS: 53-56 in the Sequence Listing. In some embodiments, the transmembrane domain includes an amino acid sequence having at least 90% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 53-56. In some embodiments, the transmembrane domain includes an amino acid sequence having at least 95% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 53-56. In some embodiments, the transmembrane domain includes an amino acid sequence having about 100% sequence identity to one or more of SEQ ID NOS: 53-56. In some embodiments, the transmembrane domain includes an amino acid sequence having a sequence selected from the group consisting of SEQ ID NOS: 53-56, wherein one, two, three, four, or five of the amino acid residues in any one of the SEQ ID NOS: 53-56 is substituted by a different amino acid residue.

Endodomain

[0131] In some embodiments, the endodomain is responsible for receptor clustering/dimerization after antigen binding and for initiation of signal transduction to the cell.

[0132] As outlined above, the chimeric receptors of the disclosure include an endodomain of an IL-9 receptor.

[0133] In some embodiments, the amino acid sequence for the IL-9 receptor endodomain is as follows in SEQ ID NO: 57 below:

VKRIFYQNVSPAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQ
EATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA GCTEWRVQTLAYLPQED
WAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHL SALPGNTQSSGPIPALAC
GLSCDHQGLETTQQGVAVVL AGHCQRPGLHEDLQGMLLP SVLSKARSWTF

[0134] In other embodiments, amino acid numbers 292 to 521 of IL-9R α (NCBI REFSEQ: NP_002177.2) can be used.

[0135] Alternatively, a truncated fragment of said endodomain of the IL-9 receptor chain also may be used. For example, the truncated fragment comprises up to 250 amino acids, or is 50 to 200 amino acids or 80 to 150 amino acids of the ILR cytoplasmic domain.

[0136] As described *supra*, one aspect of the present disclosure relates to a recombinant nucleic acid encoding a chimeric receptor including: (a) an extracellular portion comprising a binding domain of an endogenous inhibitory receptor; (b) an intracellular portion comprising an endodomain of an IL-9 receptor linked to a BOX1/2 common gamma chain domain; (c) a transmembrane domain that joins the extracellular portion and the intracellular portion. Extracellular portions comprising binding domains of inhibitory receptors are described above and are useful in the chimeric receptors described *infra* as well. In this category of chimeric receptors, signaling through the IL-9 endodomain requires recruitment of the common gamma chain. In some embodiments, the binding domains of the extracellular portion of the chimeric receptors described herein are not able to naturally recruit the common gamma chain in order to elicit signaling through the IL-9 endodomain of the chimeric receptor. Accordingly, in these embodiments, the endodomain of the IL-9 receptor can be linked to BOX1/2 domain. Receptors of the common gamma chain family contain two regions at the cytoplasmic tail, termed Box 1 and Box 2. These domains are critical for the association of JAKs with the receptor (see for example, Murakami M, Narazaki M, Hibi M, Yawata H, Yasukawa K, Hamaguchi M, Taga T, Kishimoto T (1991) Critical cytoplasmic region of the interleukin 6 signal transducer gp130 is conserved in the cytokine receptor family. *Proc Natl Acad Sci U S A* 88:11349–11353). Generally, the Box1 domain contains a proline-rich segment of amino acid residues, and the Box2 domain contains a hydrophobic segment of amino acid residues.

[0137] In some embodiments, the chimeric receptor comprises a BOX1/2 domain of the following amino acid sequence of SEQ ID NO: 58

ERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALG
EGPGASPCNQHSPYWAPPCYTLKPET

Linkers

[0138] The nucleic acid encoding the chimeric receptor can further comprise a linker between any of the portions or domains described above. As used herein, the term “linker” generally refers to an oligopeptide or polypeptide that functions to link a one region of a nucleic acid to another region of a nucleic acid. The spacer or linker may comprise up to 300 amino acids, 0-100 amino acids, 25-50 amino acids, 10-15 amino acids, for example.

[0139] Linkers useful in the chimeric receptors described herein include those in Table 3 below.

Linker	Amino acid sequence	SEQ ID NO
Gly Ser Linker	GGGGSGGGGSGGGGS	59
Q-Pro Linker	QPQPQPQPQPQP	60
K-Pro Linker	KPKPKPKPKPKP	61

[0140] In some embodiments, the linker is a Gly Ser Linker. In some embodiments, the linker comprising the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO:59).

[0141] In some embodiments, the linker is a Q-Pro Linker. In some embodiments, the linker comprising the amino acid sequence QPQPQPQPQPQP (SEQ ID NO:60).

[0142] In some embodiments, no linker is present.

[0143] In some embodiments, the linker can be a 2A self-cleaving peptide. 2A peptide are a class of 18-22 amino acid peptides, which can result in ribosomal skipping during translation of a protein in a cell. In some embodiments, a linker, such as a 2A peptide, can be included to link the nucleic acid region encoding the chimeric receptor of the disclosure to another nucleic acid region encoding a chimeric antigen receptor (CAR). In some embodiments, the CAR is anti-HER2 CAR (4D5).

Signal Sequence

[0144] A "signal sequence" can also included at the beginning of the coding sequence of the chimeric receptors disclosed herein. This sequence encodes a signal peptide, N-terminal to the

mature polypeptide, that directs the host cell to translocate the polypeptide. Translocation signal sequences can be found associated with a variety of proteins native to eukaryotes and prokaryotes, and are often functional in both types of organisms.

[0145] An exemplary signal sequence that can be used in the chimeric receptors herein includes the amino acid sequence of: MAAPALSWRLPLLILLPLATSWASA (SEQ ID NO: 62)

Nucleic Acid Molecules

[0146] Provided herein are various nucleic acid molecules including nucleotide sequences encoding the chimeric receptors of the disclosure. In some embodiments, expression cassettes and expression vectors contain these nucleic acid molecules operably linked to heterologous nucleic acid sequences such as, for example, regulatory sequences which allow *in vivo* expression of the receptor in a host cell.

[0147] The terms "nucleic acid molecule" and "polynucleotide" are used interchangeably herein, and refer to both RNA and DNA molecules, including nucleic acid molecules comprising cDNA, genomic DNA, synthetic DNA, and DNA or RNA molecules containing nucleic acid analogs. A nucleic acid molecule can be double-stranded or single-stranded (*e.g.*, a sense strand or an antisense strand). A nucleic acid molecule may contain unconventional or modified nucleotides. The terms "polynucleotide sequence" and "nucleic acid sequence" as used herein interchangeably refer to the sequence of a polynucleotide molecule. The nomenclature for nucleotide bases as set forth in 37 CFR §1.822 is used herein.

[0148] Nucleic acid molecules of the present disclosure can be of any length, including for example, between about 1.5 Kb and about 50 Kb, between about 5 Kb and about 40 Kb, between about 5 Kb and about 30 Kb, between about 5 Kb and about 20 Kb, or between about 10 Kb and about 50 Kb, for example between about 15 Kb to 30 Kb, between about 20 Kb and about 50 Kb, between about 20 Kb and about 40 Kb, about 5 Kb and about 25 Kb, or about 30 Kb and about 50 Kb.

[0149] In some embodiments, provided herein is a nucleic acid molecule including a nucleotide sequence encoding a chimeric polypeptide including: (a) an extracellular portion comprising a binding domain of an endogenous cytokine receptor; (b) a transmembrane domain; and (c) an intracellular portion comprising an endodomain of an IL-9 receptor.

[0150] In one embodiment, the nucleic acid molecule includes a sequence encoding a chimeric polypeptide including: (a) a binding domain of IL-21; (b) a transmembrane domain of IL-9; and (c) an endodomain of an IL-9 receptor.

[0151] In one embodiment, the nucleic acid molecule includes a sequence encoding a chimeric polypeptide including: (a) a binding domain of IL-4; (b) a transmembrane domain of IL-9; and (c) an endodomain of an IL-9 receptor.

[0152] In one embodiment, the nucleic acid molecule includes a sequence encoding a chimeric polypeptide including: (a) a binding domain of IL-15Ra; (b) a transmembrane domain of IL-9; and (c) an endodomain of an IL-9 receptor.

[0153] In one embodiment, the nucleic acid molecule includes a sequence encoding a chimeric polypeptide including: (a) a binding domain of IL-10Ra; (b) a transmembrane domain of IL-9; and (c) an endodomain of an IL-9 receptor.

[0154] In some embodiments, provided herein is a nucleic acid molecule including a nucleotide sequence encoding a chimeric polypeptide including: (a) an extracellular portion comprising a binding domain of an endogenous inhibitory receptor; (b) a transmembrane domain; and (c) an intracellular portion comprising an endodomain of an IL-9 receptor linked to a BOX1/2 common gamma chain domain.

[0155] The orientation of the endodomain of the IL-9 receptor linked to a BOX 1/2 common gamma chain domain may be altered depending upon desired structure and function. For example, the intracellular portion can comprise, in an N- to C-terminal direction, an endodomain of an IL-9 receptor, a linker, and a BOX 1/2 common gamma chain domain. Alternatively, the intracellular portion can comprise, in an N- to C-terminal direction, a BOX 1/2 common gamma chain domain, a linker, and an endodomain of an IL-9 receptor.

[0156] In one embodiment, the nucleic acid molecule includes a sequence encoding a chimeric polypeptide including: (a) a binding domain of Fas; (b) a transmembrane domain of IL-9; and (c) an endodomain of an IL-9 receptor linked to a BOX1/2 common gamma chain domain.

[0157] In some embodiments, provided herein is a nucleic acid molecule including a nucleotide sequence encoding a chimeric polypeptide including: (a) an extracellular portion comprising a binding domain of an endogenous inhibitory receptor linked to an agent specific for the common gamma chain; (b) a transmembrane domain; and (c) an intracellular portion comprising an endodomain of an IL-9 receptor.

[0158] The orientation of the extracellular portion comprising a binding domain of an endogenous inhibitory receptor linked to an agent specific for the common gamma chain may be altered depending upon desired structure and function. For example, the extracellular portion can comprise, in an N- to C-terminal direction, a binding domain of an endogenous inhibitory receptor, a linker, and an agent specific for the common gamma chain. Alternatively, the extracellular portion can comprise, in an N- to C-terminal direction, an agent specific for the common gamma chain, a linker, and a binding domain of an endogenous inhibitory receptor.

[0159] In some embodiments, the nucleotide sequence is incorporated into an expression cassette or an expression vector. It will be understood that an expression cassette generally includes a construct of genetic material that contains coding sequences and enough regulatory information to direct proper transcription and/or translation of the coding sequences in a recipient cell, *in vivo* and/or *ex vivo*. Generally, the expression cassette may be inserted into a vector for targeting to a desired host cell and/or into a subject. As such, in some embodiments, an expression cassette of the disclosure include a coding sequence for the chimeric polypeptide as disclosed herein, which is operably linked to expression control elements, such as a promoter, and optionally, any or a combination of other nucleic acid sequences that affect the transcription or translation of the coding sequence.

[0160] In some embodiments, the nucleotide sequence is incorporated into a cloning vector or an expression vector. It will be understood by one skilled in the art that the term “vector” generally refers to a recombinant polynucleotide construct designed for transfer between host cells, and that may be used for the purpose of transformation, *e.g.*, the introduction of heterologous DNA into a host cell. As such, in some embodiments, the vector can be a replicon, such as a plasmid, phage, or cosmid, into which another DNA segment may be inserted so as to bring about the replication of the inserted segment. In some embodiments, the expression vector can be an integrating vector. In some embodiments, the nucleotide sequence is incorporated into a cloning vector.

[0161] As described above in relation to linkers, the nucleic acid sequence encoding a chimeric receptor as described herein can also encode a CAR. Each may each be provided on separate expression vectors, each nucleic acid sequence being operably linked to one or more expression control elements to achieve expression of the CAR and chimeric receptor in the target cell, the vectors being co- transfected into the target cell. Alternatively, the nucleic acid sequences

encoding the CAR and the chimeric receptor may each be provided on a single vector each nucleic acid sequence under the control of one or more expression control elements to achieve expression of the associated nucleic acid sequence. Alternatively, both nucleic acid sequences may be under the control of a single promoter with intervening or downstream control elements that facilitate co-expression of the two sequences from the vector.

[0162] In some embodiments, the expression vector can be a viral vector. As will be appreciated by one of skill in the art, the term “viral vector” is widely used to refer either to a nucleic acid molecule (*e.g.*, a transfer plasmid) that includes virus-derived nucleic acid elements that generally facilitate transfer of the nucleic acid molecule or integration into the genome of a cell or to a viral particle that mediates nucleic acid transfer. Viral particles will generally include various viral components and sometimes also host cell components in addition to nucleic acid(s). The term viral vector may refer either to a virus or viral particle capable of transferring a nucleic acid into a cell or to the transferred nucleic acid itself. Viral vectors and transfer plasmids contain structural and/or functional genetic elements that are primarily derived from a virus. The term “retroviral vector” refers to a viral vector or plasmid containing structural and functional genetic elements, or portions thereof, that are primarily derived from a retrovirus. The term “lentiviral vector” refers to a viral vector or plasmid containing structural and functional genetic elements, or portions thereof, including LTRs that are primarily derived from a lentivirus, which is a genus of retrovirus.

[0163] In some embodiments, provided herein are nucleic acid molecules encoding a polypeptide with an amino acid sequence having at least about 80%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a chimeric receptor disclosed herein. In some embodiments, provided herein are nucleic acid molecules encoding a polypeptide with an amino acid sequence having at least about 80%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to any one of SEQ ID NOS: 63-203 as identified in the Sequence Listing.

[0164] The nucleic acid sequences encoding the chimeric receptors can be optimized for expression in the host cell of interest. For example, the G-C content of the sequence can be adjusted to average levels for a given cell, as calculated by reference to known genes expressed in the host cell. Methods for codon usage optimization are known in the art. Codon usages within the coding sequence of the chimeric receptor disclosed herein can be optimized to enhance expression in the host cell, such that about 1%, about 5%, about 10%, about 25%, about 50%,

about 75%, or up to 100% of the codons within the coding sequence have been optimized for expression in a particular host cell.

[0165] Some embodiments disclosed herein relate to vectors or expression cassettes including a recombinant nucleic acid molecule encoding the chimeric receptors disclosed herein. The expression cassette generally contains coding sequences and sufficient regulatory information to direct proper transcription and/or translation of the coding sequences in a recipient cell, *in vivo* and/or *ex vivo*. The expression cassette may be inserted into a vector for targeting to a desired host cell and/or into a subject. An expression cassette can be inserted into a plasmid, cosmid, virus, autonomously replicating polynucleotide molecule, phage, as a linear or circular, single-stranded or double-stranded, DNA or RNA polynucleotide molecule, derived from any source, capable of genomic integration or autonomous replication, including a nucleic acid molecule where one or more nucleic acid sequences has been linked in a functionally operative manner, *i.e.*, operably linked.

[0166] Also provided herein are vectors, plasmids, or viruses containing one or more of the nucleic acid molecules encoding a chimeric receptor disclosed herein. The nucleic acid molecules can be contained within a vector that is capable of directing their expression in, for example, a cell that has been transformed/transduced with the vector. Suitable vectors for use in eukaryotic and prokaryotic cells are known in the art and are commercially available, or readily prepared by a skilled artisan. See for example, Sambrook, J., & Russell, D. W. (2012). *Molecular Cloning: A Laboratory Manual* (4th ed.). Cold Spring Harbor, NY: Cold Spring Harbor Laboratory and Sambrook, J., & Russel, D. W. (2001). *Molecular Cloning: A Laboratory Manual* (3rd ed.). Cold Spring Harbor, NY: Cold Spring Harbor Laboratory (jointly referred to herein as “Sambrook”); Ausubel, F. M. (1987). *Current Protocols in Molecular Biology*. New York, NY: Wiley (including supplements through 2014); Bollag, D. M. *et al.* (1996). *Protein Methods*. New York, NY: Wiley-Liss; Huang, L. *et al.* (2005). *Nonviral Vectors for Gene Therapy*. San Diego: Academic Press; Kaplitt, M. G. *et al.* (1995). *Viral Vectors: Gene Therapy and Neuroscience Applications*. San Diego, CA: Academic Press; Lefkovits, I. (1997). *The Immunology Methods Manual: The Comprehensive Sourcebook of Techniques*. San Diego, CA: Academic Press; Doyle, A. *et al.* (1998). *Cell and Tissue Culture: Laboratory Procedures in Biotechnology*. New York, NY: Wiley; Mullis, K. B., Ferré, F. & Gibbs, R. (1994). *PCR: The Polymerase Chain Reaction*. Boston: Birkhauser Publisher; Greenfield, E. A. (2014). *Antibodies:*

A Laboratory Manual (2nd ed.). New York, NY: Cold Spring Harbor Laboratory Press; Beaucage, S. L. *et al.* (2000). *Current Protocols in Nucleic Acid Chemistry*. New York, NY: Wiley, (including supplements through 2014); and Makrides, S. C. (2003). *Gene Transfer and Expression in Mammalian Cells*. Amsterdam, NL: Elsevier Sciences B.V., the disclosures of which are incorporated herein by reference).

[0167] DNA vectors can be introduced into eukaryotic cells via conventional transformation or transfection techniques. Suitable methods for transforming or transfecting host cells can be found in Sambrook *et al.* (2012, *supra*) and other standard molecular biology laboratory manuals, such as, calcium phosphate transfection, DEAE-dextran mediated transfection, transfection, microinjection, cationic lipid-mediated transfection, electroporation, transduction, scrape loading, ballistic introduction, nucleoporation, hydrodynamic shock, and infection.

[0168] Viral vectors that can be used in the disclosure include, for example, retrovirus vectors, adenovirus vectors, and adeno-associated virus vectors, lentivirus vectors, herpes virus, simian virus 40 (SV40), and bovine papilloma virus vectors (see, for example, Gluzman (Ed.), *Eukaryotic Viral Vectors*, CSH Laboratory Press, Cold Spring Harbor, N.Y.). For example, a chimeric receptor as disclosed herein can be produced in a eukaryotic host, such as a mammalian cells (*e.g.*, COS cells, NIH 3T3 cells, or HeLa cells). These cells are available from many sources, including the American Type Culture Collection (Manassas, VA). In selecting an expression system, care should be taken to ensure that the components are compatible with one another. Artisans of ordinary skill are able to select and design expression systems suitable and functional in a selected engineered cell. If further guidance is required in selecting an expression system, skilled artisans may consult P. Jones, “Vectors: Cloning Applications”, John Wiley and Sons, New York, N.Y., 2009).

[0169] The nucleic acid molecules provided can contain naturally occurring sequences, or sequences that differ from those that occur naturally, but, due to the degeneracy of the genetic code, encode the same polypeptide, *e.g.*, antibody. These nucleic acid molecules can consist of RNA or DNA (for example, genomic DNA, cDNA, or synthetic DNA, such as that produced by phosphoramidite-based synthesis), or combinations or modifications of the nucleotides within these types of nucleic acids. In addition, the nucleic acid molecules can be double-stranded or single-stranded (*e.g.*, either a sense or an antisense strand).

Recombinant cells and Cell Cultures

[0170] The nucleic acid of the present disclosure can be introduced into a host cell, such as, for example, a human T lymphocyte, to produce a host cell containing the recombinant nucleic acid molecule. Accordingly, some embodiments of the disclosure relate to methods for making a host cell, including (a) providing a cell capable of protein expression and (b) contacting the provided cell with a recombinant nucleic acid of the disclosure.

[0171] Introduction of the nucleic acid molecules of the disclosure into cells can be achieved by methods known to those skilled in the art such as, for example, viral infection, transfection, conjugation, protoplast fusion, lipofection, electroporation, nucleofection, calcium phosphate precipitation, polyethyleneimine (PEI)-mediated transfection, DEAE-dextran mediated transfection, liposome-mediated transfection, particle gun technology, calcium phosphate precipitation, direct micro-injection, nanoparticle-mediated nucleic acid delivery, and the like.

[0172] Accordingly, in some embodiments, the nucleic acid molecules can be delivered by viral or non-viral delivery vehicles known in the art. For example, the nucleic acid molecule can be stably integrated in the host genome, or can be episomally replicating, or present in the recombinant cell as a mini-circle expression vector for transient expression. Accordingly, in some embodiments, the nucleic acid molecule is maintained and replicated in the recombinant cell as an episomal unit. In some embodiments, the nucleic acid molecule is stably integrated into the genome of the recombinant cell. Stable integration can be achieved using classical random genomic recombination techniques or with more precise techniques such as guide RNA-directed CRISPR/Cas9 genome editing, or DNA-guided endonuclease genome editing with NgAgo (*Natronobacterium gregoryi* Argonaute), or TALENs genome editing (transcription activator-like effector nucleases). In some embodiments, the nucleic acid molecule is present in the recombinant cell as a mini-circle expression vector for transient expression.

[0173] The nucleic acid molecules can be encapsulated in a viral capsid or a lipid nanoparticle, or can be delivered by viral or non-viral delivery means and methods known in the art, such as electroporation. For example, introduction of nucleic acids into cells may be achieved by viral transduction. In a non-limiting example, adeno-associated virus (AAV) is engineered to deliver nucleic acids to target cells via viral transduction. Several AAV serotypes have been described, and all of the known serotypes can infect cells from multiple diverse tissue types. AAV is

capable of transducing a wide range of species and tissues *in vivo* with no evidence of toxicity, and it generates relatively mild innate and adaptive immune responses.

[0174] Lentiviral-derived vector systems are also useful for nucleic acid delivery and gene therapy via viral transduction. Lentiviral vectors offer several attractive properties as gene-delivery vehicles, including: (i) sustained gene delivery through stable vector integration into host genome; (ii) the capability of infecting both dividing and non-dividing cells; (iii) broad tissue tropisms, including important gene- and cell-therapy-target cell types; (iv) no expression of viral proteins after vector transduction; (v) the ability to deliver complex genetic elements, such as polycistronic or intron-containing sequences; (vi) a potentially safer integration site profile; and (vii) a relatively easy system for vector manipulation and production.

[0175] In some embodiments, host cells can be genetically engineered (e.g., transduced or transformed or transfected) with, for example, a vector construct of the present application that can be, for example, a viral vector or a vector for homologous recombination that includes nucleic acid sequences homologous to a portion of the genome of the host cell, or can be an expression vector for the expression of the polypeptides of interest. These cells can be either untransformed cells or cells that have already been transfected with at least one nucleic acid molecule.

[0176] In some embodiments, the recombinant cell is a prokaryotic cell or a eukaryotic cell. In some embodiments, the cell is *in vivo*. In some embodiments, the cell is *ex vivo*. In some embodiments, the cell is *in vitro*. In some embodiments, the recombinant cell is a prokaryotic cell including a recombinant nucleic acid as disclosed herein. In some embodiments, the recombinant prokaryotic cell includes a recombinant nucleic acid which is a cloning vector. In some embodiments, the recombinant cell is a eukaryotic cell. In some embodiments, the recombinant cell is an animal cell. In some embodiments, the animal cell is a mammalian cell. In some embodiments, the animal cell is a human cell. In some embodiments, the cell is a non-human primate cell. In some embodiments, the mammalian cell is an immune cell, a neuron, an epithelial cell, and endothelial cell, or a stem cell. In some embodiments, the recombinant cell is an immune system cell, e.g., a lymphocyte (e.g., a T cell or NK cell), or a dendritic cell. In some embodiments, the immune cell is a B cell, a monocyte, a natural killer (NK) cell, a basophil, an eosinophil, a neutrophil, a dendritic cell, a macrophage, a regulatory T cell, a helper T cell (T_H),

a cytotoxic T cell (T_{CTL}), or other T cell. In some embodiments, the immune system cell is a T lymphocyte.

[0177] In some embodiments, the cell is a stem cell. In some embodiments, the cell is a hematopoietic stem cell. In some embodiments of the cell, the cell is a lymphocyte. In some embodiments, the cell is a precursor T cell or a T regulatory (Treg) cell. In some embodiments, the cell is a CD34+, CD8+, or a CD4+ cell. In some embodiments, the cell is a CD8+ T cytotoxic lymphocyte cell selected from the group consisting of naïve CD8+ T cells, central memory CD8+ T cells, effector memory CD8+ T cells, and bulk CD8+ T cells. In some embodiments of the cell, the cell is a CD4+ T helper lymphocyte cell selected from the group consisting of naïve CD4+ T cells, central memory CD4+ T cells, effector memory CD4+ T cells, and bulk CD4+ T cells. In some embodiments, the cell can be obtained by leukapheresis performed on a sample obtained from a subject. In some embodiments, the subject is a human patient.

[0178] In one embodiment, the cell expressing the recombinant nucleic acid molecule described herein is a T- cell which has been modified to surface express a chimeric antigen receptor (a 'CAR-T' cell). As used herein, a CAR-T cell may be engineered to express a chimeric receptor of the present disclosure. CARs useful in the practice of the present disclosure can be prepared in accordance with principles well known in the art. See e.g., Eshhaar et al. United States Patent No. 7,741,465 B1 issued June 22, 2010; Sadelain, et al (2013) Cancer Discovery 3(4):388-398; Jensen and Riddell (2015) Current Opinions in Immunology 33:9-15; Gross, et al. (1989) PNAS(USA) 86(24) : 10024- 10028; Curran, et al. (2012) J Gene Med 14(6): 405- 15. Examples of commercially available CAR-T cell products that may be modified to incorporate a chimeric receptor of the present disclosure include axicabtagene ciloleucel (marketed as Yescarta® commercially available from Gilead Pharmaceuticals) and tisagenlecleucel (marketed as Kymriah® commercially available from Novartis).

[0179] In some embodiments, the recombinant cell further includes a first and a second nucleic acid molecule as disclosed herein, wherein the first nucleic acid molecule and the second nucleic acid molecule do not have the same sequence. In some embodiments, the recombinant cell further includes a first and a second chimeric polypeptide as disclosed herein, wherein the first chimeric polypeptide and the second chimeric polypeptide do not have the same sequence. In some embodiments, the first second chimeric polypeptide is a CAR. In some embodiments, the

first chimeric polypeptide modulates the expression and/or activity of the second chimeric polypeptide.

[0180] In some embodiments, the recombinant cell further includes an expression cassette or vector encoding a protein of interest operably linked to a promoter, wherein expression of the protein is modulated by the chimeric receptor's transcriptional effector. In some embodiments, the protein of interest is heterologous to the recombinant cell. In some embodiments, the heterologous protein is one that is not normally found in the cell, *e.g.*, not normally produced by the cell. In some embodiments, the expression vector encodes a copy of a protein that is already present in the cell. Exemplary types of proteins suitable for use with the compositions and methods disclosed herein include cytokines, cytotoxins, chemokines, immunomodulators, pro-apoptotic factors, anti-apoptotic factors, hormones, differentiation factors, dedifferentiation factors, immune cell receptors, or reporters.

[0181] In another aspect, provided herein are compositions of cells comprising an expression vector described herein. Cell cultures including at least one host cell as disclosed herein, and a culture medium are also contemplated. Generally, the culture medium can be any suitable culture medium for culturing the cells described herein. Techniques for transforming a wide variety of the above-mentioned cells and species are known in the art and described in the technical and scientific literature. Accordingly, cell cultures including at least one recombinant cell as disclosed herein are also within the scope of this application. Methods and systems suitable for generating and maintaining cell cultures are known in the art.

Pharmaceutical compositions

[0182] In some embodiments, the nucleic acids, host cells, and/or polypeptides (*i.e.*, chimeric receptors) of the disclosure can be incorporated into compositions, including pharmaceutical compositions. Such compositions include one or more of the recombinant nucleic acids, host cells, and/or polypeptides (*i.e.*, chimeric receptors) as disclosed herein. The composition can also contain a pharmaceutically acceptable excipient, *e.g.*, a carrier.

[0183] Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.), or phosphate buffered saline (PBS). In all cases, the composition should be sterile and

should be fluid to the extent that easy syringability exists. It should be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants, *e.g.*, sodium dodecyl sulfate. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be generally to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

[0184] Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle, which contains a basic dispersion medium and the required other ingredients from those enumerated above.

[0185] In some embodiments, the chimeric receptors of the disclosure can also be administered by transfection or infection using methods known in the art, including but not limited to the methods described in McCaffrey et al. (Nature 418:6893, 2002), Xia et al. (Nature Biotechnol. 20:1006-10, 2002), or Putnam (Am. J. Health Syst. Pharm. 53:151-60, 1996, erratum at Am. J. Health Syst. Pharm. 53:325, 1996).

[0186] As described in greater detail below, in some embodiments, the host cells of the disclosure can be formulated for administration to a subject using techniques known to the skilled artisan. For example, formulations comprising populations of recombinant cells can include pharmaceutically acceptable excipient(s). Excipients included in the formulations will have different purposes depending, for example, on the recombinant cells used and the mode of administration. Examples of generally used excipients included, without limitation: saline, buffered saline, dextrose, water-for-injection, glycerol, ethanol, and combinations thereof, stabilizing agents, solubilizing agents and surfactants, buffers and preservatives, tonicity agents,

bulking agents, and lubricating agents. The formulations comprising recombinant cells can have been prepared and cultured in the absence of non-human components, *e.g.*, in the absence of animal serum. A formulation can include one population of recombinant cells, or more than one, such as two, three, four, five, six or more populations of recombinant cells.

[0187] Formulations comprising population(s) of recombinant cells can be administered to a subject using modes and techniques known to the skilled artisan. Exemplary modes include, but are not limited to, intravenous injection. Other modes include, without limitation, intratumoral, intradermal, subcutaneous (S.C., s.q., sub-Q, Hypo), intramuscular (i.m.), intraperitoneal (i.p.), intra-arterial, intramedullary, intracardiac, intra-articular (joint), intrasynovial (joint fluid area), intracranial, intraspinal, and intrathecal (spinal fluids). Devices useful for parenteral injection or infusion of the formulations can be used to effect such administration.

METHODS OF THE DISCLOSURE

Methods for modulating an activity of a cell

[0188] In one aspect, provided herein are methods for modulating an activity of an immune cell. The methods involve administering, to an immune cell, the recombinant nucleic acid as described herein. One skilled in the art upon reading the present disclosure will appreciate that the disclosed methods can be carried out *in vivo*, *ex vivo*, or *in vitro*.

[0189] Non-limiting exemplary cellular activities that can be modulated using the methods provided herein include, but are not limited to, gene expression, proliferation, apoptosis, non-apoptotic death, differentiation, dedifferentiation, migration, secretion of a gene product, cellular adhesion, and cytolytic activity.

[0190] In some embodiments, the expression of a gene product of the cell is modulated.

[0191] In some embodiments, the gene product in the cell is selected from the group consisting of a chemokine, a chemokine receptor, a chimeric antigen receptor, a cytokine, a cytokine receptor, a differentiation factor, a growth factor, a growth factor receptor, a hormone, a metabolic enzyme, a pathogen-derived protein, a proliferation inducer, a receptor, an RNA guided nuclease, a site-specific nuclease, a T cell receptor (TCR) or a component thereof, a chimeric antigen receptor (CAR), a toxin, a toxin-derived protein, a transcriptional effector, a transcriptional activator, a transcriptional repressor, a translation regulator, a translational activator, a translational repressor, an activating immuno-receptor, an antibody, an apoptosis

inhibitor, an apoptosis inducer, an engineered T cell receptor, an immuno-activator, an immuno-inhibitor, and an inhibiting immuno-receptor.

[0192] In cases where expression of a chemokine or a cytokine is modulated, in some embodiments, the expression of cytokines and chemokines is modulated such that there is an increase in type-1 polarization following ligand stimulation relative to controls. Exemplary cytokine and chemokines that can be modulated include, without limitation, FGF2, GMCSF, IFN α , IFN γ , IL-10, IL-17, IL-12, IL-2, IL-3, IL-6, IP-10, MIP1 α , and RANTES.

[0193] Methods of measuring levels of cytokines and chemokines are known in the art. Levels of cytokines and chemokines can be measured, for example, by enzyme-linked immunosorbent assay (ELISA), bead based systems (e.g. Luminex), the Cytokine Bead Array (Pharmingen) and array-based systems (e.g., EMD Biosciences' ProteoPlex).

[0194] In some embodiments, the modulation of an activity of an immune cell can involve alteration of cell signaling events within the cell. As described herein, the IL-9 receptor endodomain signals through JAK1 and JAK3 to activate various developmental pathways including STAT1, STAT3, STAT5, MAPK, and PI3K/AKT pathways. Activation of STAT family members through ligand mediated phosphorylation is believed to confer advantages in effector function, polarization and proliferation to T cells. This, in some embodiments, administration of the recombinant nucleic acid encoding the chimeric switch receptor described herein induces phosphorylation of STAT1, STAT3, and/or STAT5 when stimulated with ligand. Methods for measuring the phosphorylation status of one or more proteins is known in the art and includes, for example, western blot and phospho flow cytometry as described in the Examples herein.

[0195] Cell death (e.g., apoptosis and non-apoptotic cell death) can also be modulated by the methods described herein. In some embodiments, administration of the recombinant nucleic acid encoding the chimeric switch receptor described herein can result in increased cell death of a target cell. By way of example, real-time cytotoxicity assays can be used to analyze whether or not cells expressing a chimeric switch receptor of the present disclosure show increased cytotoxicity when exposed to ligand. In some embodiments, cells expressing a chimeric switch receptor of the present disclosure demonstrate improved killing of target cells when stimulated with ligand over unstimulated controls.

Methods of treatment

[0196] Administration of any one of the therapeutic compositions described herein, *e.g.*, chimeric receptors, nucleic acids, host cells, and pharmaceutical compositions, can be used to treat patients for relevant diseases, such as cancers, autoimmune diseases, and infections. In some embodiments, the recombinant nucleic acids, host cells, and pharmaceutical compositions described herein can be incorporated into therapeutic agents for use in methods of treating or aiding in the treatment of a subject who has, who is suspected of having, or who may be at high risk for developing one or more diseases.

[0197] One aspect of the present disclosure is directed to a method of treating a subject that involves administering, to the subject, a chimeric switch receptor of the present disclosure or a cell expressing the recombinant nucleic acid of the present disclosure.

[0198] In one embodiment, the subject is treated for cancer. A cancer may be any unwanted cell proliferation (or any disease manifesting itself by unwanted cell proliferation), neoplasm or tumor or increased risk of or predisposition to the unwanted cell proliferation, neoplasm or tumor. The cancer may be benign or malignant and may be primary or secondary (metastatic). A neoplasm or tumor may be any abnormal growth or proliferation of cells and may be located in any tissue. Examples of tissues include the adrenal gland, adrenal medulla, anus, appendix, bladder, blood, bone, bone marrow, brain, breast, cecum, central nervous system (including or excluding the brain) cerebellum, cervix, colon, duodenum, endometrium, epithelial cells (*e.g.* renal epithelia), gallbladder, oesophagus, glial cells, heart, ileum, jejunum, kidney, lacrimal gland, larynx, liver, lung, lymph, lymph node, lymphoblast, maxilla, mediastinum, mesentery, myometrium, nasopharynx, omentum, oral cavity, ovary, pancreas, parotid gland, peripheral nervous system, peritoneum, pleura, prostate, salivary gland, sigmoid colon, skin, small intestine, soft tissues, spleen, stomach, testis, thymus, thyroid gland, tongue, tonsil, trachea, uterus, vulva, white blood cells.

[0199] Tumors to be treated may be nervous or non-nervous system tumors. Nervous system tumors may originate either in the central or peripheral nervous system, *e.g.* glioma, medulloblastoma, meningioma, neurofibroma, ependymoma, Schwannoma, neurofibrosarcoma, astrocytoma and oligodendroglioma. Non-nervous system cancers/tumors may originate in any other non-nervous tissue, examples include melanoma, mesothelioma, lymphoma, myeloma, leukemia, Non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma, chronic myelogenous

leukemia (CML), acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), cutaneous T-cell lymphoma (CTCL), chronic lymphocytic leukemia (CLL), hepatoma, epidermoid carcinoma, prostate carcinoma, breast cancer, lung cancer, colon cancer, ovarian cancer, pancreatic cancer, thymic carcinoma, NSCLC, haematologic cancer and sarcoma. In particular, treatment of melanoma, kidney cancer (e.g. renal carcinoma) or bladder cancer is contemplated.

[0200] In some embodiments the cancer is an EBV or HPV positive cancer.

[0201] In one embodiment, the subject is treated for autoimmune disease. Exemplary autoimmune diseases include Crohn's disease and Multiple Sclerosis.

[0202] In one embodiment, the subject is treated for infection. An infection may be any infection or infectious disease, e.g. bacterial, viral, fungal, or parasitic infection. In some embodiments it may be particularly desirable to treat chronic/persistent infections, e.g. where such infections are associated with T cell dysfunction or T cell exhaustion. It is well established that T cell exhaustion is a state of T cell dysfunction that arises during many chronic infections (including viral, bacterial and parasitic), as well as in cancer (Wherry Nature Immunology Vol.12, No.6, p492-499, June 2011).

[0203] Examples of bacterial infections that may be treated include infection by *Bacillus* spp., *Bordetella pertussis*, *Clostridium* spp., *Corynebacterium* spp., *Vibrio cholerae*, *Staphylococcus* spp., *Streptococcus* spp. *Escherichia*, *Klebsiella*, *Proteus*, *Yersinia*, *Erwinia*, *Salmonella*, *Listeria* sp, *Helicobacter pylori*, mycobacteria (e.g. *Mycobacterium tuberculosis*) and *Pseudomonas aeruginosa*. For example, the bacterial infection may be sepsis or tuberculosis. Examples of viral infections that may be treated include infection by Epstein-Barr virus, influenza virus, measles virus, hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), lymphocytic choriomeningitis virus (LCMV), Herpes simplex virus and human papilloma virus.

[0204] Examples of fungal infections that may be treated include infection by *Alternaria* sp, *Aspergillus* sp, *Candida* sp and *Histoplasma* sp. The fungal infection may be fungal sepsis or histoplasmosis. Examples of parasitic infections that may be treated include infection by *Plasmodium* species (e.g. *Plasmodium falciparum*, *Plasmodium yoeli*, *Plasmodium ovale*, *Plasmodium vivax*, or *Plasmodium chabaudi chabaudi*). The parasitic infection may be a disease such as malaria, leishmaniasis and toxoplasmosis

Administration of recombinant cells to a subject

[0205] In some embodiments, the methods of the disclosure involve administering an effective amount or number of the recombinant cells to a subject in need of such treatment. This administering step can be accomplished using any method of implantation delivery in the art. For example, the recombinant cells can be infused directly in the subject's bloodstream or otherwise administered to the subject.

[0206] In some embodiments, the methods disclosed herein include administering, which term is used interchangeably with the terms "introducing", "implanting", and "transplanting", recombinant cells into a subject, by a method or route that results in at least partial localization of the introduced cells at a desired site such that a desired effect(s) is/are produced. The recombinant cells or their differentiated progeny can be administered by any appropriate route that results in delivery to a desired location in the subject where at least a portion of the administered cells or components of the cells remain viable. The period of viability of the cells after administration to a subject can be as short as a few hours, *e.g.*, twenty-four hours, to a few days, to as long as several years, or even the lifetime of the subject, *i.e.*, long-term engraftment.

[0207] When provided prophylactically, the recombinant cells described herein can be administered to a subject in advance of a symptom of a disease or condition to be treated. Accordingly, in some embodiments the prophylactic administration of a recombinant cell population prevents the occurrence of symptoms of the disease or condition.

[0208] When provided therapeutically in some embodiments, recombinant cells are provided at (or after) the onset of a symptom or indication of a disease or condition, *e.g.*, upon the onset of disease or condition.

[0209] For use in the various embodiments described herein, an effective amount of recombinant cells as disclosed herein, can be at least 10^2 cells, at least 5×10^2 cells, at least 10^3 cells, at least 5×10^3 cells, at least 10^4 cells, at least 5×10^4 cells, at least 10^5 cells, at least 2×10^5 cells, at least 3×10^5 cells, at least 4×10^5 cells, at least 5×10^5 cells, at least 6×10^5 cells, at least 7×10^5 cells, at least 8×10^5 cells, at least 9×10^5 cells, at least 1×10^6 cells, at least 2×10^6 cells, at least 3×10^6 cells, at least 4×10^6 cells, at least 5×10^6 cells, at least 6×10^6 cells, at least 7×10^6 cells, at least 8×10^6 cells, at least 9×10^6 cells, or multiples thereof. The recombinant cells can be derived from one or more donors or can be obtained from an autologous source. In some embodiments, the recombinant cells are expanded in culture prior to administration to a subject in need thereof.

[0210] In some embodiments, the delivery of a recombinant cell composition (*e.g.*, a composition including a plurality of recombinant cells according to any of the cells described herein) into a subject by a method or route results in at least partial localization of the cell composition at a desired site. A composition including recombinant cells can be administered by any appropriate route that results in effective treatment in the subject, *e.g.*, administration results in delivery to a desired location in the subject where at least a portion of the composition delivered, *e.g.*, at least 1×10^4 cells, is delivered to the desired site for a period of time. Modes of administration include injection, infusion, instillation. “Injection” includes, without limitation, intravenous, intramuscular, intra-arterial, intrathecal, intraventricular, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal, intracerebrospinal, and intrasternal injection and infusion. In some embodiments, the route is intravenous. For the delivery of cells, delivery by injection or infusion is a standard mode of administration.

[0211] In some embodiments, the recombinant cells are administered systemically, *e.g.*, via infusion or injection. For example, a population of recombinant cells are administered other than directly into a target site, tissue, or organ, such that it enters, the subject’s circulatory system and, thus, is subject to metabolism and other similar biological processes.

[0212] The efficacy of a treatment including any of the compositions provided herein for the treatment of a disease or condition can be determined by a skilled clinician. However, one skilled in the art will appreciate that a treatment is considered effective if any one or all of the signs or symptoms or markers of disease are improved or ameliorated. Efficacy can also be measured by failure of a subject to worsen as assessed by decreased hospitalization or need for medical interventions (*e.g.*, progression of the disease is halted or at least slowed). Methods of measuring these indicators are known to those of skill in the art and/or described herein. Treatment includes any treatment of a disease in a subject or an animal (some non-limiting examples include a human, or a mammal) and includes: (1) inhibiting the disease, *e.g.*, arresting, or slowing the progression of symptoms; or (2) relieving the disease, *e.g.*, causing regression of symptoms; and (3) preventing or reducing the likelihood of the development of symptoms.

[0213] In some embodiments of the disclosed methods, the subject is a mammal. In some embodiments, the mammal is a human.

Additional therapies

[0214] As discussed above, the recombinant cells, and pharmaceutical compositions described herein can be administered in combination with one or more additional therapeutic agents such as, for example, chemotherapeutics or anti-cancer agents or anti-cancer therapies. Administration “in combination with” one or more additional therapeutic agents includes simultaneous (concurrent) and consecutive administration in any order. In some embodiments, the one or more additional therapeutic agents, chemotherapeutics, anti-cancer agents, or anti-cancer therapies is selected from the group consisting of chemotherapy, radiotherapy, immunotherapy, hormonal therapy, toxin therapy, and surgery. “Chemotherapy” and “anti-cancer agent” are used interchangeably herein. Various classes of anti-cancer agents can be used. Non-limiting examples include: alkylating agents, antimetabolites, anthracyclines, plant alkaloids, topoisomerase inhibitors, podophyllotoxin, antibodies (*e.g.*, monoclonal or polyclonal), tyrosine kinase inhibitors (*e.g.*, imatinib mesylate (Gleevec® or Glivec®)), hormone treatments, soluble receptors and other antineoplastics.

[0215] Accordingly, in some embodiments, the disclosed treatment methods further include administering to the subject a second therapy. Generally, the second therapy can be any therapy known in the art. Non-limiting examples of therapies suitable for use in combination with the therapeutic compositions disclosed herein include chemotherapy, radiotherapy, immunotherapy, hormonal therapy, toxin therapy, and surgery. In some embodiments, the second therapy includes one or more additional therapeutic agents such as, for example, chemotherapeutics or anti-cancer agents or anti-cancer therapies. In some embodiments, the first therapy and the second therapy are administered together in the same composition. In some embodiments, the first therapy and the second therapy are administered in separate compositions. In some embodiments, the first therapy and the second therapy are administered at the same time. In some embodiments, the first therapy and the second therapy are administered sequentially. In some embodiments, the first therapy is administered before the second therapy. In some embodiments, the first therapy is administered after the second therapy. In some embodiments, the first therapy and the second therapy are administered in rotation.

SYSTEMS AND KITS

[0216] Also provided herein are kits including the recombinant nucleic acids, recombinant cells, or pharmaceutical compositions provided and described herein as well as written instructions for making and using the same. For example, provided herein, in some

embodiments, are kits that include one or more of the following: (i) a recombinant nucleic acids as described herein, (ii) a recombinant cell as described herein, and (iii) a pharmaceutical composition as described herein. In some embodiments, the systems and/or kits of the disclosure further include one or more syringes (including pre-filled syringes) and/or catheters (including pre-filled syringes) used to administer one any of the provided recombinant nucleic acids, recombinant cells, or pharmaceutical compositions to a subject. In some embodiments, a kit can have one or more additional therapeutic agents that can be administered simultaneously or sequentially with the other kit components for a desired purpose, *e.g.*, for modulating an activity of a cell, inhibiting a target cancer cell, or treating a disease in a subject in need thereof.

[0217] Any of the above-described systems and kits can further include one or more additional reagents, where such additional reagents can be selected from: dilution buffers; reconstitution solutions, wash buffers, control reagents, control expression vectors, negative control polypeptides, positive control polypeptides, reagents for in vitro production of the chimeric receptor polypeptides.

[0218] In some embodiments, a system or kit can further include instructions for using the components of the kit to practice the methods. The instructions for practicing the methods are generally recorded on a suitable recording medium. For example, the instructions can be printed on a substrate, such as paper or plastic, etc. The instructions can be present in the kits as a package insert, in the labeling of the container of the kit or components thereof (*i.e.*, associated with the packaging or sub-packaging), etc. The instructions can be present as an electronic storage data file present on a suitable computer readable storage medium, *e.g.* CD-ROM, diskette, flash drive, etc. In some instances, the actual instructions are not present in the kit, but means for obtaining the instructions from a remote source (*e.g.*, via the internet), are provided. An example of this embodiment is a kit that includes a web address where the instructions can be viewed and/or from which the instructions can be downloaded. As with the instructions, this means for obtaining the instructions can be recorded on a suitable substrate.

[0219] No admission is made that any reference cited herein constitutes prior art. The discussion of the references states what their authors assert, and the inventors reserve the right to challenge the accuracy and pertinence of the cited documents. It will be clearly understood that, although a number of information sources, including scientific journal articles, patent documents,

and textbooks, are referred to herein; this reference does not constitute an admission that any of these documents forms part of the common general knowledge in the art.

[0220] The discussion of the general methods given herein is intended for illustrative purposes only. Other alternative methods and alternatives will be apparent to those of skill in the art upon review of this disclosure, and are to be included within the spirit and purview of this application.

[0221] Throughout this specification, various patents, patent applications and other types of publications (e.g., journal articles, electronic database entries, *etc.*) are referenced. The disclosure of all patents, patent applications, and other publications cited herein are hereby incorporated by reference in their entirety to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

EXAMPLES

[0222] The practice of the present disclosure will employ, unless otherwise indicated, conventional techniques of molecular biology, microbiology, cell biology, biochemistry, nucleic acid chemistry, and immunology, which are well known to those skilled in the art. Such techniques are explained fully in the literature cited above.

[0223] Additional embodiments are disclosed in further detail in the following examples, which are provided by way of illustration and are not in any way intended to limit the scope of this disclosure or the claims.

EXAMPLE 1

[0224] *Cloning of chimeric receptors.* DNA encoding the binding domains of IL-2rb, IL-2ra, IL-4r, IL-7ra, IL-15ra, IL-21ra, TGF-beta R1, TGF-beta R2, IL-10ra, FAS, CTLA4, LAG3, TIM3, PD1, ILT2, ILT3, ILT4, ILT5, VEGF; the transmembrane domains of IL-9, IL-7ra and IL-2rb; the endodomain of the IL-9 receptor; the BOX 1/2 common gamma chain domain; and an agent specific for the common gamma chain are cloned, in various configurations, into mammalian expression vectors driven by a CMV or elongation factor (EF)-1 promoter. The vector contains a mammalian selection cassette.

[0225] Similarly, DNA encoding the binding domains of IL-2rb, IL-2ra, IL-4r, IL-7ra, IL-15ra, IL-21ra, TGF-beta R1, TGF-beta R2, IL-10ra, FAS, CTLA4, LAG3, TIM3, PD1, ILT2, ILT3, ILT4, ILT5, VEGF; the transmembrane domains of IL-9, IL-7ra and IL-2rb; the endodomain of

the IL-9 receptor; the BOX $\frac{1}{2}$ common gamma chain domain; and an agent specific for the common gamma chain are cloned, in various configurations, into lentiviral vectors.

EXAMPLE 2

[0226] *Lentivirus expression.* Lentivirus is produced as previously described in [Tiscornia G. et al. Nature Protocols 27 June 2006; doi: 10.1038/nprot.2006.37].

EXAMPLE 3

[0227] *Assessment of surface expression of chimeric receptors.* Mammalian expression constructs encoding for chimeric receptors are transfected into 293 cells using methods well known in the art such as lipofection 2000 (Invitrogen) or electroporation. 24 to 48 hours later, cell surface expression is assessed by flow cytometry using fluorescently labeled antibodies specific for the ectodomains chimeric receptors. An example would be FITC labeled anti-IL4R antibody for 293 cells transduced with construct 73.

[0228] Alternatively, Jurkat T cell are transduced with purified lentivirus expressing the chimeric receptors of interest at an MOI of 20. 24 to 48 hours later, cell surface expression is assessed by flow cytometry using fluorescently labeled antibodies specific for the ectodomains chimeric receptors.

EXAMPLE 4

[0229] *Ligand stimulation and STAT5 activation.* Transfected 293 cells and virally transduced Jurkat T cells are stimulated with individual ligands to analyze the ability of the ligands to bind the chimeric receptors and induce STAT5 activation. Briefly, after stimulation with ligand for various time points, cells are lysed and protein is collected. The phosphorylation status of STAT5 is analyzed by Western Blot using phosphor STAT5 specific antibodies and assessed relative to a negative control comprising an empty vector. STAT5 phosphorylation status of ligand activated cells relative to empty vector controls is also assessed by flow cytometry as previously described. (<http://rhlcflow.facilities.northwestern.edu/files/2011/09/intracellular-phospho-protein-staining.pdf>)

EXAMPLE 5

[0230] *STAT5 reporter assay.* STAT5 reporter assays are done in 293 cells for activated JAK1-3 induced activity. Cells are seeded in a 48 well plate. The next day, cells are transfected by Lipofectamine 2000 (Invitrogen) with the STAT5-Luciferase vector and an internal control plasmid together with other plasmids expressing genes of interest. 24 hours later, the cells are stimulated with appropriate ligand for various time points, then lysed and subjected to internal control fluorescence and luciferase luminescence measurement using a plate reader. The reporter gene activity is shown after being normalized against internal control readings.

EXAMPLE 6

[0231] *Ligand stimulation and cytokine expression.* Jurkat T cell are transduced with purified lentivirus expressing the chimeric receptors of interest. 24 to 48 hours later, cells are stimulated with appropriate ligands for various time points from 0, 15, 30 45 and 60 minutes. Cells are then collected for analysis of expression of IFN γ , IL-4, IL-5, IP-10, IL-2, MIP1 α , MIP1 β , and TNF α using intracellular flow cytometry. Supernatants from the culture are collected analyzed for the expression of 30 cytokines and chemokines (Thermo Fisher) (<https://www.thermofisher.com/order/catalog/product/LHC6003M#/LHC6003M>) by Luminex analysis.

EXAMPLE 7

[0232] *Cytotoxicity Assays.* The ability of the recombinant nucleic acids described herein to stimulate CTL cytotoxicity can be measured by methods known to the skilled person. Cytotoxicity of a T cell to a given target cell can be investigated, for example, using any of the methods reviewed in Zaritskaya et al. Expert Rev Vaccines (2011), 9(6):601 -616, hereby incorporated by reference in its entirety. Additionally, the ability of the chimeric cytokine receptor to enhanced cell killing of a GPC3 CAR is assessed by measuring cellular killing of cell line targets in real time by electrical impedance as described in (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5834184/>). GPC3 CAR (scFv-41BB-CD3 ζ) expressing Lentivirus will be purchased from Creative Biolabs (CAR-M0158-YC) and used to transduce T cells. Briefly, T cells will be isolated from the PBMC fraction of peripheral blood by negative selection. Cells will be stimulated with TransAct (Miltenyi) for 72 hours in the presence of IL-2 prior to Lentiviral transduction. Cells will be incubated for 48 hours and CAR

expressing cells sorted by FACS. The CAR positive fraction will then be transduced with the chimeric cytokine receptor constructs. Cell surface expression of the chimeric cytokine receptor will be assessed 48 hours post transduction, by flow cytometry. Cells will be stimulated with the appropriate ligand for an additional 48 hours, washed and cultured with HEPG2 target cells on XCelligence plates (<https://www.agilent.com/en/product/cell-analysis/real-time-cell-analysis/rtca-analyzers/xcelligence-rtca-mp-multiple-plates-741230>). Transduced T cells and target cells will be cocultured for 96 hours. Target killing will be measured in real time according to the manufacturer's protocol.

EXAMPLE 8

MATERIALS AND METHODS FOR EXAMPLES 9-12

[0233] *Cloning of chimeric receptors.* DNA encoding the binding domains of various endogenous cytokine and inhibitory receptors; the transmembrane domains of IL-9 or TNFR1; the endodomain of the IL-9 receptor; and/or the BOX 1/2 common gamma chain domain; were cloned, in various configurations, into pTRPE backbone lentiviral transfer plasmid. Some receptors were co-expressed with anti-HER2 CAR (4D5) via a 2A linker sequence. The 4D5 amino acid sequence is as follows:

MDFQVQIFSLLISASVIMSRGDIQMTQSPSSLSASVGDRVITICRASQDVNTAVAWYQQ
KPGKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISLQPEDFATYYCQQHYTTPPTFG
QGTVKVEIKRTGSTSGSGKPGSGEGSEVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIH
WVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTA
VYYCSRWGGDGFYAMDVWGQGTLLTVSSTTPAPRPPTPAPTIASQPLSLRPEACRPAA
GGAVHTRGLDFACDIYWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQT
TQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDK
RRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLS
TATKDTYDALHMQALPPR* (SEQ ID NO: 204)

[0234] Similarly, DNA encoding the binding domains of IL-21R, IL-15ra, IL-4ra, IL-10ra, IL-7ra, TWEAKR, CTLA4, TIM3, LAG3, PD1, DCR1, CD40, Fas, Dr4, TNFRSF1B, TGFBR2, TIGIT, 2B4 ; the transmembrane domains of IL-9 and TNFR1; the endodomain of the IL-9

receptor; the BOX $\frac{1}{2}$ common gamma chain domain; were cloned, in various configurations, into lentiviral vectors.

[0235] *Assessment of surface expression of chimeric receptors.* Lentiviral transfer plasmids encoding for chimeric receptors were transfected into 293 cells using Lipofectamine 3000 and 500 ng of lentiviral expression plasmids. 24 hours later, cell surface expression was assessed by flow cytometry using fluorescently labeled antibodies specific for the ectodomains of the chimeric receptors. Expression of chimeric receptors on primary human T cells was measured by transducing primary human T cells with a dilution series of lentiviral supernatants and analyzed by flow cytometry 72 hours later.

[0236] *Lentivirus.* Lentiviruses for transduction of primary human CD3⁺ T cells were produced in 293T cells by lipofection (Lipofectamine 3000, Thermo Fisher Scientific) of transfer and packaging plasmids, and purified by ultracentrifugation. T cells activated with human CD3/CD28 Dynabeads (3:1 beads to cell ratio) in the presence of recombinant IL-7 and IL-15 were infected with lentiviruses one day after activation, de-beaded on Day 3, and expanded until Day 5.

[0237] *Flow Cytometry.* Flow cytometric detection of chimeric cytokine receptors and chimeric antigen receptors was performed by incubating lentivirally transduced primary human T cells with receptor-specific antibodies for 20 minutes in room temperature in the dark followed by acquisition of at least 10,000 events on FACSymphony A3 flow cytometer (BD Biosciences). Data was analyzed with FlowJo software (BD Biosciences). Transiently transfected 293T cells were treated similarly to detect chimeric cytokine receptors and chimeric antigen receptors 24 hours after lipofection (Lipofectamine 3000, Thermo Fisher Scientific) of 500 ng of lentiviral expression plasmids.

[0238] *pSTAT Detection.* In phosphoflow experiments, transduced human T cells were stimulated by addition of ligands for 30 minutes at 37°C, and the reaction was terminated by fixation with 1.5% paraformaldehyde (PFA) for 15 min at room temperature with agitation. Cells were washed and permeabilized with ice-cold 100% methanol for 60 minutes on ice or stored at -80 °C overnight. Cells were washed with FACS buffer before staining with pSTAT antibodies (Thermo Fisher Scientific) for 1 h at 4 °C in the dark. Cells were washed and analyzed on FACSymphony A3 flow cytometer. Data represent the mean fluorescence intensity (MFI).

[0239] *xCELLigence Real-Time Cell Analysis.* Tumor cell killing was assessed using the xCELLigence Real-Time Cell Analysis (RTCA) Analyzer (Agilent). SKOV-3 human ovarian adenocarcinoma tumor cells were seeded on a 96-well xCELLigence E-Plate at 10,000 cells per well. Twenty-four hours later, transduced T cells with or without 48 hours of pre-incubation with ligands for switch receptors were added in triplicate at various effector-to-target ratios with or without continued ligand stimulation. At the end of the assay, supernatant from each experimental well of the E-Plate was harvested, centrifuged to remove debris, then immediately frozen at -80C.

[0240] *Cytokine Multiplex Analysis.* Samples were analyzed for cytokines and chemokines using the Milliplex cytokine assay kit (Millipore) as per manufacturer's protocol. Briefly, samples were diluted 1:2.5 assay diluent buffer and loaded onto a Millipore Multiscreen BV 96-well filter plate. Serial dilutions of cytokine standards were prepared in parallel and added to the plate. Milliplex 42-Plex Cytokine beads were vortexed for 30 sec. and 25 μ l was added to each well with culture supernatants. Samples were then incubated on a plate shaker at 600rpm in the dark at room temperature for 2 hours. The plate was applied to a Millipore Multiscreen Vacuum Manifold, washed twice with 50 μ l of assay buffer (PBS, pH7.4, 1% BSA, 0.05% Tween20, 0.05% sodium azide), and each well resuspended with 75 μ l assay buffer. 25 μ l of biotinylated Anti-Human Multi-Cytokine Reporter was added to each well. The plate was incubated on a plate shaker at 600rpm in the dark at room temperature for 1.5 hours. Streptavidin-Phycoerythrin was diluted 1:12.5 in assay buffer, and then 25 μ l was added directly to each well. The plate was incubated on a plate shaker at 600rpm in the dark at room temperature for 30 minutes. 25 μ l of stop solution (0.2% (v/v) formaldehyde in PBS, pH 7.4) was added to each well and incubated at room temperature for 5 minutes. The plate was then applied to the vacuum manifold and each well resuspended in 125 μ l assay buffer and shaken for 1 minute. Assay plate was the transferred to the Bio-Plex Luminex 200 XYP instrument for analysis. Cytokine concentrations were calculated using Bio-Plex Manager 6.2 software with a 5 parameter curve fitting algorithm applied for standard curve calculations.

EXAMPLE 9

CHIMERIC SWITCH RECEPTORS ARE EXPRESSED ON THE SURFACE OF CELLS

[0241] In order to analyze whether the chimeric switch receptors were able to be correctly folded and expressed on the surface of cells, 293T cells were transiently transfected with lentiviral transfer plasmids encoding for the chimeric switch receptors. 24 hours later, cell surface expression was assessed by flow cytometry. The expression levels of various constructs are shown in Table 4 below.

Table 4.

Sequence ID	Ligand-binding domain	Transmembrane domain	Intracellular domain	Linker	% expression transduced sample	% expression control sample	% positive cells	% double-positive cells
SEQ63+CAR+	IL21R	IL9R	IL9R	N/A	45.4	0.031		45.369
SEQ72+CAR+	IL4Ra	IL9R	IL9R	N/A	16.7	0.5		16.2
SEQ89+CAR+	CTLA4	IL9R	IL9R	G ₄ S	28.8	0.72		28.08
SEQ90+CAR+	CTLA4	IL9R	IL9R	QP	26.6	0.22		26.38
SEQ91	TIM3	IL9R	IL9R	G ₄ S	21.5	3.42	18.08	
SEQ93	LAG3	IL9R	IL9R	QP	1.33	0.13	1.2	
SEQ94	LAG3	IL9R	IL9R	G ₄ S	3.35	2.25	1.1	
SEQ95+CAR+	PD1	IL9R	IL9R	G ₄ S	18.3	0.49		17.81
SEQ96+CAR+	PD1	IL9R	IL9R	QP	12.2	0.21		11.99
SEQ109	DCR1	IL9R	IL9R	G ₄ S	26	11.2	14.8	
SEQ110	DCR1	IL9R	IL9R	QP	17.6	7.66	9.94	
SEQ111	CD40	IL9R	IL9R	G ₄ S	24	1.42	22.58	
SEQ112	CD40	IL9R	IL9R	QP	19.2	0.31	18.89	
SEQ113+CAR+	Fas	IL9R	IL9R	G ₄ S	22.9	1.1		21.8
SEQ114+CAR+	Fas	IL9R	IL9R	QP	24.9	1.03		23.87
SEQ115	DR4	IL9R	IL9R	G ₄ S	54.5	34.7	19.8	
SEQ116	DR4	IL9R	IL9R	QP	38.3	21.4	16.9	
SEQ123	TNFRSF1B	IL9R	IL9R	G ₄ S	44.9	1.59	43.31	
SEQ124	TNFRSF1B	IL9R	IL9R	QP	52.2	1.11	51.09	
SEQ153+CAR+	IL10Ra	IL9R	IL9R	G ₄ S	19.2	0.68		18.52
SEQ155	TGFBR2	IL9R	IL9R	G ₄ S	6.22	0.45	5.77	
SEQ156	TGFBR2	IL9R	IL9R	QP	10.7	0.17	10.53	
SEQ159+CAR+	TIGIT	IL9R	IL9R	G ₄ S	13.8	0.16		13.64
SEQ160+CAR+	TIGIT	IL9R	IL9R	QP	19.9	0.023		19.877
SEQ165	2B4	IL9R	IL9R	G ₄ S	30.4	28.5	1.9	
SEQ166	2B4	IL9R	IL9R	QP	18.1	15.3	2.8	
SEQ187	DCR1	TNFR1	IL9R	G ₄ S	35.3	15.5	19.8	
SEQ188	DCR1	TNFR1	IL9R	QP	47	11.4	35.6	

SEQ189	CD40	TNFR1	IL9R	G ₄ S	31.1	1.03	30.07	
SEQ190	CD40	TNFR1	IL9R	QP	29	1.45	27.55	
SEQ193	DR4	TNFR1	IL9R	G ₄ S	65.8	45.3	20.5	
SEQ194	DR4	TNFR1	IL9R	QP	63.7	49.6	14.1	
SEQ200	TNFRSF1B	TNFR1	IL9R	G ₄ S	29.1	1.31	27.79	
SEQ201	TNFRSF1B	TNFR1	IL9R	QP	47.3	0.95	46.35	

[0242] As demonstrated by the data in Table 4, all constructs exhibited some level of cell surface expression in 293T cells. These results indicate that the constructs produced properly folded proteins capable of endocytic transport and resistant to general proteolysis.

[0243] Constructs that exhibited cell surface expression in 293T cells were then packaged in lentivirus and titered on human primary T cells. The expression analysis over transduced primary human T cells is show in Table 5 below

Table 5.

Sequence ID	Ligand-binding domain	Transmembrane domain	Intracellular domain	Linker	Fold-dilution of lentivirus	% positive T cells	% double-positive T cells (average of duplicates)	% positive T cells in unstained T cells (average of duplicates)	% positive T cells in stained untransduced T cells (endogenous expression)
SEQ63 +CAR+	IL21R	IL9R	IL9R	N/A	2		61	0.46	20.6
					6		39.85		
					18		28.4		
					54		14.8		
					162		4.725		
					486		0.845		
					1458		0.495		
SEQ66	IL15Ra	IL9R	IL9R	N/A	2	63.1		0.2	32.3
					6	60.6			
					18	33.85			
					54	40.6			
					162	39.6			
					486	38			
					1458	36			
SEQ69	IL7Ra	IL9R	IL9R	N/A	2	90.6		1.02	55.5
					6	83.4			
					18	77.25			
					54	66.6			
					162	60.45			

WO 2023/044461

PCT/US2022/076618

					486	54.4			
					1458	52.8			
SEQ72 +CAR+	IL4Ra	IL9R	IL9R	N/A	2		38.95	0.15	44.6
					6		29.85		
					18		18.1		
					54		10.8		
					162		7.01		
					486		2.915		
					1458		1.41		
SEQ89 +CAR+	CTLA4	IL9R	IL9R	G ₂ S	2		30	N/A	N/A
					6		18.45		
					18		9.895		
					54		3.97		
					162		1.355		
					486		0.635		
					1458		0.485		
SEQ90 +CAR+	CTLA4	IL9R	IL9R	QP	2		41.3	0.058	0.63
					6		31.5		
					18		20.05		
					54		12.6		
					162		3.06		
					486		1.255		
					1458		0.68		
SEQ91	TIM3	IL9R	IL9R	G ₂ S	2	83.4		1.71	88.4
					6	84.15			
					18	85.5			
					54	81.8			
					162	88.3			
					486	86.6			
					1458	77			
					4374	84.9			
SEQ95 +CAR+	PD1	IL9R	IL9R	G ₂ S	2		32.45	0.027	0.64
					6		18.75		
					18		14.45		
					54		6.965		
					162		2.43		
					486		1.19		
					1458		0.88		
SEQ96 +CAR+	PD1	IL9R	IL9R	QP	2		30.5	0.01	85.8
					6		25.1		

WO 2023/044461

PCT/US2022/076618

					18		12.85		
					54		9.4		
					162		3.31		
					486		1.33		
					1458		0.645		
SEQ109	DCR1	IL9R	IL9R	G ₂ S	2	77.8		0.033	0.7
					6	60.95			
					18	44.6			
					54	29.45			
					162	13.4			
					486	4.285			
					1458	2.985			
SEQ110	DCR1	IL9R	IL9R	QP	2	89.1		0.059	1.14
					6	74.9			
					18	49.65			
					54	28.9			
					162	15.6			
					486	10.755			
					1458	8.61			
SEQ111	CD40	IL9R	IL9R	G ₂ S	2	50.25		0.44	12.1
					6	48.2			
					18	38.1			
					54	40.25			
					162	21.8			
					486	9.285			
					1458	9.3			
SEQ112	CD40	IL9R	IL9R	QP	2	85.05		0.049	3.41
					6	78.2			
					18	62.4			
					54	39.1			
					162	31.75			
					486	13.65			
					1458	12.13			
SEQ113 +CAR+	Fas	IL9R	IL9R	G ₂ S	2		42.45	N/A	N/A
					6		17.3		
					18		8.735		
					54		4.84		
					162		2.05		
					486		0.98		
					1458		0.625		
SEQ114 +CAR+	Fas	IL9R	IL9R	QP	2		87.15	0.34	98.1

WO 2023/044461

PCT/US2022/076618

					6		81.25		
					18		71.4		
					54		54.15		
					162		30		
					486		13		
					1458		4.52		
SEQ116	DR4	IL9R	IL9R	QP	2	93.1		0.2	33.9
					6	87.85			
					18	77.75			
					54	63.8			
					162	50.1			
					486	39			
					1458	34.6			
SEQ123	TNFRSF1B	IL9R	IL9R	G ₂ S	2	90.9		0.019	68.5
					6	86.45			
					18	77.85			
					54	57.75			
					162	78			
					486	72.45			
					1458	72.5			
SEQ124	TNFRSF1B	IL9R	IL9R	QP	2	81.05		0.086	72.7
					6	78.25			
					18	70			
					54	70.75			
					162	71.9			
					486	73.6			
					1458	71.65			
SEQ154 +CAR+	IL10Ra	IL9R	IL9R	QP	2		28.2	0.33	1.34
					6		22.4		
					18		10.9		
					54		4.49		
					162		1.635		
					486		1.055		
					1458		1.075		
SEQ155	TGFBR2	IL9R	IL9R	G ₂ S	2	27.55		0.67	0.68
					6	17.6			
					18	14.14			
					54	4.305			
					162	1.425			
					486	2.1			
					1458	1.6			

WO 2023/044461

PCT/US2022/076618

SEQ156	TGFBR2	IL9R	IL9R	QP	2	77.45		0.056	68.9
					6	76.8			
					18	70.55			
					54	70.9			
					162	63.45			
					486	67.5			
					1458	71.05			
SEQ171	TWEAKR	IL9R	IL9R	G ₂ S	2	77.35		0.54	62.8
					6	68.45			
					18	53.65			
					54	46.8			
					162	59.7			
					486	63.4			
					1458	63.75			
SEQ172	TWEAKR	IL9R	IL9R	QP	2	74		0.39	32.9
					6	53.85			
					18	44.9			
					54	47.4			
					162	36.45			
					486	34.75			
					1458	34.1			
SEQ173	TWEAKR	TNFR1	IL9R	G ₂ S	2	92.7		0.37	30.5
					6	80.85			
					18	64.65			
					54	46.55			
					162	36.1			
					486	32.95			
					1458	31			
SEQ174	TWEAKR	TNFR1	IL9R	QP	2	87.2		0.29	23.6
					6	68.95			
					18	47.75			
					54	37.15			
					162	30			
					486	25.7			
					1458	26.75			
SEQ187	DCR1	TNFR1	IL9R	G ₂ S	2	86.65		0.16	4.81
					6	70.25			
					18	50.15			
					54	29			
					162	19.8			
					486	6.475			

WO 2023/044461

PCT/US2022/076618

					1458	3.325			
SEQ188	DCR1	TNFR1	IL9R	QP	2	63.85		0.02	8.63
					6	60.8			
					18	48.65			
					54	35.7			
					162	15.08			
					486	14.7			
					1458	8.65			
SEQ189	CD40	TNFR1	IL9R	G ₄ S	2	91.05		0.079	11.9
					6	79			
					18	55.8			
					54	24.3			
					162	20.55			
					486	10.65			
					1458	10.365			
SEQ190	CD40	TNFR1	IL9R	QP	2	58.15		0.32	34
					6	56.3			
					18	53.5			
					54	48.5			
					162	38.65			
					486	33.15			
					1458	31.3			
SEQ193	DR4	TNFR1	IL9R	G ₄ S	2	86		0.22	40
					6	69.3			
					18	61			
					54	50.3			
					162	48.85			
					486	47			
					1458	43.2			
SEQ194	DR4	TNFR1	IL9R	QP	2	87		0.089	60.6
					6	84.3			
					18	83.4			
					54	84.15			
					162	75.6			
					486	74			
					1458	64.85			
SEQ200	TNFRSF1B	TNFR1	IL9R	G ₄ S	2	96.95		1.84	93.6
					6	95.35			
					18	93.65			
					54	94.25			
					162	92.7			

					486	91.65			
					1458	92			
SEQ201	TNFRSF1B	TNFR1	IL9R	QP	2	95.85		0.39	92.8
					6	96.2			
					18	94.15			
					54	93.5			
					162	94.15			
					486	92.1			
					1458	93.8			

[0244] As demonstrated in Table 5 above, lentiviruses for all constructs were successfully produced and transduced primary human T cells exhibited at least some level of cell surface expression. Despite their general resistance to viral transduction and sensitivity unfolded protein responses (UPR) [Lopez-Soto et al., “Cancer-induced Endoplasmic Reticulum Stress in T Cells Subverts Immunosurveillance,” *Cell Metabolism* 28(6):803-805 (2018); Li et al., “The Emerging Roles of Endoplasmic Reticulum Stress in Balancing Immunity and Tolerance in Health and Diseases: Mechanisms and Opportunities,” *Front. Immunol.* Volum 10, Article 3154], the constructs produced properly folded proteins capable of endocytic transport and resistant to general proteolysis in primary T cells.

EXAMPLE 10

EXPRESSION OF CHIMERIC SWITCH RECEPTORS RESULTS IN PHOSPHORYLATION OF STAT RECEPTORS

[0245] Some constructs were then tested for their ability to induce phosphorylation of STAT1, STAT3, and/or STAT5. Briefly, primary human T cells were transduced with a lentiviral vector encoding switch receptors of SEQ ID NO:63+CAR+ (IL21R ECD + IL9R TM + IL9R ICD and CAR 4D5), SEQ ID NO:66 (IL15Ra + IL9R TM + IL9R ICD), SEQ ID NO:72+CAR+ (IL4R ECD + IL9R TM + IL9R ICD and CAR 4D5), or SEQ ID NO:153+CAR+ (IL10Ra ECD + IL9R TM + IL9R ICD and CAR 4D5). Cells transduced with SEQ ID NO:63+CAR+ were left either unstimulated or stimulated with 200ng/mL IL-21 for 30 minutes. Cells transduced with SEQ ID NO:66 were left either unstimulated or stimulated with 200ng/mL IL-15 for 30 minutes. Cells transduced with SEQ ID NO:72+CAR+ were left either unstimulated or stimulated with

200ng/mL IL-4 for 30 minutes. Cells transduced with SEQ ID NO:153+CAR+ were left either unstimulated or stimulated with 200ng/mL IL-4 for 30 minutes. The fold increase in gMFI of ligand stimulated versus no stimulation was calculated and is shown in **FIG. 1**.

[0246] As shown in **FIG. 1**, all constructs induced phosphorylation of STAT1, STAT3, and STAT5 when stimulated with ligand. Activation of STAT family members through ligand mediated phosphorylation is believed to confer advantages in effector function, polarization and proliferation to T cells.

EXAMPLE 11

PRIMARY T CELLS EXPRESSING CHIMERIC SWITCH RECEPTORS EXHIBIT ENHANCED TUMOR CELL KILLING

[0247] Real-time cytotoxicity assays were then used to analyze whether or not cells expressing a chimeric switch receptor of the present disclosure would show increased cytotoxicity when exposed to ligand. As shown in **FIGs. 2-4**, upon stimulation with ligand, cells expressing either SEQ ID NO:63+CAR+ (IL21R ECD + IL9R TM + IL9R ICD and CAR 4D5) (**FIG. 2**), SEQ ID NO:72+CAR+ (IL4R ECD + IL9R TM + IL9R ICD and CAR 4D5) (**FIG. 3**), or SEQ ID NO:113+CAR+ (Fas ECD + IL9R TM + IL9R ICD and CAR 4D5) (**FIG. 4**), demonstrated an increase in killing of SKOV-3 human ovarian adenocarcinoma cells expressing HER2 when preconditioned with ligand as compared to untransduced, stimulated cells. Consistent with the observed activation of STAT transcription factors following ligand stimulation, T cells transduced with hybrid IL9R receptors demonstrated improved killing over unstimulated controls. It should be noted that in the case of Seq ID NO 113, the presence of natural ligand (TNFSF6) increases background killing in the assay. That said, the addition of exogenous ligand enhances T cell killing above controls.

EXAMPLE 12

PRIMARY T CELLS EXPRESSING CHIMERIC SWITCH RECEPTORS EXHIBIT INCREASED CYTOKINE AND CHEMOKINE ACTIVITY

[0248] Culture supernatants from primary human T cells transduced with either SEQ ID NO:63+CAR+ (IL21R ECD + IL9R TM + IL9R ICD and CAR 4D5) (**FIG. 5**) or SEQ ID NO:72+CAR+ (IL4R ECD + IL9R TM + IL9R ICD and CAR 4D5) (**FIG. 6**) were then analyzed for the presence of cytokines and chemokines. Supernatants were taken from cells stimulated with ligand before the real-time cytotoxicity assay of Example 11 (first bar, “pre”), cells stimulated with ligand during the real-time cytotoxicity assay of Example 11 (second bar, “post”), or cells stimulated at both points in the real-time cytotoxicity assay of Example 11 (third bar, “both”). The fold increase over unstimulated was calculated and is shown in **FIGs. 5 and 6**. As shown in **FIGs. 5 and 6**, several cytokines and chemokines, such as IFN γ , FGF2, GMCSF, IL-3, IL-6, IP10, MIP1a, and RANTES, demonstrated increased production. The magnitude and quality of cytokines produced following ligand stimulation (either “pre”, “post” or “both”) indicates a robust improvement in T cell response with hybrid-IL9R engagement. Furthermore, the pattern of cytokine response indicates an increase in type-1 polarization following ligand stimulation relative to controls.

[0249] **FIGs. 7-19** depict results from the same experiment, however, the data is shown in concentration of cytokine or chemokine (in pg.mL) for each of the above described experimental conditions. Similarly, the magnitude and quality of cytokines produced following ligand stimulation (either “pre”, “post” or “both”) indicates a robust improvement in T cell response with hybrid-IL9R engagement, and the pattern of cytokine response indicates an increase in type-1 polarization following ligand stimulation relative to controls.

Informal Sequence Listing

SEQ ID NO: 63

IL21r/IL9R

CPDLVCYTDYLQTVICILEMWNLHPSTLTLTWQDQYEELKDEATSCSLHRSAHNATHATY
 TCHMDVHFHMADDIFSVNITDQSGNYSQECGSFLLAESIKPAPPFNVTVTFSGQYNISWR
 SDYEDPAFYMLKGKLQYELQYRNRGDPWAVSPRRKLISVDSRSVSLLPLEFRKDSSYELQ
 VRAGPMPGSSYQGTWSEWSDPVIFQTQSEELKELIPWGWPGNTLVAVSIFLLTGPTYLLFKLSPRVKRIFYQNVPSPA
 MFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLP
 GNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNNYCALGCYGGWHLSALPGNTQ
 SSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLKARSWTF

SEQ ID NO: 64

IL21r/IL9R/IL7RaTM

CPDLVCYTDYLQTVICILEMWNLHPSTLTLTWQDQYEELKDEATSCSLHRSAHNATHATY
 TCHMDVHFHMADDIFSVNITDQSGNYSQECGSFLLAESIKPAPPFNVTVTFSGQYNISWR
 SDYEDPAFYMLKGKLQYELQYRNRGDPWAVSPRRKLISVDSRSVSLLPLEFRKDSSYELQ
 VRAGPMPGSSYQGTWSEWSDPVIFQTQSEELKEPILLTISILSFFSVALLVILACVLWVKRIFYQNVPSPAMFFQPLYSVH
 NGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLP
 GNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNNYCALGCYGGWHLSALPGNTQ
 SSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLKARSWTF

SEQ ID NO: 65

IL21r/IL9R/IL2RbTM

CPDLVCYTDYLQTVICILEMWNLHPSTLTLTWQDQYEELKDEATSCSLHRSAHNATHATY
 TCHMDVHFHMADDIFSVNITDQSGNYSQECGSFLLAESIKPAPPFNVTVTFSGQYNISWR
 SDYEDPAFYMLKGKLQYELQYRNRGDPWAVSPRRKLISVDSRSVSLLPLEFRKDSSYELQ
 VRAGPMPGSSYQGTWSEWSDPVIFQTQSEELKE IPWLGHLLVGLSGAFGFIIILVYLLI
 VKRIFYQNVPSPAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSV
 EEEQEGPGTRLP
 GNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNNYCALGCY
 GWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLKARSWTF

SEQ ID NO: 66

IL15r-alpha/IL9R

ITCPPPMSVEHADIWVKSYSLYRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTTPS
 LKCIDPALVHQRAPPSTVTAGVTPQPESLSPSGKEPAASSPSSNNTAATTAAIVPGS
 QLMPKSPSTGTTEISSHESSHGTPSQTTAKNWELTASASHQPPGVYPQGHSDTLIPPWGWPGNTLVAVSIFLLTG
 P
 TYLLFKLSPRVKRIFYQNVPSPAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGP
 ARPWKSVALEEEQEGPGTRLP
 GNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNN
 NYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLKAR
 SWTF

SEQ ID NO: 67

IL15r-alpha/IL9R/IL7RaTM

ITCPPPMSVEHADIWVKSYSLYRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTTPS
 LKCIDPALVHQRAPPSTVTAGVTPQPESLSPSGKEPAASSPSSNNTAATTAAIVPGS
 QLMPKSPSTGTTEISSHESSHGTPSQTTAKNWELTASASHQPPGVYPQGHSDTTPILLTISILSFFSVALLVILACVLW

VKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVAL
 EEEQEGPGTRLPGNLSSSEDLVAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYG
 GWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 68

IL15r-alpha/IL9R/IL2RbTM

ITCPPPMSVEHADIWVKSYSLSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPS
 LKCRDPALVHQRAPPSTVTTAGVTPQPELSPSGKEPAASSPSSNNTAATTAAIVPGS
 QLMPSKSPSTGTTEISSHESSHGTPSQTTAKNWELTASASHQPPGVYPQGHSDTT IPWLGHLLVGLSGAFGFIIIVYLLI
 VKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVAL
 EEEQEGPGTRLPGNLSSSEDLVAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYG
 GWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 69

IL7r-alpha /IL9R

ESGYAQNGDLEDAELDDYSFSCYSQLEVNGSQHSLTCAFEDPDVNITNLEFEICGALVEV
 KCLNFRKLQEIYFIETKKFLLIGKSNICVKVGEKSLTCKKIDLTIVKPEAPFDLSVVYR
 EGANDFVVTFTNTSHLQKKYVKVLMHADVAYRQEKDENKWTHVNLSTKLTLQKRLQPAAM
 YEIKVRSIPDHYFKGFWEWSPSYFRTPEINNSSGEMDLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSPRVKRIFYQN
 VPSPAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGP
 GTRLPGNLSSSEDLVAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHLSAL
 PGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 70

IL7r-alpha /IL9R/IL7RaTM

ESGYAQNGDLEDAELDDYSFSCYSQLEVNGSQHSLTCAFEDPDVNITNLEFEICGALVEV
 KCLNFRKLQEIYFIETKKFLLIGKSNICVKVGEKSLTCKKIDLTIVKPEAPFDLSVVYR
 EGANDFVVTFTNTSHLQKKYVKVLMHADVAYRQEKDENKWTHVNLSTKLTLQKRLQPAAM
 YEIKVRSIPDHYFKGFWEWSPSYFRTPEINNSSGEMD PILLTISILSFFSVALLVILACVLW
 VKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVAL
 EEEQEGPGTRLPGNLSSSEDLVAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYG
 GWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 71

IL7r-alpha /IL9R/IL2RbTM

ESGYAQNGDLEDAELDDYSFSCYSQLEVNGSQHSLTCAFEDPDVNITNLEFEICGALVEV
 KCLNFRKLQEIYFIETKKFLLIGKSNICVKVGEKSLTCKKIDLTIVKPEAPFDLSVVYR
 EGANDFVVTFTNTSHLQKKYVKVLMHADVAYRQEKDENKWTHVNLSTKLTLQKRLQPAAM
 YEIKVRSIPDHYFKGFWEWSPSYFRTPEINNSSGEMD IPWLGHLLVGLSGAFGFIIIVYLLI
 VKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVAL
 EEEQEGPGTRLPGNLSSSEDLVAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYG
 GWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 72

IL4r-alpha/IL9R

MKVLQEPTCVSDYMSISTCEWKMNPTNCSTELRLLYQLVFLSEAHTCIPENNGGAGCV
 CHLLMDDVVSADNYTLDLWAGQQLWKGSFKPSEHVKPRAPGNLTVHTNVSDTLLLTWSN
 PYPPDNYLYNHLTYAVNIWSENDPADFRIYNVTYLEPSLRIAASTLKSGISYRVRVRAWA
 QCYNTTWSEWSPSTKWHNSYREPFEQHLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSPRVKRIFYQNVPSAMFFQP
 LYSVHNGNFQWTWGAHAGVLLSQDCAGTPQGALEPCVQEATAALLTCGPAPWKSVALEEEQEGPGTRLPGNLSSE
 DVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIP
 ALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 73

IL4r-alpha/IL9R/IL7RaTM

MKVLQEPTCVSDYMSISTCEWKMNPTNCSTELRLLYQLVFLSEAHTCIPENNGGAGCV
 CHLLMDDVVSADNYTLDLWAGQQLWKGSFKPSEHVKPRAPGNLTVHTNVSDTLLLTWSN
 PYPPDNYLYNHLTYAVNIWSENDPADFRIYNVTYLEPSLRIAASTLKSGISYRVRVRAWA
 QCYNTTWSEWSPSTKWHNSYREPFEQH PILLTISILSFFSVALLVILACVLW
 VKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHAGVLLSQDCAGTPQGALEPCVQEATAALLTCGPAPWKSVAL
 EEEQEGPGTRLPGNLSSEDLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYG
 GWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 74

IL4r-alpha/IL9R/IL2RbTM

MKVLQEPTCVSDYMSISTCEWKMNPTNCSTELRLLYQLVFLSEAHTCIPENNGGAGCV
 CHLLMDDVVSADNYTLDLWAGQQLWKGSFKPSEHVKPRAPGNLTVHTNVSDTLLLTWSN
 PYPPDNYLYNHLTYAVNIWSENDPADFRIYNVTYLEPSLRIAASTLKSGISYRVRVRAWA
 QCYNTTWSEWSPSTKWHNSYREPFEQH IPWLGHLLVGLSGAFGFILVYLLI
 VKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHAGVLLSQDCAGTPQGALEPCVQEATAALLTCGPAPWKSVAL
 EEEQEGPGTRLPGNLSSEDLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYG
 GWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 75

IL2r-beta Ectodomain /IL9R

AVNGTSQFTCFYNSRANISCVWSQDQALQDTSCQVHAWPDORRRWNQTCELLPVSQASWAC
 NLILGAPDSQKLTTVDIVTLRVLCREGVRWRVMAIQDFKPFENLRMAPISLQVVHVETH
 RCNISWEISQASHYFERHLEFEARTLSPGHTWEEAPLLTLKQKQEWICLETLPDTQYEF
 QVRVKPLQGEFTTWSPWSQPLAFRTKPAALGKDTLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSPRVKRIFYQNVPS
 AMFFQPLYSVHNGNFQWTWGAHAGVLLSQDCAGTPQGALEPCVQEATAALLTCGPAPWKSVALEEEQEGPGTRL
 PGNLSSEDLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLALPGNT
 QSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 76

IL2r-beta Ectodomain /IL9R/IL7RaTM

AVNGTSQFTCFYNSRANISCVWSQDQALQDTSCQVHAWPDORRRWNQTCELLPVSQASWAC

NLILGAPDSQKLTTVDIVTLRVLCREGVRWRVMAIQDFKPFENLRMAPISLQVVHVETH
 RCNISWEISQASHYFERHLEFEARTLSPGHTWEEAPLLTLKQKQEWICLETLPDTQYEF
 QVRVKPLQGEFTTWSPWSQPLAFRTKPAALGKDT PILLTISILSFFSVALLVILACVLW
 VKRIFYQNVPSAMFFQPLYSVHNGNFQWTWMAHAGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVAL
 EEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYG
 GWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 77

IL2r-beta Ectodomain /IL9R/IL2RbTM

AVNGTSQFTCFYNSRANISCVWSQDGALQDTSQCVHAWPDORRRWNQTCELLPVSQASWAC
 NLILGAPDSQKLTTVDIVTLRVLCREGVRWRVMAIQDFKPFENLRMAPISLQVVHVETH
 RCNISWEISQASHYFERHLEFEARTLSPGHTWEEAPLLTLKQKQEWICLETLPDTQYEF
 QVRVKPLQGEFTTWSPWSQPLAFRTKPAALGKDT IPWLGHLLVGLSGAFGFIIIVYLLI
 VKRIFYQNVPSAMFFQPLYSVHNGNFQWTWMAHAGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVAL
 EEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYG
 GWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 78

IL2r-alpha Ectodomain/IL9R

ELCDDDPPEIPHATFKAMAYKEGTMLNCECKRGFRRIKSGSLYMLCTGNSSHSSWDNQCQ
 CTSSATRNNTTKQVTPQPEEQKERKTTEMQSPMQPVDQASLPGHCREPPPWENEATERIYH
 FVVGQMVYYQCVQGYRALHRGAESVCKMTHGKTRWTQPQLICTGEMETSQFPGEKPKQA
 SPEGRPESETSCLVTTTDFQIQTEMAATMETSIFTTEYQLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNV
 PSPAMFFQPLYSVHNGNFQWTWMAHAGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPG
 TRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHLSALP
 GNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 79

IL2r-alpha Ectodomain/IL9R/IL7RaTM

ELCDDDPPEIPHATFKAMAYKEGTMLNCECKRGFRRIKSGSLYMLCTGNSSHSSWDNQCQ
 CTSSATRNNTTKQVTPQPEEQKERKTTEMQSPMQPVDQASLPGHCREPPPWENEATERIYH
 FVVGQMVYYQCVQGYRALHRGAESVCKMTHGKTRWTQPQLICTGEMETSQFPGEKPKQA
 SPEGRPESETSCLVTTTDFQIQTEMAATMETSIFTTEYQ PILLTISILSFFSVALLVILACVLW
 VKRIFYQNVPSAMFFQPLYSVHNGNFQWTWMAHAGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVAL
 EEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYG
 GWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 80

IL2r-alpha Ectodomain/IL9R/IL2RbTM

ELCDDDPPEIPHATFKAMAYKEGTMLNCECKRGFRRIKSGSLYMLCTGNSSHSSWDNQCQ
 CTSSATRNNTTKQVTPQPEEQKERKTTEMQSPMQPVDQASLPGHCREPPPWENEATERIYH
 FVVGQMVYYQCVQGYRALHRGAESVCKMTHGKTRWTQPQLICTGEMETSQFPGEKPKQA

SPEGRPESETSCLVTTTDFQIQTEMAATMETSIFTTEYQ IPWLGHLLVGLSGAFGFILVYLLI
VKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVAL
EEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCY
GWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTF

SEQ ID NO: 81

ILT5/IL9R/cGC-F

GPFPKPTLWAEPGSVISWGSPVTIWCQGSQEAQEYRLHKEGSPEPLDRNNPLEPKNKARF
SIPSMTEHHAGRYRCHYSSAGWSEPSDPLEMVMGTGAYSKPTLSALPSPVVASGGNMTLR
CGSQKGYHHFVLMKEGEHQLPRTLDSQQLHSRGFQALFPVGPVTPSHRWRFTCYYYTNT
PWVWSPDPLEILPSGVSRKPSLLTLQGPVLAPGQSLTLQCGSDVGYNRFVLYKEGERD
FLQRPQGQPQAGLSQANFTLGPVSPSNGGQYRCYGAHNLSSEWSAPSDPLNLMAGQIYD
TVLSAQPGPTVASGENVTLLCQSWWQFDTLLTKEGAHPPPLRLRSMYGAHKYQAEFPM
SPVTSAHAGTYRCYGSYSSNPHLLSHPSPELVLVSGHSGGSSLPPTGPPSTPGLGRYLELIPPWGWPGNTLVAVSIFLL
TGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLT
CGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSN
NNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSK
ARSWTFGGGGSGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGG
ALGEGPGASPCNQHSPLYWAPPCYTLKPET

SEQ ID NO: 82

ILT5/IL9R/cGC-S

GPFPKPTLWAEPGSVISWGSPVTIWCQGSQEAQEYRLHKEGSPEPLDRNNPLEPKNKARF
SIPSMTEHHAGRYRCHYSSAGWSEPSDPLEMVMGTGAYSKPTLSALPSPVVASGGNMTLR
CGSQKGYHHFVLMKEGEHQLPRTLDSQQLHSRGFQALFPVGPVTPSHRWRFTCYYYTNT
PWVWSPDPLEILPSGVSRKPSLLTLQGPVLAPGQSLTLQCGSDVGYNRFVLYKEGERD
FLQRPQGQPQAGLSQANFTLGPVSPSNGGQYRCYGAHNLSSEWSAPSDPLNLMAGQIYD
TVLSAQPGPTVASGENVTLLCQSWWQFDTLLTKEGAHPPPLRLRSMYGAHKYQAEFPM
SPVTSAHAGTYRCYGSYSSNPHLLSHPSPELVLVSGHSGGSSLPPTGPPSTPGLGRYLELIPPWGWPGNTLVAVSIFLL
TGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLT
CGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSN
NNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSK
ARSWTFQPPQPPQPPPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALG
EGPGASPCNQHSPLYWAPPCYTLKPET

SEQ ID NO: 83

ILT3/IL9R/cGC-F

QAGPLPKPTLWAEPGSVISWGNSVTIWCQGTLEAREYRLDKEESPAPWDRQNPLEPKNKA
RFSIPSMTEYDAGRYRCYRSPVGWSQPSDPLELVMGTGAYSKPTLSALPSPLVTS GKSVT
LLCQSRSPMDTFLLIKERAHPLHLRSEHGAQQHQAEPMSPVTSVHGGTYRCFSSHGF
SHYLLSHPSDPLELIVSGSLEDPRPSPTRSVSTAAGPEDQPLMPTGSVPHSGLRRHWE
LIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDC
AGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTS
LTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHC

QRPGLHEDLQGMILLPSVLSKARSWTFGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAE
SLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 84

ILT3/IL9R/cGC-S

QAGPLPKPTLWAEPGSVISWGNSTIWCQGTLEAREYRLDKEESPAPWDRQNPLEPKNKA
RFSIPSMTEDYAGRYRCYYRSPVGWSQPSDPLELVMGTGAYSKPTLSALPSPLVTS GKSVT
LLCQSRSPMDTFLLIKERAHPLLHLRSEHGAQQHQAEPMPSPVTSVHGGTYRCFSSHGF
SHYLLSHPSDPLELIVSGSLEDPRPSPTRSVSTAAGPEDQPLMPTGSPVPHSGLRRHWELIPWGWPGNTLVAVSIFLLT
GPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQTMGAHAGVLLSQDCAGTPQGALEPCVQEATALLTC
GPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA GCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSN
NNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSDHQLETQQGVAWVLAGHCQRPGLHEDLQGMILLPSVLSK
ARSWTFQPQPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALG
EGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 85

ILT4 IL9R/cGC-F

QTGTIPKPTLWAEPDSVITQGSPVTLSCQGSLEAQEYRLYREKKSASWITRIRPELVKNG
QFHIPSITWEHTGRYGCQYYSRARWSELSDPLVLVMTGAYPKPTLSAQSPVVTSGGRVT
LQCESQVAFGGFILCKEGEEHPQCLNSQPHARGSSRAIFSVGPVSPNRRWSHRCYGYDL
NSPYVWSSPSDLELLVPGVSKKPSLSVQPGPVVAPGESLTLCVSDVGYDRFVLYKEGE
RDLRQLPGRQPQAGLSQANFTLGPVSRSYGGQYRCYGAHNLSSECSAPSDPLDILITGQI
RGTPFISVQPGPTVASGENVTLLCQSWRQFHTFLLTKAGAADAPLRRLRSIHEYPKYQAEF
PMSPVTSAHAGTYRCYGLNSDPYLLSHPSEPLELVVSGPSMGSSPPPTGPSTPAGPED
QPLTPTGSDPQSGLRHLGVLI PPWGWPGNTLVAVSIFLLTGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGN
FQTMGAHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA GCT
EWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSC
DHQLETQQGVAWVLAGHCQRPGLHEDLQGMILLPSVLSKARSWTFGGGSGGGGSGGGGSERTMPRIPTLKNLED
LVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 86

ILT4 IL9R/cGC-S

QTGTIPKPTLWAEPDSVITQGSPVTLSCQGSLEAQEYRLYREKKSASWITRIRPELVKNG
QFHIPSITWEHTGRYGCQYYSRARWSELSDPLVLVMTGAYPKPTLSAQSPVVTSGGRVT
LQCESQVAFGGFILCKEGEEHPQCLNSQPHARGSSRAIFSVGPVSPNRRWSHRCYGYDL
NSPYVWSSPSDLELLVPGVSKKPSLSVQPGPVVAPGESLTLCVSDVGYDRFVLYKEGE
RDLRQLPGRQPQAGLSQANFTLGPVSRSYGGQYRCYGAHNLSSECSAPSDPLDILITGQI
RGTPFISVQPGPTVASGENVTLLCQSWRQFHTFLLTKAGAADAPLRRLRSIHEYPKYQAEF
PMSPVTSAHAGTYRCYGLNSDPYLLSHPSEPLELVVSGPSMGSSPPPTGPSTPAGPED
QPLTPTGSDPQSGLRHLGVLI PPWGWPGNTLVAVSIFLLTGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGN
FQTMGAHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA GCT
EWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSC

DHQGLETQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTMPRIPTLKNLEDLVTE
YHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 87

ILT2 IL9R/cGC-F

GHLPKPTLWAEPGSVITQGSPVTLRCQGGQETQEYRLYREKKTALWITRIPQELVKKGQF
PIPSITWEHAGRYRCYGSDDTAGRSESSDPLELVVTGAYIKPTLSAQSPVNVNSGGNVIL
QCDSQVAFDGFSLCKEGEDHPQCLNSQPHARGSSRAIFSVGPVSPSRRWWYRCYAYDSN
SPYEWSLPSDLELLVLGVSKKPSLSVQPGPIVAPEETLTLCGSDAGYNRFVLYKDGER
DFLQLAGAQPQAGLSQANFTLGPVRSYGGQYRCYGAHNSSEWSAPSDPLDILIAGQFY
DRVSLSVQPGPTVASGENVTLLCQSQGWMQTFLLTKEGAADDPWRLRSTYQSQKYQAEFP
MGPVTSAHAGTYRCYGSQSSKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQP
LTPTGSDPQSGLGRHLGVLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNVPSAMFFQPLYSVHNGNFQ
TWMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPACTEW
RVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYALGCGYGGWHLALPGNTQSSGPIPALACGLSCDH
QGLETQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGSGGGGSERTMPRIPTLKNLEDLV
TEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 88

ILT2 IL9R/cGC-S

GHLPKPTLWAEPGSVITQGSPVTLRCQGGQETQEYRLYREKKTALWITRIPQELVKKGQF
PIPSITWEHAGRYRCYGSDDTAGRSESSDPLELVVTGAYIKPTLSAQSPVNVNSGGNVIL
QCDSQVAFDGFSLCKEGEDHPQCLNSQPHARGSSRAIFSVGPVSPSRRWWYRCYAYDSN
SPYEWSLPSDLELLVLGVSKKPSLSVQPGPIVAPEETLTLCGSDAGYNRFVLYKDGER
DFLQLAGAQPQAGLSQANFTLGPVRSYGGQYRCYGAHNSSEWSAPSDPLDILIAGQFY
DRVSLSVQPGPTVASGENVTLLCQSQGWMQTFLLTKEGAADDPWRLRSTYQSQKYQAEFP
MGPVTSAHAGTYRCYGSQSSKPYLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQP
LTPTGSDPQSGLGRHLGVLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNVPSAMFFQPLYSVHNGNFQ
TWMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPACTEW
RVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYALGCGYGGWHLALPGNTQSSGPIPALACGLSCDH
QGLETQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTMPRIPTLKNLEDLVTEYH
GNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 89

CTLA4 IL9R/cGC-F

KAMHVAQPAVVLASSRGIAFVCEYASPGKATEVRVTVLRQADSQVTEVCAATYMMGNEL
TFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELMYPPPYLGIGNGTQIYVIDPE
PCPDSDLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNVPSAMFFQPLYSVHNGNFQTWMGAHGAGV
LLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPACTEW
RVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYALGCGYGGWHLALPGNTQSSGPIPALACGLSCDH
QGLETQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGSGGGGSERTMPRIPTLKNLEDLVTEYH
GNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 90

CTLA4 IL9R/cGC-S

KAMHVAQPAVVLASSRGIA SFVCEYASPGKATEVRVTVLRQADSQVTEVCAATYMMGNEL
 TFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELMYPPPYLGIGNGTQIYVIDPE
 PCPDSDLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMFFQPLYSVHNGNFQTMGAHGAGV
 LLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSSEDVLPAGCTEWRVQTLAYLPQED
 WAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAV
 VLAGHCQRPGHLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPQPMPRIPTLKNLEDLVTEYHGNFSAWSGVSK
 GLAESLQPDYSERLCLVSEIPPKG GALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 91

TIM3/IL9R/cGC-F

SEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWKGACPVFECGNVVLRTDERDVNYWTSR
 YWLNGDFRKG DVSLTIENVT LADSGIYCCRIQIPGIMNDEKFNKLVIKPAKVTPAPTRQ
 RDFTAAFPRMLTTRGHGPAETQTLGSLPDINLTQISTLANELRDSRLANDLRDSGATIRI
 GLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMFFQPLYSVHNGNFQTMGAHGAGVLLSQD
 CAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSSEDVLPAGCTEWRVQTLAYLPQEDWAPT
 SLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVVLAGH
 CQRPGHLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSGERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGL
 AESLQPDYSERLCLVSEIPPKG GALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 92

TIM3/IL9R/cGC-S

SEVEYRAEVGQNAYLPCFYTPAAPGNLVPVCWKGACPVFECGNVVLRTDERDVNYWTSR
 YWLNGDFRKG DVSLTIENVT LADSGIYCCRIQIPGIMNDEKFNKLVIKPAKVTPAPTRQ
 RDFTAAFPRMLTTRGHGPAETQTLGSLPDINLTQISTLANELRDSRLANDLRDSGATIRI
 GLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMFFQPLYSVHNGNFQTMGAHGAGVLLSQD
 CAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSSEDVLPAGCTEWRVQTLAYLPQEDWAPT
 SLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVVLAGH
 CQRPGHLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPQPMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESL
 QPDYSERLCLVSEIPPKG GALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO:93

LAG3/IL9R/cGC-S

LQPGAEPV VWAQEGAPAQLPCSPTIPLQDLSLLRRAGVTWQHQPDSGPPAAAPGHPLAP
 GPHPAAPSSWGPRPRRYTVLSVPGGLRSGRLPLQPRVQLDERGRQRGDFSLWLRPARRA
 DAGEYRAAVHLRDRALSCRLRLRLGQASMTASPPGSLRASDWVILNCSFSRPDRPASVHW
 FRNRGQGRVPVRESPHHHLAESFLPLQVSPMDSGPWGCILTYRDGFNVSIMYNLTVLGL
 EPPTPLTVYAGAGSRVGLPCRLPAGVGTRSF LTAKWTPPGGGPDLLVTGDNGDFTLRLED
 VSQAQAGTYTCHIHLEQQLNATVTLAIITVTPKSFSGPSLGKLLCEVTPVSGQERFVW
 SSLDTPSQRFSFGPWLEAQEAQLLSQPWQCQLYQGERLLGAAYFTELSSPGAQRSGRAP

GALPAGHLLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMFFQPLYSVHNGNFQWTWMAHGA
 GVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQ
 EDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQLETQQGVA
 WVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPMPRIPTLKNLEDLVTEYHGNFSAWSGV
 KGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 94

LAG3/IL9R/cGC-F

LQPGAEPVWVWAQEGAPALPCSTIPLQDLSLLRRAGVTWQHQPDSGPPAAAPGHPLAP
 GHPAAPSWSGPRPRRYTVLSVPGGLRSGRLPLQPRVQLDERGRQGDLSLWLRPARRA
 DAGEYRAAVHLRDRALSCRLRLRGQASMTASPPGSLRASDWVILNCSFSRDPASVHW
 FRNRGQGRVPVRESPPHHLAESFLPLQVSPMDSGPWGCILTYRDGFNVSIMYNLTVLGL
 EPPTPLTVYAGAGSRVGLPCRLPAGVGTRSFLLTAKWTPPGGGPDLLVTGDNGDFTLRLED
 VSQAQAGTYTCHIHLQEQLNATVTLAITVTPKSFSGPSGLKLLCEVTPVSGQERFVW
 SSLDTPSQRSFSGPWLEAQEAQLSQPWQCQLYQGERLLGAAYFTELSSPGAQRSGRAP
 GALPAGHLLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMFFQPLYSVHNGNFQWTWMAHGA
 GVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQ
 EDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQLETQQGVA
 WVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWS
 GVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 95

PD1/IL9R/cGC-F

FTVTVPKDLVVEYGSNMTIECKFPVEKQLDLAALIVYWEMEDKNIIQFVHGEEDLKVQH
 SSYRQARLLKQSLGNAALQITDVKLQDAGVYRCMISYGGADYKRITVKVNAPYNKIN
 QRILVVDVPTSEHELTCAEGYPKAEVIWTSSDHQVLSGKTTTTNSKREEKLFNVTSTLR
 INTTNEIFYCTFRRLDPEENHTAELVPELPLAHPNERLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNV
 PSPAMFFQPLYSVHNGNFQWTWMAHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPG
 TRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLALP
 GNTQSSGPIPALACGLSCDHQLETQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGG
 GGS ERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALG
 EGPASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 96

PD1/IL9R/cGC-S

FTVTVPKDLVVEYGSNMTIECKFPVEKQLDLAALIVYWEMEDKNIIQFVHGEEDLKVQH
 SSYRQARLLKQSLGNAALQITDVKLQDAGVYRCMISYGGADYKRITVKVNAPYNKIN
 QRILVVDVPTSEHELTCAEGYPKAEVIWTSSDHQVLSGKTTTTNSKREEKLFNVTSTLR
 INTTNEIFYCTFRRLDPEENHTAELVPELPLAHPNERLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNV
 PSPAMFFQPLYSVHNGNFQWTWMAHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPG
 TRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLALP
 GNTQSSGPIPALACGLSCDHQLETQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQP
 ERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALG
 EGPASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 97

OPG/IL9R/cGC-F

ETFPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKTVCAPCPDHYYTDSWHTSDECL
 YCSPVCKELQYVVKQECNRTHNRVCECKEGRYLEIEFCLKHRSCPPGFGVVQAGTPERNVT
 CKRCPDGFNETSSKAPCRKHTNCSVFGLLTQKGNATHDNICSGNSESTQKCGIDVTL
 CEEAFFRFAVPTKFTPNWLSVLVDNLPGTKVNAESVERIKRQHSSQEQTFLKLWKHQN
 KDQDIVKKIQQIDLCENSQVRHIGHANLTFEQLRSLMESLPGKKVGAEDIEKTIKACKP
 SDQILKLLSLWRIKNGDQDTLKGLMHALKHSHKTYHFPKTVTQSLKKTIRFLHSFTMYKLY
 QKLFLEMIGNQVQSVKISCLLIPWGWPGNTLVAVSIFLLLTGPTYLLFKLSRVKRIFYQNVSPAMFFQPLYSVHNGNF
 QTWMGAGHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTE
 WRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCGGWHLALPGNTQSSGPIPALACGLSCD
 HQGLETQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSGERTMPRIPTLKNLEDL
 VTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 98

OPG/IL9R/cGC-S

ETFPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKTVCAPCPDHYYTDSWHTSDECL
 YCSPVCKELQYVVKQECNRTHNRVCECKEGRYLEIEFCLKHRSCPPGFGVVQAGTPERNVT
 CKRCPDGFNETSSKAPCRKHTNCSVFGLLTQKGNATHDNICSGNSESTQKCGIDVTL
 CEEAFFRFAVPTKFTPNWLSVLVDNLPGTKVNAESVERIKRQHSSQEQTFLKLWKHQN
 KDQDIVKKIQQIDLCENSQVRHIGHANLTFEQLRSLMESLPGKKVGAEDIEKTIKACKP
 SDQILKLLSLWRIKNGDQDTLKGLMHALKHSHKTYHFPKTVTQSLKKTIRFLHSFTMYKLY
 QKLFLEMIGNQVQSVKISCLLIPWGWPGNTLVAVSIFLLLTGPTYLLFKLSRVKRIFYQNVSPAMFFQPLYSVHNGNF
 QTWMGAGHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTE
 WRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCGGWHLALPGNTQSSGPIPALACGLSCD
 HQGLETQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQPQPQPERTMPRIPTLKNLEDLVTEY
 HGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO:99

TACI/IL9R/cGC-F

MSGLGSRRRGGRSRVDQEERFPQGLWTGVAMRSCPEEQYWDPLLGTCSCKTICNHQSQR
 TCAAFCRSLSCRKEQGKFYDHLRDCISCASICGQHPKQCAFCENKLRSPVNLPELRR
 QRSGEVENNSDNSGRYQGLEHRGSEASPALPGLKLSADQVALVYS
 LIPWGWPGNTLVAVSIFLLLTGPTYLLFKLSRVKRIFYQNVSPAMFFQPLYSVHNGNFQTWMGAGHAGVLLSQDC
 AGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTS
 TRPAPPDSEGRSSSSSSSSNNNNYCALGCGGWHLALPGNTQSSGPIPALACGLSCDHQGLETQQGVAVVLAGHC
 QRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSGERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAE
 SLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 100

TACI/IL9R/cGC-S

MSGLGSRRRGGRSRVDQEERFPQGLWTGVAMRSCPEEQYWDPLLGTCSCKTICNHQSQR
 TCAAFCRSLSCRKEQGKFYDHLRDCISCASICGQHPKQCAFCENKLRSPVNLPELRR

QRSGEVENNSDNSGRYQGLEHRGSEASPALPGLKLSADQVALVYS
 LIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDC
 AGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTS
 TRPAPPDSEGRSSSSSSSSSSNNNNYCALGCGYGGWHLALPGNTQSSGPIPALACGLSCDHQGLTQQGVAVVLAGHC
 QRPGLHEDLQGMLLPSVLSKARSWTFQPPQPPQPPQPPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQ
 PDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 101

BCMA/IL9R/cGC-F

MLQMAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNALIPPWGWPGNTLVAVSIFLLLTGP
 TYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGP
 ARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNN
 NYCALGCGYGGWHLALPGNTQSSGPIPALACGLSCDHQGLTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKAR
 SWTFGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGAL
 GEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 102

BCMA/IL9R/cGC-S

MLQMAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNALIPPWGWPGNTLVAVSIFLLLTGP
 TYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGP
 ARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNN
 NYCALGCGYGGWHLALPGNTQSSGPIPALACGLSCDHQGLTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKAR
 SWTFQPPQPPQPPQPPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEG
 PGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 103

NGFR/IL9R/cGC-F

KEACPTGLYTHSGECKKACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTE
 CVGLQSMSAPCVEADDAVCRCAHYGYQDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEE
 CPDGTYSDEANHVDPCLPCTVCEDTERQLRECTRWADAEECEIPGRWITRSTPPEGSDST
 APSTQEPEAPPEQDLIASTVAGVVTTVMGSSQPVVTRGTTDNLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIF
 YQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQ
 EGPGRTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCGYGGWHL
 SALPGNTQSSGPIPALACGLSCDHQGLTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGG
 SGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSP
 YWAPPCYTLKPET

SEQ ID NO: 104

NGFR/IL9R/cGC-S

KEACPTGLYTHSGECKKACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTE
 CVGLQSMSAPCVEADDAVCRCAHYGYQDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEE
 CPDGTYSDEANHVDPCLPCTVCEDTERQLRECTRWADAEECEIPGRWITRSTPPEGSDST
 APSTQEPEAPPEQDLIASTVAGVVTTVMGSSQPVVTRGTTDNLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIF
 YQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQ

EGPGTRLPGNLSSSEVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHL
SALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQ
QPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPKGGALGEGPGASPCNQHSPYWA
PPCYTLKPET

SEQ ID NO: 105

EDAR/IL9R/cGC-F

EYSNCGENEYNNQTTGLCQECPPCGPGEOPYLSCGYGTKDEYGCVPCEAEKFSKGGYQI
CRRHKDCEGFFRATVLTGDMENDAECGPCLPGYYMLENRPRNIYGMVCYSCLLAPPNTK
ECVGATSGASANFPGTSGSSTLSPFQHAHKELSGQGLHATALIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVKRIFY
QNVSPAMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQE
GPGTRLPGNLSSSEVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHL
ALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGS
GGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPKGGALGEGPGASPCNQHSPY
WAPPCYTLKPET

SEQ ID NO: 106

EDAR/IL9R/cGC-S

EYSNCGENEYNNQTTGLCQECPPCGPGEOPYLSCGYGTKDEYGCVPCEAEKFSKGGYQI
CRRHKDCEGFFRATVLTGDMENDAECGPCLPGYYMLENRPRNIYGMVCYSCLLAPPNTK
ECVGATSGASANFPGTSGSSTLSPFQHAHKELSGQGLHATALIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVKRIFY
QNVSPAMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQE
GPGTRLPGNLSSSEVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHL
ALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQ
QPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPKGGALGEGPGASPCNQHSPYWAP
PCYTLKPET

SEQ ID NO: 107

DCR2 (TNFRSF10D) /IL9R/cGC-F

ATIPRQDEVPPQTVAPQQRRSLKEEECPAGSHRSEYTGACNPCTEGVDYTIASNNLPSC
LLCTVCKSGQTNKSSCTTTRDTCQCEKGSFQDKNSPEMCRCTGCPRGMVKVSNTCP
SDIKCKNESAASSTGKTPAAETVTTLGMLASPHYHLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVKRIFYQNVSP
AMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPTRL
PGNLSSSEVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHL
SALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGS
GGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPKGGALGEGPGASPCNQHSPYWAPPC
YTLKPET

SEQ ID NO: 108

DCR2 (TNFRSF10D) /IL9R/cGC-S

ATIPRQDEVPPQTVAPQQRRSLKEEECPAGSHRSEYTGACNPCTEGVDYTIASNNLPSC
LLCTVCKSGQTNKSSCTTTRDTCQCEKGSFQDKNSPEMCRCTGCPRGMVKVSNTCP
SDIKCKNESAASSTGKTPAAETVTTLGMLASPHYHLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVKRIFYQNVSP
AMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPTRL
PGNLSSSEVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHL
SALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGS
GGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPKGGALGEGPGASPCNQHSPYWAPPC
YTLKPET

QSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPT
MPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTL
KPET

SEQ ID NO: 109

DCR1 (TNFRSF10C) /IL9R/cGC-F

ATTARQEEVPQQTVAAPQQQRHSFKGEECPAGSHRSEHTGACNPCTEGVDYTNASNNPSC
FPCTVCKSDQKHKSCTMTRDTCQCKEGTFRNENSPENCRKCSRCPGSEVQVSNCTSWD
DIQCVEEFGANATVETPAAEETMNTSPGTPAPAAEETMNTSPGTPAPAAEETMTTSPGTP
APAAEETMTTSPGTPAPAAEETMNTSPGTPALIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVKRIFYQNVPSAMF
FQPLYSVHNGNFQWTWGAHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPAPWKSVALEEEQEGPGTRLPGNL
SSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSPALPGNTQSSG
PIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTM
PRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKP
ET

SEQ ID NO: 110

DCR1 (TNFRSF10C) /IL9R/cGC-S

ATTARQEEVPQQTVAAPQQQRHSFKGEECPAGSHRSEHTGACNPCTEGVDYTNASNNPSC
FPCTVCKSDQKHKSCTMTRDTCQCKEGTFRNENSPENCRKCSRCPGSEVQVSNCTSWD
DIQCVEEFGANATVETPAAEETMNTSPGTPAPAAEETMNTSPGTPAPAAEETMTTSPGTP
APAAEETMTTSPGTPAPAAEETMNTSPGTPALIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVKRIFYQNVPSAMF
FQPLYSVHNGNFQWTWGAHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPAPWKSVALEEEQEGPGTRLPGNL
SSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSPALPGNTQSSG
PIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTMPRIPT
TLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 111

CD40/IL9R/cGC-F

EPPTACREKQYLINSQCCSLCQPGQKLVSDDCTEFTETECPCGESEFLDTWNRETHCHQH
KYCDPNLGLRVQKGTSETDTICTCEEGWHCTSEACESCVLHRSCSPGFGVKQIATGVSD
TICEPCPVGFFSNVSSAFEKHPWTSCETKDLVVQQAGTNKTDVVCQPQDRRLIPPWGWPGNTLVAVSIFLLTGPTY
LLFKLSRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPAP
PWKSVALEEEQEGPGTRLPGNLSSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNY
CALGCYGGWHLSPALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSW
TFGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGE
GPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 112

CD40/IL9R/cGC-S

EPPTACREKQYLINSQCCSLCQPGQKLVSDDCTEFTETECPCGESEFLDTWNRETHCHQH
KYCDPNLGLRVQKGTSETDTICTCEEGWHCTSEACESCVLHRSCSPGFGVKQIATGVSD
TICEPCPVGFFSNVSSAFEKHPWTSCETKDLVVQQAGTNKTDVVCQPQDRRLIPPWGWPGNTLVAVSIFLLTGPTY
LLFKLSRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPAP
PWKSVALEEEQEGPGTRLPGNLSSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNY

CALGCYGGWHLSPALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSW
TFQPQPQPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGA
SPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 113

FAS/IL9R/cGC-F

QVTDINSKGLELRKTVTTVETQNLEGLHHDGQFCHKPCPPGERKARDCTVNGDEPDCVPC
QEGKEYTDKAHFSSKRRRCRLCDEGHGLEVEINCTRTQNTKCRCKPNFFCNSTVCEHCDP
CTKCEHGIIKECTLTSTNKCKEEGSRSNLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSRVKRIFYQNVSPAMFFQPLY
SVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPTRLPGNLSSDV
LPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHLSPALPGNTQSSGPIPAL
ACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGSGGGGSGGGGSERTMPRIPT
LKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 114

FAS/IL9R/cGC-S

QVTDINSKGLELRKTVTTVETQNLEGLHHDGQFCHKPCPPGERKARDCTVNGDEPDCVPC
QEGKEYTDKAHFSSKRRRCRLCDEGHGLEVEINCTRTQNTKCRCKPNFFCNSTVCEHCDP
CTKCEHGIIKECTLTSTNKCKEEGSRSNLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSRVKRIFYQNVSPAMFFQPLY
SVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPTRLPGNLSSDV
LPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHLSPALPGNTQSSGPIPAL
ACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTMPRIPTLKN
LEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 115

DR4/IL9R/cGC-F

ASGTEAAAATPSKVWSSAGRIEPRGGGRGALPTSMGQHGPSARARAGRAPGPRPAREAS
PRLRVHKTFFKVVVGVLLQVVPSSAATIKLHDQSIGTQQWEHSPLGELCPPGSHRSEHPG
ACNRCTEGVGYTNASNNLFACLPCTACKSDEEERSPCTTTRNTACQCKPGTFRNDNSAEM
CRKCSRGCPRGMVVKDCTPWSIDIECVHKESGNHNLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSRVKRIFYQNV
PSPAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPG
TRLPGNLSSDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHLSPAL
GNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGSGGGGSGG
GGERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWA
PPCYTLKPET

SEQ ID NO: 116

DR4/IL9R/cGC-S

ASGTEAAAATPSKVWSSAGRIEPRGGGRGALPTSMGQHGPSARARAGRAPGPRPAREAS
PRLRVHKTFFKVVVGVLLQVVPSSAATIKLHDQSIGTQQWEHSPLGELCPPGSHRSEHPG
ACNRCTEGVGYTNASNNLFACLPCTACKSDEEERSPCTTTRNTACQCKPGTFRNDNSAEM
CRKCSRGCPRGMVVKDCTPWSIDIECVHKESGNHNLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSRVKRIFYQNV
PSPAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPG

TRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYALGCYGGWHLALP
 GNTQSSGPIPALACGLSDHQLETQQGVAWVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQP
 ERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPKGGALGEGPGASPCNQHSPYWAPPC
 YTLKPET

SEQ ID NO: 117

DR6/IL9R/cGC-F

QPEQKASNLIGTYRHVDRATGQVLTCDKCPAGTYVSEHCTNTSLRVCSSCPVGTFTRHEN
 GIEKCHDCSQPCPWPMIEKLPCAALTDRECTCPPGMFQSNATCAPHTVCPVGWGVRRKKGT
 ETEDVRCKQCARGTFSDVPSSVMKCKAYTDCLSQNLVVIKPGTKETDNVCGTLPSFSSST
 SPSPGTAIFRPEHMETHEVPSSTYVPKGMNSTESNSSASVRPKVLSSIQEGTVPDNTSS
 ARGKEDVNKTLPNLQVVNHQQGPHHRHILKLLPSMEATGGEKSSTPIKGPGRGHPRQNLH
 KHFDINEHLIPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVKRIFYQNVPSAMFFQPLYSVHNGNFQWVMGAHGA
 GVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQ
 EDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYALGCYGGWHLALPGNTQSSGPIPALACGLSDHQLETQQGVA
 WVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWS
 GVSGLAESLQPDYSERLCLVSEIPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 118

DR6/IL9R/cGC-S

QPEQKASNLIGTYRHVDRATGQVLTCDKCPAGTYVSEHCTNTSLRVCSSCPVGTFTRHEN
 GIEKCHDCSQPCPWPMIEKLPCAALTDRECTCPPGMFQSNATCAPHTVCPVGWGVRRKKGT
 ETEDVRCKQCARGTFSDVPSSVMKCKAYTDCLSQNLVVIKPGTKETDNVCGTLPSFSSST
 SPSPGTAIFRPEHMETHEVPSSTYVPKGMNSTESNSSASVRPKVLSSIQEGTVPDNTSS
 ARGKEDVNKTLPNLQVVNHQQGPHHRHILKLLPSMEATGGEKSSTPIKGPGRGHPRQNLH
 KHFDINEHLIPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVKRIFYQNVPSAMFFQPLYSVHNGNFQWVMGAHGA
 GVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQ
 EDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYALGCYGGWHLALPGNTQSSGPIPALACGLSDHQLETQQGVA
 WVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPQPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVS
 KGLAESLQPDYSERLCLVSEIPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 119

DR5/IL9R/cGC-F

ITQQDLAPQQRAAPQQKRSSPSEGLCPPGHHISEDGRDCISCKYQDYSTHWNDLLFCLR
 CTRCDSGEVELSPCTTTRNTVCQCEEGTFREEDSPEMCRKCRGTGCPRGMVKVGDCPTWSD
 IECVHKESGTHKSGEVPVEETVTSSPGTPASPCSLIPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVKRIFYQNVPSA
 MFFQPLYSVHNGNFQWVMGAHGAHVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLP
 GNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYALGCYGGWHLALPGNTQ
 SSGPIPALACGLSDHQLETQQGVAWVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSE
 RTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPKGGALGEGPGASPCNQHSPYWAPPCY
 TLKPET

SEQ ID NO: 120

DR5/IL9R/cGC-S

ITQQDLAPQQRAAPQQKRSSPSEGLCPPGHHISEDGRDCISCKYQQDYSTHWNDLLFCLR
 CTRCDSGEVELSPCTTTRNTVCQCEEGTFREEDSPEMCRKCRGTGCPRGMVKVGDCTPWSD
 IECVHKESGTHKSHGEVPAVEETVTSSPGTPASPCSLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSPRVKRIFYQNVPSPA
 MFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLP
 GNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCGYGGWHLALPGNTQ
 SSGPIPALACGLSCDHQGLTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTM
 PRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKP
 ET

SEQ ID NO: 121

DR3/IL9R/cGC-F

QGGTRSPRCDACAGDFHKKIGLFCCRGCPAGHYLKAPCTEPCGNSTCLVCPQDFTLAWENH
 HNSECARCQACDEQASQVALENCASAVADTRCGCKPGWFVECCQVSQCVSSSPFYCQPCLCD
 GALHRHTRLLCSRRDTCGTCLPGFYEHDGCVSCTSTLGSCEPERCAAVCGWRQLIPPWGWPGNTLVAVSIFLLTG
 TYLLFKLSPRVKRIFYQNVPSPAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGP
 ARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNN
 NYCALGCGYGGWHLALPGNTQSSGPIPALACGLSCDHQGLTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKAR
 SWTFGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGAL
 GEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 122

DR3/IL9R/cGC-S

QGGTRSPRCDACAGDFHKKIGLFCCRGCPAGHYLKAPCTEPCGNSTCLVCPQDFTLAWENH
 HNSECARCQACDEQASQVALENCASAVADTRCGCKPGWFVECCQVSQCVSSSPFYCQPCLCD
 GALHRHTRLLCSRRDTCGTCLPGFYEHDGCVSCTSTLGSCEPERCAAVCGWRQLIPPWGWPGNTLVAVSIFLLTG
 TYLLFKLSPRVKRIFYQNVPSPAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGP
 ARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNN
 NYCALGCGYGGWHLALPGNTQSSGPIPALACGLSCDHQGLTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKAR
 SWTFQPQPQPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEG
 PGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 123

TNFRSF1B/IL9R/cGC-F

LPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKSDTVCDSCEDST
 YTQLWNWVPECLSCGSRSSDQVETQACTREQNRICRPGWYCALSKQEGCRLCAPLRK
 CRPGFGVARPGTETSDVVKPCAPGTFSNTTSSTDICRPHQICNVVAIPGNASMDAVCTS
 TSPTRSMAAGAVHLPQPVSTRSQHTQPTPEPSTAPSTSFLPMGPSPPAEGSTGDLIPPWGWPGNTLVAVSIFLLTG
 TYLLFKLSPRVKRIFYQNVPSPAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGP
 ARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNN
 NYCALGCGYGGWHLALPGNTQSSGPIPALACGLSCDHQGLTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKAR
 SWTFGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGAL
 GEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 124

TNFRSF1B/IL9R/cGC-S

LPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKSDTVCDSCEDST
 YTQLWNWVPECLSCGSRSSDQVETQACTREQNRICRCRPGWYCALSKEGCRCLCAPLRK
 CRPGFGVARPGTETSDVVCKPCAPGTFSNTTSSTDICRPHQICNVVAIPGNASMDAVCTS
 TSPTRSMAPGAVHLPQPVSTRSQHTQPTPEPSTAPSTSFLPMGPSPPAEGSTGDLIPWGWPGNTLVAVSIFLLLTGP
 TYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGP
 ARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNN
 NYCALGCGYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKAR
 SWTFQPQPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEG
 PGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 125

TNFRSF1/IL9R/cGC-F

LVPHLGDRKRDVCPQGKYIHPQNNISICCTKCHKGTLYNDCPGPGQDTCRECESGSF
 TASENHLRHCLSCSKCRKEMGQVEISSCTVDRDTCGCRKNQYRHYWSENLFQCFNCSLC
 LNGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSELECTKLCLPQIENVKGTEDSG
 TTLIPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQ
 DCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAP
 TSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCGYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAG
 HCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKG
 LAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 126

TNFRSF1/IL9R/cGC-S

LVPHLGDRKRDVCPQGKYIHPQNNISICCTKCHKGTLYNDCPGPGQDTCRECESGSF
 TASENHLRHCLSCSKCRKEMGQVEISSCTVDRDTCGCRKNQYRHYWSENLFQCFNCSLC
 LNGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSELECTKLCLPQIENVKGTEDSG
 TTLIPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQ
 DCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAP
 TSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCGYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAG
 HCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAES
 LQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 127

BMPR1B/IL9R/cGC-F

KKEDGESTAPTRPKVLRCKCHHCPEDSVNNICSTDGYCFTMIEEDDSGLPVVTSGCLG
 LEGSDFQCRDTPIPHQRRSIECCTERNECNKDLHPTLPPLKNRDFVDGPIHHRILIPWGWPGNTLVAVSIFLLLTGPTYLL
 FKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARP
 WKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNY
 ALGCGYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWT

FGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEG
PGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 128

BMPR1B/IL9R/cGC-S

KKEDGESTAPTRPKVLRCKCHHHCPEDSVNNICSTDGYCFTMIEEDDSGLPVVTSGLG
LEGSDFQCRDTPIPHQRRSIECCTERNECNKDLHPTLPPLKNRDFVDGPIHHRIPPWGWPGNTLVAVSIFLLLTGPTYLL
FKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARP
WKSVALEEEQEGPGTRLPGNLSSDVLPACTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYC
ALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWT
FQPQPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGAS
PCNQHSPYWAPPCYTLKPET

SEQ ID NO: 129

BMPR1A/IL9R/cGC-F

QNLDSMLHGTGMKSDSDQKXSENGVTLAPEDTLPFLKCYCSGHCPCDDAINNTCITNGHCF
AIIEDDQGETTLASGCMKYEGSDFQCKDSPKAQLRRTIECCRTNLCNQYLQPTLPPVVI
GPFFDGSIRLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGA
GVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPACTEWRVQTLAYLPQ
EDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVA
WVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWS
GVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 130

BMPR1A/IL9R/cGC-S

QNLDSMLHGTGMKSDSDQKXSENGVTLAPEDTLPFLKCYCSGHCPCDDAINNTCITNGHCF
AIIEDDQGETTLASGCMKYEGSDFQCKDSPKAQLRRTIECCRTNLCNQYLQPTLPPVVI
GPFFDGSIRLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGA
GVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPACTEWRVQTLAYLPQ
EDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVA
WVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGV
KGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 131

BMPR2/IL9R/cGC-F

SQNQERLCAFKDPYQQDLGIGESRISHENGITLCSKGSTCYGLWEKSGDINLVKQGCWS
HIGDPQECHYECCVTTTPPSIQNGTYRFCCSTDLCNVNFTENFPPDTPPLSPHSFN
RDETLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLL
SQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPACTEWRVQTLAYLPQEDW
APTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWV
LAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGV
KGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 132

BMPR2/IL9R/cGC-S

SQNQERLCAFKDPYQQDLGIGESRISHENGITILCSKGSTCYGLWEKSGDINLVKQGCWS
 HIGDPQECHYEECVVTTPPSIQNGTYRFCCCSTDLCNVNFTENFPPDTPPLSPPHSFN
 RDETLIPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNVSPAMFFQPLYSVHNGNFQTMGAHGAGVLL
 SQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPACTEWRVQTLAYLPQEDW
 APTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVL
 AGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGL
 AESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 133**CSF3R/IL9R/cGC-F**

ECGHISVSAPIVHLGDPITASCIKQNCSHLDPEPQILWRLGAELQPGGRQQRLSDGTQE
 SIITLPHLNHTQAFLLSCCLNWGNSLQILDQVELRAGYPPAIPHNLSCLMNLTTSSLICQW
 EPGPETHLPTSFTLKSFKSRGNCQTQGDSDILDCVPGDQSHCCIPRKHLLYQNMGIWVQ
 AENALGTSMSPLCLDPMDDVVKLEPPMLRTMDPSPEAAPPQAGCLQLCWEPWQPLHINQ
 KCELRHKPQRGEASWALVGPLPLEALQYELCGLLPATAYTLQIRCIRWPLPGHWSWSPS
 LELRTTERAPTVRDLTWWRQRQLDPRTVQLFWKPVPLEEDSGRIQGYVVSWRPSGQAGAI
 LPLCNTTELSCTFHLPSEAQEVALLVAYNSAGTSRPTPVVFSESRGPALTRLHAMARDPHS
 LWVGWEPPNPWPQGYVIEWGLGPPSASNSNKTWRMEQNGRATGFLLENIRPFQLYEIV
 TPLYQDTMGPSQHVYAYSQEMAPSHAPELHLKHIGKTWAQLEWVPEPPELGKSPPLTHYTI
 FWTNAQNSFSAILNASSRGFVLHGLEPASLYHIHLMAASQAGATNSTVLTMTLTPEGS
 ELHLIPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNVSPAMFFQPLYSVHNGNFQTMGAHGAGVLLS
 QDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPACTEWRVQTLAYLPQEDWA
 PTLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLA
 GHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSEMTMPRIPTLKNLEDLVTEYHGNFSAWSGVSK
 GLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO:134**CSF3R/IL9R/cGC-S**

ECGHISVSAPIVHLGDPITASCIKQNCSHLDPEPQILWRLGAELQPGGRQQRLSDGTQE
 SIITLPHLNHTQAFLLSCCLNWGNSLQILDQVELRAGYPPAIPHNLSCLMNLTTSSLICQW
 EPGPETHLPTSFTLKSFKSRGNCQTQGDSDILDCVPGDQSHCCIPRKHLLYQNMGIWVQ
 AENALGTSMSPLCLDPMDDVVKLEPPMLRTMDPSPEAAPPQAGCLQLCWEPWQPLHINQ
 KCELRHKPQRGEASWALVGPLPLEALQYELCGLLPATAYTLQIRCIRWPLPGHWSWSPS
 LELRTTERAPTVRDLTWWRQRQLDPRTVQLFWKPVPLEEDSGRIQGYVVSWRPSGQAGAI
 LPLCNTTELSCTFHLPSEAQEVALLVAYNSAGTSRPTPVVFSESRGPALTRLHAMARDPHS
 LWVGWEPPNPWPQGYVIEWGLGPPSASNSNKTWRMEQNGRATGFLLENIRPFQLYEIV
 TPLYQDTMGPSQHVYAYSQEMAPSHAPELHLKHIGKTWAQLEWVPEPPELGKSPPLTHYTI
 FWTNAQNSFSAILNASSRGFVLHGLEPASLYHIHLMAASQAGATNSTVLTMTLTPEGS
 ELHLIPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNVSPAMFFQPLYSVHNGNFQTMGAHGAGVLLS
 QDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPACTEWRVQTLAYLPQEDWA
 PTLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLA
 GHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAE
 SLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 135

CSF1R/IL9R/cGC-F

IPVIEPSVPELVVKPGATVTLRCVGNGSVEWDGPPSPHWTLYSDGSSSILSTNNATFQNT
 GTYRCTEPGDPLGGSAAIHLVVKDPAWPWNVLAQEVVVFEDQDALLPCLLTDPVLEAGVS
 LVRVRGRPLMRHTNYSFSPWHGFTIHRAKFIQSQDYQCSALMGGRKVMSSIRLKVQKVI
 PGPPALTLVPAELVRIRGEAAQIVCSASSVDVNFDFLQHNNTKLAIPQQSDFHNNRYQK
 VLTNLNDQVDFQHAGNYSCVASNVQGHSTSMFFRVVESAYLNLSSSEQNLIQEVTVGEG
 NLKVMVEAYPGLQGFNWTYLGPFSDHQPEPKLANATTKDTYRHTFTLSLPRLPSEAGRY
 SFLARNPGGWRAITFELTLRYPPEVSVIWTFFINGSGTLLCAASGYPQPNVTWLQCSGHTD
 RCDEAQVLQVWDDPYPEVLSQEPFHKVTVQSLTETLEHNQTYECRAHNSVSGSGWAFI
 PISAGATHPPDEFLEFTLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNPVSPAMFFQPLYSVHNGNFQT
 WMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPTRLPGNLSSEDLVLPAGCTEWR
 VQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQ
 GLETQQGVAWVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGGSGGGGSEMTMPRIPTLKNLEDLVTE
 YHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPLYWAPPCYTLKPET

SEQ ID NO: 136

CSF1R/IL9R/cGC-S

IPVIEPSVPELVVKPGATVTLRCVGNGSVEWDGPPSPHWTLYSDGSSSILSTNNATFQNT
 GTYRCTEPGDPLGGSAAIHLVVKDPAWPWNVLAQEVVVFEDQDALLPCLLTDPVLEAGVS
 LVRVRGRPLMRHTNYSFSPWHGFTIHRAKFIQSQDYQCSALMGGRKVMSSIRLKVQKVI
 PGPPALTLVPAELVRIRGEAAQIVCSASSVDVNFDFLQHNNTKLAIPQQSDFHNNRYQK
 VLTNLNDQVDFQHAGNYSCVASNVQGHSTSMFFRVVESAYLNLSSSEQNLIQEVTVGEG
 NLKVMVEAYPGLQGFNWTYLGPFSDHQPEPKLANATTKDTYRHTFTLSLPRLPSEAGRY
 SFLARNPGGWRAITFELTLRYPPEVSVIWTFFINGSGTLLCAASGYPQPNVTWLQCSGHTD
 RCDEAQVLQVWDDPYPEVLSQEPFHKVTVQSLTETLEHNQTYECRAHNSVSGSGWAFI
 PISAGATHPPDEFLEFTLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNPVSPAMFFQPLYSVHNGNFQT
 WMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPTRLPGNLSSEDLVLPAGCTEWR
 VQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQ
 GLETQQGVAWVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFQPPQPPQPPPERTMPRIPTLKNLEDLVTEYHG
 NFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPLYWAPPCYTLKPET

SEQ ID NO: 137

VEGF Receptor 1/IL9R/cGC-F

SKLKDPELSLKGTHIMQAGQTLHLQCRGEAAHKWSLPEMVSKESESLITKSACGRNGK
 QFCSTLTNTAQANHTGFYSCKYLAVPTSKKKETESAIYIFISDTGRPFVEMYSEIPEII
 HMTGRELVIPCRVTSPNITVTLKKFPLDTLIPDGKRIIWDNRKGFISNATYKEIGLLT
 CEATVNGHLYKTNLYLTHRQNTIIVQJSTPRPVKLLRGHTLVLNCTATTPLNTRVQMTW
 SYPDEKNKRASVRRRIDQSNHANIFYSVLTIDKMQNKDKGLYTCRVRSGPSFKSVNTSV
 HIYDKAFITVKKRQVLETVAGKRSYRLSMKVKAFFPSPEVVWLKDGLPATEKSARYLTR
 GYSIIKDVTEEDAGNYTILLSIKQSNVFNLTATLIVNVKPKIYEKAVSSFPDPALYPL
 GSRQILTCTAYGIPQPTIKWFWHPCNHNHSEARCDFCNNNEESFILDADSNMGNRIESIT

QRMAIIEGKNKMASTLVVADSRISGIYICIASNKVGTVGRNISFYITDVPNGFHVNLEKM
 PTEGEDLKLSTVNKFLYRDVTWILLRTVNNRTMHYSISQKQMAITKEHSITLNLTIMNV
 SLQDSGTYACRARNVYTGEILQKKEITIRDQEPYLLRNLSDHVAISSSTLDCHANG
 VPEPQITWFKNNHKIQQEPGILGPSSTLFIERVTEEDEGVYHCKATNQKGSVESSAYL
 TVQGTSDKSNLELIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVRKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGMG
 AHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTL
 AYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLT
 QQGVAVWLAGHCQRPLGHEDLQGMLLPSVLSKARSWTFGGGGSGGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHG
 NFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 138

VEGF Receptor 1/IL9R/cGC-S

SKLKDPESLKGQTQHIMQAGQTLHLQCRGEAAHKWSLPEMVSKESESLITKSACGRNGK
 QFCSTLTNTAQANHTGFYCKYLAVPTSKKKETESAIYIFISDTGRPFVEMYSEIPEII
 HMTGRELVIPCRVTPNITVTLLKFLDTPDYGKRIIWDNRKGFISNATYKEIGLLT
 CEATVNGHLYKTNLTHRQNTNIDVQISTPRPVKLLRGHTLVNCTATTPLNTRVQMTW
 SYPDEKNKRASVRRRIDQSNHANIFYSVLTIDKMQNKDKGLYTCRVRSGPSFKSVNTSV
 HIYDKAFITVHKRQKQVLETVAGKRSYRLSMKVKAFPSPPEVVWLKDGLPATEKSARYLTR
 GYSLIKDVTEEDAGNYTILLSIKQSNVFNLTATLIVNVKPKIYEKAVSSFPDPALYPL
 GSRQILTCTAYGIPQPTIKWFHPCNHNHSEARCDFCSNNEESFILDADSNMGNRIESIT
 QRMAIIEGKNKMASTLVVADSRISGIYICIASNKVGTVGRNISFYITDVPNGFHVNLEKM
 PTEGEDLKLSTVNKFLYRDVTWILLRTVNNRTMHYSISQKQMAITKEHSITLNLTIMNV
 SLQDSGTYACRARNVYTGEILQKKEITIRDQEPYLLRNLSDHVAISSSTLDCHANG
 VPEPQITWFKNNHKIQQEPGILGPSSTLFIERVTEEDEGVYHCKATNQKGSVESSAYL
 TVQGTSDKSNLELIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSRVRKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGMG
 AHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTL
 AYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLT
 QQGVAVWLAGHCQRPLGHEDLQGMLLPSVLSKARSWTFQPPQPPQPPQPPERTMPRIPTLKNLEDLVTEYHGNFSA
 WSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO:139

VEGF Receptor 2/IL9R/cGC-F

ASVGLPSVSLDLPRLSIQKDILTILKANTTLQITCRGQRDLWLWPNNQSGSEQRVEVTEC
 SDGLFCKTLTIPKVIGNDTGAYKCFYRETDLASVIYVVYQDYRSPFIASVSDQHGVVYIT
 ENKNKTVVIPCLGSISNLNVSLCARYPEKRFVPDGNRISWDSKKGFTIPSYMISYAGMVF
 CEAKINDESYQSIMYIVVVVGYRIYDVVLSPSHGIELSVGEKLVNCTARTELNVGIDFN
 WEYPSSKHQHKLVNRDLKTQSGSEMKKFLSTLTIDGVTRSDQGLYTCAASSGLMTKKNS
 TFVRVHEKPFVAFGSGMESLVEATVGERVRIPAKYLGYPPEIKWYKNGIPLESNHTIKA
 GHVLTIMEVSEKRDGTNYTVILTNPISKEKQSHVVSLLVYVPPQIGEKSLISPVDYQYGT
 TQTLTCTVYAIPPPHHIHWYWLQEEECANEPSQAVSVTNYPCEEWRSDVDFQGGNKIEV
 NKNQFALIEGKNKTVSTLVIQAANVSALYKCEAVNKVGRGERVISFHVTRGPEITLQPDM
 QPTEQESVSLWCTADRSTFENLTWYKLGPPQPLPIHVGELEPTPVCKNLDTLWKLNATMFSN
 STNDILIMELKNASLQDQGDYVCLAQDRKTKKRHCVRQLTVLERVAPTITGNLENQTTT
 IGESIEVSTASGNPPPQIMWFKDNETLVEDSGIVLKDGNRNLTIIRVRKEDEGLYTCAQ

CSVLGCAKVEAFFIIEGAQEKTNLELIPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMFFQPLYSVH
 NGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSSEDLPA
 GCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACG
 LSCDHQGLETTQQGVAVVLAGHCQRPLGHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSGERTMPRIPTLKN
 LEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPCKGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 140

VEGF Receptor 2/IL9R/cGC-S

ASVGLPSVSLDPLRLSIQKDILTILKANTTLQITCRGQRDLWLWPNNQSGSEQRVEVTEC
 SDGLFCKTLTIPKVGINDTGAYKCFYRETDLASVIYVYVQDYRSPFIASVSDQHGVVYIT
 ENKNKTVVIPCLGSISNLNVLSCARYPEKRFVDPGNRISWDSKKGFTIPSYMISYAGMVF
 CEAKINDESYQSIMYIVVVVGYRIYDVVLSPSHGIELSVGEKLVNCTARTELVNVDIFN
 WEYPSSKHQHKLVNRDLKTQSGSEMKKFLSTLTIDGVTRSDQGLYTCAASSGLMTKKNS
 TFVRVHEKPFVAFSGMESLVEATVGERVRIPAKYLGYPPEIKWYKNGIPLESNHTIKA
 GHVLTIMEVSEKRDGTNYTVILTNPISKEKQSHVVSLLVYVPPQIGEKSLISPVDSYQYGT
 TQTLTCTVYAIPPPHHIHWYWQLEEECANEPSQAVSVTNYPCEEWRSEDFQGGNKIEV
 NKNQFALIEGKNKTVSTLVIQAANVSALYKCEAVNKVGRGERVISFHVTRGPEITLQPD
 QPTEQESVSLWCTADRSTFENLTWYKLGPPQLPIHVGELEPTPVCKNLDTLWKLNATMFSN
 STNDILIMELKNASLQDQGDYVCLAQDRKTKKRHCVRQLTVLERVAPTITGNLENQTT
 IGESIEVSTASGNPPPQIMWFKDNETLVEDSGIVLKDGNRNLTIIRVRKEDEGLYTCA
 CSVLGCAKVEAFFIIEGAQEKTNLELIPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMFFQPLYSVH
 NGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSSEDLPA
 GCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACG
 LSCDHQGLETTQQGVAVVLAGHCQRPLGHEDLQGMLLPSVLSKARSWTFQPPQPQPQPQPPTMPRIPTLKNLEDL
 VTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPCKGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 141

VEGF Receptor 3/IL9R/cGC-S

YSMTPTPLNITEESHVIDTGDSLSISCRGQHPLEWAWPGAQEAPATGDKDSEDTGVVRDC
 EGTDPARPYCKVLLLHEVHANDTGSYVCYKIKARIEGTTAASSYVFVRDFEQPFINKPD
 TLLVNRKDAMWVPCLVSIPGLNVTLSQSSVLWPDGQEVVWDDRRGMLVSTPLLHDALYL
 QCETTWGDQDFLSNPFLVHITGNELYDIQLLPRKSLELLVGEKLVNCTVWAEFNSGVTF
 DWDYPGKQAERGKWWPERRSQQTHTELSSILTIHNVSQHDLGSYVCKANNGIQRFRETE
 VIVHENPFISVEWLKGPILAEATAGDELVKLPVKLAAYPPPEFQWYKDGKALSGRHSFHAL
 VLKEVTEASTGTYTLALWNSAAGLRRNISLELVNVPPQIHEKEASSPSIYSRHSRQALT
 CTAYGVPLPLSIQWHWRPWTPCKMFAQSRSLRRRQQQLMPQCRDWRAVTTQDAVNPIESL
 DTWTEFVEGKNKTVSKLVIQANANVSAMYKCVVSNKVGQDERLIYFYVTTIPDGFTIESKP
 SEELLEGQPVLLSCQADSYKYEHLRWYRLNLSTLHDAHGNPLLLDCKNVHLFATPLAASL
 EEVAPGARHATLSLSIPRVAPEHEGHYVCEVQDRRSHDKHCHKYLSVQALEAPRLTQNL
 TDLLVNVSDSLEMQLVAGAHAPSIVWYKDERLLEEKSGVDLADSNQKLSIQRVREEDAG
 RYLCSVCNAKGCVNSSASVAVEGSEDKGSMELIPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMF
 FQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNL
 SSSEDLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLSALPGNTQSSG

PIPALACGLSCDHQGLETTQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQPQPQPPTMPRIPTLNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 142

VEGF Receptor 3/IL9R/cGC-F

YSMTPTLNITEESHVIDTGDLSISCRGQHPLAWWPGAQEAQATGDKDSED TGVRDC
EGTDARPYCKVLLLHEVHANDTGSYVCYKYIKARIEGTTAASSYVFVRDFEQPFINKPD
TLLVNRKDAMWVPCLVSIPLNVTLSQS SVLWPDGQEVVWDDRRGMLVSTPLLHDALYL
QCETTWGDQDFLSNPFLVHITGNELYDIQLPRKSLELLVGEKLVNCTVWAEFNSGVTF
DWDYPGKQAEGRKWVPERRSQQTHTELSSILTIHNVSQHDLGSYVCKANNGIQRFRESTE
VIVHENPFISVEWLKGPILAEATAGDELVKLPVKLAAYPPPEFQWYKDGKALSGRHS PHAL
VLKEVTEASTGTYTALWNSAAGLRRNISLELVNVPPQIHEKEASSPSIYSRHSRQALT
CTAYGVPLPLSIQWHWRPWTPCKMFAQRSLRRRQQQDLMPQCRDWRAVTTQDAVNPIESL
DTWTEFVEGKNKTVSKLVIQANVNSAMYKCVVSNKVGQDERLIYFYVTTIPDGFTIESKP
SEELLEGQPVLLSCQADS YKYEHLRWYRLNLSTLHDAHGNPLLLDCKNVHLFATPLAASL
EEVAPGARHATLSLIPRVAPEHEGHYVCEVQDRRSHDKHCHKYLSVQALEAPRLTQNL
TDLLVNVSDSLEMQLVAGAHAPSIVWYKDERLLEEKSGVDLADSNQKLSIQRVREEDAG
RYLCSVCNAKGCVNSSASVAVEGSEDKGSMELIPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVPS PAMF
FQPLYSVHNGNFQWTWGAHAGAVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNL
SSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHL SALPGNTQSSG
PIPALACGLSCDHQGLETTQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTM
PRIPTLNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKP
ET

SEQ ID NO: 143

Activin R1A ectodomain/IL9R/cGC-F

MEDEKPKVNPPLYMCVCEGLSCGNEDHCEGQQCFSSLSINDGFHVYQKGCQVYEQGKMT
CKTPPSPGQAVECCQGDWCNRNITAQLPTKGKSFPGTQNFHLELIPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVK
RIFYQNVPS PAMFFQPLYSVHNGNFQWTWGAHAGAVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEE
EQEGPGTRLPGNLSSSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGW
HLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGG
GGSGGGGSERTMPRIPTLNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQH
SPYWAPPCYTLKPET

SEQ ID NO: 144

Activin R1A ectodomain/IL9R/cGC-S

MEDEKPKVNPPLYMCVCEGLSCGNEDHCEGQQCFSSLSINDGFHVYQKGCQVYEQGKMT
CKTPPSPGQAVECCQGDWCNRNITAQLPTKGKSFPGTQNFHLELIPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVK
RIFYQNVPS PAMFFQPLYSVHNGNFQWTWGAHAGAVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEE
EQEGPGTRLPGNLSSSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGW
HLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQPQ
PQPQPPTMPRIPTLNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPY
WAPPCYTLKPET

SEQ ID NO: 145

Activin R1B ectodomain/IL9R/cGC-F

SGPRGVQALLCACTSCAQANYTCETDGACMVSIFNLDGMEHHVRTCIPKVELVPAGKPFY
 CLSSEDLRNTHCCYTDYCNRIDLRVPSGHLKEPEHPSMWGPVELIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRI
 FYQNVSPAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEE
 QEGPGTRLPGNLSSSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGW
 HLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGG
 GGGGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQH
 SPYWAPPCYTLKPET

SEQ ID NO: 146

Activin R1B ectodomain/IL9R/cGC-S

SGPRGVQALLCACTSCAQANYTCETDGACMVSIFNLDGMEHHVRTCIPKVELVPAGKPFY
 CLSSEDLRNTHCCYTDYCNRIDLRVPSGHLKEPEHPSMWGPVELIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRI
 FYQNVSPAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEE
 QEGPGTRLPGNLSSSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGW
 HLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQ
 PQQPQPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPY
 WAPPCYTLKPET

SEQ ID NO: 147

Activin R1C ectodomain/IL9R/cGC-F

LSPGLKCVCLLCDSSNFTCQTEGACWASVMLTNGKEQVIKSCVSLPELNAQVFCHSSNNV
 TKTECCFTDFCNITLHLPTASPNAPKLGPMELIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMF
 FQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNL
 SSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSG
 PIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGGSGGGGSERTM
 PRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKP
 ET

SEQ ID NO: 148

Activin R1C ectodomain/IL9R/cGC-S

LSPGLKCVCLLCDSSNFTCQTEGACWASVMLTNGKEQVIKSCVSLPELNAQVFCHSSNNV
 TKTECCFTDFCNITLHLPTASPNAPKLGPMELIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMF
 FQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNL
 SSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSG
 PIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQPPQPQPERTMPRI
 PTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 149

Activin R2B ectodomain/IL9R/cGC-F

SGRGEAETRECIYYNANWELERTNQSLERCEGEQDKRLHCYASWRNSSGTIELVKKGCW

LDDFNCYDRQECVATEENPQVYFCCCEGNFCNERFTHLPEAGGPEVTYEPPTAPTLLTLIPPWGWPNGNTLVAVSIFLLL
TGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLT
CGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSN
NNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSK
ARSWTFGGGGSGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGG
ALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 150

Activin R2B ectodomain/IL9R/cGC-S

SGRGEAETRECIYYNANWELERTNQSGLERCEGEQDKRLHCYASWRNSSGTIELVKKGCW

LDDFNCYDRQECVATEENPQVYFCCCEGNFCNERFTHLPEAGGPEVTYEPPTAPTLLTLIPPWGWPNGNTLVAVSIFLLL
TGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLT
CGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSN
NNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSK
ARSWTFQPPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALG
EGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 151

Activin R2A ectodomain/IL9R/cGC-F

AILGRSETQECLFFNANWEKDRTNQTGVEPCYGDKDKRRHCFATWKNISGSIEIVKQGCW

LDDINCYDRTDCVEKKDSPEVYFCCCEGNMCNEKFSYFPEMEVTQPTSNPVTPKPPLIPPWGWPNGNTLVAVSIFLLLTG
PTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCG
PARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNN
NNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKA
RSWTFGGGGSGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGA
LGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 152

Activin R2A ectodomain/IL9R/cGC-S

AILGRSETQECLFFNANWEKDRTNQTGVEPCYGDKDKRRHCFATWKNISGSIEIVKQGCW

LDDINCYDRTDCVEKKDSPEVYFCCCEGNMCNEKFSYFPEMEVTQPTSNPVTPKPPLIPPWGWPNGNTLVAVSIFLLLTG
PTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCG
PARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNN
NNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKA
RSWTFQPPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGE
GPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 153

IL10R-alpha/IL9R/cGC-F

HGTELSPSPSVWFEEFFHHILHWTPIPNQSESTCYEVALLRYGIESWNSISNCSQTLSTY

DLTAVTLDLYHSNGYRARVRAVDGSRHSNWTVTNTRFSVDEVTLTVGSVNLEIHNGFILG

KIQLPRPKMAPANDTYESIFSHFREYEIAIRKVPGNFTFTHKKVKHENFSLTSGEVGEF

CVQVKPSVASRSNKGMSKEECISLTRQYFTVTNLIPPWGWPNGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNVPS
 AMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRL
 PGNLSSDVLPAAGTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNT
 QSSGPIPALACGLSCDHQGLETTQQGVAVWVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGS
 ERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPLYWAPPC
 YTLKPET

SEQ ID NO: 154

IL10R-alpha/IL9R/cGC-S

HGTLPSPPSVWFEEFFHHILHWTPIPNQSESTCYEVALLRYGIESWNSISNCSQTL
 DLTAVTLDLYHSNGYRARVRAVDGSRHSNWTVTNTRFSVDEVTLTVGSVNLEIHNGFILG
 KIQLPKPKMAPANDTYESIFSHFREYEIAIRKVPGNFTFTHKKVKHENFSLTSGEVGEF
 CVQVKPSVASRSNKGMSKEECISLTRQYFTVTNLIPPWGWPNGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNVPS
 AMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRL
 PGNLSSDVLPAAGTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNT
 QSSGPIPALACGLSCDHQGLETTQQGVAVWVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFQPPQPPQPPPERT
 MPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPLYWAPPCYTL
 KPET

SEQ ID NO: 155

TGFBR2 ectodomain/IL9R/cGC-F

TIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQE
 VCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDE
 CNDNIIFSEYNTSNPDLLLVIQFQLIPPWGWPNGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNVPSAMFFQPLYSVHN
 GNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA
 GTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGL
 SCDHQGLETTQQGVAVWVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMPRIPTLKNL
 EDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPLYWAPPCYTLKPET

SEQ ID NO: 156

TGFBR2 ectodomain/IL9R/cGC-S

TIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQE
 VCVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDE
 CNDNIIFSEYNTSNPDLLLVIQFQLIPPWGWPNGNTLVAVSIFLLTGPTYLLFKLSRVRKIFYQNVPSAMFFQPLYSVHN
 GNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA
 GTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGL
 SCDHQGLETTQQGVAVWVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFQPPQPPQPPPERTMPRIPTLKNLEDLV
 TEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPLYWAPPCYTLKPET

SEQ ID NO: 157

TGFBR1 ectodomain/IL9R/cGC-F

LQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPRDRPFVCA PSSKTG

SVTTTYCCNQDHCNKIELPTTVKSSPGLGPVELLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSPRVKRIFYQNVPSAM
 FFQPLYSVHNGNFQWTWMAHAGAVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPTRLPGN
 LSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCGYGGWHLSALPGNTQSS
 GPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERT
 MPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTL
 KPET

SEQ ID NO:158

TGFBFR1 ectodomain/IL9R/cGC-S

LQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPDRPFVCPASSKTG
 SVTTTYCCNQDHCNKIELPTTVKSSPGLGPVELLIPPWGWPGNTLVAVSIFLLTGPTYLLFKLSPRVKRIFYQNVPSAM
 FFQPLYSVHNGNFQWTWMAHAGAVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPTRLPGN
 LSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCGYGGWHLSALPGNTQSS
 GPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPPQPPQPPERTMPRI
 PTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO:159

TIGIT/IL9R/cGC-F

MMTGTIETTGNISAEKGGSIILQCHLSSTTAQVTQVNWEQQDQLLAICNADLGWHISPSF
 KDRVAPGPGGLGLTLQSLTVNDTGEYFCIYHTYPDGTYTGRIFLEVLESSVAEHGARFQIPLIPPWGWPGNTLVAVSIFLL
 TGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWMAHAGAVLLSQDCAGTPQGALEPCVQEATALLT
 CGPARPWKSVALEEEQEGPTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSN
 NNNYCALGCGYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSK
 ARSWTFGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGG
 ALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 160

TIGIT/IL9R/cGC-S

MMTGTIETTGNISAEKGGSIILQCHLSSTTAQVTQVNWEQQDQLLAICNADLGWHISPSF
 KDRVAPGPGGLGLTLQSLTVNDTGEYFCIYHTYPDGTYTGRIFLEVLESSVAEHGARFQIPLIPPWGWPGNTLVAVSIFLL
 TGPTYLLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWMAHAGAVLLSQDCAGTPQGALEPCVQEATALLT
 CGPARPWKSVALEEEQEGPTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSN
 NNNYCALGCGYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSK
 ARSWTFQPPQPPQPPQPPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALG
 EGPASPCNQHSPYWAPPCYTLKPET

SEQ ID NO:161

FCGR2B/IL9R/cGC-F

TPAAPPKAVLKLEPQWINVLQEDSVTLTCRGTHSPESDSIQWFHNGNLIPTHTQPSYRFK
 ANNNDSGEYTCQTGQTSLSDPVHLTVLSEWLVLQTPHLEFQEGETIVLRCHSWKDKPLVK
 VTFFQNGKSKKFSRSDPNFSIPQANHSHSGDYHCTGNIGYTYSSKPVITITVQAPLIPPWGWPGNTLVAVSIFLLTGPTY
 LLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWMAHAGAVLLSQDCAGTPQGALEPCVQEATALLTCGP
 PARPWKSVALEEEQEGPTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNY

CALGCGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKARSW
TFGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLPDYSERLCLVSEIPPKGKALGE
GPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 162

FCGR2B/IL9R/cGC-S

TPAAPPKAVLKLEPQWINVLQEDSVTLTCRGTHSPESDSIQWFHNGNLIPTHTQPSYRFK
ANNNDSGEYTCQTGQTSLSDPVHLTVLSEWLVLQTPHLEFQEGETIVLRCHSWKDKPLVK
VTFFQNGKSKKFSRSDPNFSIPQANHSHSGDYHCTGNIGYTLYSSKPVITITVQAPLIPPWGWPGNTLVAVSIFLLTGPTY
LLFKLSPRVKRIFYQNVPSAMFFQPLYSVHNGNFQTMWGAHGAGVLLSQDCAGTPQGALEPCVQEATAALLTCGP
PWKSVALEEEQEGPGRPLGNLSSDVLPACTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNY
CALGCYGGWHLSPALPGNTQSSGPIALACGLSCDHQGLTQQGVAWVLVAGHCQRPLGHEDLQGMLLPSVLSKARS
TFQPQPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCVSEIPPKGGALGEGPGA
SPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 163

FCGR1/IL9R/cGC-F

QVDDTTKAVITLQPPWVSFQEETVTLHCEVLHLPSSSTQWFLNGTATQTSTPSYRITSA
SVNDSGEYRCQRGLSGRSDPIQLEIHRGWLLLQVSSRVFTEGEPLALRCHAWKDKLVYNV
LYYRNGKAFKFFHWNSNLTKTNISHNGTYHCSGMGKHRYTSAGISVTVKELFPAPVLN
ASVTSPILLEGNLVTLSCETKLLLRPGLQLYFSFYMGSKTLRGRNTSSEYQILTARREDS
GLYWCEAATEDGNVLKRSPLELEQLVLGLQLPTPVWFHLIPWPWGPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNV
PSPAMFFQPLYSVHNGNFQTWMGAGHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPG
TRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLALP
GNTQSSGPIPALACGLSCDHQGLTQQGVAVVLAGHCQRPLGHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGG
GGSERTMPRIPTLKNLEDLVTEYHGNSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGKGGALGEGPGASPCNQHSPYWA
PPCYTLKPET

SEQ ID NO: 164

FCGR1/IL9R/cGC-S

QVDDTTKAVITLQPPWVSFQEETVTLHCEVLHLPGSSSTQWFLNGTATQTSTPSYRITSA
SVNDSGEYRCQRGLSGRSDPIQLEIHRGWLLQVSSRVFTEGEPLALRCHAWKDKLVYNV
LYYRNGKAFKFFHWNSNLTKTNISHNGTYHCSGMGKHRYTSAGISVTVKELFPAPVLN
ASVTSPLLEGNLVTLSCETKLLLRPGLQLYFSFYMGSKTLRGRNTSSEYQILTARREDS
GLYWCEAATEDGNVLKRSPLELEQLVLGLQLPTPVWFHlippwGwpgNTLVAVSIFLLLTGPTYLLFKLSprvKRIFYQNV
PSPAMFFQPLYSVHNGNFQTWmGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPG
TRLPGNLSSSEDLVPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALP
GNTQSSGPIPALACGLSCDHQGLTQQGVAVVLAGHCQRPGlhEDLQGMllPSVLSKARSWTFQPQPQPQPQP
ERTMPRIPTLKNLEDLVTEYHGnFSAWSGVSKGLAESLQPDYserLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPP
YTLKPET

SEQ ID NO: 165

2B4/IL9R/cCG-F

CQGSADHVVVISGVPLQLQPNSIQTKVDSIAWKKLLPSQNGFHHILKWENGLSPSNTSND

RFSFIVKNLSLLIKAAQQQDSGLYCLEVTSISGKVQTATFQVVFESLLPDKVEKPRLQG
 QGKILDRGRCQVALSCLVSRDGNVSYAWYRGSKLIQTAGNLTYLDEEVDINGTHYTCNV
 SNPVSWEHTLNLTDQCNAHQEFRWPLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMFFQ
 PLYSVHNGNFQWTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSS
 EDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCGYGGWHLSALPGNTQSSGPI
 PALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMP
 RIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPE
 T

SEQ ID NO: 166

2B4/IL9R/cCG-S

CQGSADHVVISGVPLQLQPNISQTKVDSIAWKKLLPSQNGFHHILKWENGSLPSNTSND
 RFSFIVKNLSLLIKAAQQQDSGLYCLEVTSISGKVQTATFQVVFESLLPDKVEKPRLQG
 QGKILDRGRCQVALSCLVSRDGNVSYAWYRGSKLIQTAGNLTYLDEEVDINGTHYTCNV
 SNPVSWEHTLNLTDQCNAHQEFRWPLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMFFQ
 PLYSVHNGNFQWTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSS
 EDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCGYGGWHLSALPGNTQSSGPI
 PALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQPQPQPPTMPRIPTL
 KNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 167

LAIR1/IL9R/cGC-F

QEEDLPRPSISAEPGTVIPLGSHVTFVCRGPVGVQTFRLERESRSTYNDTEDVSQASPSE
 SEARFRIDSVSEGNAGPYRCIYYKPPKWSEQSDYLELLVKETSGGPDSPDTEPGSSAGPT
 QRPSDNSHNEHAPASQGLKAEHLYLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMFFQPLYSV
 HNGNFQWTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSS
 AGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCGYGGWHLSALPGNTQSSGPIPALAC
 GLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMPRIPTL
 KNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 168

LAIR1/IL9R/cGC-S

QEEDLPRPSISAEPGTVIPLGSHVTFVCRGPVGVQTFRLERESRSTYNDTEDVSQASPSE
 SEARFRIDSVSEGNAGPYRCIYYKPPKWSEQSDYLELLVKETSGGPDSPDTEPGSSAGPT
 QRPSDNSHNEHAPASQGLKAEHLYLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVSPAMFFQPLYSV
 HNGNFQWTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSS
 AGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCGYGGWHLSALPGNTQSSGPIPALAC
 GLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQPQPQPPTMPRIPTLKNLE
 DLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 169

CD5/IL-9R/cGC-F

RLSWYDPDFQARLTRNSKCGQLEVYLKDGWHMVCQSQSWGRSSKQWEDPSQASKVCQRL

NCGVPLSLGPFLVTYTPQSSIICYGQLGSFSNCSHSRNDMCHSLGLTCLPQKTTPTTR
 PPPTTTPEPTAPRRLQLVAQSGGQHCAGVVEFYSGSLGGTISYEAQDKTQDLENFLC>NNL
 QCGSFLKHLPETEAGRAQDPGEPREHQPLPIQWKIQNSSCTSLEHCFRKKIKPKSGRVLA
 LLCSGFQPKVQSRLVGGSSICEGTVEVRQGAQWAALCDSSSARSSLRWEEVCREQQCGSV
 NSYRVLDAGDPTSRGLFCPHQKLSQCHELWERNYSYCKKVFTVCQDPNPLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLS
 PRVKRIFYQNVPSAMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSV
 ALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCY
 GGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGG
 GSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASP
 CNQHSPYWAPPCYTLKPET

SEQ ID NO: 170

CD5/IL-9R/cGC-S

RLSWYDPDFQARLTRNSKCGQLLEVYLDGWHMVCSSQSWGRSSKQWEDPSQASKVCQRL
 NCGVPLSLGPFLVTYTPQSSIICYGQLGSFSNCSHSRNDMCHSLGLTCLPQKTTPTTR
 PPPTTTPEPTAPRRLQLVAQSGGQHCAGVVEFYSGSLGGTISYEAQDKTQDLENFLC>NNL
 QCGSFLKHLPETEAGRAQDPGEPREHQPLPIQWKIQNSSCTSLEHCFRKKIKPKSGRVLA
 LLCSGFQPKVQSRLVGGSSICEGTVEVRQGAQWAALCDSSSARSSLRWEEVCREQQCGSV
 NSYRVLDAGDPTSRGLFCPHQKLSQCHELWERNYSYCKKVFTVCQDPNPLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLS
 PRVKRIFYQNVPSAMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSV
 ALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCY
 GGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQ
 PQPQPQPQPRTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQ
 HSPYWAPPCYTLKPET

SEQ ID NO: 171

TWEAKR/IL9R/cGC-F

EQAPGTAPCSRGSWSADLDKCMDCASCRRPHSDFCLGCAAAPPAPFRLLWPLIPPWGWPGNTLVAVSIFLLLTGPT
 YLLFKLSRPRVKRIFYQNVPSAMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPA
 RPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNN
 YCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKARS
 WTFGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALG
 EGPASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 172

TWEAKR/IL9R/cGC-S

EQAPGTAPCSRGSWSADLDKCMDCASCRRPHSDFCLGCAAAPPAPFRLLWPLIPPWGWPGNTLVAVSIFLLLTGPT
 YLLFKLSRPRVKRIFYQNVPSAMFFQPLYSVHNGNFQTMGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPA
 RPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNN
 YCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKARS
 WTFQPQPQPQPQPRTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGP
 GASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 173

TWEAKR/IL9R/cGC-F/TNFR1-TM

EQAPGTAPCSRGSWSADLDKCMDCASCRRPHSDFCLGCAAAPPAPFRLLWPVLLPLVIFFGLCLLSLLFIGLMYVKRI
 FYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEE
 QEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGW
 HLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGG
 GGGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQH
 SPYWAPPCYTLKPET

SEQ ID NO: 174

TWEAKR/IL9R/cGC-S/TNFR1-TM

EQAPGTAPCSRGSWSADLDKCMDCASCRRPHSDFCLGCAAAPPAPFRLLWPVLLPLVIFFGLCLLSLLFIGLMYVKRI
 FYQNVPSAMFFQPLYSVHNGNFQWTWGAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEE
 QEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGW
 HLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQ
 PQQPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPY
 WAPPCYTLKPET

SEQ ID NO: 175

OPG/IL9R/cGC-F/TNFR1-TM

ETFPKYLHYDEETSHQLLCKCPPGTLYLKQHCTAKWKTVCAPCPDHYYTDSWHTSDECL
 YCSPVCKELQYVKQECNRTHNRVCECKEGRYLEIEFCLKHRSCPPGFGVVQAGTPERNVT
 CKRCPDGGFSNETSSKAPCRKHTNCSVFGLLTQKGNATHDNICSGNSESTQKCGIDVTL
 CEEAFFRFAVPTKFTPNWLSVLVDNLPGTKVNAESVERIKRQHSSQEQTQQLKLWKHQN
 KDQDIVKKIQQIDLCENSQQRHIGHANLTFEQLRSLMESLPGKKVGAEDIEKTIKACKP
 SDQILKLLSLWRIKNGDQDTLKGMLHALKHSKTYHFPKTVTQSLKKTIRFLHSFTMYKLY
 QKLFLMIGNQVQSVKISCLVLLPLVIFFGLCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGA
 GVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQ
 EDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLALSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVA
 WVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWS
 GVSGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 176

OPG/IL9R/cGC-S/TNFR1-TM

ETFPKYLHYDEETSHQLLCKCPPGTLYLKQHCTAKWKTVCAPCPDHYYTDSWHTSDECL
 YCSPVCKELQYVKQECNRTHNRVCECKEGRYLEIEFCLKHRSCPPGFGVVQAGTPERNVT
 CKRCPDGGFSNETSSKAPCRKHTNCSVFGLLTQKGNATHDNICSGNSESTQKCGIDVTL
 CEEAFFRFAVPTKFTPNWLSVLVDNLPGTKVNAESVERIKRQHSSQEQTQQLKLWKHQN
 KDQDIVKKIQQIDLCENSQQRHIGHANLTFEQLRSLMESLPGKKVGAEDIEKTIKACKP
 SDQILKLLSLWRIKNGDQDTLKGMLHALKHSKTYHFPKTVTQSLKKTIRFLHSFTMYKLY
 QKLFLMIGNQVQSVKISCLVLLPLVIFFGLCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWGAHGA
 GVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQ
 EDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNNYCALGCYGGWHLALSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVA

WVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQPQPQPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 177

TACI/IL9R/cGC-F/TNFR1-TM

MSGLGSRRRGGRSRVDQEERFPQGLWTGVAMRSCPEEQYWDPLLGTCTMSCKTICNHQSQR

TCAAFCRSLSCRKEQGKFYDHLRDCISCASICGQHPKQCAYFCENKLRSPVNLPPELRR

QRSGEVENNSDNGSRYQGLEHRGSEASPALPGLKLSADQVALVYS

VLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCV

QEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGS

SSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQGVAVWLAGHCQRPGLHEDLQG

MLLPSVLSKARSWTFGGGGSGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCL

VSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 178

TACI/IL9R/cGC-S/TNFR1-TM

MSGLGSRRRGGRSRVDQEERFPQGLWTGVAMRSCPEEQYWDPLLGTCTMSCKTICNHQSQR

TCAAFCRSLSCRKEQGKFYDHLRDCISCASICGQHPKQCAYFCENKLRSPVNLPPELRR

QRSGEVENNSDNGSRYQGLEHRGSEASPALPGLKLSADQVALVYS

VLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCV

QEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGS

SSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQGVAVWLAGHCQRPGLHEDLQG

MLLPSVLSKARSWTFQPPQPQPQPQPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEI

PPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 179

BCMA/IL9R/cGC-F/TNFR1-TM

MLQMAGQCSQNEYFDSLLHACIPCQLRCSNTPPLTCQRYCNASVTNSVKGTNAVLLPLVIFFGCLLSLLFIGLMYVKRI

FYQNVPSAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEE

QEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGW

HLALPGNTQSSGPIPALACGLSCDHQGLETTQGVAVWLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGG

GGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQH

SPYWAPPCYTLKPET

SEQ ID NO: 180

BCMA/IL9R/cGC-S/TNFR1-TM

MLQMAGQCSQNEYFDSLLHACIPCQLRCSNTPPLTCQRYCNASVTNSVKGTNAVLLPLVIFFGCLLSLLFIGLMYVKRI

FYQNVPSAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEE

QEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGW

HLALPGNTQSSGPIPALACGLSCDHQGLETTQGVAVWLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQPQ

PQPQPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPY

WAPPCYTLKPET

SEQ ID NO:181

NGFR/IL9R/cGC-F/TNFR1-TM

KEACPTGLYTHSGECKACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTE
 CVGLQMSAPCVEADDAVCRCAYGYQDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEE
 CPDGTYSDEANHVDPCLPCTVCEDTERQLRECTRWADAEECEIPGRWITRSTPPEGSDST
 APSTQEPEAPPEQDLIASTVAGVVTTVMGSSQPVVTRGTTDNVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFF
 QPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLS
 SEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGP
 IPALACGLSCDHQGLETTQQGVAWVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMP
 RIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPE
 T

SEQ ID NO: 182

NGFR/IL9R/cGC-S/TNFR1-TM

KEACPTGLYTHSGECKACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTE
 CVGLQMSAPCVEADDAVCRCAYGYQDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEE
 CPDGTYSDEANHVDPCLPCTVCEDTERQLRECTRWADAEECEIPGRWITRSTPPEGSDST
 APSTQEPEAPPEQDLIASTVAGVVTTVMGSSQPVVTRGTTDNVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFF
 QPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLS
 SEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGP
 IPALACGLSCDHQGLETTQQGVAWVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFQPPQPQPQPQPPTMPRIPT
 LKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 183

EDAR/IL9R/cGC-F/TNFR1-TM

EYSNCGENEYNNQTTGLCQECPPCGPEEPYLSGCGYGTKDEDYGCVPCEPAEKFSKGGYQI
 CRRHKDCGFFRATVLTTPGDMENDAECGPCLPGYYMLENRPRNIYGMVCYSCLLAPPNTK
 ECVGATSGASANFPGTSGSSTLSPFQHAHKELSGQGHATAVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQ
 PLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLS
 EDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPI
 PALACGLSCDHQGLETTQQGVAWVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMP
 RIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPE
 T

SEQ ID NO: 184

EDAR/IL9R/cGC-S/TNFR1-TM

EYSNCGENEYNNQTTGLCQECPPCGPEEPYLSGCGYGTKDEDYGCVPCEPAEKFSKGGYQI
 CRRHKDCGFFRATVLTTPGDMENDAECGPCLPGYYMLENRPRNIYGMVCYSCLLAPPNTK
 ECVGATSGASANFPGTSGSSTLSPFQHAHKELSGQGHATAVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQ
 PLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLS
 EDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPI

PALACGLSCDHQGLETQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTMPRIPTL
KNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 185

DCR2 (TNFRSF10D) /IL9R/cGC-F/TNFR1-TM

ATIPRQDEVPPQTVAPQQRRSLKEECPAGSHRSEYTGACNPCTEGVDYTIASNNLPSC
LLCTVCKSGQTNKSSCTTTRDVCQCEKGSFQDKNSPEMCRCTGCPRGMVKVSNCTPR
SDIKCKNESAASSTGKTPAAEETVTTLGMLASPHYVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHN
GNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA
CTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGL
SCDHQGLETQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGSGGGGSGGGGSERTMPRIPTLKNL
EDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO:186

DCR2 (TNFRSF10D) /IL9R/cGC-S/TNFR1-TM

ATIPRQDEVPPQTVAPQQRRSLKEECPAGSHRSEYTGACNPCTEGVDYTIASNNLPSC
LLCTVCKSGQTNKSSCTTTRDVCQCEKGSFQDKNSPEMCRCTGCPRGMVKVSNCTPR
SDIKCKNESAASSTGKTPAAEETVTTLGMLASPHYVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHN
GNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA
CTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGL
SCDHQGLETQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTMPRIPTLKNLEDLV
TEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 187

DCR1 (TNFRSF10C) /IL9R/cGC-F/TNFR1-TM

ATTARQEEVPQQTVPAPQQRHSFKGEECPAGSHRSEHTGACNPCTEGVDYTNASNNEPSC
FPCTVCKSDQKHKSCTMTTRDVCQCKEGTFRNENSPEMCRKCSRCPGSEVQVSNCTSWD
DIQCVEEFGANATVETPAAEETMNTSPGTPAPAAEETMNTSPGTPAPAAEETMTTSPGTP
APAAEETMTTSPGTPAPAAEETMITSPGTPAVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHNGNF
QWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA
CTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCD
HQGLETQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGSGGGGSGGGGSERTMPRIPTLKNLEDL
VTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 188

DCR1 (TNFRSF10C) /IL9R/cGC-S/TNFR1-TM

ATTARQEEVPQQTVPAPQQRHSFKGEECPAGSHRSEHTGACNPCTEGVDYTNASNNEPSC
FPCTVCKSDQKHKSCTMTTRDVCQCKEGTFRNENSPEMCRKCSRCPGSEVQVSNCTSWD
DIQCVEEFGANATVETPAAEETMNTSPGTPAPAAEETMNTSPGTPAPAAEETMTTSPGTP
APAAEETMTTSPGTPAPAAEETMITSPGTPAVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHNGNF
QWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA
CTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCD
HQGLETQQGVAVWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPQPQPQPQPPTMPRIPTLKNLEDLVTEY
HGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO:189

CD40/IL9R/cGC-F/TNFR1-TM

EPPTACREKQYLINSQCCSLCQPGQKLVSDCTEFTETECLPCGESEFLDTWNRETHCHQH
 KYCDPNLGLRVQQGTSETDTICTCEEGWHCTSEACESCVLHRSCSPGFGVKQIATGVSD
 TICEPCVGGFFSNVSSAFEKCHPWTSCETKDLVVQQAGTNKTDVVCQPQDRLRVLLPLVIFFGCLLSLLFIGLMYVKRIFY
 QNVPSAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQE
 GPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLS
 ALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGSGGGGS
 GGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPY
 WAPPCYTLKPET

SEQ ID NO: 190

CD40/IL9R/cGC-S/TNFR1-TM

EPPTACREKQYLINSQCCSLCQPGQKLVSDCTEFTETECLPCGESEFLDTWNRETHCHQH
 KYCDPNLGLRVQQGTSETDTICTCEEGWHCTSEACESCVLHRSCSPGFGVKQIATGVSD
 TICEPCVGGFFSNVSSAFEKCHPWTSCETKDLVVQQAGTNKTDVVCQPQDRLRVLLPLVIFFGCLLSLLFIGLMYVKRIFY
 QNVPSAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQE
 GPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLS
 ALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQPQP
 QPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAP
 PCYTLKPET

SEQ ID NO: 191

FAS/IL9R/cGC-F/TNFR1-TM

QVTDINSKLELRKTVTTVETQNLGLHHDGQFCHKPCPPGERKARDCTVNGDEPDCVPC
 QEGKEYTDKAHFSSKRRRCRLCDEGHGLEVEINCTRTQNTKCRCKPNFFCNSTVCEHCDP
 CTKEHGIIKECTLSNTKCKEEGSRSNVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHNGNFQWTW
 MAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGLTRLPGNLSSDVLPAAGCTEWRV
 QTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQ
 LETQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGSGGGSGGGGSERTMPRIPTLKNLEDLVTEY
 HGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 192

FAS/IL9R/cGC-S/TNFR1-TM

QVTDINSKLELRKTVTTVETQNLGLHHDGQFCHKPCPPGERKARDCTVNGDEPDCVPC
 QEGKEYTDKAHFSSKRRRCRLCDEGHGLEVEINCTRTQNTKCRCKPNFFCNSTVCEHCDP
 CTKEHGIIKECTLSNTKCKEEGSRSNVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHNGNFQWTW
 MAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGLTRLPGNLSSDVLPAAGCTEWRV
 QTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQ
 LETQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQPQPQPPERTMPRIPTLKNLEDLVTEYHGN
 FSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

PATENT

SEQ ID NO: 193

DR4/IL9R/cGC-F/TNFR1-TM

ASGTEAAAATPSKVWGSSAGRIEPRGGGRGALPTSMGQHGPSARARAGRAPGPRPAREAS
 PRLRVHKTfKFVVVGVLQVVPSSAATIKLHDQSIGTQQWEHSPLGELCPPGSHRSEHPG
 ACNRCTEGVGYTNASNNLFACLPCTACKSDEEERSPCTTTRNTACQCKPGTFRNDNSAEM
 CRKCSRGCPRGMVKVKDCTPWSIDIECVHKESGNGHNVLLPLVIFFGLCLLSLLFIGLMYVKRIFYQNVSPAMFFQPLYS
 VHNGNFQTWMGAGHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVL
 PAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALA
 CGLSCDHQGLETTQQGVAVVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMPRIPTL
 KNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPLYWAPPCYTLKPET

SEQ ID NO: 194

DR4/IL9R/cGC-S/TNFR1-TM

ASGTEAAAATPSKVWGSSAGRIEPRGGGRGALPTSMGQHGPSARARAGRAPGPRPAREAS
 PRLRVHKTfKFVVVGVLQVVPSSAATIKLHDQSIGTQQWEHSPLGELCPPGSHRSEHPG
 ACNRCTEGVGYTNASNNLFACLPCTACKSDEEERSPCTTTRNTACQCKPGTFRNDNSAEM
 CRKCSRGCPRGMVKVKDCTPWSIDIECVHKESGNGHNVLLPLVIFFGLCLLSLLFIGLMYVKRIFYQNVSPAMFFQPLYS
 VHNGNFQTWMGAGHAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVL
 PAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALA
 CGLSCDHQGLETTQQGVAVVLAGHCQRPLHEDLQGMLLPSVLSKARSWTFQPPQPQPQPQPQPERTMPRIPTLKNLE
 DLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPLYWAPPCYTLKPET

SEQ ID NO: 195

DR6/IL9R/cGC-S/TNFR1-TM

QPEQKASNLIGTYRHVD RATGQVLTCDKCPAGTYVSEHCTNTSLRVCSSCPVGTFTRHEN
 GIEKCHDCSQPCWPWMIKLP CAALTDRECTCPPGMFQSNATCAPHTVCPVGWGVRRKGT
 ETEDVRCKQCARGTFSDVPSSVMKCKAYTDCLSQNLVVIKPGTKETDNVCGTLPFSFSST
 SPSPGTAIFRPEHMETHEVPSSTYVPKGMNSTESNSSASVRPKVLSSIQEGTVPDNTSS
 ARGKEDVNKTLPNLQVVNHQQGPHHRHILKLLPSMEATGGEKSSTPIKGPKRGHPRQNLH
 KHFDINEHVLLPLVIFFGLCLLSLLFIGLMYVKRIFYQNVSPAMFFQPLYSVHNGNFQTWMGAGHAGVLLSQDCAGTP
 QGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPA
 PPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVVLAGHCQRPG
 LHEDLQGMLLPSVLSKARSWTFQPPQPQPQPQPQPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSE
 RLCLVSEIPPKGGALGEGPGASPCNQHSPLYWAPPCYTLKPET

PATENT

SEQ ID NO: 196

DR5/IL9R/cGC-F/TNFR1-TM

ITQQDLAPQQRAAPQQKRSSPSEGLCPPGHHISEDGRDCISCKYGGDYSTHWNDLLFCLR
 CTRCDSGEVELSPCTTTRNTVCQCEEGTFREEDSPEMCRKCRTGCPRGMVKVGDCTPWSD
 IECVHKESGTHKSGEVPVEETVTSSPGTPASPCSVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHN
 GNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA
 CTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGL
 SCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMPRIPTLKNL
 EDLVTEYHGNSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 197

DR5/IL9R/cGC-S/TNFR1-TM

ITQQDLAPQQRAAPQQKRSSPSEGLCPPGHHISEDGRDCISCKYGGDYSTHWNDLLFCLR
 CTRCDSGEVELSPCTTTRNTVCQCEEGTFREEDSPEMCRKCRTGCPRGMVKVGDCTPWSD
 IECVHKESGTHKSGEVPVEETVTSSPGTPASPCSVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHN
 GNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPA
 CTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIPALACGL
 SCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPPQPPQPPERTMPRIPTLKNLEDLV
 TEYHGNSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

SEQ ID NO: 198

DR3/IL9R/cGC-F/TNFR1-TM

QGGTRSPRCDACAGDFHKKIGLFCCRGCPAGHYLKAPCTEPCGNSTCLVCPQDFTLAWENH
 HNSECARCAQACDEQASQVALENCASAVADTRCGCKPGWFVECVSQCVSSSPFYCQPCLD
 GALHRHTRLLCSRRDTCGTCLPGFYEHDGCVSCPTSTLGSCPERCAAVCGWRQVLLPLVIFFGCLLSLLFIGLMYVKR
 IFYQNVPSAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEE
 QEGPGTRLPGNLSSDVLPACTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGW
 HLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGG
 GGGGGGSERTMPRIPTLKNLEDLVTEYHGNSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQH
 SPYWAPPCYTLKPET

SEQ ID NO: 199

DR3/IL9R/cGC-S/TNFR1-TM

QGGTRSPRCDACAGDFHKKIGLFCCRGCPAGHYLKAPCTEPCGNSTCLVCPQDFTLAWENH
 HNSECARCAQACDEQASQVALENCASAVADTRCGCKPGWFVECVSQCVSSSPFYCQPCLD
 GALHRHTRLLCSRRDTCGTCLPGFYEHDGCVSCPTSTLGSCPERCAAVCGWRQVLLPLVIFFGCLLSLLFIGLMYVKR
 IFYQNVPSAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEE
 QEGPGTRLPGNLSSDVLPACTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGRSSSSSSSSNNNNYCALGCYGGW
 HLSALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPPQ
 PQQPPERTMPRIPTLKNLEDLVTEYHGNSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPY
 WAPPCYTLKPET

PATENT

SEQ ID NO: 200

TNFRSF1B/IL9R/cGC-F/TNFR1-TM

LPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKTSDTVCDSCEDST
YTQLWNWVPECLSCGSRCSDDQVETQACTREQNRICTRPGWYCALSKEGCRCLCAPLRK
CRPGFGVARPGTETSDVVCKPCAPGTFSNTTSSTDICRPHQICNVVAIPGNASMDAVCTS
TSPTRSMAPGAVHLPQPVSTRSQHTQPTPEPSTAPSTSFLPMGSPPPAEGSTGDVLLPLVIFFGCLLSLLFIGLMYVKRI
FYQNVPSAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEE
QEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGW
HLSALPGNTQSSGPIALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFGGGGSGG
GGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGALGEGPGASPCNQH
SPYWAPPCYTLKPET

SEQ ID NO: 201

TNFRSF1B/IL9R/cGC-S/TNFR1-TM

LPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKTSDTVCDSCEDST
YTQLWNWVPECLSCGSRCSDDQVETQACTREQNRICTRPGWYCALSKEGCRCLCAPLRK
CRPGFGVARPGTETSDVVCKPCAPGTFSNTTSSTDICRPHQICNVVAIPGNASMDAVCTS
TSPTRSMAPGAVHLPQPVSTRSQHTQPTPEPSTAPSTSFLPMGSPPPAEGSTGDVLLPLVIFFGCLLSLLFIGLMYVKRI
FYQNVPSAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEE
QEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSSNNNNYCALGCYGGW
HLSALPGNTQSSGPIALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKARSWTFQPPQPQ
PQPQPERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGALGEGPGASPCNQHSPY
WAPPCYTLKPET

SEQ ID NO: 202

TNFRSF1/IL9R/cGC-F/TNFR1-TM

LVPHLGDREKRDSVCPQGYIHPQNNISCTKCHKGTLYNDGPGGQDTCRECESGSF
TASENHLRHCLSCSKCRKEMGQVEISSCTVDRDTCGCRKNQYRHYWSENLFQCFNCSLC
LNGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIENVKGTEDSG
TTVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHNGNFQWTWMAHGAGVLLSQDCAGTPQGALEP
CVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEG
SRSSSSSSSSNNNNYCALGCYGGWHLSALPGNTQSSGPIALACGLSCDHQGLETTQQGVAWVLAGHCQRPGLHEDLQ
GMILLPSVLSKARSWTFGGGGSGGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLC
LVSEIPPKGALGEGPGASPCNQHSPYWAPPCYTLKPET

PATENT

SEQ ID NO: 203

TNFRSF1/IL9R/cGC-S/TNFR1-TM

LVPHLGDREKRDSVCPQGKYIHPQNNISICCTKCHKGTLYNDPCPGGQDTCRECESGSF
TASENHLRHCLSCSKRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLC
LNGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIENVKGTEDSG
TTVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHNGNFQTWMGAGAGVLLSQDCAGTPQGALEP
CVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEG
SRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVVLAGHCQRPLHEDLQ
GMLLPVLSKARSWTFQPQPQPQPQPPTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVS
EIPPKGGALGEGPGASPCNQHSPLYWAPPCYTLKPET

SEQ ID NO: 205

DR6/IL9R/cGC-F/TNFR1-TM

QPEQKASNLIGTYRHVDRTGQVLTCDKCPAGTYVSEHCTNTSLRVCSSCPVGTFTRHEN
GIEKCHDCSQPCWPWMIKLPAAALTDRECTCPPGMFQSNATCAPHTVCPVGWGVRRKGT
ETEDVRCKQCARGTFSDVPSSVMKCKAYTDCLSQLVVIKPGTKETDNVCGTLPSFSSST
SPSPGTAIFRPEHMETHEVPSSTYVPKGMNSTESNSSASVRPKVLSSIQEGTVPDNTSS
ARGKEDVNKTLPNLQVVNHQQGPHHRHILKLLPSMEATGGEKSSTPIKGPGRGHPRQNLH
KHFDINEHVLLPLVIFFGCLLSLLFIGLMYVKRIFYQNVPSAMFFQPLYSVHNGNFQTWMGAGAGVLLSQDCAGTP
QGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSDVLPAAGCTEWRVQTLAYLPQEDWAPTSLTRPA
PPDSEGRSSSSSSSSNNNNYCALGCYGGWHLALPGNTQSSGPIPALACGLSCDHQGLETTQQGVAVVLAGHCQRPG
LHEDLQGMLLPSVLSKARSWTFGGGGSGGGGSGGGGSERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPD
YSERLCLVSEIPPKGGALGEGPGASPCNQHSPLYWAPPCYTLKPET

CLAIMS

WHAT IS CLAIMED IS:

1. A recombinant nucleic acid molecule encoding a chimeric receptor, said chimeric receptor comprising:
 - an extracellular portion comprising a binding domain of an endogenous cytokine receptor;
 - an intracellular portion comprising an endodomain of an IL-9 receptor; and
 - a transmembrane domain that joins the extracellular portion and the intracellular portion.
2. The recombinant nucleic acid molecule of claim 1 further comprising one or more linkers.
3. The recombinant nucleic acid molecule of claim 1, wherein the endogenous cytokine receptor is selected from IL-2rb, IL-2ra, IL-4r, IL-7ra, IL-15ra, and IL-21ra.
4. The recombinant nucleic acid molecule according to any one of claims 1 or 2, wherein the endogenous cytokine receptor comprises an amino acid sequence having at least 80% sequence identity to an amino acid sequence selected from SEQ ID Nos: 1-6.
5. The recombinant nucleic acid molecule according to any one of claims 1 to 4, wherein the transmembrane domain is selected from the transmembrane domain of IL-9, IL-7ra, IL-2rb, and TNFR1.
6. The recombinant nucleic acid molecule according to any one of claims 1 to 5, wherein the transmembrane domain comprises an amino acid sequence selected from SEQ ID Nos: 53-56.
7. The recombinant nucleic acid molecule according to any one of claims 1 to 5, wherein the chimeric receptor comprises an amino acid sequence having at least 80% sequence identity to an amino acid sequence selected from SEQ ID Nos: 63-80.

8. The recombinant nucleic acid molecule according to any one of claims 1 to 5, wherein the chimeric receptor comprises the amino acid sequence selected from SEQ ID Nos: 63 and 72.

9. The recombinant nucleic acid molecule according to any one of claims 1 to 8, wherein the recombinant nucleic acid molecule is incorporated into a vector.

10. The recombinant nucleic acid molecule according to any one of claims 1 to 9, further comprising a signal sequence.

11. The recombinant nucleic acid molecule according to claim 10, wherein the signal sequence comprises the amino acid sequence of MAAPALSWRLPLLILLPLATSWASA (SEQ ID NO: 62).

12. The recombinant nucleic acid molecule according to any one of claims 1 to 11 further comprising a 2A linker.

13. The recombinant nucleic acid molecule according to according to any one of claims 1 to 12 further comprising a nucleic acid sequence encoding a chimeric antigen receptor.

14. An expression vector comprising the recombinant nucleic acid molecule of any one of claims 1-13.

15. A recombinant host cell comprising the recombinant nucleic acid of claims 1-13 or the expression vector of claim 14.

16. The recombinant cell of claim 15, wherein the recombinant cell is a eukaryotic cell.

17. The recombinant cell of claims 15-16, wherein the eukaryotic cell is an animal cell.

18. The recombinant cell of claims 15-17, wherein the animal cell is a mammalian cell.

19. The recombinant cell of claims 15-18, wherein the mammalian cell is an immune cell, a neuron, an epithelial cell, and endothelial cell, or a stem cell.

20. The recombinant cell of claim 19, wherein the recombinant cell is an immune cell

or a dendritic cell.

21. The recombinant cell of claim 20, wherein the immune cell is a B cell, a monocyte, a natural killer (NK) cell, a basophil, an eosinophil, a neutrophil, a dendritic cell, a macrophage, a regulatory T cell, a helper T cell (T_H), a cytotoxic T cell (T_{CTL}), or other T cell.

22. A composition comprising a recombinant nucleic acid of any one of claims 1-13.

23. A composition of cells comprising the expression vector of claim 14.

24. A polypeptide encoded by the recombinant nucleic acid of any one of claims 1-13.

25. A composition of one or more polypeptides encoded by the one or more recombinant nucleic acids of any one of claims 1-13.

26. The polypeptide of claim 24, wherein the polypeptide comprises an amino acid sequence having at least 80% sequence identity to an amino acid sequence selected from SEQ ID Nos: 1-6.

27. The polypeptide of claim 24, wherein the polypeptide comprises an amino acid sequence selected from SEQ ID Nos: 53-56.

28. The polypeptide of claim 24, wherein the polypeptide comprises an amino acid sequence having at least 80% sequence identity to an amino acid sequence selected from SEQ ID Nos: 63-80.

29. A composition of cells capable of expressing the chimeric receptor encoded by the recombinant nucleic acid of any one of claims 1-13.

30. A composition of cells comprising a chimeric receptor comprising an amino acid sequence selected from SEQ ID Nos: 63-203.

31. A method for modulating the activity of an immune cell, said method comprising: administering, to an immune cell, the recombinant nucleic acid of any one of claims 1-13.

32. The method of claim 31, wherein the immune cell is a B cell, a monocyte, a natural killer (NK) cell, a basophil, an eosinophil, a neutrophil, a dendritic cell, a macrophage, a regulatory T cell, a helper T cell (T_H), a cytotoxic T cell (T_{CTL}), or other T cell.

33. The method of claim 31, wherein the immune cell is a T cell.

34. The method of claim 31, wherein the T cell is a CAR-T cell.

35. A method of treating a subject, said method comprising:
administering, to the subject, the chimeric switch receptor expressed by the recombinant nucleic acid of any one of claims 1-13 or a cell expressing the recombinant nucleic acid of any one of claims 1-13.

36. The method of claim 35, wherein the subject is treated for cancer.

37. The method of claim 35, wherein the subject is treated for autoimmune disease.

38. The method of claim 35, wherein the subject is treated for infection.

Sequence ID	Ligand-binding domain	Transmembrane domain	Intracellular domain	Linker	pSTAT type	No Ligand Stimulation (gMFI)	Ligand Stimulated (gMFI)	Fold increase in gMFI
SEQ63+CAR+	IL21R	IL9R	IL9R	N/A	pSTAT1	620	1478	2.38
					pSTAT3	345	1831	5.31
					pSTAT5	700	870	1.24
SEQ66	IL15Ra	IL9R	IL9R	N/A	pSTAT1	491	917	1.87
					pSTAT3	330	594	1.80
					pSTAT5	669	2283	3.41
SEQ72+CAR+	IL4Ra	IL9R	IL9R	N/A	pSTAT1	471	770	1.63
					pSTAT3	243	444	1.83
					pSTAT5	536	660	1.23
SEQ153+CAR+	IL10Ra	IL9R	IL9R	G ₄ S	pSTAT1	261	1900	7.28
					pSTAT3	78	1569	20.12
					pSTAT5	284	663	2.33

FIG. 1

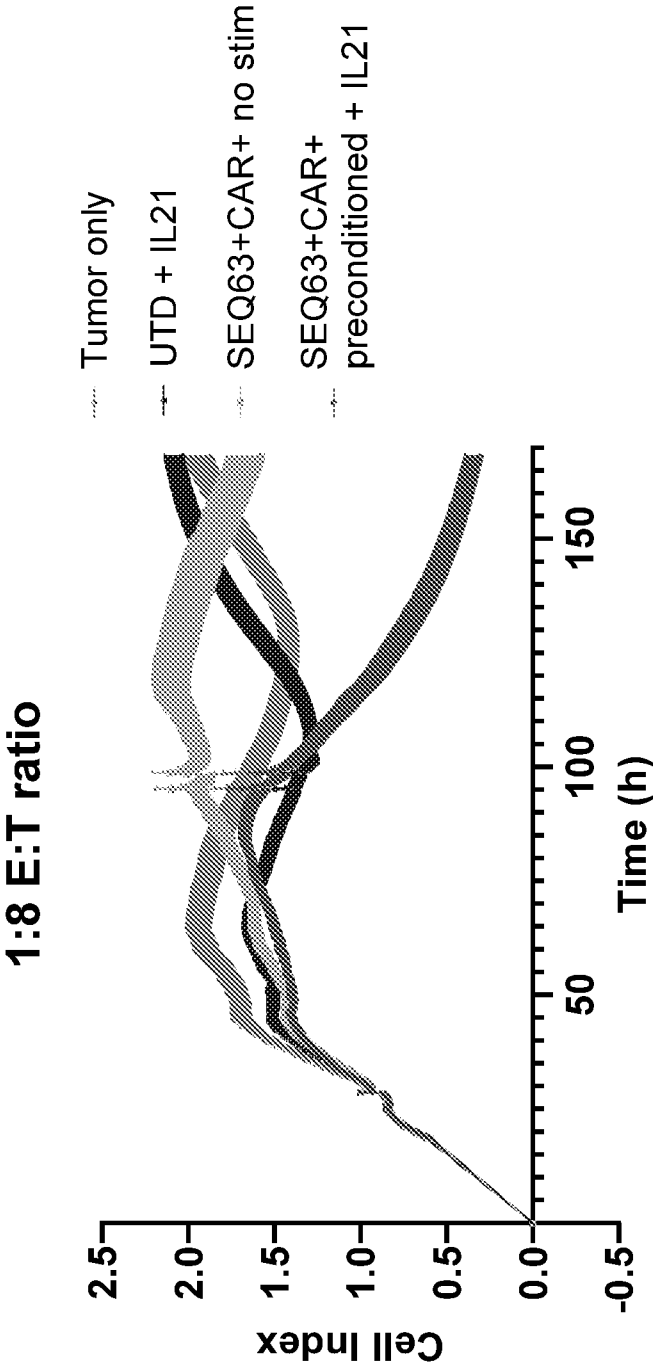


FIG. 2

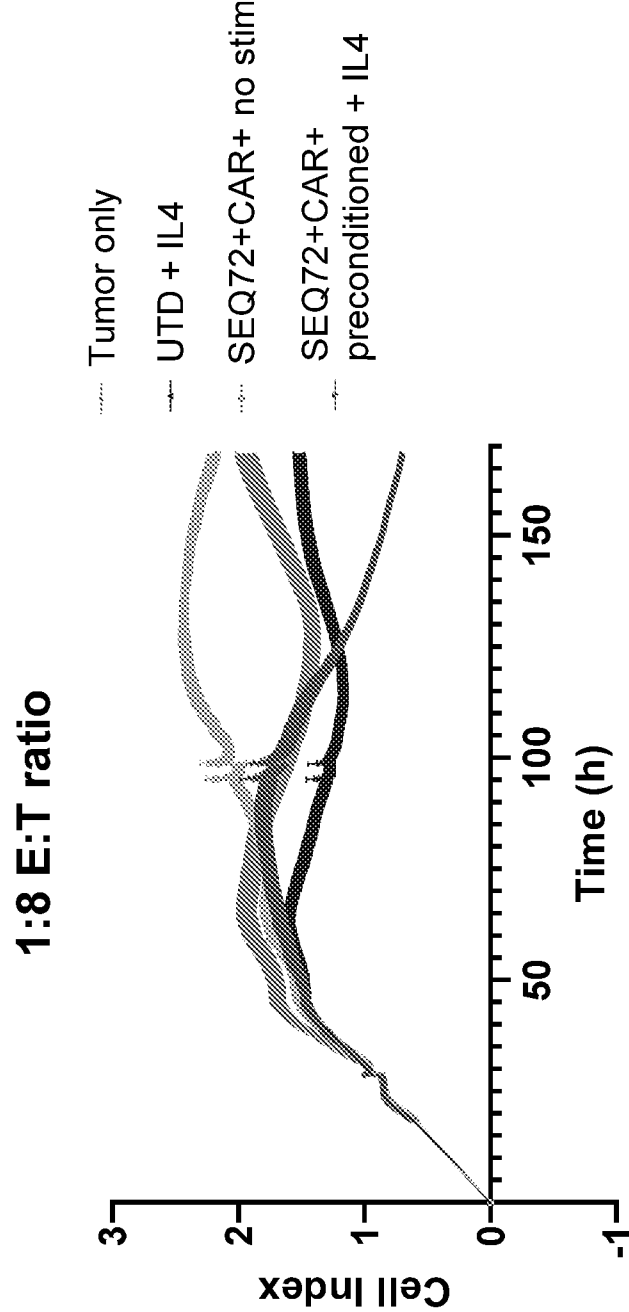


FIG. 3

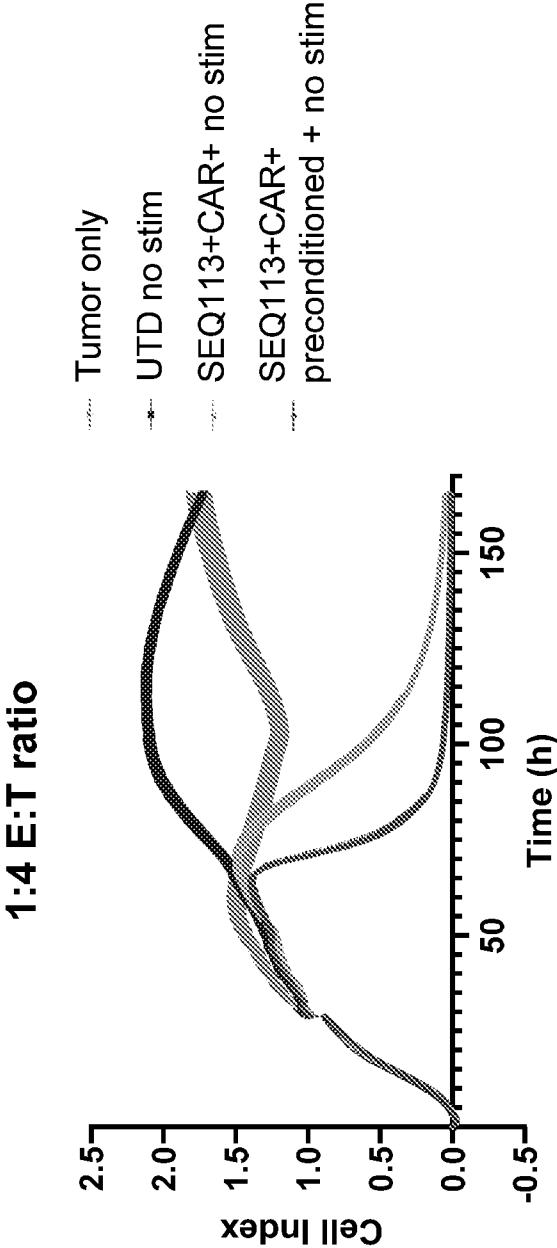


FIG. 4

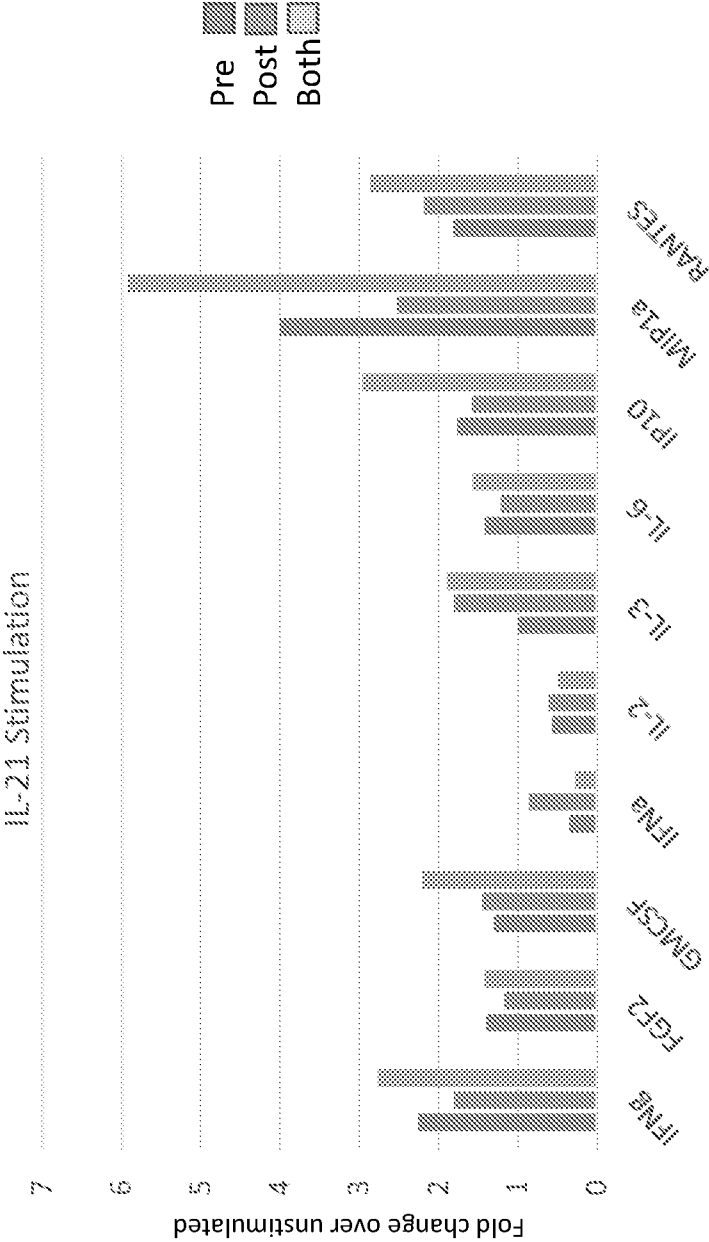


FIG. 5

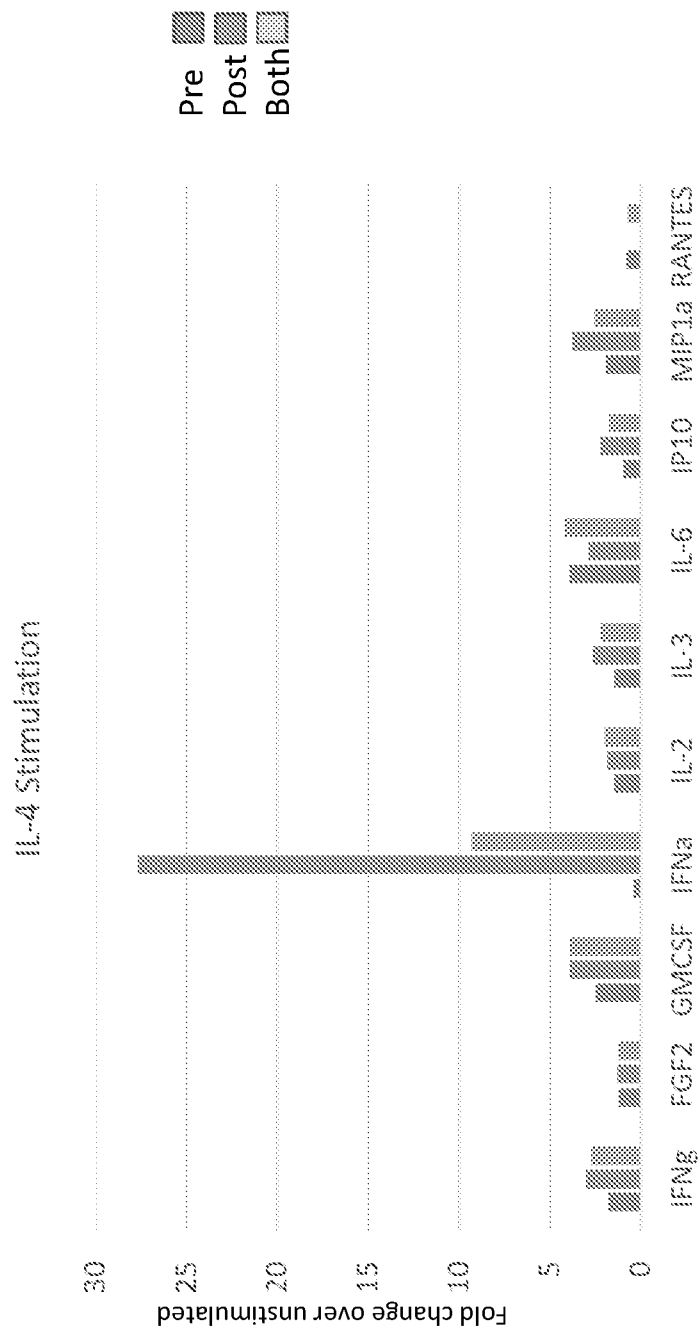


FIG. 6

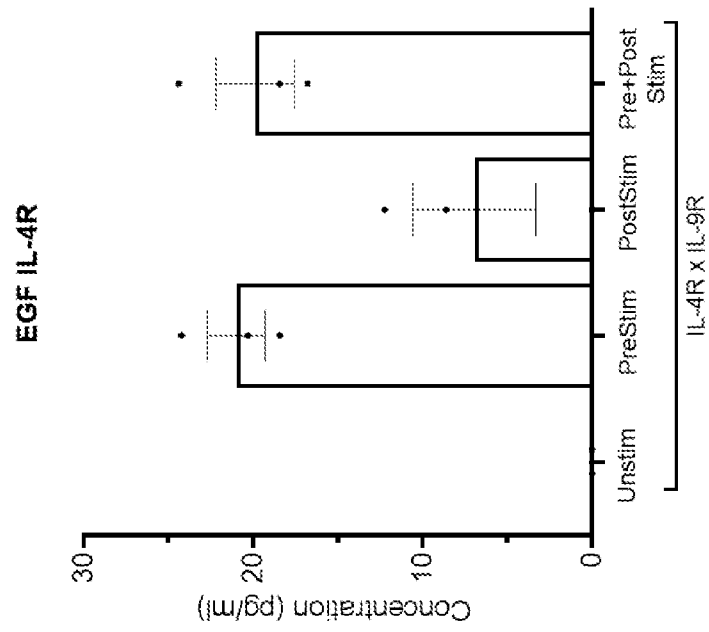


FIG. 7

FIG. 8B

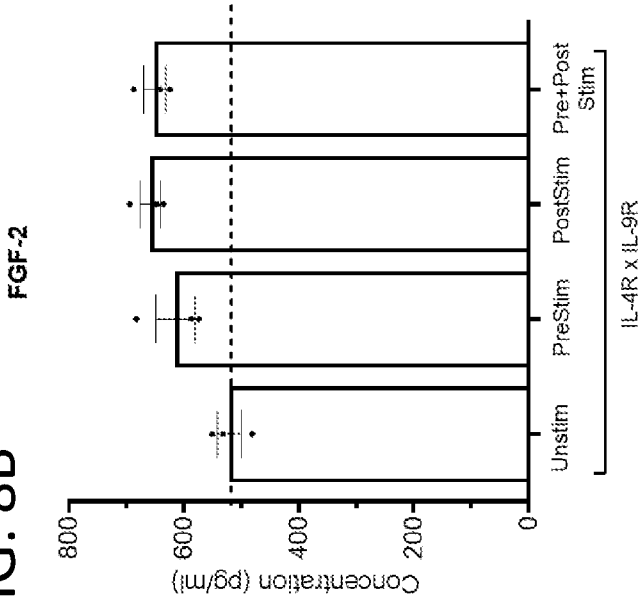


FIG. 8A

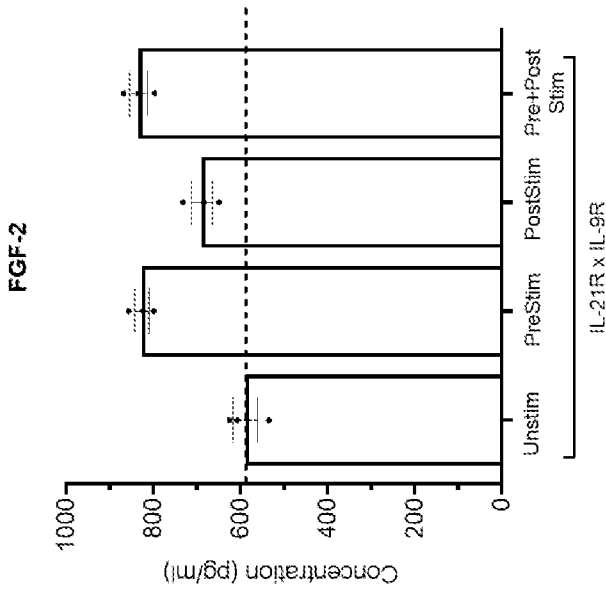


FIG. 9A

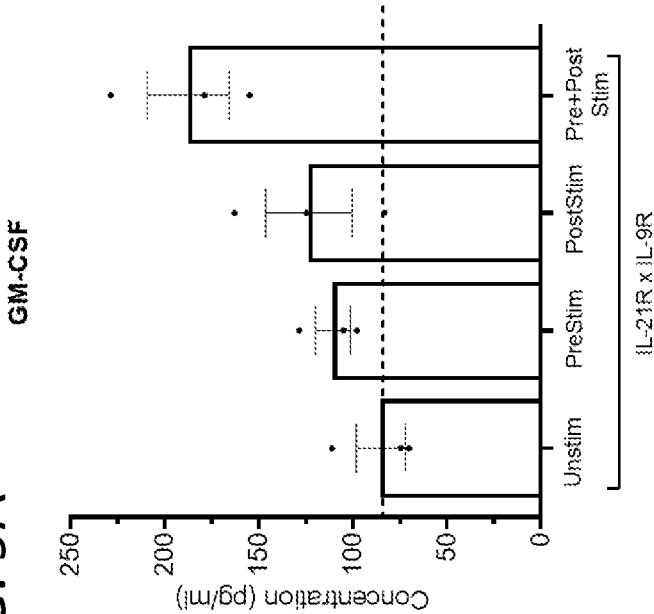
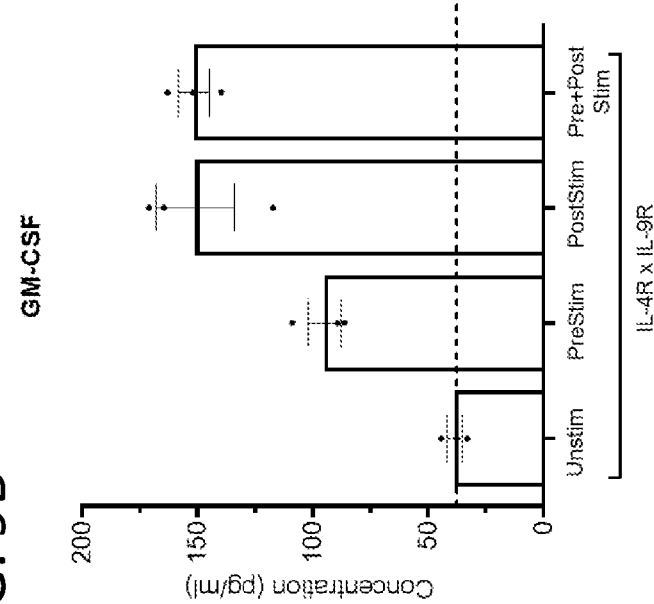


FIG. 9B



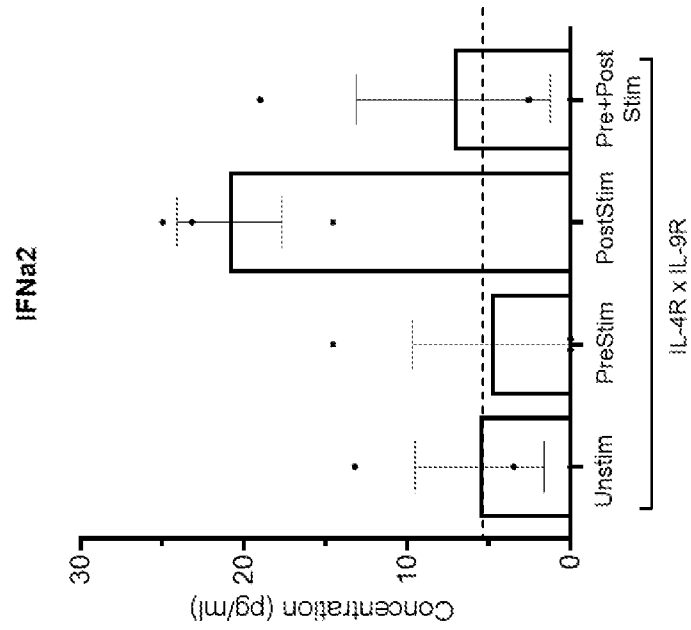


FIG. 10

FIG. 11A

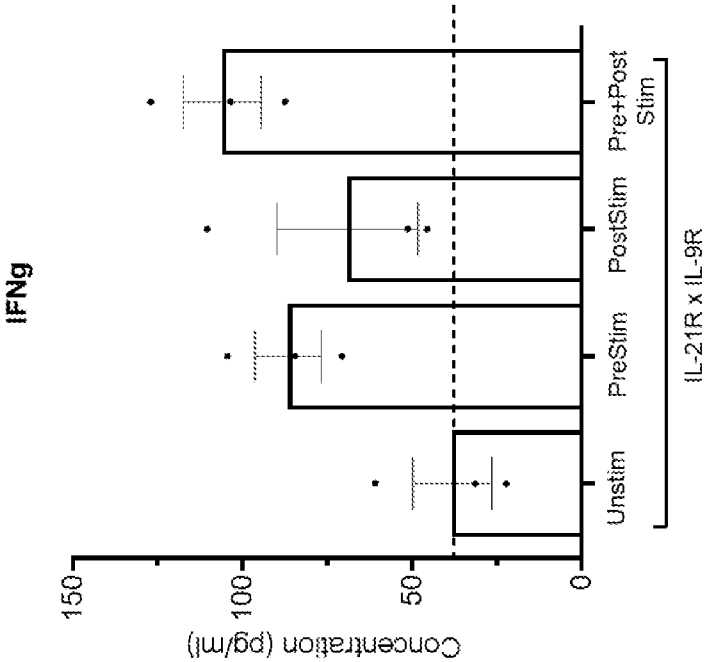
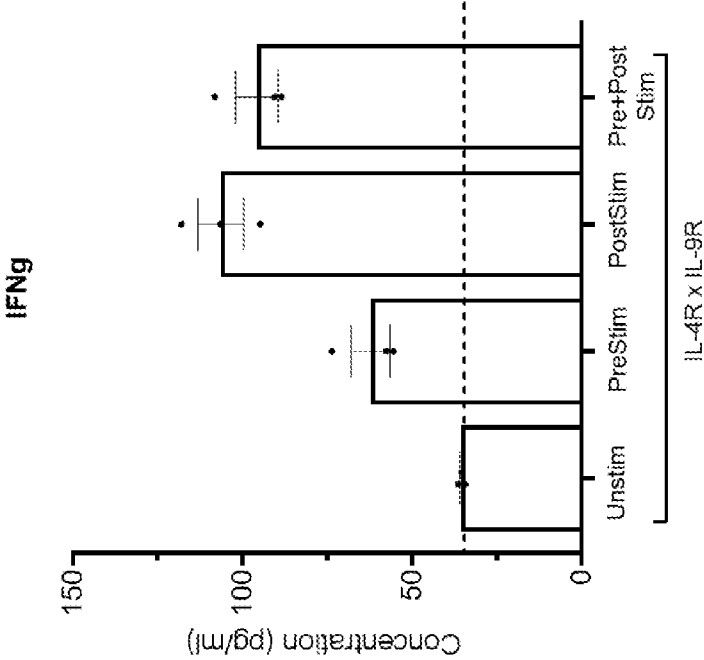


FIG. 11B



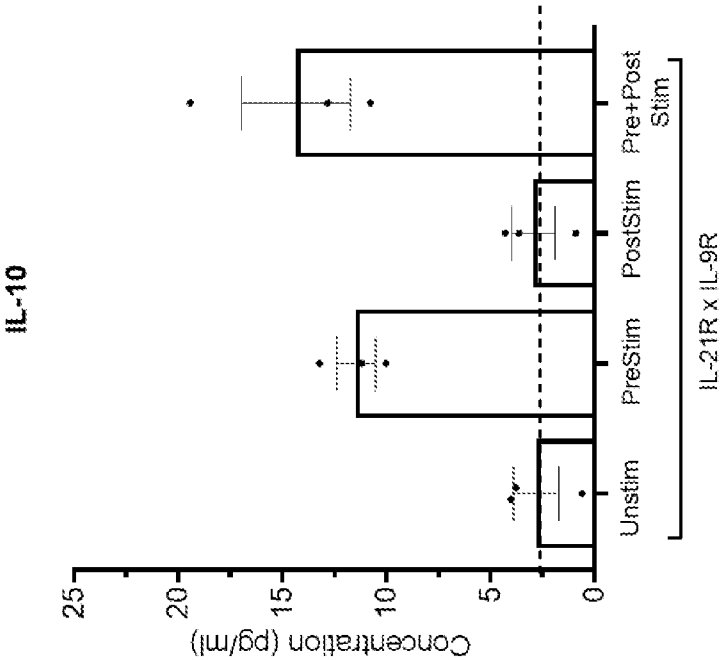
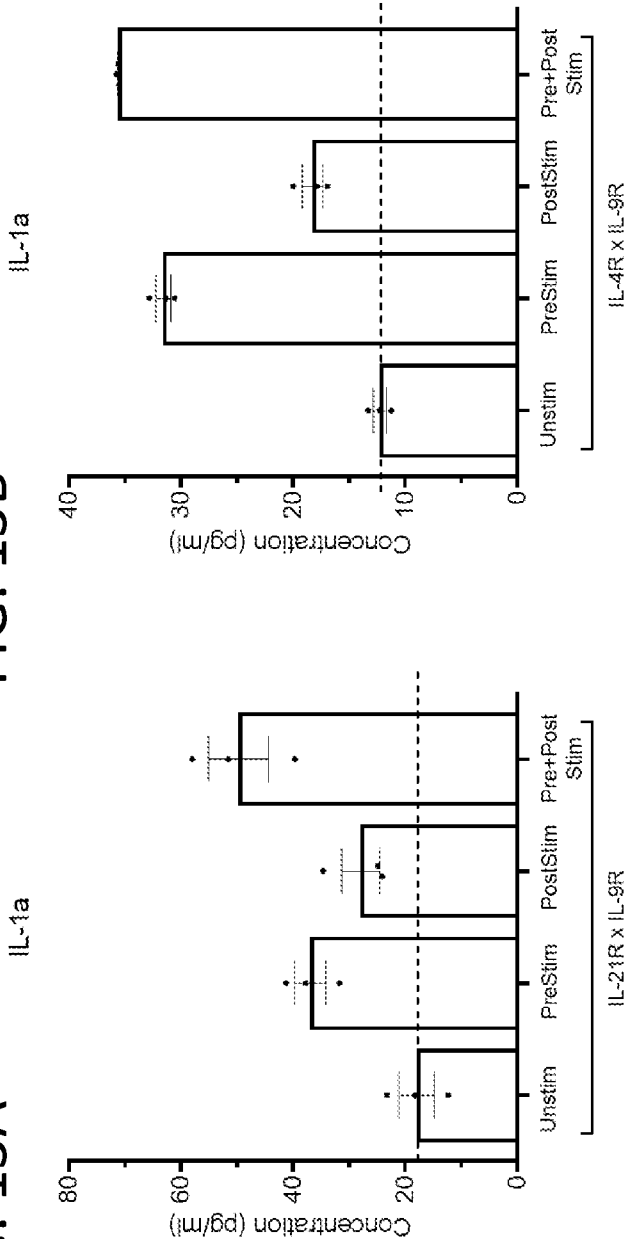


FIG. 12

FIG. 13A

FIG. 13B



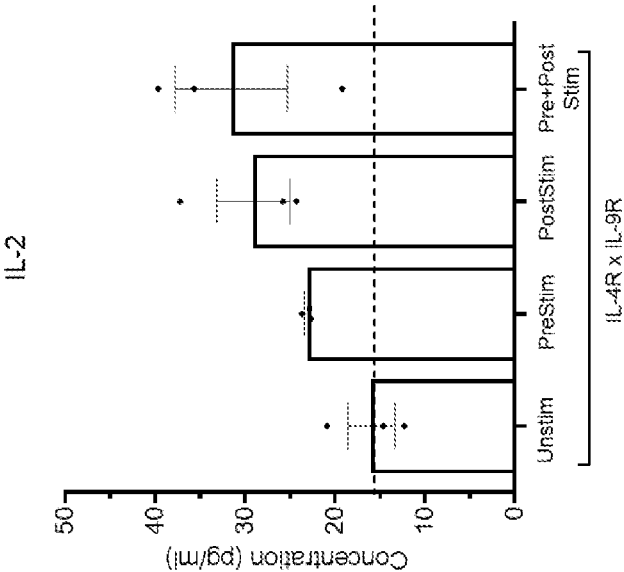


FIG. 14

FIG. 15A

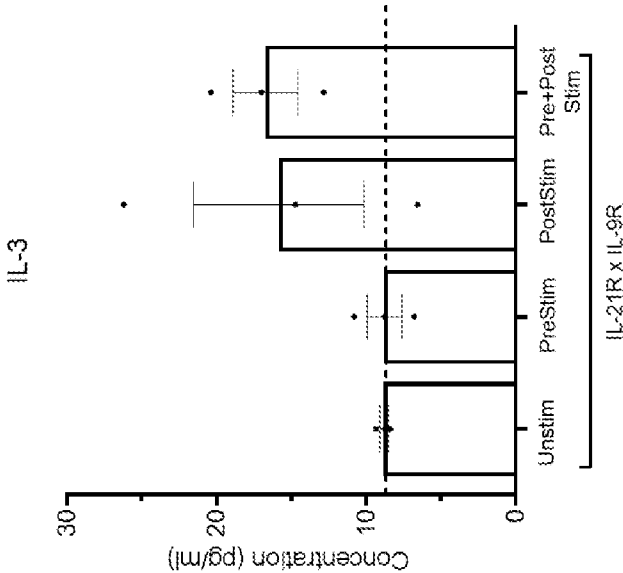


FIG. 15B

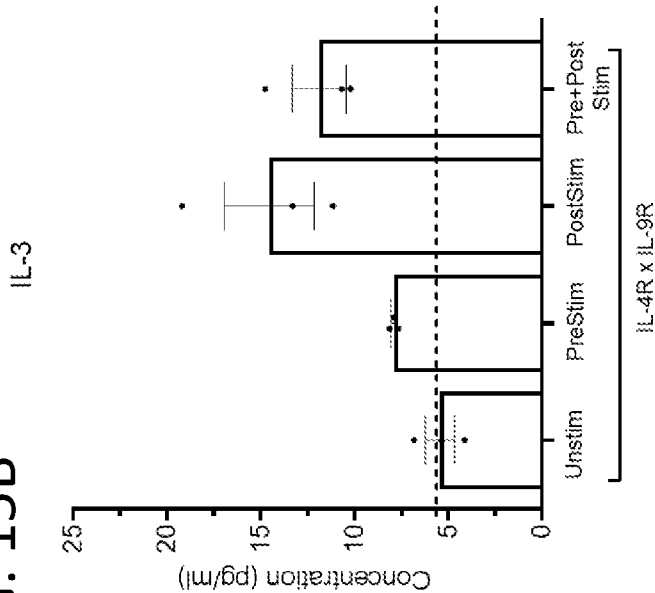


FIG. 16A

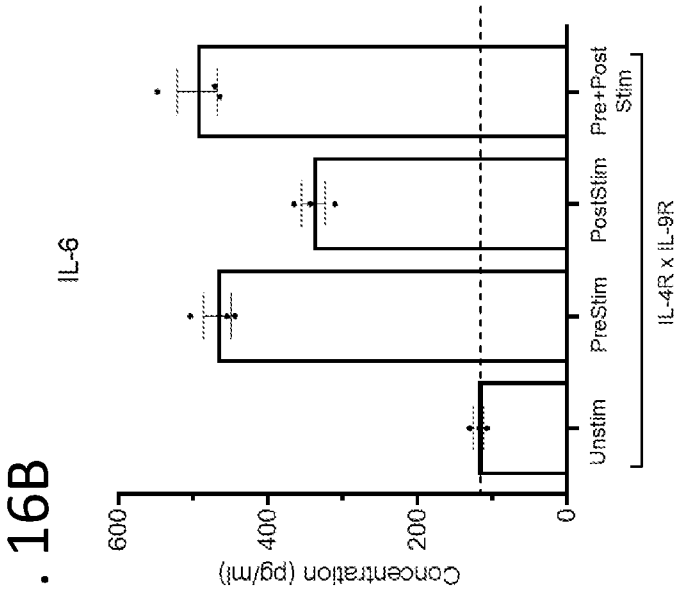
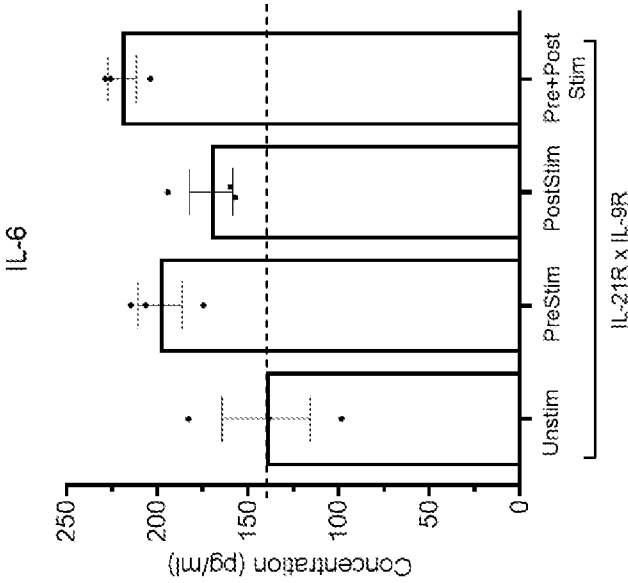


FIG. 17A

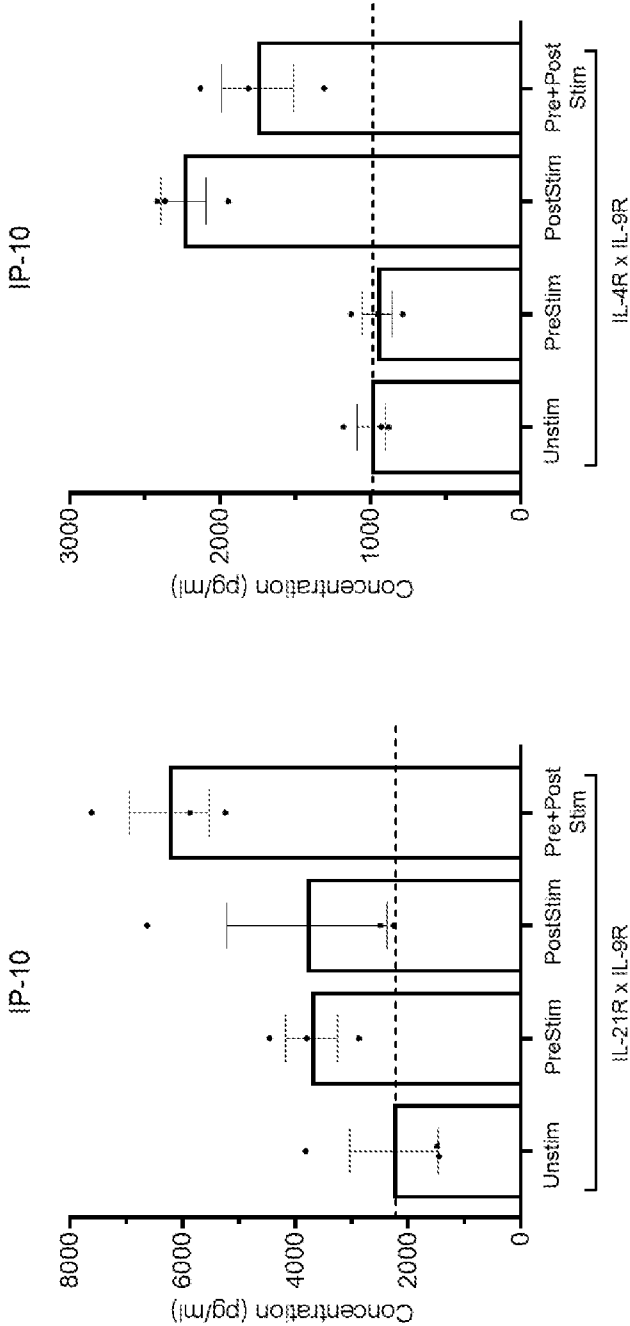


FIG. 17B

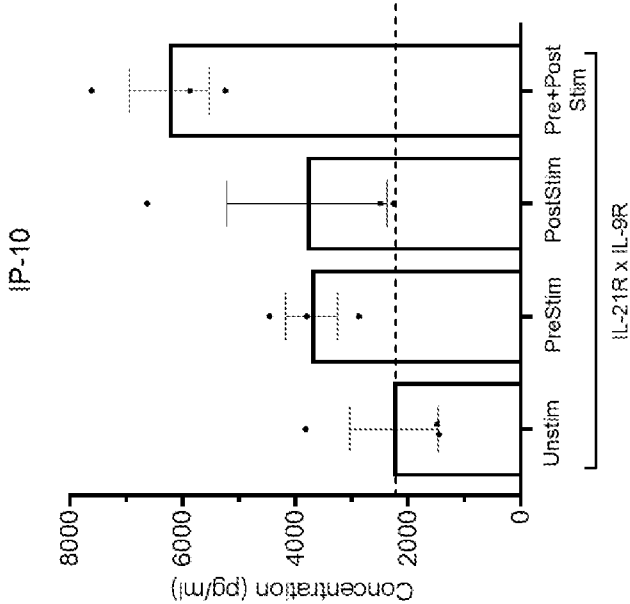


FIG. 18B

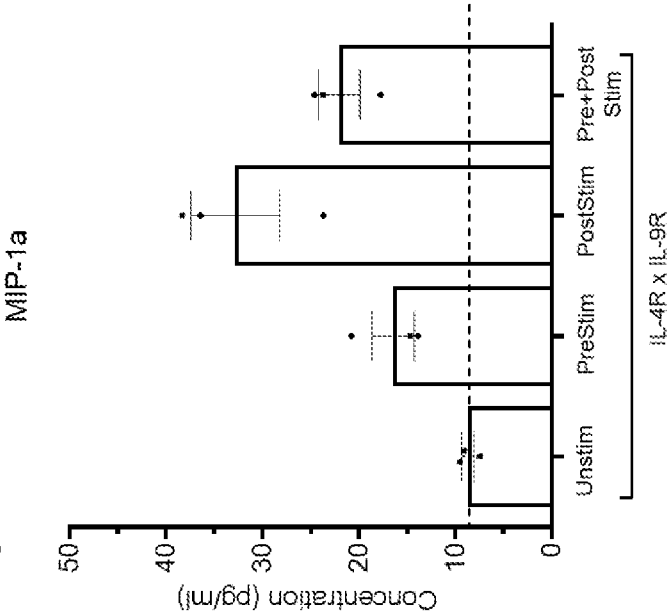
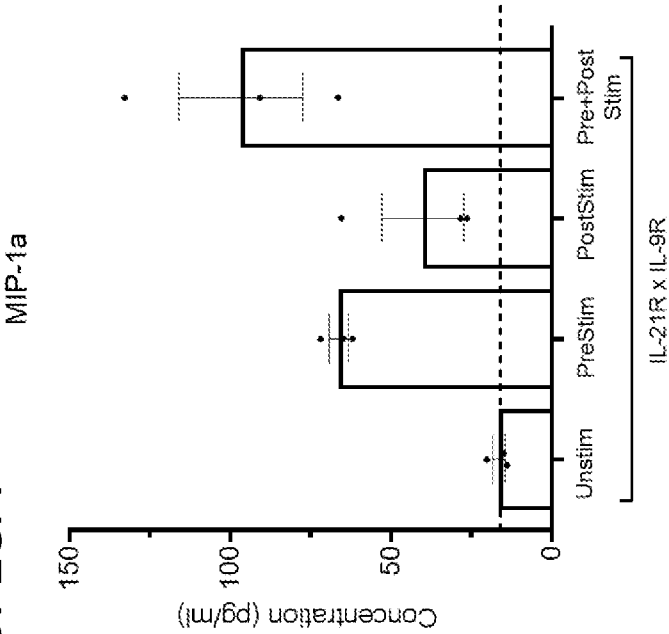


FIG. 18A



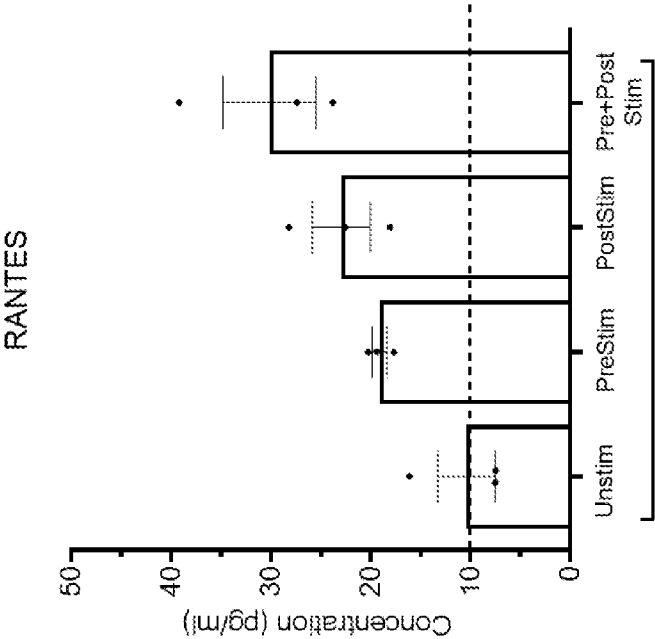


FIG. 19