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- 一 国際調査報告 (条約第21条(3))
- 一 明細書の別個の部分として表した配列リスト (規則5.2(a))

(54) Title: ANTIGEN-PRESENTING EXTRACELLULAR VESICLES, COMPOSITION CONTAINING SAME, AND METHODS FOR PRODUCTION THEREOF

(54) 発明の名称: 抗原提示細胞外小胞、それを含む組成物、及びそれらを製造するための方法

(57) Abstract: To provide extracellular vesicles capable of satisfactorily activating, etc., antigen-specific T cells. Provided are said antigen-presenting extracellular vesicles that present an antigen-presenting MHC molecule and a T-cell-stimulating cytokine extramembranously.

(57) 要約: 抗原特異的なT細胞を満足に活性化等することが可能な細胞外小胞を提供すること。抗原提示MHC分子及びT細胞刺激性サイトカインを膜外に提示する該抗原提示細胞外小胞を提供する。

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DESCRIPTION

TITLE OF INVENTION: ANTIGEN-PRESENTING EXTRACELLULAR
VESICLES, COMPOSITION CONTAINING SAME, AND METHOD FOR
5 PRODUCTION THEREOF

Technical Field

[0001] The present invention relates to antigen-presenting extracellular vesicles, a
composition containing the same, and a method for preparing the same.

10

Background Art

[0002] It is known that antigen-specific T cells (for example, cytotoxic T cells, helper
T cells, and the like) play a central role in an immune reaction such as elimination of
cancer cells and the like by living bodies or regulation of responses to auto-antigens,
15 allergic substances, and the like. The antigen-specific T cells recognize a binding
complex of MHC molecules on cell surfaces of antigen-presenting cells such as
dendritic cells or macrophages, and antigens derived from cancer, allergic substances,
and the like, at a T cell receptor, and activate, proliferate, and differentiate. The
activated antigen-specific T cells specifically injure cancer cells and the like presenting
20 antigens, and regulate responses to auto-antigens, allergic substances, and the like.
Therefore, it is considered that activation, proliferation, and differentiation of the
antigen-specific T cells are particularly important in the immune reaction.

[0003] As a method for activating the antigen-specific T cells, not only a method for
expressing a chimeric antigen receptor in T cells that has already been put into practical
25 use, but also other methods have been developed. For example, Patent Literature 1
discloses that nanoparticles containing MHC molecules and T-cell costimulatory
molecules on surfaces thereof proliferate antigen-specific T cells. In addition, Non
Patent Literature 1 discloses that exosomes in which IL-12 is expressed on membranes
via PTGFRN proliferate tumor antigen-specific CD8-positive T cells.

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Citation List

Patent Literature

[0004] Patent Literature 1: JP 2016-520518 A

35 Non Patent Literatures

[0005] Non Patent Literature 1: Katherine Kirwin, et al., "Exosome Surface Display of

IL-12 Results in Tumor-Retained Pharmacology with Superior Potency and Limited Systemic Exposure Compared to Recombinant IL-12”, November 6, 2019, 34th Annual Meeting of the Society for Immuno-therapy of Cancer

Non Patent Literature 2: Journal of Extracellular Vesicles (2018); 7:1535750

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Summary of Invention

Technical Problem

[0006] As a novel method capable of activating antigen-specific T cells, the present inventors tried a method using extracellular vesicles containing MHC molecules and T-cell costimulatory molecules in membranes. However, when an attempt was made to active antigen-specific T cells using the extracellular vesicles, it was found for the first time that antigen-specific T cells could not be satisfactorily activated.

[0007] Therefore, an object of the present invention is to provide extracellular vesicles capable of satisfactorily activating antigen-specific T cells.

15

Solution to Problem

[0008] In view of the above problems, as a result of conducting intensive studies, the present inventors have surprisingly found that antigen-specific T cells can be satisfactorily activated using extracellular vesicles containing MHC molecules and T-cell stimulatory cytokines in membranes, thereby completing the present invention.

[0009] Therefore, the present invention includes the followings.

[0] An extracellular vesicle presenting an antigen-presenting MHC molecule and a T-cell stimulatory cytokine outside membrane thereof.

[1] An antigen-presenting extracellular vesicle, the membrane of which contains:

(A) a protein which comprises an antigen-presenting MHC molecule and is capable of presenting the antigen outside the membrane; and

(B) a protein which comprises a first T-cell stimulatory cytokine or a subunit thereof and is capable of presenting the first T-cell stimulatory cytokine outside the membrane.

[2] The antigen-presenting extracellular vesicle according to [1], wherein the membrane of the antigen-presenting extracellular vesicle contains:

(A) a fusion protein or a protein complex which comprises an antigen-presenting MHC molecule, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof, and is

capable of presenting the antigen outside the membrane; and

(B) a fusion protein which comprises a first T-cell stimulatory cytokine or a subunit thereof, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding
5 to membrane of an extracellular vesicle or a domain thereof, and is capable of presenting the first T-cell stimulatory cytokine outside the membrane.

[3] The antigen-presenting extracellular vesicle according to [1] or [2], wherein the membrane of the antigen-presenting extracellular vesicle contains:

(A) a fusion protein or a protein complex which comprises an antigen-
10 presenting MHC molecule and a tetraspanin or a transmembrane domain thereof or MFG-E8 or a domain thereof, and is capable of presenting the antigen outside the membrane; and

(B) a fusion protein which comprises a first T-cell stimulatory cytokine or a subunit thereof and a partial sequence of a tetraspanin, and is capable of presenting the
15 first T-cell stimulatory cytokine outside the membrane, in which the partial sequence of the tetraspanin contains at least two transmembrane domains, and the first T-cell stimulatory cytokine is disposed between the two transmembrane domains, or

(B) a fusion protein which comprises a first T-cell stimulatory cytokine or a subunit thereof and MFG-E8 or a domain thereof, and is capable of presenting the first
20 T-cell stimulatory cytokine outside the membrane.

[4] The antigen-presenting extracellular vesicle according to any one of [1] to [3], wherein the membrane of the antigen-presenting extracellular vesicle contains:

(A) a fusion protein capable of presenting an antigen peptide outside the membrane, wherein the fusion protein comprises an amino acid sequence consisting of,
25 from an N-terminal side thereof,

(A-1) an MHC molecule-restricted antigen peptide,
(A-2) a spacer sequence which may be optionally present,
(A-3) a single chain MHC molecule,
(A-4) a spacer sequence which may be optionally present, and
30 (A-5) a tetraspanin, or

(A) a protein complex capable of presenting an antigen peptide outside the membrane, wherein the protein complex contains:

a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

35 (A-1) an MHC molecule-restricted antigen peptide,
(A-2) a spacer sequence which may be optionally present,

(A-3) an MHC class I α chain, β_2 microglobulin, an MHC class II α chain, or an MHC class II β chain,

(A-4) a spacer sequence which may be optionally present, and

(A-5) a tetraspanin; and

5 (A-6) a protein comprising an amino acid sequence of β_2 microglobulin, an MHC class I α chain, an MHC class II β chain, or an MHC class II α chain; and

(B) a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

10 (B-1) a partial sequence of a tetraspanin containing, from an N-terminal side thereof, a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3,

(B-2) a spacer sequence which may be optionally present,

(B-3) a first T-cell stimulatory cytokine,

(B-4) a spacer sequence which may be optionally present, and

15 (B-5) a partial sequence of a tetraspanin containing a transmembrane domain 4,

the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside the membrane, or

20 (B) a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

(B-3) a first T-cell stimulatory cytokine,

(B-4) a spacer sequence which may be optionally present, and

(B-5) MFG-E8,

25 the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside the membrane.

[5] The antigen-presenting extracellular vesicle according to [4], wherein the membrane of the antigen-presenting extracellular vesicle contains:

30 (A) a fusion protein capable of presenting an antigen peptide outside the membrane, in which the fusion protein comprises an amino acid sequence consisting of, from an N-terminal side thereof,

(A-1) an MHC class I molecule-restricted antigen peptide,

(A-2) a spacer sequence which may be optionally present,

(A-3) a single chain MHC class I molecule,

(A-4) a spacer sequence which may be optionally present, and

35 (A-5) a tetraspanin.

[6] The antigen-presenting extracellular vesicle according to [4], wherein the

membrane of the antigen-presenting extracellular vesicle contains:

(A) a protein complex capable of presenting an antigen peptide outside the membrane, wherein the protein complex contains:

a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

- (A-1) an MHC class II molecule-restricted antigen peptide,
- (A-2) a spacer sequence which may be optionally present,
- (A-3) an MHC class II β chain,
- (A-4) a spacer sequence which may be optionally present, and
- (A-5) a tetraspanin; and
- (A-6) a protein comprising an amino acid sequence of an MHC class II α chain.

[7] The antigen-presenting extracellular vesicle according to any one of [1] to [6], wherein the first T-cell stimulatory cytokine is IL-2, IL-4, IL-6, IL-12, a subunit of IL-12, or TGF- β .

[8] The antigen-presenting extracellular vesicle according to any one of [1] to [7], wherein the membrane of the antigen-presenting extracellular vesicle contains:

(C) a protein which comprises a T-cell costimulatory molecule and is capable of allowing the T-cell costimulatory molecule to interact with T cells.

[9] The antigen-presenting extracellular vesicle according to any one of [1] to [8], wherein the membrane of the antigen-presenting extracellular vesicle contains:

(C) a fusion protein which comprises a T-cell costimulatory molecule, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof, and is capable of allowing the T-cell costimulatory molecule to interact with T cells.

[10] The antigen-presenting extracellular vesicle according to any one of [1] to [9], wherein the membrane of the antigen-presenting extracellular vesicle contains:

(C) a fusion protein which comprises a T-cell costimulatory molecule, and a tetraspanin or a transmembrane domain thereof or MFG-E8 or a domain thereof, and is capable of allowing the T-cell costimulatory molecule to interact with T cells.

[11] The antigen-presenting extracellular vesicle according to any one of [1] to [10], wherein the membrane of the antigen-presenting extracellular vesicle contains:

(C) a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

(C-1) a T-cell costimulatory molecule,

(C-2) a spacer sequence which may be present, and

(C-3) a tetraspanin,

the fusion protein being capable of allowing the T-cell costimulatory molecule to interact with T cells.

5 [12] The antigen-presenting extracellular vesicle according to any one of [1] to [11], wherein the extracellular vesicle is an exosome.

[13] Polynucleotides encoding any one of:

(i) the fusion protein or protein complex of (A) defined in any one of [2] to [6];

(ii) the fusion protein of (B) defined in any one of [2] to [4]; and

10 (iii) the fusion protein of (C) defined in any one of [9] to [11].

[14] A vector comprising at least one polynucleotide selected from the polynucleotides according to [13].

[15] A cell transformed with a single vector or a combination of two or more vectors, the vector comprising:

15 (i) a polynucleotide encoding the fusion protein or protein complex of (A) defined in any one of [2] to [6];

(ii) a polynucleotide encoding the fusion protein of (B) defined in any one of [2] to [4]; and optionally,

20 (iii) a polynucleotide encoding the fusion protein of (C) defined in any one of [9] to [11].

[16] A culture supernatant obtained by culturing the cell according to [15].

[17] An antigen-presenting extracellular vesicle obtained from the culture supernatant according to [16].

25 [18] A method for preparing the antigen-presenting extracellular vesicle according to any one of [1] to [12], the method comprising a step of collecting a culture supernatant obtained by culturing the cell according to [15].

[19] A pharmaceutical composition comprising the antigen-presenting extracellular vesicle according to any one of [1] to [12] and [17] or the culture supernatant according to [16].

30 [20] A pharmaceutical composition for treating or preventing an infectious disease, comprising the antigen-presenting extracellular vesicle according to any one of [1] to [12] and [17] or the culture supernatant according to [16].

[21] A pharmaceutical composition for treating or preventing cancer, comprising the antigen-presenting extracellular vesicle according to any one of [5] and
35 [7] to [12].

[22] A pharmaceutical composition for treating or preventing an autoimmune

disease, comprising the antigen-presenting extracellular vesicle according to any one of [6] to [12].

[23] A pharmaceutical composition for treating or preventing an allergic disease, comprising the antigen-presenting extracellular vesicle according to any one of
5 [6] to [12].

[24] A method for activating and/or proliferating T cells against a specific antigen, comprising contacting the antigen-presenting extracellular vesicle according to any one of [1] to [12] and [17] with T cells in vitro or ex vivo.

[0010] [25]

10 The antigen-presenting extracellular vesicle according to any one of [1] to [11], wherein the protein or protein complex defined in (A) and the protein or protein complex defined in (B) are fused to each other.

[26]

The antigen-presenting extracellular vesicle according to any one of [8] to [11],
15 wherein the protein or protein complex defined in (A) and the protein or protein complex defined in (C) are fused to each other.

[27]

The antigen-presenting extracellular vesicle according to any one of [8] to [11], wherein the protein or the protein complex defined in (B) and the protein or protein
20 complex defined in (C) are fused to each other.

[28]

The antigen-presenting extracellular vesicle according to any one of [8] to [11], wherein the protein or the protein complex defined in (A), the protein or protein complex defined in (B), and the protein or protein complex defined in (C) are fused to
25 each other.

[29] The antigen-presenting extracellular vesicle according to any one of [25] to [27], wherein the extracellular vesicle is an exosome.

[0011] [30] The pharmaceutical composition according to [21], further containing an immune checkpoint inhibitor.

30 [31] The pharmaceutical composition according to [30], wherein the immune checkpoint inhibitor is present on the membrane of the antigen-presenting extracellular vesicle.

[32] The pharmaceutical composition according to [30] or [31], wherein the immune checkpoint inhibitor is selected from the group consisting of an anti-PD-1
35 antibody or an active fragment thereof, an anti-CTLA-4 antibody or an active fragment thereof, and a PD-L1 antibody or an active fragment thereof.

[0012] [1A]

An antigen-presenting extracellular vesicle, the membrane of which contains,
(D) a fusion protein which comprises an antigen-presenting MHC molecule
and at least one T-cell stimulatory cytokine or subunit thereof, and is capable of
5 presenting the antigen and the T-cell stimulatory cytokine outside the membrane.

[2A] The antigen-presenting extracellular vesicle according to [1A], in wherein
the fusion protein comprises the antigen-presenting MHC molecule, the at least one T-
cell stimulatory cytokine or subunit thereof, and a membrane protein capable of being
localized to membrane of an extracellular vesicle or a transmembrane domain thereof or
10 a protein capable of binding to membrane of an extracellular vesicle or a membrane-
binding domain thereof.

[3A] The antigen-presenting extracellular vesicle according to [2A], wherein
the membrane protein capable of being localized on membrane of an extracellular
vesicle or the protein capable of binding to membrane of an extracellular vesicle is a
15 tetraspanin or MFG-E8.

[4A] The antigen-presenting extracellular vesicle according to [3A], wherein
the fusion protein comprises an amino acid sequence encoding, from an N-terminal side
thereof,

(D-1) an MHC molecule-restricted antigen peptide,
20 (D-2) a spacer sequence which may be present,
(D-3) a single chain MHC molecule,
(D-4) a spacer sequence which may be present, and
(D-5) a fusion peptide comprising a tetraspanin or a transmembrane domain
thereof or MFG-E8 or a transmembrane domain thereof, and the at least one T-cell
25 stimulatory cytokine or subunit thereof, in this order.

[5A] The antigen-presenting extracellular vesicle according to [3A], wherein
the fusion protein contains an amino acid sequence encoding, from an N-terminal side
thereof,

(D-1) a fusion peptide comprising a tetraspanin or a transmembrane domain
30 thereof or MFG-E8 or a transmembrane domain thereof, and the at least one T-cell
stimulatory cytokine or subunit thereof,
(D-2) a spacer sequence which may be optionally present,
(D-3) a single chain MHC molecule,
(D-4) a spacer sequence which may be optionally present, and
35 (D-5) an MHC molecule-restricted antigen peptide, in this order.

[6A]

The antigen-presenting extracellular vesicle according to [4A] or [5A], in which the fusion peptide comprises an amino acid sequence encoding, from an N-terminal side thereof,

- (1) a partial sequence of a tetraspanin containing a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3,
- (2) a spacer sequence which may be optionally present,
- (3) the at least one T-cell stimulatory cytokine or subunit thereof,
- (4) a spacer sequence which may be optionally present, and
- (5) a partial sequence of a tetraspanin containing a transmembrane domain 4, in this order.

[7A]

The antigen-presenting extracellular vesicle according to [4A] or [5A], wherein the fusion peptide comprises an amino acid sequence encoding, from an N-terminal side thereof,

- (1) the at least one T-cell stimulatory cytokine or subunit thereof,
- (2) a spacer sequence which may be optionally present, and
- (3) MFG-E8, in this order.

[8A]

The antigen-presenting extracellular vesicle according to [4A] or [5A], wherein the MHC molecule-restricted antigen peptide is an MHC class I molecule-restricted antigen peptide, and the single chain MHC molecule comprises an extracellular domain of an MHC class I α chain.

[9A]

The antigen-presenting extracellular vesicle according to [4A] or [5A], wherein the MHC molecule-restricted antigen peptide is an MHC class II molecule-restricted antigen peptide, and the single chain MHC molecule comprises an extracellular domain of an MHC class II α chain and/or an extracellular domain of an MHC class II β chain.

[0013] [10A]

The antigen-presenting extracellular vesicle according to any one of [1A] to [9A], wherein the membrane of the antigen-presenting extracellular vesicle further contains (C) a protein which comprises at least one T-cell costimulatory molecule and is capable of allowing the T-cell costimulatory molecule to interact with T cells.

[11A]

The antigen-presenting extracellular vesicle according to [10A], wherein the protein capable of interacting with T cells comprises the at least one T-cell

costimulatory molecule, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof.

[12A]

5 The antigen-presenting extracellular vesicle according to [11A], wherein the protein capable of interacting with T cells comprises the at least one T-cell costimulatory molecule, and a tetraspanin or a transmembrane domain thereof or MFG-E8 or a domain thereof.

[13A]

10 The antigen-presenting extracellular vesicle according to [12A], wherein the protein capable of interacting with T cells comprises

(C) an amino acid sequence encoding, from an N-terminal side thereof,

(C-1) the at least one T-cell costimulatory molecule,

(C-2) a spacer sequence which may be optionally present, and

15 (C-3) a tetraspanin, in this order.

[14A] The antigen-presenting extracellular vesicle according to any one of [10A] to [13A], wherein the fusion protein (D) is fused to the protein (C) capable of interacting with T cells.

20 [15A] The antigen-presenting extracellular vesicle according to any one of [1A] to [14A], wherein the extracellular vesicle is an exosome.

[0014] [1B] A pharmaceutical composition comprising the antigen-presenting extracellular vesicle according to any one of [1A] to [15A] and a pharmacologically acceptable carrier.

[0015] [1C] A pharmaceutical composition for treating or preventing cancer
25 comprising the antigen-presenting extracellular vesicle according to any one of [1A] to [15A], wherein the antigen peptide preferably includes a cancer antigen peptide.

[2C] A pharmaceutical composition for treating or preventing an autoimmune disease comprising the antigen-presenting extracellular vesicle according to any one of [1A] to [15A], wherein the antigen peptide preferably includes an auto-antigen peptide.

30 [3C] A pharmaceutical composition for treating or preventing an allergic disease comprising the antigen-presenting extracellular vesicle according to any one of [1A] to [15A], wherein the antigen peptide preferably includes an allergen.

[4C] The pharmaceutical composition according to [1C], further containing an immune checkpoint inhibitor.

35 [5C] The pharmaceutical composition according to [4C], wherein the immune checkpoint inhibitor is present on the membrane of the antigen-presenting extracellular

vesicle.

[6C] The pharmaceutical composition according to [4C] or [5C], wherein the immune checkpoint inhibitor is selected from the group consisting of an anti-PD-1 antibody or an active fragment thereof, an anti-CTLA-4 antibody or an active fragment thereof, and a PD-L1 antibody or an active fragment thereof.

[7C] A pharmaceutical composition for treating or preventing an infectious disease comprising the antigen-presenting extracellular vesicle according to any one of [1A] to [15A] and a pharmacologically acceptable carrier, wherein the antigen peptide is preferably derived from an infectious pathogen that causes an infectious disease.

[0016] [1D] The antigen-presenting extracellular vesicle according to any one of [1A] to [15A] for use in treating or preventing cancer, wherein the antigen peptide preferably includes a cancer antigen peptide.

[2D] The antigen-presenting extracellular vesicle according to any one of [1A] to [15A] for use in treating or preventing an autoimmune disease, wherein the antigen peptide preferably includes an auto-antigen peptide.

[3D] The antigen-presenting extracellular vesicle according to any one of [1A] to [15A] for use in treating or preventing an allergic disease, wherein the antigen peptide preferably includes an allergen.

[4D] The antigen-presenting extracellular vesicle for use according to [1D] used together with an immune checkpoint inhibitor.

[5D] The antigen-presenting extracellular vesicle for use according to [4D], wherein the immune checkpoint inhibitor is present on the membrane of the antigen-presenting extracellular vesicle.

[6D] The antigen-presenting extracellular vesicle for use according to [4D] or [5D], wherein the immune checkpoint inhibitor is selected from the group consisting of an anti-PD-1 antibody or an active fragment thereof, an anti-CTLA-4 antibody or an active fragment thereof, and a PD-L1 antibody or an active fragment thereof.

[7D] The antigen-presenting extracellular vesicle according to any one of [1A] to [15A] for use in treating or preventing an infectious disease, wherein the antigen peptide is preferably derived from an infectious pathogen that causes an infectious disease.

[0017] [1E] Use of the antigen-presenting extracellular vesicle according to any one of [1A] to [15A] in the manufacture of a medicament for treating or preventing cancer, wherein the antigen peptide preferably includes a cancer antigen peptide.

[2E] Use of the antigen-presenting extracellular vesicle according to any one of [1A] to [15A] in the manufacture of a medicament for treating or preventing an

autoimmune disease, wherein the antigen peptide preferably includes an auto-antigen peptide.

[3E] Use of the antigen-presenting extracellular vesicle according to any one of [1A] to [15A] in the manufacture of a medicament for treating or preventing an allergic disease, wherein the antigen peptide preferably includes an allergen.

[4E] The use according to [1E], wherein the pharmaceutical is used together with an immune checkpoint inhibitor.

[5E] The use according to [4E], wherein the immune checkpoint inhibitor is present on the membrane of the antigen-presenting extracellular vesicle.

[6E] The use according to [4E] or [5E], wherein the immune checkpoint inhibitor is selected from the group consisting of an anti-PD-1 antibody or an active fragment thereof, an anti-CTLA-4 antibody or an active fragment thereof, and a PD-L1 antibody or an active fragment thereof.

[7E] Use of the antigen-presenting extracellular vesicle according to any one of [1A] to [15A] the manufacture of a medicament for treating or preventing an infectious disease, wherein the antigen peptide is preferably derived from an infectious pathogen that causes an infectious disease.

[0018] [1F] A method for treating or preventing cancer in a subject, the method comprising:

administering an effective amount of the antigen-presenting extracellular vesicle according to any one of [1A] to [15A] to the subject to activate and/or proliferate T cells that recognize a cancer antigen in the subject and to allow the activated and/or proliferated T cells to attack cancer cells; wherein the activated and/or proliferated T cells are preferably CD8-positive cytotoxic T cells, and the antigen peptide preferably includes a cancer antigen peptide.

[2F] A method for treating or preventing an autoimmune disease in a subject, the method comprising administering an effective amount of the antigen-presenting extracellular vesicle according to any one of [1A] to [15A] to the subject to activate and/or proliferate T cells that recognize an auto-antigen in the subject and to desensitize an immune response to the auto-antigen in the subject, wherein the activated and/or proliferated T cells are preferably CD4-positive regulatory T cells (Treg), and the antigen peptide preferably includes an auto-antigen peptide.

[3F] A method for treating or preventing an allergic disease in a subject, wherein a method for treating or preventing an autoimmune disease comprises administering an effective amount of the antigen-presenting extracellular vesicle according to any one of [1A] to [15A] to the subject to activate and/or proliferate T cells

that recognize an allergen in the subject and to desensitize an immune response to the auto-antigen in the subject, wherein the activated and/or proliferated T cells are preferably CD4-positive regulatory T cells (Treg), and the antigen peptide preferably includes an auto-antigen peptide.

5 [4F] The method according to [1F], wherein the antigen-presenting extracellular vesicle is administered together with an immune checkpoint inhibitor.

 [5F] The method according to [4F], wherein the immune checkpoint inhibitor is present on the membrane of the antigen-presenting extracellular vesicle.

 [6F] The method according to [4F] or [5F], wherein the immune checkpoint
10 inhibitor is selected from the group consisting of an anti-PD-1 antibody or an active fragment thereof, an anti-CTLA-4 antibody or an active fragment thereof, and a PD-L1 antibody or an active fragment thereof.

 [7F] A method for treating or preventing an infectious disease in a subject, the method comprising:

15 administering an effective amount of the antigen-presenting extracellular vesicle according to any one of [1A] to [15A] to the subject to,

 1) secrete inflammatory cytokines and to activate innate immunity of the subject, and/or

 2) provide acquired immunity to an infectious pathogen that causes the
20 infectious disease to the subject,

 so that, in the subject's body, the infectious pathogen that causes the infectious disease is eliminated and/or a proliferation of the infectious pathogen is suppressed.

[0019] [1G] A method for activating and/or proliferating T cells against a specific antigen, the method comprising contacting the antigen-presenting extracellular
25 vesicle according to any one of [1A] to [15A] with T cells in vitro or ex vivo.

[0020] [1H] A polynucleotide encoding:

 (i) the fusion protein or protein complex (D) defined in any one of [1A] to [9A];

 (ii) the protein (C) capable of interacting with T cells defined in any one of
30 [10A] to [13A]; or

 (iii) the fusion protein of the fusion protein (D) and the protein (C) capable of interacting with T cells defined in [14A].

 [2H] A vector comprising the nucleic acid according to [1H].

35 Advantageous Effects of Invention

[0021] According to the present invention, it is possible to satisfactorily activate

antigen-specific T cells by using an extracellular vesicle (i.e., antigen-presenting extracellular vesicle) containing an MHC molecule and a T-cell stimulatory cytokine in membrane thereof.

5 Brief Description of Drawings

[0022] Fig. 1A illustrates a model diagram of an antigen peptide-single chain MHC class I molecule (sc-Trimer)-CD81 fusion protein.

 Fig. 1B illustrates an amino acid sequence of the antigen peptide-single chain MHC class I molecule (sc-Trimer)-CD81 fusion protein.

10 Fig. 1C illustrates a model diagram of a CD80-CD9 fusion protein.

 Fig. 1D illustrates an amino acid sequence of the CD80-CD9 fusion protein.

 Fig. 1E illustrates a model diagram of a CD63-IL-2 fusion protein.

 Fig. 1F illustrates an amino acid sequence of the CD63-IL-2 fusion protein.

 Fig. 1G illustrates a model diagram of an antigen peptide-MHC class II β chain (sc-Dimer)-CD81 fusion protein.

 Fig. 1H illustrates an amino acid sequence of the antigen peptide-MHC class II β chain (sc-Dimer)-CD81 fusion protein.

 Fig. 1I illustrates an amino acid sequence of an MHC class II α chain.

 Fig. 1J illustrates a model diagram of a TGF- β -MFG-E8 fusion protein.

20 Fig. 1K illustrates an amino acid sequence of the TGF- β -MFG-E8 fusion protein.

 Fig. 1L illustrates a model diagram of a CD81-IL-4 fusion protein.

 Fig. 1M illustrates an amino acid sequence of the CD81-IL-4 fusion protein.

 Fig. 2A illustrates a model diagram of an antigen-presenting extracellular vesicle of Example 1.

 Fig. 2B illustrates a model diagram of an antigen-presenting extracellular vesicle of Example 2.

 Fig. 2C illustrates a model diagram of an antigen-presenting extracellular vesicle of Example 3.

30 Fig. 2D illustrates a model diagram of an antigen-presenting extracellular vesicle of Example 4.

 Fig. 2E illustrates a model diagram of an antigen-presenting extracellular vesicle of Example 5.

 Fig. 2F illustrates a model diagram of an antigen-presenting extracellular vesicle of Example 6.

 Fig. 2G illustrates a model diagram of an antigen-presenting extracellular

vesicle of Example 7.

Fig. 2H illustrates a model diagram of an antigen-presenting extracellular vesicle of Example 8.

Fig. 2I illustrates a model diagram of an antigen-presenting extracellular
5 vesicle of Example 9.

Fig. 2J illustrates a model diagram of antigen-presenting extracellular vesicles of other embodiments.

Fig. 3A illustrates results obtained by analyzing fusion proteins contained in the membrane of the antigen-presenting extracellular vesicle of Example 2 by flow
10 cytometry in Test Example 1-1.

Fig. 3B illustrates results obtained by analyzing fusion proteins contained in the membrane of the antigen-presenting extracellular vesicle of Example 3 by flow cytometry in Test Example 1-2.

Fig. 3C illustrates results obtained by analyzing fusion proteins contained in
15 the membrane of the antigen-presenting extracellular vesicle of Example 4 by flow cytometry in Test Example 1-3.

Fig. 3D illustrates results obtained by analyzing fusion proteins contained in the membrane of the antigen-presenting extracellular vesicle of Example 5 by flow cytometry in Test Example 1-4.

Fig. 3E illustrates results obtained by analyzing fusion proteins contained in the
20 membrane of the antigen-presenting extracellular vesicle of Example 6 by flow cytometry in Test Example 1-5.

Fig. 3F illustrates results obtained by analyzing fusion proteins contained in the
25 membrane of the antigen-presenting extracellular vesicle of Example 7 by flow cytometry in Test Example 1-6.

Fig. 3G illustrates results obtained by analyzing fusion proteins contained in the membrane of the antigen-presenting extracellular vesicle of Example 8 by flow cytometry in Test Example 1-7.

Fig. 3H illustrates results obtained by analyzing fusion proteins contained in
30 the membrane of the antigen-presenting extracellular vesicle of Example 9 by flow cytometry in Test Example 1-8.

Fig. 4 illustrates results obtained by evaluating whether the antigen-presenting extracellular vesicles of Examples 1 and 2 activate antigen-specific CD8-positive T cells (OT-1 T cells) in vitro in Test Example 2.

Fig. 5 illustrates results obtained by evaluating whether the antigen-presenting
35 extracellular vesicle of Example 2 activates antigen-specific CD8-positive T cells (OT-

1) in vivo in Test Example 3.

Fig. 6 illustrates results obtained by evaluating whether the antigen-presenting extracellular vesicle of Example 3 activates antigen-specific CD4-positive T cells in vitro in Test Example 4.

5 Fig. 7 illustrates results obtained by evaluating whether the antigen-presenting extracellular vesicle of Example 4 induces differentiation of antigen-specific CD4-positive T cells (OT-2 T cells) into regulatory T cells in vitro in Test Example 5.

Fig. 8 illustrates results obtained by evaluating whether the antigen-presenting extracellular vesicles of Examples 3 and 5 induce differentiation of antigen-specific
10 CD4-positive T cells (OT-2 T cells) into Th2T cells in vitro in Test Example 6.

Fig. 9 illustrates results obtained by evaluating whether the antigen-presenting extracellular vesicle of Example 6 induces differentiation of antigen-specific CD4-positive T cells into Th1 cells in vitro in Test Example 7.

Fig. 10 illustrates results obtained by evaluating whether the antigen-presenting
15 extracellular vesicle of Example 7 induces differentiation of antigen-specific CD4-positive T cells into Th17 cells in vitro in Test Example 8.

Fig. 11 illustrates that antigen-specific CD8-positive T cells are remarkably proliferated by the antigen-presenting extracellular vesicles of Examples 1 and 8 in Test Example 9.

20 Fig. 12 illustrates that B16 melanoma cells are remarkably suppressed by the antigen-presenting extracellular vesicle of Example 8 in Test Example 10.

Description of Embodiments

[0023] Definitions

25 [0024] Extracellular vesicle

[0025] The “extracellular vesicle” used in the present specification is not particularly limited as long as it is a vesicle secreted from cells, and examples thereof include exosomes, microvesicles (MV), and apoptotic bodies.

[0026] The “exosome” used in the present specification means a vesicle of about 20 to
30 about 500 nm (preferably about 20 to about 200 nm, more preferably about 25 to about 150 nm, and still more preferably about 30 to about 100 nm), the vesicle being derived from an endocytosis pathway. Examples of constituent components of the exosome include a protein and a nucleic acid (mRNA, miRNA, or non-coated RNA). The exosome has a function of controlling intercellular communication. Examples of a
35 maker molecule of the exosome include Alix, Tsg101, a tetraspanin, a flotillin, and phosphatidylserine.

[0027] The “microvesicle” used in the present specification means a vesicle of about 50 to about 1,000 nm, the vesicle being derived from a cytoplasmic membrane.

Examples of constituent components of the microvesicle include a protein and a nucleic acid (mRNA, miRNA, non-coated RNA, or the like). The microvesicle has a function of controlling intercellular communication and the like. Examples of a marker molecule of the microvesicle include integrin, selectin, CD40, and CD154.

[0028] The “apoptotic body” used in the present specification means a vesicle of about 500 to about 2,000 nm, the vesicle being derived from a cytoplasmic membrane.

Examples of constituent components of the apoptotic body include a fragmented nucleus and a cell organelle. The apoptotic body has a function of inducing phagocytosis and the like. Examples of a marker molecule of the apoptotic body include Annexin V and phosphatidylserine.

[0029] The “antigen-presenting extracellular vesicle” used in the present specification means an extracellular vesicle presenting an antigen outside membrane thereof.

[0030] Major Histocompatibility Gene Complex Molecule

[0031] The “major histocompatibility complex (hereinafter, also referred to as “MHC”) molecule” used in the present specification is not particularly limited as long as it has an antigen-binding gap and can bind to an antigen to be presented to a T cell, a T cell precursor, or the like. Examples of the MHC molecule include an MHC class I molecule and an MHC class II molecule. The MHC molecule may be derived from any animal species. Examples thereof include a human leukocyte antigen (HLA) in a human and an H2 system in a mouse.

[0032] HLA corresponding to the MHC class I molecule may be classified into subtypes such as HLA-A, HLA-B, HLA-Cw, HLA-F, and HLA-G. Polymorphism (allele) is known for these subtypes. Examples of polymorphism of HLA-A include HLA-A1, HLA-A0201, and HLA-A24, examples of polymorphism of HLA-B include HLA-B7, HLA-B40, and HLA-B4403, and examples of polymorphism of HLA-Cw include HLA-Cw0301, HLA-Cw0401, and HLA-Cw0602.

[0033] HLA corresponding to the MHC class II molecule may be classified into subtypes such as HLA-DR, HLA-DQ, and HLA-DP.

[0034] The MHC molecule described in the present specification is not limited as long as the function thereof can be exhibited, and an amino acid sequence identity of a wild-type amino acid sequence (for example, in a case of an MHC class I molecule: for example, an MHC class I α chain of SEQ ID NO: 9 or the like, β_2 microglobulin of SEQ ID NO: 7 or the like, a single chain MHC class I molecule of SEQ ID NO: 65 or the like, and the like; and in a case of an MHC class II molecule: for example, an MHC

class II α chain of SEQ ID NO: 71 or the like, an MHC class II β chain of SEQ ID NO: 37 or the like, a single chain MHC class II molecule, and the like) may be 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more. Alternatively, the MHC molecule described in the present specification may be obtained by deletion, insertion, and/or substitution of one or a plurality of amino acids with respect to the wild-type amino acid sequence as long as it can exhibit the function thereof.

[0035] The “antigen-presenting MHC molecule” used in the present specification is not particularly limited as long as it is an MHC molecule presenting an antigen, and examples thereof include an antigen-presenting MHC class I molecule and an antigen-presenting MHC class II molecule. Examples of the “antigen-presenting MHC class I molecule” include a complex of an antigen, an MHC class I α chain or an extracellular domain thereof, and β_2 microglobulin; a complex of an antigen and a single chain MHC class I molecule; a fusion protein in which an antigen and a single chain MHC class I molecule are bound; and a complex an antigen, and a fusion protein of an extracellular domain of an MHC class I α chain and another protein or a domain thereof or a fragment thereof (for example, a fusion protein of an extracellular domain of an MHC class I α chain and an Fc portion of an antibody, a fusion protein of an extracellular domain of an MHC class I α chain and a transmembrane domain of another membrane protein, and the like) Examples of the “antigen-presenting MHC class II molecule” include a complex of an antigen, an MHC class II α chain or an extracellular domain thereof, and an MHC class II β chain or an extracellular domain thereof; a complex of an antigen and a single chain MHC class II molecule; a complex of a fusion protein in which an antigen and an MHC class II β chain are bound and an MHC class II α chain; and a complex of a fusion protein of an antigen, an extracellular domain of an MHC class II α chain and another protein or a domain thereof or a fragment thereof (for example, a fusion protein of an extracellular domain of an MHC class II α chain and an Fc portion of an antibody; a fusion protein of an extracellular domain of an MHC class II α chain and a transmembrane domain of another membrane protein; and the like), and a fusion protein of an extracellular domain of an MHC class II β chain and another protein or a domain thereof or a fragment thereof (for example, a fusion protein of an extracellular domain of an MHC class II β chain and an Fc portion of an antibody; a fusion protein of an amino acid sequence containing an extracellular domain of an MHC class II β chain and a transmembrane domain of another membrane protein; and the like).

[0036] The “single chain MHC molecule”, the “single chain MHC class I molecule”, or the “single chain MHC class II molecule” used in the present specification means a

fusion protein in which an α chain of an MHC molecule (or an MHC class I molecule or an MHC class II molecule) or an extracellular domain thereof, and a β chain or an extracellular domain thereof or β_2 microglobulin are linked by a spacer sequence, if necessary. Examples of the “single chain MHC class I molecule” include a fusion

5 protein in which an MHC class I α chain and β_2 microglobulin are linked by a spacer sequence, if necessary. Examples of the “single chain MHC class II molecule” include a fusion protein in which an MHC class II α chain and an MHC class II β chain are linked by a spacer sequence, if necessary.

[0037] The “protein (or a fusion protein, a protein complex, or the like) which

10 comprises an antigen-presenting MHC molecule and is capable of presenting the antigen (or an antigen peptide) outside membrane” used in the present specification means a protein comprising at least an antigen-presenting MHC molecule and presenting an antigen (or an antigen peptide) outside membrane, in which the protein is capable of presenting an antigen to T cells and the like (a fusion protein, a protein

15 complex, or the like). The “protein (or a fusion protein, a protein complex, or the like) comprising an antigen-presenting MHC molecule and presenting an antigen (or an antigen peptide) outside the membrane” may be expressed in the form of a fusion protein, a protein complex, or the like using a plasmid or the like so that the protein is expressed in membrane of an extracellular vesicle. Alternatively, in a case where a

20 soluble antigen-presenting MHC molecule (although not limited thereto, a fusion protein comprising an MHC class I α chain and an immunoglobulin heavy chain described in Patent Literature 1; a soluble MHC class I molecule described in JP 2007-161719 A, or the like) is used, the “protein (or a fusion protein, a protein complex, or the like) which comprises an antigen-presenting MHC molecule and is capable of

25 presenting an antigen (or an antigen peptide) outside the membrane” may be a protein in which a soluble antigen-presenting MHC molecule and an extracellular vesicle are bound to membrane of the extracellular vesicle by a lipid linker, a peptide linker, or the like, if necessary (for example, the method described in JP 2018-104341 A or the like may be referred to). Alternatively, the protein may be a mixture of a protein in which

30 a desired tag (for example, a His tag, a FLAG tag, a PNE tag (SEQ ID NO: 79: NYHLENEVARLKKL), or the like) is added to the N-terminus or C-terminus of a soluble antigen-presenting MHC molecule (the tag may be expressed as a fusion protein together with other constituent elements, for example, may be bound to an additionally prepared soluble antigen-presenting MHC molecule by a linker or the like, if

35 necessary), and an extracellular vesicle containing a protein comprising an antibody against the tag or an antigen-binding fragment thereof (for example, scFv, Fab, or a

nanobody) (for example, an antibody itself against the tag or an antigen-binding fragment thereof (for example, scFv, Fab, or a nanobody) bound to the membrane of the extracellular vesicle by a linker or the like, if necessary; a fusion protein in which a nanobody for the tag is bound to the N-terminus or C-terminus of a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof) in membrane under desired conditions (for example, the method using a PNE tag and an antibody against the tag described in Raj D, et al., Gut., 2019 Jun; 68(6): 1052-1064, and the like, may be referred to).

[0038] Antigen

10 [0039] The “antigen” used in the present specification is not particularly limited as long as it can have antigenicity, and includes not only peptide antigens but also non-peptide antigens (for example, constituent elements of a bacterial membrane such as mycolic acid and lipoarabinomannan) such as phospholipids and complex carbohydrates.

15 [0040] The “antigen peptide” used in the present specification is not particularly limited as long as it is a peptide that can be an antigen, and may be naturally derived, synthetically derived, or commercially available. Examples of the antigen peptide include, but are not limited to, tumor-associated antigen peptides such as WT-1, an α -fetal protein, MAGE-1, MAGE-3, placental alkaline phosphatase Sialyl-Lewis X, CA-
20 125, CA-19, TAG-72, epithelial glycoprotein 2, 5T4, an α -fetal protein receptor, M2A, tyrosinase, Ras, p53, Her-2/neu, EGF-R, an estrogen receptor, a progesterone receptor, myc, BCR-ABL, HPV-type 16, melanotransferrin, MUC1, CD10, CD19, CD20, CD37, CD45R, an IL-2 receptor α chain, a T cell receptor, prostatic acid phosphatase, GP100, MelanA/Mart-1, gp75/brown, BAGE, S-100, itokeratin, CYFRA21-1, and Ep-CAM;
25 self-antigen peptides such as insulin, glutamic acid decarboxylase, ICA512/IA-2 protein tyrosine phosphatase, ICA12, ICA69, preproinsulin, HSP60, carboxypeptidase H, periferin, GM1-2, vitronectin, β -crystallin, carreticulin, serotransferase, keratin, pyruvate carboxylase, C1, billin 2, nucleosome, ribonucleoprotein, myelin oligodendrocyte glycoprotein, myelin-associated glycoprotein, myelin/oligodendrocyte
30 basic protein, oligodendrocyte-specific protein, myelin basic protein, and proteolipid protein; antigen peptides derived from infectious pathogens such as protozoa (for example, plasmodium, leishmania, and trypanosoma), bacteria (for example, gram-positive cocci, gram-positive rods, gram-negative bacteria, and anaerobic bacteria), fungi (for example, *Aspergillus*, *Blastomycosis*, *Candida*, *Coccidioidomycosis*,
35 *Cryptococcus*, *Histoplasma*, *Paracoccidioidomycosis*, and *Sporoslix*), viruses (for example, adenovirus, simple herpesvirus, papillomavirus, respiratory synthiavirus,

poxvirus, HIV, influenza virus, and coronavirus such as SARS-CoV or SARS-CoV2), intracellular parasites (for example, Chlamydiaceae, Mycoplasmataceae, Acholeplasma, and Rickettsiaceae), and helminths (for example, nematodes, trematodes, and tapeworms); and other antigen peptides such as prion.

- 5 The antigen peptide may comprise an allergen that causes allergic symptoms. Examples of the allergen include exogenous peptides such as peptides derived from house dust, mites, animals (for example, companion animals such as cats and dogs), and pollens (for example, Japanese cedar or Japanese cypress), in addition to the peptides derived from protozoa, bacteria, fungi, intracellular parasites, and helminths. More
10 specifically, proteins contained in Japanese cedar such as Cryj1 are exemplified. Alternatively, the allergen that causes allergic symptoms may be derived from food. Examples of the allergen that causes allergic symptoms for food include peptides derived from chicken egg, cow milk, wheat, buckwheat, crab, shrimp, and peanut.
- [0041] The “MHC molecule-restricted antigen peptide” used in the present
15 specification means an antigen peptide capable of binding to an MHC molecule in vitro, in vivo, and/or ex vivo. The number of amino acid residues of the “MHC molecule-restricted antigen peptide” is usually about 7 to about 30. Examples of the “MHC molecule-restricted antigen peptide” include an MHC class I molecule-restricted antigen peptide and an MHC class II molecule-restricted antigen peptide.
- 20 [0042] The “MHC class I molecule-restricted antigen peptide” used in the present specification means an antigen peptide capable of binding to an MHC class I molecule in vitro, in vivo, and/or ex vivo. When the MHC class I molecule-restricted antigen peptide is presented outside membrane of the extracellular vesicle, for example, the antigen peptide is recognized by precursor T cells or the like, and cytotoxic T cells or
25 the like can be induced. The number of amino acid residues of the “MHC class I molecule-restricted antigen peptide” is usually about 7 to about 30, preferably about 7 to about 25, more preferably about 7 to about 20, still more preferably about 7 to about 15, and further still more about 7 to about 12.
- [0043] The “MHC class II molecule-restricted antigen peptide” used in the present
30 specification means an antigen peptide capable of binding to an MHC class II molecule in vitro, in vivo, and/or ex vivo. When the MHC class II molecule-restricted antigen peptide is presented outside membrane of the extracellular vesicle, for example, the antigen peptide is recognized by precursor T cells or the like, and α -T cells or the like can be induced. The number of amino acid residues of the “MHC class II molecule-restricted antigen peptide” is usually about 7 to about 30, preferably about 10 to about
35 25, and more preferably about 12 to about 24.

[0044] The “MHC molecule-restricted antigen peptide”, the “MHC class I molecule-restricted antigen peptide”, or the “MHC class II molecule-restricted antigen peptide” is not particularly limited as long as it is an antigen peptide capable of binding to an MHC molecule, an MHC class I molecule, or an MHC class II molecule.

5 [0045] T-Cell Stimulatory Cytokine

[0046] The “T-cell stimulatory cytokine” used in the present specification is not particularly limited as long as it is a cytokine capable of stimulating (for example, activating, suppressing, or the like) T cells via a receptor or the like expressed on the membrane of the T cell. Examples of the T-cell stimulatory cytokine include, are not
10 limited to, IL-2, IL-4, IL-6, IL-12, TGF- β , IFN- α , and IFN- γ . Among them, a T-cell stimulatory cytokine capable of forming a multimer of homo or hetero subunits (for example, IL-12, TGF- β , or the like) may be a T-cell stimulatory cytokine comprising a continuous amino acid sequence linked by a peptide linker or the like, if necessary, as long as it is functional (that is, as long as it can have a desired pharmacological
15 activity).

[0047] The T-cell stimulatory cytokines described in the present specification may be derived from any animal species. Examples of the T-cell stimulatory cytokine include T-cell stimulatory cytokines derived from animals such as mammals, for example, rodents such as a mouse and a rat; lagomorph such as a rabbit; ungulates such as a pig, a
20 cow, a goat, a horse, and a sheep; carnivora such as a dog and a cat; and primates such as a human, a monkey, a rhesus monkey, a crab-eating macaque, a marmoset, an orangutan, and a chimpanzee. The T-cell stimulatory cytokine described in the present specification is preferably derived from rodents or primates, and more preferably derived from a mouse or a human.

25 [0048] The T-cell stimulatory cytokine described in the present specification may have an amino acid sequence identity of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more with respect to a wild-type amino acid sequence thereof (for example, in the case of IL-2, for example, SEQ ID NO: 25 or the like; and in the case of
30 IL-4, for example, SEQ ID NO: 53 or the like), as long as it can exhibit the function thereof. Alternatively, the T-cell stimulatory cytokine described in the present specification may be obtained by deletion, insertion, and/or substitution of one or a plurality of amino acids with respect to the wild-type amino acid sequence as long as it can exhibit the function thereof.

35 [0049] The “protein which comprises a (first or second) T-cell stimulatory cytokine and is capable of presenting the (first or second) T-cell stimulatory cytokine outside

membrane” used in the present specification means a protein which comprises at least a T-cell stimulatory cytokine and is capable of presenting the T-cell stimulatory cytokine outside membrane of an extracellular vesicle. The “protein which comprises a (first or second) T-cell stimulatory cytokine and is capable of presenting the (first or second) T-cell stimulatory cytokine outside membrane” may be expressed by using a plasmid or the like as a fusion protein having a fragment comprising a T-cell stimulatory cytokine and a membrane protein or a transmembrane domain thereof so that the protein is expressed in the membrane of the extracellular vesicle. Alternatively, in a case where a soluble T-cell stimulatory cytokine (examples thereof include, but are not limited to, a T-cell stimulatory cytokine itself; a fusion protein of a T-cell stimulatory cytokine and an Fc portion of an antibody; and a complex of a T-cell stimulatory cytokine and an antibody that recognizes the T-cell stimulatory cytokine or an antigen-binding fragment thereof (for example, scFv, Fab, or a nanobody)) is used, the “protein which comprises a (first or second) T-cell stimulatory cytokine and is capable of presenting the (first or second) T-cell stimulatory cytokine outside membrane” may be a protein in which a soluble T-cell stimulatory cytokine and an extracellular vesicle are bound to membrane of an extracellular vesicle by a lipid linker, a peptide linker, or the like, if necessary (for example, the method described in JP 2018-104341 A or the like may be referred to). Alternatively, the protein may be a mixture of a protein in which a desired tag (for example, a His tag, a FLAG tag, or a PNE tag) is added to the N-terminus or C-terminus of a soluble T-cell stimulatory cytokine (the tag may be expressed as a fusion protein together with other constituent elements, for example, may be bound to an additionally prepared soluble T-cell stimulatory cytokine by a linker or the like, if necessary), and an extracellular vesicle containing a protein comprising an antibody against the tag or an antigen-binding fragment thereof (for example, scFv, Fab, or a nanobody) (for example, an antibody itself against the tag or an antigen-binding fragment thereof (for example, scFv, Fab, or a nanobody) bound to the membrane of the extracellular vesicle by a linker or the like, if necessary; a fusion protein in which a nanobody for the tag is bound to the N-terminus or C-terminus of a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof) in membrane under desired conditions (for example, the method using a PNE tag and an antibody against the tag described in Raj D, et al., Gut., 2019 Jun; 68(6): 1052-1064, and the like, may be referred to). Note that in a case of a T-cell stimulatory cytokine formed by multimers of subunits, when one of the subunits is a protein that can be presented outside membrane of an extracellular vesicle, the remaining subunits do not need to be in a form that can be presented outside the membrane. When one of the subunits is a

protein capable of being presented outside membrane of an extracellular vesicle, a functional T-cell stimulatory cytokine can be constructed outside the membrane of the extracellular vesicle by adding or co-expressing other subunits.

[0050] T-Cell Costimulatory Molecule

5 [0051] The “T-cell costimulatory molecule” used in the present specification means a molecule that can contribute to activation of T cells by interacting with a molecule present on membrane of a T cell such as CD28 or CD134. Examples of the T-cell costimulatory molecule include, but are not limited to, molecules such as CD80 and CD86, or extracellular domains thereof or functional fragments thereof; antibodies such
10 as an anti-CD28 antibody and an anti-CD134 antibody or antigen-binding fragments thereof (for example, scFv, Fab, or a nanobody); and a fusion protein (or a complex or an aggregate) of them with a transmembrane domain of another protein or an Fc portion of an antibody.

[0052] The T-cell costimulatory molecule described in the present specification may
15 be derived from any animal species. Examples of the T-cell costimulatory molecule include T-cell costimulatory molecules derived from animals such as mammals, for example, rodents such as a mouse, a rat, a hamster, and a guinea pig; lagomorph such as a rabbit; ungulates such as a pig, a cow, a goat, a horse, and a sheep; carnivora such as a dog and a cat; and primates such as a human, a monkey, a rhesus monkey, a crab-eating
20 macaque, a marmoset, an orangutan, and a chimpanzee. The T-cell costimulatory molecule described in the present specification is preferably derived from rodents or primates, and more preferably derived from a mouse or a human.

[0053] The T-cell costimulatory molecule described in the present specification may have an amino acid sequence identity of 80% or more, preferably 90% or more, more
25 preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more with respect to a wild-type amino acid sequence thereof (for example, in the case of CD80, for example, SEQ ID NO: 67 or the like), as long as it can exhibit the function described above. Alternatively, the T-cell costimulatory molecule described in the present specification may be obtained by deletion, insertion,
30 and/or substitution of one or a plurality of amino acids with respect to the wild-type amino acid sequence as long as it can exhibit the function thereof.

[0054] The “protein which comprises a T-cell costimulatory molecule and is capable of allowing the T-cell costimulatory molecule to interact with T cells” used in the present specification means a protein which comprises at least a T-cell costimulatory
35 molecule and is capable of interacting with a molecule present in membrane of the T cell. That is, it means that the at least a portion capable of interacting with T cells

present in the T-cell costimulatory molecule is located outside the membrane of the extracellular vesicle. The “protein which comprises a T-cell costimulatory molecule and is capable of allowing the T-cell costimulatory molecule to interact with T cells” may be expressed by using a plasmid or the like so that it is expressed in the membrane

5 of the extracellular vesicle. Alternatively, in a case where a soluble T-cell costimulatory molecule (examples thereof include, but are not limited to, a fusion protein of an extracellular domain of CD80 and an Fc portion of an antibody; and an anti-CD28 antibody or an antigen-binding fragment thereof (for example, scFv, Fab, or a nanobody)) is used, the “protein which comprises a T-cell costimulatory molecule and

10 is capable of allowing the T-cell costimulatory molecule to interact with T cells” may be a protein in which a soluble T-cell costimulatory molecule and an extracellular vesicle are bound to membrane of the extracellular vesicle by a lipid linker, a spacer sequence, or the like, if necessary (for example, the method described in JP 2018-104341 A or the like may be referred to). Alternatively, the protein may be a mixture

15 of a protein in which a desired tag (for example, a His tag, a FLAG tag, or a PNE tag) is added to the N-terminus or C-terminus of a soluble T-cell costimulatory molecule (the tag may be expressed as a fusion protein together with other constituent elements, for example, may be bound to an additionally prepared soluble T-cell costimulatory molecule by a linker or the like, if necessary), and an extracellular vesicle containing a

20 protein comprising an antibody against the tag or an antigen-binding fragment thereof (for example, scFv, Fab, or a nanobody) (for example, an antibody itself against the tag or an antigen-binding fragment thereof (for example, scFv, Fab, or a nanobody) bound to the membrane of the extracellular vesicle by a linker or the like, if necessary; a fusion protein in which a nanobody for the tag is bound to the N-terminus or C-terminus of a

25 membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof) in membrane under desired conditions (for example, the method using a PNE tag and an antibody against the tag described in Raj D, et al., Gut., 2019 Jun; 68(6): 1052-1064, and the like, may be referred to).

[0055] As the “membrane protein capable of being expressed in membrane of an

30 extracellular vesicle or the transmembrane domain thereof” used in the present specification, any membrane protein or a transmembrane domain thereof can be selected as long as it can be expressed in the membrane of the extracellular vesicle. The “membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof” is preferably a membrane protein known to

35 be capable of being expressed in an extracellular vesicle (for example, exosome or the like) (for example, a tetraspanin, CD58, ICAM-1, PTGFRN (for example, see Non

Patent Literature 1, WO 2019/183578 A, and the like), and the like), or a transmembrane domain thereof.

[0056] As the “protein capable of binding to membrane of an extracellular vesicle or the domain thereof” used in the present specification, any protein or a domain thereof
5 can be selected as long as it can be bound in the membrane of the extracellular vesicle. The “protein capable of binding to membrane of an extracellular vesicle or the domain thereof” is preferably a protein known to be capable of binding to membrane of an extracellular vesicle (for example, exosome or the like) (for example, MFG-E8 or a domain thereof (for example, a C1 or C2 domain of MFG-E8 described in Alain
10 Delcayre, et al., Blood Cells, Molecules, and Diseases 35 (2005) 158-168)).

[0057] The “membrane protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof” or the “protein capable of binding to membrane of an extracellular vesicle or the domain thereof” described in the present specification may be derived from any animal species. Examples of the T-cell
15 stimulatory cytokine include T-cell stimulatory cytokines derived from animals such as mammals, for example, rodents such as a mouse and a rat; lagomorph such as a rabbit, ungulates such as a pig, a cow, a goat, a horse, and a sheep; carnivora such as a dog and a cat; and primates such as a human, a monkey, a rhesus monkey, a crab-eating macaque, a marmoset, an orangutan, and a chimpanzee. The “membrane protein
20 capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof” or the “protein capable of binding to membrane of an extracellular vesicle or the domain thereof” described in the present specification is preferably derived from rodents or primates, and is more preferably derived from a mouse or a human.

25 [0058] According to Non Patent Literature 2, markers of mammalian extracellular vesicles are classified as follows.

Examples of a membrane protein or a GPI anchor protein that can be used as a marker protein of an extracellular vesicle include:

- 1) tissue non-specific
- 30 tetraspanins (CD63, CD9, CD81, and CD82), other multiple transmembrane type membrane proteins (CD47 and hetero trimer G proteins (guanine nucleotide-binding proteins (GNA)),
- MHC class I (HLA-A/B/C,H2-K/D/Q),
- integrin (ITGA/ITGB), a transferrin receptor (TFR2);
- 35 LAMP1/2;
- heparan sulfate proteoglycans ((including syndecan (SDC));

extracellular matrix metalloprotease inducer (EMMPRIN) (also referred to as BSG or CD147);

ADAM10;

CD73 that is a GPI anchored 5' nucleotidase (NT5E),

5 CD55 and CD59 that are GPI anchored complement binding proteins; and sonic hedgehog protein (SHH); and

2) cell/tissue specific

several tetraspanins: TSPAN8 (epithelial specific), CD37, and CD53 (leukocyte-specific);

10 PECAM1 (endothelial specific);

ERBB2 (breast cancer specific);

EPCAM (epithelial specific);

CD90 (THY1) (mesenchymal stem cell-specific);

CD45 (PTPRC) (immune cell-specific), CD41 (ITGA2B), or CD42a (GP9) (platelet-specific);

glycophorin A (GYPA) (erythroid specific);

CD14 (monocyte specific), MHC class II (HLA-DR/DP/DQ,H2-A);

CD3 (T cell specific);

acetylcholinesterase/AChE-S (neuronal cell-specific), AChE-E (erythroid specific); and

20 amyloid β A4/APP (neuronal cell-specific).

Therefore, although not limited thereto, a protein that is a marker of an extracellular vesicle may be used as the "membrane protein capable of being expressing in membrane of an extracellular vesicle" or the "the protein capable of binding to membrane of an extracellular vesicle" in the present invention.

[0059] The "tetraspanin" used in the present specification means a protein belonging to a tetraspanin family (for example, but are not limited to, CD9, CD53, CD63, CD81, CD82, CD151, and the like). The tetraspanin usually contains, from an N-terminal side thereof, a transmembrane domain 1 (hereinafter, referred to as "TM1"), a small extracellular loop (hereinafter, referred to as "SEL"), a transmembrane domain 2 (hereinafter, referred to as "TM2"), a small intracellular loop (hereinafter, referred to as "SIL"), a transmembrane domain 3 (hereinafter, referred to as "TM3"), a large extracellular loop (hereinafter, referred to as "LEL"), and a transmembrane domain 4 (hereinafter, referred to as "TM4"), and thus is a quadruple transmembrane type, and both the N-terminus and the C-terminus are present on the cytoplasmic side. For example, in a case where the tetraspanin is mouse CD63 (amino acid sequences: 1 to

238, SEQ ID NO: 27), the tetraspanin may typically contain TM1, SEL, TM2, SIL, and TM3 in the amino acid sequence from about 1 to about 110, LEL in the amino acid sequence from about 111 to about 200, and TM4 in the amino acid sequence from about 201 to about 238.

5 [0060] Each domain (for example, TM1, SEL, SIL, LTL, or the like) in the “tetraspanin” described in the present specification may be derived from the same tetraspanin, or may be derived from different tetraspanins in whole or in part.

[0061] The tetraspanin described in the present specification may have an amino acid sequence identity of 80% or more, preferably 90% or more, more preferably 95% or
10 more, still more preferably 98% or more, and further still more preferably 99% or more with respect to a wild-type amino acid sequence thereof (for example, in the case of CD9 with a full length, for example, SEQ ID NO: 21 or the like; in the case of CD63 with a full length, for example, SEQ ID NO: 27 or the like; and in the case of CD81 with a full length, for example, SEQ ID NO: 15 or the like), as long as it can be
15 expressed in the membrane of the extracellular vesicle. Alternatively, the tetraspanin described in the present specification may be obtained by deletion, insertion, and/or substitution of one or a plurality of amino acids with respect to the wild-type amino acid sequence as long as it can be expressed in the membrane of the extracellular vesicle.

[0062] A partial sequence of the tetraspanin (for example, each domain; a partial
20 sequence containing TM1, SEL, TM2, SIL, and TM3 (for example, in the case of CD63, SEQ ID NO: 57 or the like; and in the case of CD81, SEQ ID NO: 61 or the like); a partial sequence containing TM4 (for example, in the case of CD63, SEQ ID NO: 59 or the like; and in the case of CD81, SEQ ID NO: 63 or the like)) described in the present specification may have an amino acid sequence identity of 80% or more,
25 preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more with respect to a wild-type amino acid sequence thereof. Alternatively, the partial sequence of the tetraspanin described in the present specification may be obtained by deletion, insertion, and/or substitution of one or a plurality of amino acids with respect to the wild-type amino acid sequence.

30 [0063] MFG-E8 described in the present specification may have an amino acid sequence identity of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more with respect to a wild-type amino acid sequence thereof (for example, SEQ ID NO: 49 or the like), as long as it can bind to the membrane of the extracellular vesicle.

35 Alternatively, MFG-E8 described in the present specification may be obtained by deletion, insertion, and/or substitution of one or a plurality of amino acids with respect

to the wild-type amino acid sequence as long as it can bind to the membrane of the extracellular vesicle.

[0064] CD58, PTGFRN, or the like described in the present specification may have an amino acid sequence identity of 80% or more, preferably 90% or more, more preferably 5 95% or more, still more preferably 98% or more, and further still more preferably 99% or more with respect to a wild-type amino acid sequence thereof, as long as it can be expressed in the membrane of the extracellular vesicle or can bind to the membrane of the extracellular vesicle. Alternatively, CD58, PTGFRN, or the like described in the present specification may be obtained by deletion, insertion, and/or substitution of one 10 or a plurality of amino acids with respect to the wild-type amino acid sequence as long as it can be expressed in the membrane of the extracellular vesicle or can bind to the membrane of the extracellular vesicle.

[0065] Spacer Sequence

[0066] The "spacer sequence" used in the present specification means any sequence 15 having at least one amino acid residue that is present between two or more proteins or partial sequences or domains thereof. The spacer sequence can be used, for example, when two or more proteins or partial sequences or domains thereof are linked. The spacer sequence contains a peptide linker. A length of the amino acid residue of the spacer sequence is usually 1 to about 50, preferably about 2 to about 28, and more 20 preferably about 4 to about 25. Examples of the spacer sequence include, but are not limited to, $(GGGXS)_nG_m$ (wherein, X is independently A or G each time it appears, n is 1 to 8, and m is 0 to 3) (for example, SEQ ID NO: 5, 11, 29, 39, or the like); $(GGGS)_nG_m$ (wherein, n is 1 to 10, and m is 0 to 3); and $T_aS_b(GGX)_nG_m$ (wherein, X is independently S or T each time it appears, n is 1 to 8, m is 0 to 3, a is 0 or 1, and b is 0 25 or 1) (for example, SEQ ID NO: 77 or the like).

[0067] Antigen-Presenting Extracellular Vesicles Described in Present Specification

[0068] In an embodiment of the present invention, there is provided an extracellular vesicle presenting an antigen-presenting MHC molecule and a T-cell stimulatory cytokine outside membrane (the model is illustrated in (1) of Fig. 2J).

30 Such an extracellular vesicle may present an antigen-presenting MHC molecule and a T-cell stimulatory cytokine outside membrane thereof by containing proteins specified in the following (A) and (B), or may present an antigen-presenting MHC molecule and a T-cell stimulatory cytokine outside membrane thereof by containing a protein specified in (D).

35 Alternatively, an antigen-presenting MHC molecule and a T-cell stimulatory cytokine may be attached to membrane surface of an isolated extracellular vesicle later.

An attachment method is not particularly limited, an antigen-presenting MHC molecule and a T-cell stimulatory cytokine may be attached to membrane surface by binding each phospholipid to an antigen-presenting MHC molecule and a T-cell stimulatory cytokine and incorporating a new lipid moiety into membrane of an extracellular vesicle.

5 Phosphatidylserine is present on the surface of the extracellular vesicle. Therefore, each protein obtained by fusing an antigen-presenting MHC molecule or a T-cell stimulatory cytokine desired to be presented to MFG-E8 binding to phosphatidylserine is synthesized and purified, and the fusion protein and an extracellular vesicle are mixed, such that an extracellular vesicle presenting an antigen-presenting MHC
10 molecule and a T-cell stimulatory cytokine on membrane surface can be prepared. In addition, an antigen-presenting MHC molecule to which a PNEtag is attached and a T-cell stimulatory cytokine may be added later to an extracellular vesicle pre-expressing a peptide neoepitope (PNE) nanobody to be presented on membrane surface of the extracellular vesicle. A biotinylated antigen-presenting MHC molecule and a T-cell
15 stimulatory cytokine may be added to the extracellular vesicle expressing streptavidin to be presented on the membrane surface of the extracellular vesicle.

[0069] In an embodiment of the present invention, the extracellular vesicle may present a plurality of kinds (2, 3, 4, and 5 kinds) of antigen-presenting MHC molecules and a plurality of kinds (2, 3, 4, and 5 kinds) of T-cell stimulatory cytokines (in order to
20 identify each T-cell stimulatory cytokine, hereinafter, it may be referred to as a first T-cell stimulatory cytokine, a second T-cell stimulatory cytokine, third or higher T-cell stimulatory cytokines, and the like) outside the membrane. Alternatively, the extracellular vesicle may be an extracellular vesicle presenting one kind of an antigen-presenting MHC molecule and a plurality of kinds of cell stimulatory cytokines outside
25 membrane (a model of an extracellular vesicle presenting one kind of an antigen-presenting MHC molecule and two kinds of T-cell stimulatory cytokines outside membrane is illustrated in (3) of Fig. 2J).

[0070] In an embodiment of the present invention, there is provided an antigen-presenting extracellular vesicle the membrane of which contains:

30 (A) a protein which contains an antigen-presenting MHC molecule and is capable of presenting the antigen outside membrane; and

(B) a protein which contains a first T-cell stimulatory cytokine and is capable of presenting the first T-cell stimulatory cytokine outside membrane.

[0071] Constitutional Requirement (A)

35 The “protein which comprises an antigen-presenting MHC molecule and is capable of presenting the antigen outside membrane” of the (A) above may comprise

another protein or a domain thereof, or the like in addition to the antigen-presenting MHC molecule as long as it is a protein capable of presenting an antigen outside membrane of an extracellular vesicle.

[0072] In an embodiment of the present invention, the (A) above is a fusion protein or
5 a protein complex which comprises an antigen-presenting MHC molecule, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof, and is capable of presenting the antigen outside membrane.

10 [0073] In an embodiment of the present invention, the (A) above is a fusion protein or a protein complex which comprises an antigen-presenting MHC molecule, and a tetraspanin or a transmembrane domain thereof or MFG-E8 or a domain thereof, and is capable of presenting the antigen outside membrane.

[0074] In an embodiment of the present invention, the (A) above is
15 (A) a fusion protein capable of presenting an antigen peptide outside membrane, in which the fusion protein comprises an amino acid sequence consisting of, from an N-terminal side thereof,

- (A-1) an MHC molecule-restricted antigen peptide,
- (A-2) a spacer sequence which may be present,
- 20 (A-3) a single chain MHC molecule,
- (A-4) a spacer sequence which may be present, and
- (A-5) a tetraspanin, or

(A) a protein complex capable of presenting an antigen peptide outside membrane, in which the protein complex contains,
25 a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

- (A-1) an MHC molecule-restricted antigen peptide,
- (A-2) a spacer sequence which may be present,
- (A-3) an MHC class Ia chain, β_2 microglobulin, an MHC class II α chain, or
- 30 an MHC class II β chain,
- (A-4) a spacer sequence which may be present, and
- (A-5) a tetraspanin;

and
(A-6) a protein comprising an amino acid sequence of β_2 microglobulin, an
35 MHC class Ia chain, an MHC class II β chain, or an MHC class II α chain.

[0075] In an embodiment of the present invention, the (A) above is

(A) a fusion protein capable of presenting an antigen peptide outside membrane, in which the fusion protein comprises an amino acid sequence consisting of, from an N-terminal side thereof,

- (A-1) an MHC class I molecule-restricted antigen peptide,
- 5 (A-2) a spacer sequence which may be present,
- (A-3) a single chain MHC class I molecule,
- (A-4) a spacer sequence which may be present, and
- (A-5) a tetraspanin.

In addition, in an embodiment of the present invention, the (A) above is
10 (A) a fusion protein capable of presenting an antigen peptide outside membrane, in which the fusion protein contains an amino acid sequence consisting of, from an N-terminal side thereof,

- (A-1) an MHC class II molecule-restricted antigen peptide,
- (A-2) a spacer sequence which may be present,
- 15 (A-3) a single chain MHC class II molecule,
- (A-4) a spacer sequence which may be present, and
- (A-5) a tetraspanin.

[0076] In an embodiment of the present invention, the (A) above is

(A) a protein complex capable of presenting an antigen peptide outside
20 membrane, in which the protein complex contains:
a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

- (A-1) an MHC class I molecule-restricted antigen peptide,
- (A-2) a spacer sequence which may be present,
- 25 (A-3) β_2 microglobulin,
- (A-4) a spacer sequence which may be present, and
- (A-5) a tetraspanin;

and

(A-6) a protein comprising an amino acid sequence of an MHC class Ia chain.

30 In addition, in an embodiment of the present invention, the (A) above is

(A) a protein complex capable of presenting an antigen peptide outside membrane, in which the protein complex contains:

a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

- 35 (A-1) an MHC class I molecule-restricted antigen peptide,
- (A-2) a spacer sequence which may be present,

(A-3) an MHC class I α chain,
(A-4) a spacer sequence which may be present, and
(A-5) a tetraspanin;

and

5 (A-6) a protein comprising an amino acid sequence of β_2 microglobulin.

In addition, in an embodiment of the present invention, the (A) above is

(A) a protein complex capable of presenting an antigen peptide outside
membrane, in which the protein complex contains:

10 a fusion protein comprising an amino acid sequence consisting of, from an N-
terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence which may be present,

(A-3) an MHC class II β chain,

(A-4) a spacer sequence which may be present, and

15 (A-5) a tetraspanin; and

(A-6) a protein comprising an amino acid sequence of an MHC class II α chain.

In addition, in an embodiment of the present invention, the (A) above is

(A) a protein complex capable of presenting an antigen peptide outside
membrane, in which the protein complex contains:

20 a fusion protein comprising an amino acid sequence consisting of, from an N-
terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence which may be present,

(A-3) an MHC class II α chain,

25 (A-4) a spacer sequence which may be present, and

(A-5) a tetraspanin;

and

(A-6) a protein comprising an amino acid sequence of an MHC class II β chain.

[0077] In an embodiment of the present invention, in a case where the (A-3) above is a
30 "single chain MHC class I molecule", the "single chain MHC class I molecule" consists
of, from an N-terminal side thereof, β_2 microglobulin (for example, SEQ ID NO: 7 or
the like, or a sequence having an amino acid sequence identity thereto of 80% or more,
preferably 90% or more, more preferably 95% or more, still more preferably 98% or
more, and further still more preferably 99% or more), a spacer sequence which may be
35 present (when present, for example, SEQ ID NOS: 5, 11, 29, 39, 77, and the like), and
an MHC class I α chain (for example, SEQ ID NO: 9 or the like, or a sequence having an

amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more). In an embodiment of the present invention, in a case where the (A-3) above is a "single chain MHC class I molecule", the "single chain MHC class I molecule" contains SEQ ID NO: 65 or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more.

[0078] In an embodiment of the present invention, in a case where the (A-3) above is a "single chain MHC class II molecule", the "single chain MHC class II molecule"

consists of, from an N-terminal side thereof, an MHC class II β chain, a spacer sequence which may be present, and an MHC class II α chain.

[0079] In an embodiment of the present invention, in a case where the (A-3) and/or (A-6) above is " β_2 microglobulin", the " β_2 microglobulin" comprises SEQ ID NO: 7 or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more.

[0080] In an embodiment of the present invention, in a case where the (A-3) and/or (A-6) above is an "MHC class I α chain", the "MHC class I α chain" comprises SEQ ID NO: 9 or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more.

[0081] In an embodiment of the present invention, in a case where the (A-3) and/or (A-6) above is an "MHC class II β chain", the "MHC class II β chain" comprises SEQ ID NO: 37 or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more.

[0082] In an embodiment of the present invention, in a case where the (A-3) and/or (A-6) above is an "MHC class II α chain", the "MHC class II α chain" comprises SEQ ID NO: 71 or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more.

[0083] The "spacer sequence which may be present" of (A-2) and (A-4) in each of the embodiments may be independently selected when present. When (A-2) is present, for example, the spacer sequence may be, for example, a spacer sequence of SEQ ID NO: 5, 11, 29, 39, 77, or the like. When (A-4) is present, for example, the spacer sequence may be, for example, a spacer sequence of SEQ ID NO: 5, 11, 29, 39, 77, or the like.

[0084] In an embodiment of the present invention, the tetraspanin of (A-5) in each of the embodiments is selected from the group consisting of CD9, CD63, and CD81. In an embodiment of the present invention, the tetraspanin of (A-5) in each of the embodiments is CD81 (preferably, SEQ ID NO: 15 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

[0085] In an embodiment of the present invention, the (A) above is
(A) a fusion protein capable of presenting an antigen peptide outside
10 membrane, in which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class I molecule-restricted antigen peptide,
(A-2) a spacer sequence of SEQ ID NO: 5,
(A-3) a single chain MHC class I molecule of SEQ ID NO: 65 (or a
15 sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

[0086] In an embodiment of the present invention, the (A) above is
(A) a protein complex capable of presenting an antigen peptide outside
membrane, in which the protein complex contains:

25 a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,
(A-2) a spacer sequence of SEQ ID NO: 39,
(A-3) an MHC class II β chain of SEQ ID NO: 37 (or a sequence having an
30 amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

and

(A-6) an MHC class II α chain of SEQ ID NO: 71 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

[0087] Constitutional Requirement (B)

The “protein which comprises a first T-cell stimulatory cytokine and is capable of presenting the first T-cell stimulatory cytokine outside membrane” of the (B) above may comprise another protein or a domain thereof, or the like in addition to the first T-cell stimulatory cytokine as long as it is a protein capable of presenting the first T-cell stimulatory cytokine outside membrane.

[0088] In an embodiment of the present invention, the (B) above is a fusion protein which comprises a first T-cell stimulatory cytokine, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof, and is capable of presenting the first T-cell stimulatory cytokine outside membrane.

[0089] In an embodiment of the present invention, the (B) above is

(B) a fusion protein which comprises a first T-cell stimulatory cytokine and a partial sequence of a tetraspanin and is capable of presenting the first T-cell stimulatory cytokine outside membrane, in which the partial sequence of the tetraspanin contains at least two transmembrane domains and the first T-cell stimulatory cytokine is disposed between the two transmembrane domains, or

(B) a fusion protein which comprises a first T-cell stimulatory cytokine and MFG-E8 or a domain thereof and is capable of presenting the first T-cell stimulatory cytokine.

[0090] Examples of the expression “the partial sequence of the tetraspanin contains at least two transmembrane domains and the first T-cell stimulatory cytokine is disposed between the two transmembrane domains” used in the present specification include a case where the partial sequence of the tetraspanin contains at least TM1 and TM2 of the tetraspanin, and the first T-cell stimulatory cytokine is disposed between TM1 and TM2, and a case where the partial sequence of the tetraspanin contains at least TM3 and TM4 of the tetraspanin, and the first T-cell stimulatory cytokine is disposed between TM3 and TM4.

[0091] In an embodiment of the present invention, the (B) above is

(B) a fusion protein comprising an amino acid sequence consisting of, from an

N-terminal side thereof,

(B-1) a partial sequence of a tetraspanin containing, from an N-terminal side thereof, a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3,

5 (B-2) a spacer sequence which may be present,

(B-3) a first T-cell stimulatory cytokine,

(B-4) a spacer sequence which may be present, and

(B-5) a partial sequence of a tetraspanin containing a transmembrane domain 4,

10 (B) the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane, or

(B) a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

(B-3) a first T-cell stimulatory cytokine,

15 (B-4) a spacer sequence which may be present, and

(B-5) MFG-E8,

the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane.

[0092] As disclosed in WO 2016/139354 A, it has been reported that the tetraspanin can be expressed in membranes even when a large extracellular loop (LEL) thereof is entirely or partially replaced by a different amino acid sequence. Therefore, the first T-cell stimulatory cytokine of (B-3) may be inserted in place of the LEL of the tetraspanin or may be inserted at any site in the LEL of the tetraspanin or a partial sequence thereof, by a spacer sequence which may be present.

25 [0093] The “partial sequence of the tetraspanin containing a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3” of (B-1) usually does not contain a transmembrane domain 4 of the tetraspanin. The “partial sequence of the tetraspanin containing a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3” of (B-1) may contain a large extracellular loop or a partial sequence thereof. In (B-1), the transmembrane domain 1, the small extracellular loop, the transmembrane domain 2, the small intracellular loop, and the transmembrane domain 3 may be sequences derived from different tetraspanins, respectively, or all the domains may be sequences derived from the same tetraspanin. Preferably, in (B-1), all the transmembrane domain 1, the small extracellular loop, the transmembrane domain 2, the small intracellular loop, and the

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transmembrane domain 3 may be sequences derived from the same tetraspanin.

[0094] In an embodiment of the present invention, in (B-1), all the partial sequences of the tetraspanin containing a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3 are
5 partial sequences derived from CD9, CD63, or CD81. In an embodiment of the present invention, all the partial sequences of the tetraspanin containing a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3 of (B-1) are preferably partial sequences derived from CD63 or CD81 (preferably, SEQ ID NO: 57, SEQ ID NO: 61,
10 or the like, or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

[0095] The “partial sequence of the tetraspanin containing a transmembrane domain 4” of (B-5) usually does not contain a transmembrane domain 1, a small extracellular
15 loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3 of the tetraspanin. The “partial sequence of the tetraspanin containing a transmembrane domain 4” of (B-5) may contain a large extracellular loop or a partial sequence thereof. The transmembrane domain 4 in (B-5) may be a sequence derived from a tetraspanin different from that in (B-1), or may be a sequence derived from the
20 same tetraspanin as that in (B-1). Preferably, the transmembrane domain 4 in (B-5) is a sequence derived from the same tetraspanin as that in (B-1). In an embodiment of the present invention, in (B-5), the partial sequence of the tetraspanin containing a transmembrane domain 4 is a partial sequence derived from CD9, CD63, or CD81. In an embodiment of the present invention, the partial sequence of the tetraspanin
25 containing a transmembrane domain 4 of (B-5) is a partial sequence derived from CD63 or CD81 (preferably, SEQ ID NO: 59, SEQ ID NO: 63, or the like, or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

[0096] In an embodiment of the present invention, the “partial sequence of the tetraspanin containing a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3” of
30 (B-1) is a partial sequence derived from CD63 (preferably, SEQ ID NO: 57 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and the “partial sequence of the

tetraspanin containing a transmembrane domain 4” of (B-5) is a partial sequence derived from CD63 (preferably, SEQ ID NO: 59 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more). In an embodiment of the present invention, the “partial sequence of the tetraspanin containing a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3” of (B-1) is a partial sequence derived from CD81 (preferably, SEQ ID NO: 61 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and the “partial sequence of the tetraspanin containing a transmembrane domain 4” of (B-5) is a partial sequence derived from CD81 (preferably, SEQ ID NO: 63 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

[0097] The fusion protein of the (B) above is a fusion protein comprising a partial sequence of a tetraspanin, and in a case where one or more of the (A) above and (C) present in some cases described below contain a fusion protein comprising an amino acid sequence of a tetraspanin, the fusion protein of the (B) above may be a fusion protein different from the fusion protein of the (A) above and/or (C) present in some cases described below, or may constitute a part of the fusion protein of the (A) above and/or (C) present in some cases described below. The expression that the fusion protein of the (B) above “constitutes a part of the fusion protein of the (A) above and/or (C) present in some cases described below” includes, for example, a case where the tetraspanin of (A-5) constitutes the fusion protein of (B), and/or a case where a tetraspanin of (C-3) present in some cases described below is the fusion protein of (B).

[0098] The “MFG-E8” of the (B-5) above is preferably SEQ ID NO: 49 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more.

[0099] In an embodiment of the present invention, in (B-3) of each of the embodiments, the first T-cell stimulatory cytokine is IL-2, IL-4, IL-6, IL-12, or TGF- β . In an embodiment of the present invention, the first T-cell stimulatory cytokine in (B-3) in each of the embodiments is IL-2 (preferably, SEQ ID NO: 25 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably

90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), IL-4 (preferably, SEQ ID NO: 53 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), or TGF- β (preferably, SEQ ID NO: 73 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

[0100] The "spacer sequence which may be present" in (B-2) and (B-4) in each of the embodiments may be independently selected when present. When (B-2) is present, for example, the spacer sequence may be, for example, a spacer sequence of SEQ ID NO: 5, 11, 29, 39, 77, or the like. When (B-4) is present, for example, the spacer sequence may be, for example, a spacer sequence of SEQ ID NO: 5, 11, 29, 39, 77, or the like.

[0101] In an embodiment of the present invention, the (B) above is
(B) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(B-1) a partial sequence of a tetraspanin of SEQ ID NO: 57 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-2) a spacer sequence of SEQ ID NO: 29,

(B-3) a first T-cell stimulatory cytokine that is IL-2 of SEQ ID NO: 25 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 29, and

(B-5) a partial sequence of a tetraspanin of SEQ ID NO: 59 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane.

[0102] In an embodiment of the present invention, the (B) above is a fusion protein capable of presenting the first T-cell stimulatory cytokine of SEQ ID NO: 31 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and

further still more preferably 99% or more), outside membrane.

[0103] In an embodiment of the present invention, the (B) above is

(B) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

5 (B-1) a partial sequence of a tetraspanin of SEQ ID NO: 61 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-2) a spacer sequence of SEQ ID NO: 29,

10 (B-3) a first T-cell stimulatory cytokine that is IL-4 of SEQ ID NO: 53 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 29, and

15 (B-5) a partial sequence of a tetraspanin of SEQ ID NO: 63 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

20 the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane.

[0104] In an embodiment of the present invention, the (B) above is a fusion protein capable of presenting the first T-cell stimulatory cytokine of SEQ ID NO: 55 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and
25 further still more preferably 99% or more), outside membrane.

[0105] In an embodiment of the present invention, the above (B) is

(B) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

30 (B-3) a first T-cell stimulatory cytokine that is TGF- β of SEQ ID NO: 73 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 29, and

35 (B-5) MFG-E8 of SEQ ID NO: 49 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99%

or more),

the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane.

5 [0106] In an embodiment of the present invention, the (B) above is a fusion protein capable of presenting the first T-cell stimulatory cytokine of SEQ ID NO: 75 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), outside membrane.

[0107] Second (or Higher) T-Cell Stimulatory Cytokines

10 The antigen-presenting extracellular vesicle described in the present specification may further contain second (or higher) T-cell stimulatory cytokines in addition to the first T-cell stimulatory cytokine. Therefore, in an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification may further contain a second T-cell stimulatory cytokine. In particular,
15 in a case where the MHC molecule capable of presenting an antigen is an MHC class II molecule capable of presenting an antigen, it is preferable that the antigen-presenting extracellular vesicle described in the present specification contains a second T-cell stimulatory cytokine.

[0108] The second (or higher) T-cell stimulatory cytokines may be inserted into, for
20 example, the (B) above (for example, the second (or higher) T-cell stimulatory cytokines may be linked to the N-terminus and/or the C-terminus of the "first T-cell stimulatory cytokine" of (B-3) by a spacer sequence or the like, if necessary).

Alternatively, similar to the first T-cell stimulatory cytokine, the second (or higher) T-cell stimulatory cytokines may be contained in the membrane of the antigen-presenting
25 extracellular vesicle described in the present specification as a protein (or a fusion protein) different from the protein (or the fusion protein) of the constitutional requirement (B) described in the present specification by having the same configuration as that of the constitutional requirement (B) described in the present specification.

[0109] In an embodiment of the present invention, the second T-cell stimulatory
30 cytokine is IL-2, IL-4, IL-6, IL-12, or TGF- β . In an embodiment of the present invention, the second T-cell stimulatory cytokine is TGF- β (preferably, SEQ ID NO: 73 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

35 [0110] In an embodiment of the present invention, the first T-cell stimulatory cytokine is IL-2 or IL-4 (preferably, SEQ ID NO: 25, SEQ ID NO: 53, or the like or a sequence

having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and the second T-cell stimulatory cytokine is TGF- β (preferably, SEQ ID NO: 73 or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

[0111] In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a fusion protein or a protein complex which contains an antigen-presenting MHC molecule, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof, and is capable of presenting the antigen outside membrane; and

(B) a fusion protein which contains a first T-cell stimulatory cytokine, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof, and is capable of presenting the first T-cell stimulatory cytokine outside membrane.

[0112] In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a fusion protein or a protein complex which contains an antigen-presenting MHC molecule and a tetraspanin or a transmembrane domain thereof or MFG-E8 or a domain thereof, and is capable of presenting the antigen outside membrane; and

(B) a fusion protein which contains a first T-cell stimulatory cytokine and a partial sequence of a tetraspanin, and is capable of presenting the first T-cell stimulatory cytokine outside membrane, in which the partial sequence of the tetraspanin contains at least two transmembrane domains, and the first T-cell stimulatory cytokine is disposed between the two transmembrane domains, or

(B) a fusion protein which contains a first T-cell stimulatory cytokine and MFG-E8 or a domain thereof, and is capable of presenting the first T-cell stimulatory cytokine outside membrane.

[0113] In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a fusion protein capable of presenting an antigen peptide outside membrane, in which the fusion protein contains an amino acid sequence consisting of, from an N-terminal side thereof,

- (A-1) an MHC molecule-restricted antigen peptide,
- 5 (A-2) a spacer sequence which may be present,
- (A-3) a single chain MHC molecule,
- (A-4) a spacer sequence which may be present, and
- (A-5) a tetraspanin, or

(A) a protein complex capable of presenting an antigen peptide outside
10 membrane, in which the protein complex contains,
a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

- (A-1) an MHC molecule-restricted antigen peptide,
- (A-2) a spacer sequence which may be present,
- 15 (A-3) an MHC class I α chain, β_2 microglobulin, an MHC class II α chain, or an MHC class II β chain,
- (A-4) a spacer sequence which may be present, and
- (A-5) a tetraspanin,

and

- 20 (A-6) a protein comprising an amino acid sequence of β_2 microglobulin, an MHC class I α chain, an MHC class II β chain, or an MHC class II α chain; and

(B) a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

- (B-1) a partial sequence of a tetraspanin containing, from an N-terminal side
25 thereof, a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3,
- (B-2) a spacer sequence which may be present,
- (B-3) a first T-cell stimulatory cytokine,
- (B-4) a spacer sequence which may be present, and
- 30 (B-5) a partial sequence of a tetraspanin containing a transmembrane domain

4,

the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane, or

- (B) a fusion protein comprising an amino acid sequence consisting of, from an
35 N-terminal side thereof,
- (B-3) a first T-cell stimulatory cytokine,

(B-4) a spacer sequence which may be present, and

(B-5) MFG-E8,

the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane.

5 [0114] In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a fusion protein capable of presenting an antigen peptide outside membrane, in which the fusion protein contains an amino acid sequence consisting of,
10 from an N-terminal side thereof,

(A-1) an MHC class I molecule-restricted antigen peptide,

(A-2) a spacer sequence which may be present,

(A-3) a single chain MHC class I molecule,

(A-4) a spacer sequence which may be present, and

15 (A-5) a tetraspanin.

[0115] In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a protein complex capable of presenting an antigen peptide outside
20 membrane, in which the protein complex contains:

a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence which may be present,

25 (A-3) an MHC class II β chain,

(A-4) a spacer sequence which may be present, and

(A-5) a tetraspanin;

and

(A-6) a protein comprising an amino acid sequence of an MHC class II α
30 chain.

[0116] In an embodiment of the present invention, the first T-cell stimulatory cytokine is IL-2, IL-4, IL-6, IL-12, or TGF- β , and provides the antigen-presenting extracellular vesicle described in the present specification.

[0117] In an embodiment of the present invention, the antigen-presenting extracellular
35 vesicle is the extracellular vesicle described in the present specification that further presents a T-cell costimulatory molecule outside membrane (exemplifying a model

thereof in (2) of Fig. 2J).

Such an extracellular vesicle may present a T-cell costimulatory molecule outside membrane by containing a protein specified in the following (C) in membrane thereof.

5 Alternatively, a T-cell costimulatory molecule may be attached to membrane surface of an isolated extracellular vesicle later. An attachment method is not particularly limited, an antigen-presenting MHC molecule and a T-cell stimulatory cytokine may be attached to membrane surface by binding each phospholipid to a T-cell costimulatory molecule and incorporating a new lipid moiety into membrane of an
10 extracellular vesicle.

In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(C) a protein which comprises a T-cell costimulatory molecule and is capable
15 of allowing the T-cell costimulatory molecule to interact with T cells.

[0118] Constitutional Requirement (C)

The “protein which comprises a T-cell costimulatory molecule and is capable
of allowing the T-cell costimulatory molecule to interact with T cells” of the (C) above
may contain another protein or a domain thereof, or the like in addition to the T-cell
20 costimulatory molecule as long as it is a protein capable of allowing a T-cell
costimulatory molecule to interact with T cells.

[0119] In an embodiment of the present invention, the (C) above is a fusion protein
which comprises a T-cell costimulatory molecule, and a membrane protein capable of
being expressed in membrane of an extracellular vesicle or a transmembrane domain
25 thereof or a protein capable of binding to membrane of an extracellular vesicle or a
domain thereof, and is capable of allowing the T-cell costimulatory molecule to interact
with T cells.

[0120] In an embodiment of the present invention, the (C) above is a fusion protein
which comprises a T-cell costimulatory molecule, and a tetraspanin or a transmembrane
30 domain thereof or MFG-E8 or a domain thereof, and is capable of allowing the T-cell
costimulatory molecule to interact with T cells.

[0121] In an embodiment of the present invention, the above (C) is

(C) a fusion protein comprising an amino acid sequence consisting of, from an
N-terminal side thereof,

35 (C-1) a T-cell costimulatory molecule,
 (C-2) a spacer sequence which may be present, and

(C-3) a tetraspanin,

the fusion protein being capable of allowing the T-cell costimulatory molecule to interact with T cells.

[0122] In an embodiment of the present invention, the T-cell costimulatory molecule of (C-1) is CD80 or CD86. In an embodiment of the present invention, the T-cell costimulatory molecule in (C-1) is CD80 (preferably, SEQ ID NO: 67 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

[0123] The "spacer sequence which may be present" of (C-2) may be, for example, a spacer sequence of SEQ ID NO: 5, 11, 29, 39, 77, or the like when present.

[0124] In an embodiment of the present invention, the tetraspanin of (C-3) is selected from the group consisting of CD9, CD63, and CD81. In an embodiment of the present invention, the tetraspanin in (C-3) is CD9 (preferably, SEQ ID NO: 21 or the like or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

[0125] In an embodiment of the present invention, the above (C) is

(C) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(C-1) a T-cell costimulatory molecule that is CD80 of SEQ ID NO: 67 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(C-3) a tetraspanin of SEQ ID NO: 21 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein being capable of allowing the T-cell costimulatory molecule to interact with T cells.

[0126] In an embodiment of the present invention, the (C) above is a fusion protein capable of allowing the T-cell costimulatory molecule of SEQ ID NO: 69 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), to interact with T cells.

[0127] In an embodiment of the present invention, the antigen-presenting extracellular

vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

5 (A-1) an MHC class I molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 5,

(A-3) a single chain MHC class I molecule of SEQ ID NO: 65 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and
10 further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

15 the fusion protein being capable of presenting an antigen peptide outside membrane; and

(B) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(B-1) a partial sequence of a tetraspanin of SEQ ID NO: 57 (or a sequence
20 having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-2) a spacer sequence of SEQ ID NO: 29,

(B-3) a first T-cell stimulatory cytokine that is IL-2 of SEQ ID NO: 25 (or a
25 sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 29, and

(B-5) a partial sequence of a tetraspanin of SEQ ID NO: 59 (or a sequence
30 having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane.

35 [0128] In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular

vesicle the membrane of which contains:

(A) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class I molecule-restricted antigen peptide,

5 (A-2) a spacer sequence of SEQ ID NO: 5,

(A-3) a single chain MHC class I molecule of SEQ ID NO: 65 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

10 (A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

15 the fusion protein being capable of presenting an antigen peptide outside membrane; and

(B) a fusion protein capable of presenting the first T-cell stimulatory cytokine of SEQ ID NO: 31 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), outside
20 membrane.

[0129] In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

25 (A) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class I molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 5,

(A-3) a single chain MHC class I molecule of SEQ ID NO: 65 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably
30 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99%
35 or more),

the fusion protein capable of presenting an antigen peptide outside membrane;

(B) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(B-1) a partial sequence of a tetraspanin of SEQ ID NO: 57 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-2) a spacer sequence of SEQ ID NO: 29,

(B-3) a first T-cell stimulatory cytokine that is IL-2 of SEQ ID NO: 25 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 29, and

(B-5) a partial sequence of a tetraspanin of SEQ ID NO: 59 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane; and

(C) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(C-1) a T-cell costimulatory molecule that is CD80 of SEQ ID NO: 67 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(C-3) a tetraspanin of SEQ ID NO: 21 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein being capable of allowing the T-cell costimulatory molecule to interact with T cells.

[0130] In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class I molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 5,

(A-3) a single chain MHC class I molecule of SEQ ID NO: 65 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and
5 further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

10 the fusion protein capable of presenting an antigen peptide outside membrane;

(B) a fusion protein capable of presenting the first T-cell stimulatory cytokine of SEQ ID NO: 31 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), outside
15 membrane; and

(C) a fusion protein capable of allowing the T-cell costimulatory molecule of SEQ ID NO: 69 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), to interact with T cells.
20 [0131] In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a protein complex capable of presenting an antigen peptide outside membrane, in which the protein complex contains:

25 a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 39,

(A-3) an MHC class II β chain of SEQ ID NO: 37 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and
30

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);
35

and

(A-6) an MHC class II α chain of SEQ ID NO: 71 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

(B) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(B-1) a partial sequence of a tetraspanin of SEQ ID NO: 57 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-2) a spacer sequence of SEQ ID NO: 29,

(B-3) a first T-cell stimulatory cytokine that is IL-2 of SEQ ID NO: 25 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 29, and

(B-5) a partial sequence of a tetraspanin of SEQ ID NO: 59 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane; and

(C) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(C-1) a T-cell costimulatory molecule that is CD80 of SEQ ID NO: 67 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(C-3) a tetraspanin of SEQ ID NO: 21 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein being capable of allowing the T-cell costimulatory molecule to interact with T cells.

[0132] In an embodiment of the present invention, the antigen-presenting extracellular

vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a protein complex capable of presenting an antigen peptide outside membrane, in which the protein complex contains:

5 a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 39,

(A-3) an MHC class II β chain of SEQ ID NO: 37 (or a sequence having an
10 amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid
sequence identity thereto of 80% or more, preferably 90% or more, more preferably
15 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

and

(A-6) an MHC class II α chain of SEQ ID NO: 71 (or a sequence having an
amino acid sequence identity thereto of 80% or more, preferably 90% or more, more
20 preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

(B) a fusion protein capable of presenting the first T-cell stimulatory cytokine of SEQ ID NO: 31 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more
25 preferably 98% or more, and further still more preferably 99% or more), outside membrane; and

(C) a fusion protein capable of allowing the T-cell costimulatory molecule of SEQ ID NO: 69 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably
30 98% or more, and further still more preferably 99% or more), to interact with T cells.

[0133] In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a protein complex capable of presenting an antigen peptide outside
35 membrane, in which the protein complex contains:

a fusion protein of which an amino acid sequence consists of, from an N-

terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 39,

(A-3) an MHC class II β chain of SEQ ID NO: 37 (or a sequence having an
5 amino acid sequence identity thereto of 80% or more, preferably 90% or more, more
preferably 95% or more, still more preferably 98% or more, and further still more
preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid
sequence identity thereto of 80% or more, preferably 90% or more, more preferably
10 95% or more, still more preferably 98% or more, and further still more preferably 99%
or more);

and

(A-6) an MHC class II α chain of SEQ ID NO: 71 (or a sequence having an
amino acid sequence identity thereto of 80% or more, preferably 90% or more, more
15 preferably 95% or more, still more preferably 98% or more, and further still more
preferably 99% or more);

(B) a fusion protein of which an amino acid sequence consists of, from an N-
terminal side thereof,

(B-1) a partial sequence of a tetraspanin of SEQ ID NO: 57 (or a sequence
20 having an amino acid sequence identity thereto of 80% or more, preferably 90% or
more, more preferably 95% or more, still more preferably 98% or more, and further still
more preferably 99% or more),

(B-2) a spacer sequence of SEQ ID NO: 29,

(B-3) a first T-cell stimulatory cytokine that is IL-2 of SEQ ID NO: 25 (or a
25 sequence having an amino acid sequence identity thereto of 80% or more, preferably
90% or more, more preferably 95% or more, still more preferably 98% or more, and
further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 29, and

(B-5) a partial sequence of a tetraspanin of SEQ ID NO: 59 (or a sequence
30 having an amino acid sequence identity thereto of 80% or more, preferably 90% or
more, more preferably 95% or more, still more preferably 98% or more, and further still
more preferably 99% or more),

the fusion protein being capable of presenting the first T-cell stimulatory
cytokine outside membrane;

(B') a fusion protein of which an amino acid sequence consists of, from an N-
35 terminal side thereof,

(B-3) a second T-cell stimulatory cytokine that is TGF- β of SEQ ID NO: 73 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

5 (B-4) a spacer sequence of SEQ ID NO: 29, and

(B-5) MFG-E8 of SEQ ID NO: 49 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

10 the fusion protein being capable of presenting the second T-cell stimulatory cytokine outside membrane; and

(C) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

15 (C-1) a T-cell costimulatory molecule that is CD80 of SEQ ID NO: 67 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

20 (C-3) a tetraspanin of SEQ ID NO: 21 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein being capable of allowing the T-cell costimulatory molecule to interact with T cells.

[0134] In an embodiment of the present invention, the antigen-presenting extracellular
25 vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a protein complex capable of presenting an antigen peptide outside membrane, in which the protein complex contains:

30 a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 39,

35 (A-3) an MHC class II β chain of SEQ ID NO: 37 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

5 and

(A-6) an MHC class II α chain of SEQ ID NO: 71 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

10 (B) a fusion protein capable of presenting the first T-cell stimulatory cytokine of SEQ ID NO: 31 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), outside membrane;

15 (B') a fusion protein capable of presenting the second T-cell stimulatory cytokine of SEQ ID NO: 75 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), outside membrane; and

20 (C) a fusion protein capable of allowing the T-cell costimulatory molecule of SEQ ID NO: 69 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), to interact with T cells.

[0135] In an embodiment of the present invention, the antigen-presenting extracellular
25 vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a protein complex capable of presenting an antigen peptide outside membrane, in which the protein complex contains:

30 a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 39,

(A-3) an MHC class II β chain of SEQ ID NO: 37 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and
35

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

5 and

(A-6) an MHC class II α chain of SEQ ID NO: 71 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

10 (B) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(B-1) a partial sequence of a tetraspanin of SEQ ID NO: 61 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

15 (B-2) a spacer sequence of SEQ ID NO: 29,

(B-3) a first T-cell stimulatory cytokine that is IL-4 of SEQ ID NO: 53 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

20 (B-4) a spacer sequence of SEQ ID NO: 29, and

(B-5) a partial sequence of a tetraspanin of SEQ ID NO: 63 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

25 the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane; and

(C) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

30 (C-1) a T-cell costimulatory molecule that is CD80 of SEQ ID NO: 67 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(C-3) a tetraspanin of SEQ ID NO: 21 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99%

35

or more),

the fusion protein being capable of allowing the T-cell costimulatory molecule to interact with T cells.

[0136] In an embodiment of the present invention, the antigen-presenting extracellular vesicle described in the present specification is an antigen-presenting extracellular vesicle the membrane of which contains:

(A) a protein complex capable of presenting an antigen peptide outside membrane, in which the protein complex contains:

a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 39,

(A-3) an MHC class II β chain of SEQ ID NO: 37 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

and

(A-6) an MHC class II α chain of SEQ ID NO: 71 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

(B) a fusion protein capable of presenting the first T-cell stimulatory cytokine of SEQ ID NO: 55 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), outside membrane; and

(C) a fusion protein capable of allowing the T-cell costimulatory molecule of SEQ ID NO: 69 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), to interact with T cells.

[0137] In an embodiment of the present invention, as for the (A), (B), and (C) above, (A) and (B) may be fused to form one molecule, (B) and (C) may be fused to form one

molecule, and (A), (B), and (C) are fused to form one molecule. Such a fusion molecule may be translated as one protein molecule with or without a spacer sequence between (A), (B), and (C), or the proteins of (A), (B), and (C) may be fused by chemical crosslinking (for example, a disulfide bond between cysteine residues) to form one
5 molecule.

Alternatively, the (A), (B), and (C) above may be functionally fused by sharing an element for localizing the proteins thereof in the extracellular vesicle, that is, a site of a “membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof” or a “protein capable of binding to
10 membrane of an extracellular vesicle or a domain thereof”.

For example, in an embodiment of the present invention,
the antigen-presenting extracellular vesicle may also contain (D) a fusion protein comprising:

- (1) an antigen-presenting MHC molecule;
- 15 (2) at least one T-cell stimulatory cytokine; and
- (3) a “membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof” or a “protein capable of binding to membrane of an extracellular vesicle or a domain thereof”,

the fusion protein being fused in a form of sharing the site of the “membrane protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof” or the “protein capable of binding to membrane of an extracellular vesicle or the domain thereof” in (A) and (B);

a fusion protein (F) comprising:

- (1) an antigen-presenting MHC molecule;
- 25 (2) a T-cell costimulatory molecule; and
- (3) a “membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof” or a “protein capable of binding to membrane of an extracellular vesicle or a domain thereof”,

the fusion protein being fused in a form of sharing the site of the “membrane protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof” or the “protein capable of binding to membrane of an extracellular vesicle or the domain thereof” in (A) and (C);

a fusion protein (G) comprising:

- (1) at least one T-cell stimulatory cytokine;
- 35 (2) a T-cell costimulatory molecule; and
- (3) a “membrane protein capable of being expressed in membrane of an

extracellular vesicle or a transmembrane domain thereof” or a “protein capable of binding to membrane of an extracellular vesicle or a domain thereof”,

the fusion protein being fused in a form of sharing the site of the “membrane protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof” or the “protein capable of binding to membrane of an
5 extracellular vesicle or the domain thereof” in (B) and (C);

or,

a fusion protein (E) comprising:

- (1) an antigen-presenting MHC molecule;
- 10 (2) at least one T-cell stimulatory cytokine;
- (3) a T-cell costimulatory molecule; and

(4) a “membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof” or a “protein capable of binding to membrane of an extracellular vesicle or a domain thereof”,

15 the fusion protein being fused in a form of sharing the site of the “membrane protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof” or the “protein capable of binding to membrane of an extracellular vesicle or the domain thereof” in (A) to (C).

[0138] In an embodiment of the present invention, the antigen-presenting extracellular
20 vesicle may be an antigen-presenting extracellular vesicle containing a fusion protein (D) having the functions of the constitutional requirement (A) and the constitutional requirement (B) using the “protein which contains a first T-cell stimulatory cytokine and is capable of presenting the first T-cell stimulatory cytokine outside membrane” of the constitutional requirement (B), instead of the “membrane protein capable of being
25 expressed in membrane of an extracellular vesicle or the transmembrane domain thereof or the protein capable of binding to membrane of an extracellular vesicle” of the constitutional requirement (A).

[0139] Such a fusion protein (D) having the functions of the constitutional requirement (A) and the constitutional requirement (B) may be

30 (D) a fusion protein which contains an antigen-presenting MHC molecule and at least one T-cell stimulatory cytokine and is capable of presenting the antigen and the T-cell stimulatory cytokine outside membrane.

The fusion protein may contain the antigen-presenting MHC molecule, the at least one T-cell stimulatory cytokine, and a membrane protein capable of being
35 localized to membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a membrane-

binding domain thereof.

[0140] In the fusion protein (D) having the functions of the constitutional requirement (A) and the constitutional requirement (B), the membrane protein capable of being localized to membrane of an extracellular vesicle or the protein capable of binding to membrane of an extracellular vesicle may be a tetraspanin or MFG-E8.

The fusion protein may also comprise an amino acid sequence encoding, from an N-terminal side thereof,

(D-1) an MHC molecule-restricted antigen peptide,

(D-2) a spacer sequence which may be present,

(D-3) a single chain MHC molecule,

(D-4) a spacer sequence which may be present, and

(D-5) a fusion peptide comprising a tetraspanin or a transmembrane domain thereof or MFG-E8 or a transmembrane domain thereof, and the at least one T-cell stimulatory cytokine, in this order.

The fusion protein may also comprise an amino acid sequence encoding, from an N-terminal side thereof,

(D-1) a fusion peptide comprising a tetraspanin or a transmembrane domain thereof or MFG-E8 or a transmembrane domain thereof, and the at least one T-cell stimulatory cytokine,

(D-2) a spacer sequence which may be optionally present,

(D-3) a single chain MHC molecule,

(D-4) a spacer sequence which may be optionally present, and

(D-5) an MHC molecule-restricted antigen peptide, in this order.

Here, the fusion peptide may also comprise an amino acid sequence encoding, from an N-terminal side thereof,

(1) a partial sequence of a tetraspanin containing a transmembrane domain 1, a small intracellular loop, a transmembrane domain 2, a small extracellular loop, and a transmembrane domain 3,

(2) a spacer sequence which may be optionally present,

(3) the at least one T-cell stimulatory cytokine,

(4) a spacer sequence which may be optionally present, and

(5) a partial sequence of a tetraspanin containing a transmembrane domain 4, in this order.

The fusion peptide may also comprise an amino acid sequence encoding, from an N-terminal side thereof,

(1) the at least one of T-cell stimulatory cytokine,

- (2) a spacer sequence which may be optionally present, and
- (3) MFG-E8, in this order.

[0141] In an embodiment of the present invention, the MHC molecule-restricted antigen peptide is an MHC class I molecule-restricted antigen peptide, the single chain
5 MHC molecule may contain an extracellular domain of an MHC class I α chain, the MHC molecule-restricted antigen peptide is an MHC class II molecule-restricted antigen peptide, and the single chain MHC molecule may contain an extracellular domain of an MHC class II α chain and/or an extracellular domain of an MHC class II β chain.

10 [0142] In the aspect containing the fusion protein (D) having the functions of the constitutional requirement (A) and the constitutional requirement (B):

(C) a protein which comprises at least one T-cell costimulatory molecule and is capable of allowing the T-cell costimulatory molecule to interact with T cells may be further contained in the membrane;

15 the protein capable of interacting with T cells may also comprises the at least one T-cell costimulatory molecule, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof; and

20 the protein capable of interacting with T cells may also comprises the at least one T-cell costimulatory molecule, and a tetraspanin or a transmembrane domain thereof or MFG-E8 or a domain thereof.

[0143] In an embodiment of the present invention, the extracellular vesicle is an exosome.

[0144] The antigen-presenting extracellular vesicle in the present specification may
25 contain or be bound to a substance that may be therapeutically beneficial (for example, a low-molecular compound, a nucleic acid, or the like) inside the membrane thereof or in the membrane. Examples of a method for encapsulating the substance inside the membrane of the extracellular vesicle include, but are not limited to, a method in which the substance and the extracellular vesicle described in the present specification are
30 mixed in a suitable solvent.

In an embodiment of the present invention, the antigen-presenting extracellular vesicle may contain any protein preparation. The protein preparation is not particularly limited, but may be a protein that can also exist in nature such as erythropoietin, a synthetic protein that does not exist in nature such as an
35 immunoglobulin-CTLA4 fusion protein, or a monoclonal antibody or an active fragment thereof. These protein preparations are fusion proteins with a membrane

protein capable of being localized to membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a membrane-binding domain thereof, and may be localized on the surface of the antigen-presenting extracellular vesicle. Such an antigen-presenting
5 extracellular vesicle can be prepared by transfecting cells that produce antigen-presenting extracellular vesicles with a vector for expressing a fusion protein.

[0145] Each fusion protein or protein complex or a protein preparation contained in the membrane of the antigen-presenting extracellular vesicle described in the present specification may comprise one or a plurality of detectable labels. For example, the
10 fusion protein or the protein complex or the protein preparation may be labeled with a specific lipoprotein molecule, a fluorophore, a radioactive material, or an enzyme (for example, peroxidase or phosphatase), or the like by a conventional method. These labels may be linked to the N-terminus or the C-terminus of the fusion protein or the protein complex or the protein preparation, for example, as a constituent element of the
15 fusion protein or the protein complex or the protein preparation.

[0146] Polynucleotide

[0147] In an embodiment of the present invention, there is provided a polynucleotide encoding each fusion protein or protein complex in (A) and (B), and (C) present in some cases that are contained in the membrane of the antigen-presenting extracellular
20 vesicle described in the present specification. In an embodiment of the present invention, there is provided a polynucleotide encoding each fusion protein or protein complex in (A) to (G) defined in the present specification.

[0148] The “polynucleotide” used in the present specification means a single-stranded or double-stranded DNA molecule or RNA molecule, or the like. The polynucleotide
25 includes genomic DNA, cDNA, hnRNA, mRNA, and the like, and all naturally occurring or artificially modified derivatives thereof. The polynucleotide may be linear or cyclic.

[0149] The polynucleotide encoding each fusion protein or protein complex in (A) to (G) described above can be appropriately determined by those skilled in the art with
30 reference to the amino acid sequence of the fusion protein or protein complex. Note that the amino acid sequence of each fusion protein or protein complex in (A) to (G) can be appropriately determined with reference to the amino acid sequence of each constituent element (for example, in the case of (A), (A-1) to (A-5), and (A-6) in some cases) in each fusion protein or protein complex. Any type of codon can be selected
35 for use in determining a polynucleotide. For example, a polynucleotide may be determined in consideration of a frequency or the like of codons of cells to be

transformed using a vector comprising the polynucleotide.

[0150] To the N-terminus of the polynucleotide encoding each fusion protein or protein complex in (A) to (G) described above, a polynucleotide encoding a signal peptide (signal sequence) may be added, if necessary.

5 [0151] As an amino acid sequence of the signal peptide, any amino acid sequence can be used, and for example, the amino acid sequence of the signal peptide may be determined in consideration of an amino acid sequence of a fusion protein to be expressed, and the like. Examples of the polynucleotide encoding a signal peptide include a polynucleotide (for example, SEQ ID NO: 2) encoding a signal peptide (for
10 example, SEQ ID NO: 1) of β_2 microglobulin, a polynucleotide encoding a signal peptide of an MHC class I α chain, a polynucleotide encoding a signal peptide of an MHC class II α chain, and a polynucleotide (for example, SEQ ID NO: 34) encoding a signal peptide (for example, SEQ ID NO: 33) of an MHC class II β chain.

[0152] Information on each constituent element (for example, in the case of (A), (A-1)
15 to (A-5), and (A-6) in some cases) of each fusion protein or protein complex in (A) to (G) described above, the amino acid sequence such as a signal peptide, and the polynucleotide encoding them may be appropriately obtained by searching, for example, a database of known literatures, NCBI (<http://www.ncbi.nlm.nih.gov/guide/>), and the like. In addition, for the amino acid sequence in the partial sequence of the
20 tetraspanin (for example, the partial sequences in (C-1) and (C-5)) and the polynucleotide encoding the amino acid sequence, WO 2016/139354 A may be referred to.

[0153] In an embodiment of the present invention, there is provided a polynucleotide encoding any one of:

25 (A) a fusion protein capable of presenting an antigen peptide outside membrane, in which the fusion protein comprises an amino acid sequence consisting of, from an N-terminal side thereof,

(A-1) an MHC molecule-restricted antigen peptide,
(A-2) a spacer sequence which may be optionally present,
30 (A-3) a single chain MHC molecule,
(A-4) a spacer sequence which may be optionally present, and
(A-5) a tetraspanin, or

(A) a fusion protein constituting a protein complex capable of presenting an antigen peptide outside membrane,

35 in which the fusion protein comprises an amino acid sequence consisting of, from an N-terminal side thereof,

(A-1) an MHC molecule-restricted antigen peptide,
(A-2) a spacer sequence which may be optionally present,
(A-3) an MHC class I α chain, β_2 microglobulin, an MHC class II α chain, or
an MHC class II β chain,

5 (A-4) a spacer sequence which may be optionally present, and
(A-5) a tetraspanin;

(B) a fusion protein comprising an amino acid sequence consisting of, from an
N-terminal side thereof,

(B-1) a partial sequence of a tetraspanin containing, from an N-terminal side
10 thereof, a transmembrane domain 1, a small extracellular loop, a transmembrane
domain 2, a small intracellular loop, and a transmembrane domain 3,

(B-2) a spacer sequence which may be optionally present,

(B-3) a first T-cell stimulatory cytokine,

(B-4) a spacer sequence which may be optionally present, and

15 (B-5) a partial sequence of a tetraspanin containing a transmembrane domain
4,

the fusion protein being capable of presenting the first T-cell stimulatory
cytokine outside membrane, or

(B) a fusion protein comprising an amino acid sequence consisting of, from an
20 N-terminal side thereof,

(B-3) a first T-cell stimulatory cytokine,

(B-4) a spacer sequence which may be present, and

(B-5) MFG-E8,

25 the fusion protein being capable of presenting the first T-cell stimulatory
cytokine outside membrane; and

(C) a fusion protein comprising an amino acid sequence consisting of, from an
N-terminal side thereof,

(C-1) a T-cell costimulatory molecule,

(C-2) a spacer sequence which may be present, and

30 (C-3) a tetraspanin,

the fusion protein being capable of allowing the T-cell costimulatory molecule
to interact with T cells.

[0154] In an embodiment of the present invention, there provided a polynucleotide
encoding any one of:

35 (A) a fusion protein of which an amino acid sequence consists of, from an N-
terminal side thereof,

(A-1) an MHC class I molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 5,

(A-3) a single chain MHC class I molecule of SEQ ID NO: 65 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein being capable of presenting an antigen peptide outside membrane, or

(A) a fusion protein

of which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 39,

(A-3) an MHC class II β chain of SEQ ID NO: 37 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein constituting a protein complex capable of presenting an antigen peptide outside membrane;

(B) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(B-1) a partial sequence of a tetraspanin of SEQ ID NO: 57 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-2) a spacer sequence of SEQ ID NO: 29,

(B-3) a first T-cell stimulatory cytokine that is IL-2 of SEQ ID NO: 25 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and

further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 29, and

(B-5) a partial sequence of a tetraspanin of SEQ ID NO: 59 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or

5 more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane,

10 (B) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(B-1) a partial sequence of a tetraspanin of SEQ ID NO: 61 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

15 (B-2) a spacer sequence of SEQ ID NO: 29,

(B-3) a first T-cell stimulatory cytokine that is IL-4 of SEQ ID NO: 53 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

20 (B-4) a spacer sequence of SEQ ID NO: 29, and

(B-5) a partial sequence of a tetraspanin of SEQ ID NO: 63 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

25 the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane, or

(B') a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

30 (B-3) a second T-cell stimulatory cytokine that is TGF- β of SEQ ID NO: 73 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 29, and

35 (B-5) MFG-E8 of SEQ ID NO: 49 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99%

or more),

the fusion protein being capable of presenting the second (or first) T-cell stimulatory cytokine outside membrane; and

5 (C) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

(C-1) a T-cell costimulatory molecule that is CD80 of SEQ ID NO: 67 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

10 (C-3) a tetraspanin of SEQ ID NO: 21 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

15 the fusion protein being capable of allowing the T-cell costimulatory molecule to interact with T cells.

[0155] In an embodiment of the present invention, a polynucleotide encoding any one of:

(A) a fusion protein of which an amino acid sequence consists of, from an N-terminal side thereof,

20 (A-1) an MHC class I molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 5,

25 (A-3) a single chain MHC class I molecule of SEQ ID NO: 65 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

30 the fusion protein being capable of presenting an antigen peptide outside membrane, or

(A) a fusion protein

of which an amino acid sequence consists of, from an N-terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

35 (A-2) a spacer sequence of SEQ ID NO: 39,

(A-3) an MHC class II β chain of SEQ ID NO: 37 (or a sequence having an

amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

5 (A-5) a tetraspanin of SEQ ID NO: 15 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

the fusion protein constituting a protein complex capable of presenting an antigen peptide outside membrane;

10 (B) a fusion protein capable of presenting the first (or second) T-cell stimulatory cytokine of SEQ ID NO: 31, 75, or 55 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), outside membrane; and

15 (C) a fusion protein capable of allowing the T-cell costimulatory molecule of SEQ ID NO: 23 (or a sequence having an amino acid sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), to interact with T cells.
[0156] In an embodiment of the present invention, there are provided polynucleotides
20 including:

(A) a polynucleotide encoding a fusion protein capable of presenting an antigen peptide outside membrane, in which the polynucleotide comprises a sequence consisting of,

25 (A-1) a polynucleotide encoding an MHC class I molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 6,

(A-3) a single chain MHC class I molecule of SEQ ID NO: 66 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and
30

(A-5) a tetraspanin of SEQ ID NO: 16 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), or

35 (A) a polynucleotide encoding a fusion protein constituting a protein complex capable of presenting an antigen peptide outside membrane, in which the polynucleotide comprises a sequence consisting of,

(A-1) a polynucleotide encoding an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 40,

(A-3) an MHC class II β chain of SEQ ID NO: 38 (or a sequence having a
5 sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 16 (or a sequence having a sequence
10 identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

(B) a polynucleotide encoding a fusion protein capable of presenting a first T-cell stimulatory cytokine outside membrane, in which the polynucleotide comprises a sequence consisting of,

(B-1) a partial sequence of a tetraspanin of SEQ ID NO: 58 (or a sequence
15 having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-2) a spacer sequence of SEQ ID NO: 30,

(B-3) a first T-cell stimulatory cytokine that is IL-2 of SEQ ID NO: 26 (or a
20 sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 30, and

(B-5) a partial sequence of a tetraspanin of SEQ ID NO: 60 (or a sequence
25 having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B) a polynucleotide encoding a fusion protein capable of presenting a first T-cell stimulatory cytokine outside membrane, in which the polynucleotide comprises a
30 sequence consisting of,

(B-1) a partial sequence of a tetraspanin of SEQ ID NO: 62 (or a sequence
having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

35 (B-2) a spacer sequence of SEQ ID NO: 30,

(B-3) a first T-cell stimulatory cytokine that is IL-4 of SEQ ID NO: 54 (or a

sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 30, and

5 (B-5) a partial sequence of a tetraspanin of SEQ ID NO: 64 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), or

(B') a polynucleotide encoding a fusion protein capable of presenting a second
10 (or first) T-cell stimulatory cytokine outside membrane, in which the polynucleotide comprises a sequence consisting of,

(B-3) a second (or first) T-cell stimulatory cytokine that is TGF- β of SEQ ID NO: 74 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and
15 further still more preferably 99% or more),

(B-4) a spacer sequence of SEQ ID NO: 30, and

(B-5) MFG-E8 of SEQ ID NO: 50 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more); and
20 (C) a polynucleotide encoding a fusion protein capable of allowing the T-cell costimulatory molecule to interact with T cells, in which the polynucleotide comprises a sequence consisting of,

(C-1) a T-cell costimulatory molecule that is CD80 of SEQ ID NO: 68 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and
25

(C-3) a tetraspanin of SEQ ID NO: 22 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more).

30 [0157] In an embodiment of the present invention, there is provided a polynucleotide encoding:

(A) a polynucleotide encoding a fusion protein capable of presenting an antigen peptide outside membrane, in which the polynucleotide comprises a sequence consisting of,

35 (A-1) a polynucleotide encoding an MHC class I molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 6,

(A-3) a single chain MHC class I molecule of SEQ ID NO: 66 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 16 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), or

(A) a polynucleotide encoding a fusion protein constituting a protein complex capable of presenting an antigen peptide outside membrane, in which the polynucleotide comprises a sequence consisting of,

(A-1) a polynucleotide encoding an MHC class II molecule-restricted antigen peptide,

(A-2) a spacer sequence of SEQ ID NO: 40,

(A-3) an MHC class II β chain of SEQ ID NO: 38 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), and

(A-5) a tetraspanin of SEQ ID NO: 16 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more);

(B) a polynucleotide encoding a fusion protein capable of presenting the first (or second) T-cell stimulatory cytokine of SEQ ID NO: 32, 76, or 56 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), outside membrane; or

(C) a polynucleotide encoding a fusion protein capable of allowing the T-cell costimulatory molecule of SEQ ID NO: 24 (or a sequence having a sequence identity thereto of 80% or more, preferably 90% or more, more preferably 95% or more, still more preferably 98% or more, and further still more preferably 99% or more), to interact with T cells.

[0158] In an embodiment of the present invention, as for the (A), (B), and (C) above, (A) and (B) may be fused to form a polynucleotide encoding fusion proteins to be one molecule, (B) and (C) may be fused to form a polynucleotide encoding fusion proteins to be one molecule, and (A), (B), and (C) may be fused to form a polynucleotide encoding fusion proteins to be one molecule. Such a polynucleotide may encode one

fusion protein with or without a spacer sequence between (A), (B), and (C).

Alternatively, the polynucleotide in an embodiment of the present invention may encode a fusion protein obtained by functionally fusing the (A), (B), and (C) above by sharing an element for localizing the proteins thereof in the extracellular vesicle, that is, a site of a “membrane protein capable of being expressed in membrane of an
5 extracellular vesicle or a transmembrane domain thereof” or a “protein capable of binding to membrane of an extracellular vesicle or a domain thereof”.

For example, in an embodiment of the present invention,
the polynucleotide may be a polynucleotide encoding (D) a fusion protein
10 comprising:

- (1) an antigen-presenting MHC molecule;
- (2) at least one T-cell stimulatory cytokine; and
- (3) a “membrane protein capable of being expressed in membrane of an
extracellular vesicle or a transmembrane domain thereof” or a “protein capable of
15 binding to membrane of an extracellular vesicle or a domain thereof”,

the fusion protein being fused in a form of sharing the site of the “membrane protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof” or the “protein capable of binding to membrane of an extracellular vesicle or the domain thereof” in (A) and (B);

20 a polynucleotide encoding a fusion protein (F) containing:

- (1) an antigen-presenting MHC molecule;
- (2) a T-cell costimulatory molecule; and
- (3) a “membrane protein capable of being expressed in membrane of an
extracellular vesicle or a transmembrane domain thereof” or a “protein capable of
25 binding to membrane of an extracellular vesicle or a domain thereof”,

the fusion protein being fused in a form of sharing the site of the “membrane protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof” or the “protein capable of binding to membrane of an extracellular vesicle or the domain thereof” in (A) and (C);

30 a polynucleotide encoding a fusion protein (G) containing:

- (1) at least one T-cell stimulatory cytokine;
- (2) a T-cell costimulatory molecule; and
- (3) a “membrane protein capable of being expressed in membrane of an
extracellular vesicle or a transmembrane domain thereof” or a “protein capable of
35 binding to membrane of an extracellular vesicle or a domain thereof”,

the fusion protein being fused in a form of sharing the site of the “membrane

protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof” or the “protein capable of binding to membrane of an extracellular vesicle or the domain thereof” in (B) and (C);

or,

5 a polynucleotide encoding a fusion protein (E) containing:

- (1) an antigen-presenting MHC molecule;
- (2) at least one T-cell stimulatory cytokine;
- (2) a T-cell costimulatory molecule; and

(4) a “membrane protein capable of being expressed in membrane of an
10 extracellular vesicle or a transmembrane domain thereof” or a “protein capable of binding to membrane of an extracellular vesicle or a domain thereof”;

the fusion protein being fused in a form of sharing the site of the “membrane protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof” or the “protein capable of binding to membrane of an
15 extracellular vesicle or the domain thereof” in (A) to (C).

[0159] In an embodiment of the present invention, the polynucleotide may be a polynucleotide encoding a fusion protein which contains an antigen-presenting MHC molecule and at least one T-cell stimulatory cytokine and is capable of presenting the antigen and the T-cell stimulatory cytokine, the fusion protein being the fusion protein
20 (D) having the functions of the constitutional requirement (A) and the constitutional requirement (B) using the protein of the constitutional requirement (B) which contains a first T-cell stimulatory cytokine and is capable of presenting the first T-cell stimulatory cytokine outside membrane, instead of the membrane protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof
25 or the protein capable of binding to membrane of an extracellular vesicle of the constitutional requirement (A).

[0160] Such a fusion protein (D) having the functions of the constitutional requirement (A) and the constitutional requirement (B) may be a fusion protein which contains an antigen-presenting MHC molecule and at least one T-cell stimulatory
30 cytokine and is capable of presenting the antigen and the T-cell stimulatory cytokine outside membrane.

The fusion protein may comprise the antigen-presenting MHC molecule, the at least one T-cell stimulatory cytokine, and a membrane protein capable of being localized to membrane of an extracellular vesicle or a transmembrane domain thereof or
35 a protein capable of binding to membrane of an extracellular vesicle or a membrane-binding domain thereof.

[0161] In the fusion protein (D) having the functions of the constitutional requirement (A) and the constitutional requirement (B), the membrane protein capable of being localized to membrane of an extracellular vesicle or the protein capable of binding to membrane of an extracellular vesicle may be a tetraspanin or MFG-E8.

5 The fusion protein may also comprise an amino acid sequence encoding, from an N-terminal side thereof,

(D-1) an MHC molecule-restricted antigen peptide,

(D-2) a spacer sequence which may be optionally present,

(D-3) a single chain MHC molecule,

10 (D-4) a spacer sequence which may be optionally present, and

(D-5) a fusion peptide comprising a tetraspanin or a transmembrane domain thereof or MFG-E8 or a transmembrane domain thereof, and the at least one T-cell stimulatory cytokine, in this order.

15 The fusion protein may also contain an amino acid sequence encoding, from an N-terminal side thereof,

(D-1) a fusion peptide comprising a tetraspanin or a transmembrane domain thereof or MFG-E8 or a transmembrane domain thereof, and the at least one T-cell stimulatory cytokine,

(D-2) a spacer sequence which may be optionally present,

20 (D-3) a single chain MHC molecule,

(D-4) a spacer sequence which may be optionally present, and

(D-5) an MHC molecule-restricted antigen peptide, in this order.

(D-5) an MHC molecule-restricted antigen peptide, in this order.

25 Here, the fusion peptide may also comprise an amino acid sequence encoding, from an N-terminal side thereof,

(1) a partial sequence of a tetraspanin containing a transmembrane domain 1, a small intracellular loop, a transmembrane domain 2, a small extracellular loop, and a transmembrane domain 3,

(2) a spacer sequence which may be present,

30 (3) the at least one T-cell stimulatory cytokine,

(4) a spacer sequence which may be present, and

(5) a partial sequence of a tetraspanin containing a transmembrane domain 4, in this order.

35 The fusion peptide may also comprise an amino acid sequence encoding, from an N-terminal side thereof,

(1) the at least one of T-cell stimulatory cytokine,

- (2) a spacer sequence which may be present, and
- (3) MFG-E8, in this order.

[0162] In an embodiment of the present invention, the MHC molecule-restricted antigen peptide is an MHC class I molecule-restricted antigen peptide, the single chain MHC molecule may contain an extracellular domain of an MHC class Ia chain, the MHC molecule-restricted antigen peptide is an MHC class II molecule-restricted antigen peptide, and the single chain MHC molecule may contain an extracellular domain of an MHC class II α chain and/or an extracellular domain of an MHC class II β chain.

10 [0163] In the aspect containing the fusion protein (D) having the functions of the constitutional requirement (A) and the constitutional requirement (B):

(C) a protein which contains at least one T-cell costimulatory molecule and is capable of allowing the T-cell costimulatory molecule to interact with T cells may be further contained in the membrane;

15 the protein capable of interacting with T cells may also contain the at least one T-cell costimulatory molecule, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof; and

20 the protein capable of interacting with T cells may also contain the at least one T-cell costimulatory molecule, and a tetraspanin or a transmembrane domain thereof or MFG-E8 or a domain thereof.

[0164] Vector and Kit

[0165] In an embodiment of the present invention, there is provided a vector comprising at least one polynucleotide selected from the polynucleotides described in the present specification.

[0166] The "vector" used in the present specification means any vector (examples thereof include, but are not limited to, a plasmid vector, a cosmid vectors a phage vector such as a phage, a viral vector such as an adenovirus vector or a baculovirus vector, and an artificial chromosome vector). The vector includes an expression vector, a cloning vector, and the like. The expression vector may generally contain a desired coding sequence and an appropriate polynucleotide required for expression of an operably linked coding sequence in a host organism (for example, a plant, an insect, an animal, or the like) or in an in vitro expression system. The cloning vector may be used to manipulate and/or amplify a desired polynucleotide fragment. The cloning vector may delete functional sequences required for expression of a desired polynucleotide fragment.

[0167] In an embodiment of the invention, all the polynucleotides described in the present specification may be inserted into the same vector, or two or more polynucleotides may be inserted into different vectors, as long as they can be operably inserted. In an embodiment of the present invention, there is provided a kit containing
5 a combination of two or more vectors containing at least one polynucleotide selected from the polynucleotides described in the present specification.

[0168] Transformed cells

[0169] In an embodiment of the present invention, there is provided a cell transformed with a vector comprising,

- 10 (i) a polynucleotide encoding the fusion protein or the protein complex of (A) described in the present specification,
(ii) a polynucleotide encoding the fusion protein of (B) described in the present specification, and
(iii) a polynucleotide encoding the fusion protein of (C) described in the
15 present specification.

[0170] In an embodiment of the present invention, there is provided a cell transformed with a single vector or a combination of two or more vectors, the vector comprising,

- (i) a polynucleotide encoding the fusion protein or the protein complex of (A) described in the present specification,
20 (ii) a polynucleotide encoding the fusion protein of (B) described in the present specification, and optionally,
(iii) a polynucleotide encoding the fusion protein of (C) described in the present specification.

[0171] In the cell of an embodiment of the present invention, as for the (A), (B), and
25 (C) above, the cell may be transformed with a vector comprising a polynucleotide encoding fusion proteins to be one molecule obtained by fusing (A) and (B), a vector comprising a polynucleotide encoding fusion proteins to be one molecule obtained by fusing (B) and (C), or a vector comprising a polynucleotide encoding fusion proteins to be one molecule obtained by fusing (A), (B), and (C). Such a polynucleotide may
30 encode one fusion protein with or without a spacer sequence between (A), (B), and (C).

Alternatively, the polynucleotide may encode a fusion protein obtained by functionally fusing the (A), (B), and (C) above by sharing an element for localizing the proteins thereof in the extracellular vesicle, that is, a site of a “membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane
35 domain thereof” or a “protein capable of binding to membrane of an extracellular vesicle or a domain thereof”.

For example, in an embodiment of the present invention,
the cell may be transformed with a vector comprising a polynucleotide
encoding a fusion protein (D) comprising:

- (1) an antigen-presenting MHC molecule;
- 5 (2) at least one T-cell stimulatory cytokine; and
- (3) a "membrane protein capable of being expressed in membrane of an
extracellular vesicle or a transmembrane domain thereof" or a "protein capable of
binding to membrane of an extracellular vesicle or a domain thereof",

the fusion protein being fused in a form of sharing the site of the "membrane
10 protein capable of being expressed in membrane of an extracellular vesicle or the
transmembrane domain thereof" or the "protein capable of binding to membrane of an
extracellular vesicle or the domain thereof" in (A) and (B);

a vector comprising a polynucleotide encoding a fusion protein (F) comprising:

- (1) an antigen-presenting MHC molecule;
- 15 (2) a T-cell costimulatory molecule; and
- (3) a "membrane protein capable of being expressed in membrane of an
extracellular vesicle or a transmembrane domain thereof" or a "protein capable of
binding to membrane of an extracellular vesicle or a domain thereof",

the fusion protein being fused in a form of sharing the site of the "membrane
20 protein capable of being expressed in membrane of an extracellular vesicle or the
transmembrane domain thereof" or the "protein capable of binding to membrane of an
extracellular vesicle or the domain thereof" in (A) and (C);

a vector comprising a polynucleotide encoding a fusion protein (G)
comprising:

- 25 (1) at least one T-cell stimulatory cytokine;
- (2) a T-cell costimulatory molecule; and
- (3) a "membrane protein capable of being expressed in membrane of an
extracellular vesicle or a transmembrane domain thereof" or a "protein capable of
binding to membrane of an extracellular vesicle or a domain thereof",

30 the fusion protein being fused in a form of sharing the site of the "membrane
protein capable of being expressed in membrane of an extracellular vesicle or the
transmembrane domain thereof" or the "protein capable of binding to membrane of an
extracellular vesicle or the domain thereof" in (B) and (C);

or,

35 a vector comprising a polynucleotide encoding a fusion protein (E) comprising:
(1) an antigen-presenting MHC molecule;

(2) at least one T-cell stimulatory cytokine;
(3) a T-cell costimulatory molecule; and
(4) a “membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof” or a “protein capable of binding to membrane of an extracellular vesicle or a domain thereof”,

the fusion protein being fused in a form of sharing the site of the “membrane protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof” or the “protein capable of binding to membrane of an extracellular vesicle or the domain thereof” in (A) to (C).

[0172] Alternatively, in an embodiment of the present invention,

there is provided a cell transformed with a vector comprising,

(iv) a polynucleotide encoding the fusion protein of (D) described in the present specification, in which the fusion protein contains an antigen-presenting MHC molecule and at least one T-cell stimulatory cytokine and is capable of presenting the antigen and the T-cell stimulatory cytokine outside membrane, the fusion protein being the fusion protein having the functions of the constitutional requirement (A) and the constitutional requirement (B) using the protein of the constitutional requirement (B) which contains a first T-cell stimulatory cytokine and is capable of presenting the first T-cell stimulatory cytokine outside membrane, instead of the membrane protein capable of being expressed in membrane of an extracellular vesicle or the transmembrane domain thereof or the protein capable of binding to membrane of an extracellular vesicle of the constitutional requirement (A).

[0173] The expression “transformed with a single vector or a combination of two or more vectors” means that, for example, the cell may be transformed with a single vector in which all the polynucleotides (i) to (iv) are inserted into the same vector, or may be transformed with a combination of two or more vectors in which two or more of the polynucleotides (i) to (iv) are inserted into different vectors.

[0174] In a case where (A) is a fusion protein, examples of “a single vector or a combination of two or more vectors” include the followings:

- a vector comprising a polynucleotide encoding the fusion protein of (A) and a polynucleotide encoding the fusion protein of (B);
- a combination of a vector comprising a polynucleotide encoding the fusion protein of (A) and a vector comprising a polynucleotide encoding the fusion protein of (B);
- a vector comprising a polynucleotide encoding the fusion protein of (A), a polynucleotide encoding the fusion protein of (B), and a polynucleotide encoding the

fusion protein of (C);

- a combination of a vector comprising a polynucleotide encoding the fusion protein of (A) and a polynucleotide encoding the fusion protein of (B), and a vector comprising a polynucleotide encoding the fusion protein of (C);

5 • a combination of a vector comprising a polynucleotide encoding the fusion protein of (A) and a polynucleotide encoding the fusion protein of (C), and a vector comprising a polynucleotide encoding the fusion protein of (B);

 • a combination of a vector comprising a polynucleotide encoding the fusion protein of (B) and a polynucleotide encoding the fusion protein of (C), and a vector
10 comprising a polynucleotide encoding the fusion protein of (A); and

- a combination of a vector comprising a polynucleotide encoding the fusion protein of (A), a vector comprising a polynucleotide encoding the fusion protein of (B), and a vector comprising a polynucleotide encoding the fusion protein of (C).

[0175] Alternatively, in a case where (A) is a protein complex, examples of “a single
15 vector or a combination of two or more vectors” include the followings:

- a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5), a polynucleotide encoding a protein comprising (A-6), and a polynucleotide encoding the fusion protein of (B);

 • a combination of a vector comprising a polynucleotide encoding a fusion
20 protein comprising an amino acid sequence consisting of (A-1) to (A-5) and a polynucleotide encoding a protein comprising (A-6), and a vector comprising a polynucleotide encoding the fusion protein of (B);

 • a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5) and a
25 polynucleotide encoding the fusion protein of (B), and a vector comprising a polynucleotide encoding a protein comprising (A-6);

 • a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5) and a vector comprising a polynucleotide encoding a protein comprising (A-6) and a polynucleotide
30 encoding the fusion protein of (B);

 • a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5), a vector comprising a polynucleotide encoding a protein comprising (A-6), and a vector comprising a polynucleotide encoding the fusion protein of (B);

35 • a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5), a polynucleotide encoding a protein

comprising (A-6), a polynucleotide encoding the fusion protein of (B), and a polynucleotide encoding the fusion protein of (C);

- a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5), a
5 polynucleotide encoding a protein comprising (A-6), and a polynucleotide encoding the fusion protein of (B), and a vector comprising a polynucleotide encoding the fusion protein of (C);

- a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5), a
10 polynucleotide encoding the fusion protein of (B), and a polynucleotide encoding the fusion protein of (C), and a vector comprising a polynucleotide encoding a protein comprising (A-6);

- a combination of a vector comprising a polynucleotide encoding a protein comprising (A-6), a polynucleotide encoding the fusion protein of (B), and a
15 polynucleotide encoding the fusion protein of (C), and a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5);

- a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5), a
20 polynucleotide encoding a protein comprising (A-6), and a polynucleotide encoding the fusion protein of (C), and a vector comprising a polynucleotide encoding the fusion protein of (B);

- a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5) and a
25 polynucleotide encoding a protein comprising (A-6), and a vector comprising a polynucleotide encoding the fusion protein of (B) and a polynucleotide encoding the fusion protein of (C);

- a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5) and a
30 polynucleotide encoding the fusion protein of (B), and a vector comprising a polynucleotide encoding a protein comprising (A-6) and a polynucleotide encoding the fusion protein of (C);

- a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5) and a
35 polynucleotide encoding the fusion protein of (C), and a vector comprising a polynucleotide encoding a protein comprising (A-6) and a polynucleotide encoding the

fusion protein of (B);

- a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5), a vector comprising a polynucleotide encoding a protein comprising (A-6), and a vector comprising a polynucleotide encoding the fusion protein of (B) and a polynucleotide encoding the fusion protein of (C);

- a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5), a vector comprising a polynucleotide encoding the fusion protein of (B), and a vector comprising a polynucleotide encoding a protein comprising (A-6) and a polynucleotide encoding the fusion protein of (C);

- a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5), a vector comprising a polynucleotide encoding the fusion protein of (C), and a vector comprising a polynucleotide encoding a protein comprising (A-6) and a polynucleotide encoding the fusion protein of (B);

- a combination of a vector comprising a polynucleotide encoding a protein comprising (A-6), a vector comprising a polynucleotide encoding the fusion protein of (B), and a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5) and a polynucleotide encoding the fusion protein of (C);

- a combination of a vector comprising a polynucleotide encoding a protein comprising (A-6), a vector comprising a polynucleotide encoding the fusion protein of (C), and a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5) and a polynucleotide encoding the fusion protein of (B);

- a combination of a vector comprising a polynucleotide encoding the fusion protein of (B), a vector comprising a polynucleotide encoding the fusion protein of (C), and a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5) and a polynucleotide encoding a protein comprising (A-6); and

- a combination of a vector comprising a polynucleotide encoding a fusion protein comprising an amino acid sequence consisting of (A-1) to (A-5), a vector comprising a polynucleotide encoding a protein comprising (A-6), a vector comprising a polynucleotide encoding the fusion protein of (B), and a vector comprising a polynucleotide encoding the fusion protein of (C).

[0176] The cell to be transformed is not particularly limited as long as the antigen-presenting extracellular vesicle described in the present specification can be obtained after the transformation, and may be a primary cultured cell or an established cell, which may be a normal cell or a lesion cell containing cancerous or tumorigenic cells.

5 In addition, the origin of the cell to be transformed is not particularly limited, and examples thereof include cells derived from animals such as mammals, for example, rodents such as a mouse, a rat, a hamster, and a guinea pig; lagomorph such as a rabbit; ungulates such as a pig, a cow, a goat, a horse, and a sheep; carnivora such as a dog and a cat; and primates such as a human, a monkey, a rhesus monkey, a crab-eating
10 macaque, a marmoset, an orangutan, and a chimpanzee, plant-derived cells, and insect-derived cells. The cell to be transformed is preferably an animal-derived cell. Examples of the animal-derived cells include, but are not limited to, human embryonic kidney cells (including HEK293T cells and the like), human FL cells, Chinese hamster ovary cells (CHO cells), COS-7, Vero, mouse L cells, and rat GH3.

15 [0177] A method for transforming the cell is not particularly limited as long as it is a method capable of introducing a target polynucleotide into a cell. For example, the method for transforming the cell may be an electroporation method, a microinjection method, a calcium phosphate method, a cationic lipid method, a method using a liposome, a method using a non-liposomal material such as polyethyleneimine, a viral
20 infection method, or the like.

[0178] The transformed cell may be a transformed cell transiently expressing the fusion protein or protein complex of (A), (B), (C), (D), (E), (F), and/or (G), or a transformed cell (stable cell strain) stably expressing the fusion protein or protein complex of (A), (B), (C), (D), (E), (F), and/or (G).

25 [0179] The culture conditions of the cell to be transformed are not particularly limited. For example, when the transformed cell is an animal-derived cell, for example, a medium generally used for cell culture or the like (for example, an RPMI1640 medium, an Eagle's MEM medium, a Dulbecco's modified Eagle medium (DMEM medium), a Ham F12 medium, or any combination thereof), a medium obtained by adding other
30 components such as fetal bovine serum, antibiotics, and amino acids, or the like may be used, and the cell may be cultured (for example, under being left or shaking), for example, in the presence of about 1 to about 10% (preferably about 2 to about 5%) of CO₂ at about 30 to about 40°C (preferably about 37°C) for a predetermined time (for example, about 0.5 hours to about 240 hours (preferably about 5 to about 120 hours, and
35 more preferably about 12 to about 72 hours)).

[0180] A culture supernatant obtained by culturing the transformed cell may comprise

the antigen-presenting extracellular vesicles described in the present specification. Therefore, when the transformed cell is cultured to obtain the antigen-presenting extracellular vesicles described in the present specification, a medium (for example, a Dulbecco's modified Eagle medium or the like containing about 1 to about 5% fetal bovine serum from which exosomes are removed) from which extracellular vesicles such as exosomes are removed may be used, if necessary.

[0181] Culture Supernatant

[0182] In an embodiment of the present invention, a culture supernatant obtained by culturing the transformed cell described in the present specification is provided.

10 [0183] The antigen-presenting extracellular vesicles contained in the culture supernatant described in the present specification can be further collected, for example, by purifying (for example, centrifugation, chromatography, and the like), concentrating, and isolating the culture supernatant.

[0184] In an embodiment of the present invention, antigen-presenting extracellular vesicles obtained from the culture supernatant described in the present specification are provided.

[0185] Method for Preparing Antigen-Presenting Extracellular Vesicles Described in Present Specification

20 [0186] The antigen-presenting extracellular vesicles described in the present specification may be obtained by, for example, means such as genetic recombination techniques known to those skilled in the art (for example, by the method described below or by the method described in Examples), but the present invention is not limited to.

25 A polynucleotide encoding the proteins of (A) and (B) described above (or (D) instead of (A) and (B)), and if necessary, (C), respectively, is obtained by normal genetic recombination techniques, and can be operably inserted into the same or different vectors. In a case where two or more polynucleotides encoding the proteins of (A) and (B) (or (D) instead of (A) and (B)), and if necessary, (C), respectively, are inserted into the same vector, each of the polynucleotides may be operably linked to the same or different promoters. The obtained single or two or more vectors can be transformed into cells simultaneously or sequentially to obtain transformed cells (may be transformed cells that transiently express these fusion proteins, or may be transformed cells (stable strains) that stably express these fusion proteins). The obtained transformed cells are cultured under desired conditions to obtain a culture supernatant, and the obtained culture supernatant is purified (for example, purification using centrifugation, antibodies (for example, antibodies recognizing a protein or the

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like contained in membrane of an extracellular vesicle), chromatography, flow cytometry, or the like), concentrated (for example, ultrafiltration or the like), and dried, such that the antigen-presenting extracellular vesicles described in the present specification can be obtained.

5 [0187] Alternatively, in a case where soluble proteins are used as the proteins of (A) and (B) (or (D) instead of (A) and (B)) described above, and if necessary, (C), for example, the antigen-presenting extracellular vesicles described in the present specification may be obtained by the following method.

10 As soluble proteins, the (A) and (B) (or (D) instead of (A) and (B)) described above, and if necessary, (C) obtained by normal genetic recombination techniques are used, or commercially available products thereof may be used. Next, extracellular vesicles are obtained from desired cells, for example, by a known method, the method described in the present specification, or a method similar thereto. Next, the obtained extracellular vesicles and one or more the soluble proteins described above are reacted
15 in a desired solvent under desired conditions (for example, the method described in JP 2018-104341 A and the like may be referred to). The antigen-presenting extracellular vesicles described in the present specification can be obtained by carrying out this operation under appropriately changed conditions until the soluble proteins of (A) and (B) (or (D) instead of (A) and (B)), and if necessary, (C), are contained in the membrane
20 of the extracellular vesicle.

[0188] Alternatively, in a case where soluble proteins are used as the proteins of (A) and (B) (or (D) instead of (A) and (B)) described above, and if necessary, (C), for example, the antigen-presenting extracellular vesicles described in the present specification may be obtained by the following method.

25 As the soluble proteins of (A) and (B) (or (D) instead of (A) and (B)), and if necessary, (C), proteins containing a desired tag added to the N-terminus or C-terminus thereof (examples thereof include a His tag, a FLAG tag, and a PNE tag of SEQ ID NO: 79, and all the tags may be the same tag or different types of tags) are obtained by normal genetic recombination techniques. Next, extracellular vesicles are obtained
30 from the desired cells, for example, by known methods, the methods described in the present specification, or methods similar thereto, and antibodies against these tags or antigen-binding fragments thereof (for example, scFv, Fab, or a nanobody, such as an anti-PNE tag nanobody of SEQ ID NO: 83) and the like are bound to the extracellular vesicles via a peptide linker or the like, if necessary; alternatively, polynucleotides (for
35 example, SEQ ID NO: 88, 90, and the like) are obtained by normal genetic recombination techniques, the polynucleotides encoding a fusion protein (for example, a

fusion protein of SEQ ID NO: 89 of an anti-PNE nanobody (SEQ ID NO: 83), CD8a (SEQ ID NO: 85), and CD81 (SEQ ID NO: 15)) to which an antibody or an antigen-binding fragment thereof (for example, scFv, Fab, or a nanobody) at the N-terminus or C-terminus of a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof, or the like is bonded, transformed cells (the fusion protein may be a transformed cell that is transiently expressed or a transformed cell (stable strain) that is stably expressed) are obtained by transforming cells using the polynucleotides operably inserted into a vector, the obtained transformed cell are cultured or the like, and extracellular vesicles are recovered by the method described above and the like. The antigen-presenting extracellular vesicles described in the present specification may be obtained by mixing the soluble proteins (A) and (B), and if necessary, (C) to which a tag is added, and extracellular vesicles containing, in membranes thereof, proteins containing antibodies against to the tag or antigen-binding fragments thereof (for example, scFv, Fab, and a nanobody) under predetermined conditions.

[0189] Alternatively, the antigen-presenting extracellular vesicles described in the specification may be obtained from the transformed cells obtained by performing transformation using a combination of polynucleotides encoding the fusion proteins of (A) to (G).

[0190] Alternatively, the antigen-presenting extracellular vesicles described in the present specification may be obtained by a combination of two or more of the methods described above.

[0191] The antigen-presenting extracellular vesicles described in the present specification may recognize that the proteins of (A) and (B) (or (D) instead of (A) and (B)), and if necessary, (C) are contained in the membrane by, for example, methods such as flow cytometry, ELISA, and Western blotting.

[0192] In an embodiment of the present invention, there is provided a method for preparing the antigen-presenting extracellular vesicles described in the present specification, the method comprising collecting a culture supernatant obtained by culturing the transformed cells described in the present specification.

[0193] In an embodiment of the present invention, there is provided a method for preparing the antigen-presenting extracellular vesicles described in the present specification, the method comprising:

simultaneously or sequentially (preferably simultaneously) transforming cells with a single vector or a combination of two or more vectors, the vector comprising, (i) a polynucleotide encoding the fusion protein or the protein complex of (A)

described in the present specification,

(ii) a polynucleotide encoding the fusion protein of (B) described in the present specification, and optionally,

(iii) a polynucleotide encoding the fusion protein of (C) described in the present specification; and

collecting a culture supernatant obtained by culturing the obtained transformed cells.

Alternatively, in an embodiment of the present invention, there is provided a method for preparing the antigen-presenting extracellular vesicles described in the present specification, the method comprising:

simultaneously or sequentially (preferably simultaneously) transforming cells with a single vector or a combination of two or more vectors, the vector comprising,

(iv) a polynucleotide encoding the fusion protein of (D) described in the present specification, in which the fusion protein comprises an antigen-presenting MHC molecule and at least one T-cell stimulatory cytokine and is capable of the antigen and the T-cell stimulatory cytokine outside membrane, and optionally,

(iii) a polynucleotide encoding the fusion protein of (C) described in the present specification; and

collecting a culture supernatant obtained by culturing the obtained transformed cells.

Alternatively, in an embodiment of the present invention, there is provided a method for preparing the antigen-presenting extracellular vesicles described in the present specification, the method comprising:

transforming cells with a vector comprising,

(v) a polynucleotide encoding the fusion protein of (E) described in the present specification, in which the fusion protein contains an antigen-presenting MHC molecule, at least one T-cell stimulatory cytokine, and a T-cell costimulatory molecule, and is capable of the antigen and the T-cell stimulatory cytokine outside membrane; and

collecting a culture supernatant obtained by culturing the obtained transformed cells.

[0194] In an embodiment of the present invention, antigen-presenting extracellular vesicles obtained from the culture supernatant described in the present specification are provided.

[0195] In an embodiment of the present invention, there is provided an antigen-presenting extracellular vesicle obtained by a method comprising:

simultaneously or sequentially (preferably simultaneously) transforming cells

with a single vector or a combination of two or more vectors, the vector comprising,

(i) a polynucleotide encoding the fusion protein or the protein complex of (A) described in the present specification,

5 (ii) a polynucleotide encoding the fusion protein of (B) described in the present specification, and optionally,

(iii) a polynucleotide encoding the fusion protein of (C) described in the present specification; and

collecting a culture supernatant obtained by culturing the obtained transformed cells.

10 Alternatively, in an embodiment of the present invention, there is provided an antigen-presenting extracellular vesicle obtained by a method comprising:

simultaneously or sequentially (preferably simultaneously) transforming cells with a single vector or a combination of two or more vectors, the vector comprising,

15 (iv) a polynucleotide encoding the fusion protein of (D) described in the present specification, in which the fusion protein comprises an antigen-presenting MHC molecule and at least one T-cell stimulatory cytokine and is capable of the antigen and the T-cell stimulatory cytokine outside membrane, and optionally,

(iii) a polynucleotide encoding the fusion protein of (C) described in the present specification; and

20 collecting a culture supernatant obtained by culturing the obtained transformed cells.

Alternatively, in an embodiment of the present invention, there is provided an antigen-presenting extracellular vesicle obtained by a method comprising:

transforming cells with,

25 (v) a polynucleotide encoding the fusion protein of (E) described in the present specification, in which the fusion protein comprises an antigen-presenting MHC molecule, at least one T-cell stimulatory cytokine, and a T-cell costimulatory molecule, and is capable of the antigen and the T-cell stimulatory cytokine outside membrane; and

30 collecting a culture supernatant obtained by culturing the obtained transformed cells.

[0196] Composition and Use

[0197] In an embodiment of the present invention, there is provided a composition (for example, a pharmaceutical composition) containing the antigen-presenting extracellular vesicle described in the present specification, a polynucleotide and/or a vector
35 comprising the same, and/or a transformed cell and/or a culture supernatant thereof. In an embodiment of the present invention, there is provided a pharmaceutical composition

containing the antigen-presenting extracellular vesicle described in the present specification or the culture supernatant described in the present specification.

- [0198] Examples of the composition (for example, the pharmaceutical composition) described in the present specification comprise, but are not limited to, additives such as
- 5 an excipient, a lubricant, a binder, a disintegrant, a pH regulator, a solvent, a solubilizing aid, a suspending agent, an isotonicifier, a buffer, an analgesic, a preservative, an antioxidant, a colorant, a sweetener, and a surfactant. Those skilled in the art can appropriately select the types of these additives, the amount of these additives used, and the like depending on the purpose. In a case where the
- 10 pharmaceutical composition is used, these additives are preferably pharmacologically acceptable carriers. Furthermore, in a case where the composition described in the present specification contains a polynucleotide, it is preferable to contain carriers suitable for a drug delivery (DD) of nucleic acids, although not required, and examples of these carriers include lipid nanoparticles (LNP) and polymers (for example, PEI).
- 15 [0199] The composition (for example, the pharmaceutical composition) described in the present specification can be formulated into, for example, a tablet, a coated tablet, an orally disintegrating tablet, a chewable agent, a pill, granules, fine granules, a powder, a hard capsule, a soft capsule, a solution (examples thereof include a syrup, an injection, and a lotion), a suspension, an emulsion, a jelly, a patch, an ointment, a
- 20 cream, an inhalant, a suppository, and the like by a method known per se together with the additives described above. The composition may be an oral agent or a parenteral agent. The formulated composition may further contain other beneficial components (for example, other therapeutically beneficial components) depending on the purpose thereof.
- 25 [0200] The composition according to an embodiment of the present invention can enhance acquired immunity (cellular immunity and/or humoral immunity) to a specific antigen as shown in test examples, and can be used as a pharmaceutical composition for treating or preventing an infectious disease caused by an infectious pathogen when a peptide derived from an infectious pathogen (pathogenic bacteria, viruses, or the like) is
- 30 used as an antigen.

In addition, as shown in the test examples, the composition according to an embodiment of the present invention can eliminate infectious pathogens by allowing induction of inflammatory cytokines and activating innate immunity (including mobilizing and activating neutrophils, monocytes, macrophages, and the like to

35 phagocytize pathogenic bacteria), and can be used as a pharmaceutical composition for treating or preventing an infectious disease caused by infectious pathogens.

[0201] The antigen-presenting extracellular vesicle (preferably the antigen-presenting extracellular vesicle containing an MHC class I-restricted antigen peptide and an MHC class I molecule in the membrane), the polynucleotide and/or the vector comprising the same, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the composition comprising them (for example, the pharmaceutical composition) may be useful for treating or preventing cancer.

[0202] Therefore, in an embodiment of the present invention, there are provided, for treating or preventing cancer, the antigen-presenting extracellular vesicle, the polynucleotide and/or the vector comprising the polynucleotide, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the composition (for example, a pharmaceutical composition) comprising them. As shown in the test examples, the antigen-presenting extracellular vesicles and the like according to an embodiment of the present invention can proliferate and activate antigen-specific cytotoxic T cells to be used, and when a tumor-associated antigen peptide is used as an antigen to be used, the proliferated and activated cytotoxic T cells recognize and attack cancer cells, such that the cancer cells can be killed.

[0203] In another embodiment of the present invention, there is provided a use of the antigen-presenting extracellular vesicle, the polynucleotide and/or the vector comprising the polynucleotide, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the composition (for example, a pharmaceutical composition) comprising them, in the manufacture of a medicament for treating or preventing cancer.

[0204] In still another embodiment of the present invention, there is provided a method for treating or preventing cancer, the method including administering an effective amount of the antigen-presenting extracellular vesicle, the polynucleotide and/or the vector comprising the polynucleotide, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the composition comprising them to a subject in need thereof.

[0205] The cancer includes any solid cancer or blood cancer, and examples thereof include, but are not limited to, small cell lung cancer, non-small cell lung cancer, breast cancer, esophageal cancer, stomach cancer, small intestine cancer, large intestine cancer, colon cancer, rectal cancer, pancreatic cancer, prostate cancer, bone marrow cancer, kidney cancer (including kidney cell cancer), parathyroid cancer, adrenal cancer, ureteral cancer, liver cancer, bile duct cancer, cervical cancer, ovarian cancer (for example, the tissue type thereof is serous gland cancer, mucous gland cancer, clear cell adenocarcinoma cancer, and the like), testicular cancer, bladder cancer, external

5 pudendal cancer, penis cancer, thyroid cancer, head and neck cancer, craniopharyngeal cancer, pharyngeal cancer, tongue cancer, skin cancer, Merkel cell cancer, melanoma (malignant melanoma and the like), epithelial cancer, squamous cell carcinoma, basal cell cancer, childhood cancer, unknown primary cancer, fibrosarcoma, mucosal
10 sarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, spinal cord tumor, angiosarcoma, lymphangiosarcoma, lymphangiosarcoma, Kaposi's sarcoma, leiomyosarcoma, rhabdomyosarcoma, synovial tumor, mesothelioma, ewing tumor, seminoma, Wilms tumor, brain tumor, glioma, glioblastoma, astrocytoma, myeloblastoma, meningioma, neuroblastoma, medulloblastoma, retinoblastoma, spinal
15 tumor, malignant lymphoma (for example, non-Hodgkin's lymphoma, Hodgkin's lymphoma, and the like), chronic or acute lymphocytic leukemia, and adult T-cell leukemia.

[0206] In an embodiment of the present invention, immune checkpoint inhibitors can be used in combination to treat or prevent cancer. The immune checkpoint inhibitors
15 may be administered simultaneously or sequentially to a patient, or may be contained in the pharmaceutical according to the present invention.

Examples of the immune checkpoint inhibitor include, but are not limited to, a PD-1 inhibitor (for example, an anti-PD-1 antibody such as nivolumab or pembrolizumab), a CTLA-4 inhibitor (for example, an anti-CTLA-4 antibody such as
20 ipilimumab), and a PD-L1 inhibitor (for example, an anti-PD-L1 antibody such as durvalumab, atezolizumab, or avelumab). In a case where the immune checkpoint inhibitor is an antibody or an active fragment thereof, the antibody or the active fragment thereof may be bound to a membrane protein capable of being localized onto membrane of an extracellular vesicle or a transmembrane domain thereof or a protein
25 capable of binding to membrane of an extracellular vesicle or a membrane-binding domain thereof to be present on the membrane of the extracellular vesicle according to the present invention.

A combination of these immune checkpoint inhibitors enhances cytotoxicity against cancer cells.

30 [0207] The antigen-presenting extracellular vesicle (preferably the antigen-presenting extracellular vesicle containing an MHC class II-restricted antigen peptide and an MHC class II molecule in the membrane), the polynucleotide and/or the vector comprising the same, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the composition comprising them may be useful for treating or
35 preventing an autoimmune disease. As exemplified in the test examples, the antigen-presenting extracellular vesicles according to an embodiment of the present invention

can proliferate and activate antigen-specific regulatory T cells (Treg) to be used, and when an auto-antigen peptide is used as an antigen to be used, the proliferated and activated Treg induces tolerance to the auto-antigen, such that the autoimmune disease can be treated or prevented.

5 [0208] Therefore, in an embodiment of the present invention, there are provided, for treating or preventing an autoimmune disease, the antigen-presenting extracellular vesicle, the polynucleotide and/or the vector comprising the polynucleotide, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the composition (for example, a pharmaceutical composition)
10 comprising them.

[0209] In another embodiment of the present invention, there is provided a use of the antigen-presenting extracellular vesicle, the polynucleotide and/or the vector comprising the polynucleotide, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the composition (for example, a
15 pharmaceutical composition) containing them, for producing a pharmaceutical for treating or preventing an autoimmune disease.

[0210] In still another embodiment of the present invention, there is provided a method for treating or preventing an autoimmune disease, the method including administering an effective amount of the antigen-presenting extracellular vesicle, the
20 polynucleotide and/or the vector comprising the polynucleotide, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the composition containing them to a subject who requires them.

[0211] Examples of the autoimmune disease include, but are not limited to, asthma, psoriasis, systemic erythematosus, Guillain-Barre syndrome, Sjogren's syndrome,
25 multiple sclerosis, myasthenia gravis, malignant anemia, Basedow's disease, Hashimoto thyroiditis, type I diabetes, Crohn's disease, inflammatory bowel disease, and rheumatoid arthritis.

[0212] The antigen-presenting extracellular vesicle (preferably the antigen-presenting extracellular vesicle containing an MHC class II-restricted antigen peptide and an MHC class II molecule in the membrane), the polynucleotide and/or the vector comprising the
30 same, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the composition comprising them (for example, the pharmaceutical composition) may be useful for treating or preventing an allergic disease. As shown in the test examples, the antigen-presenting extracellular vesicles
35 according to an embodiment of the present invention can proliferate and activate antigen-specific regulatory T cells (Treg) to be used, and when an allergen is used as an

antigen to be used, the proliferated and activated Treg induces tolerance to the allergen, such that the allergic disease can be treated or prevented.

[0213] Therefore, in an embodiment of the present invention, there are provided, for treating or preventing an allergic disease, the antigen-presenting extracellular vesicle,
5 the polynucleotide and/or the vector comprising the polynucleotide, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the composition (for example, a pharmaceutical composition) containing them.

[0214] In another embodiment of the present invention, there is provided a use of the
10 antigen-presenting extracellular vesicle, the polynucleotide and/or the vector comprising the polynucleotide, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the composition (for example, a pharmaceutical composition) comprising them, for producing a pharmaceutical for treating or preventing an allergic disease.

[0215] In still another embodiment of the present invention, there is provided a method for treating or preventing an allergic disease, the method including
15 administering an effective amount of the antigen-presenting extracellular vesicle, the polynucleotide and/or the vector comprising the polynucleotide, and/or the transformed cell and/or the culture supernatant thereof described in the present specification, or the
20 composition containing them to a subject who requires them.

[0216] Examples of the allergic disease include, but are not limited to, allergic rhinitis, atopic dermatitis, allergic asthma, allergic conjunctivitis, allergic gastro-enteritis, food allergies, drug allergies, and urticaria.

[0217] Examples of the subject to be treated or prevented from the various diseases
25 described above include, but are not limited to, animals such as mammals, for example, rodents such as a mouse, a rat, a hamster, and a guinea pig; lagomorph such as a rabbit; ungulates such as a pig, a cow, a goat, a horse, and a sheep; carnivora such as a dog and a cat; and primates such as a human, a monkey, a rhesus monkey, a crab-eating macaque, a marmoset, an orangutan, and a chimpanzee; and plants. The subject is
30 preferably an animal, more preferably a rodent or a primate, and still more preferably a mouse or a human.

[0218] A dosage of a formulation obtained by formulating the antigen-presenting extracellular vesicle, the polynucleotide and/or the vector comprising the polynucleotide, and/or the transformed cell and/or the culture supernatant thereof
35 described in the present specification, or the composition containing them can be appropriately determined in consideration of a gender, an age, a weight, a health status,

a degree of medical condition, or a diet of a subject to be administered, an administration time, an administration method, a combination with other drugs, and other factors.

[0219] Method for Activating, Proliferating, and/or Differentiating T cells against Specific Antigen

[0220] The antigen-presenting extracellular vesicles described in the present specification can activate, proliferate, and differentiate T cells against a specific antigen by contacting with the T cells (although not limited thereto, for example, T cells or T cell populations obtained from peripheral blood, spleen, and the like) in vitro, ex vivo, and/or in vivo.

[0221] In an embodiment of the present invention, there is provided a method for activating, proliferating, and/or differentiating T cells against a specific antigen, the method comprising bringing the antigen-presenting extracellular vesicles described in the present specification into contact with T cells in vitro or ex vivo.

[0222] In an embodiment of the present invention, there are provided T cells obtained by the method described above.

[0223] The T cells obtained by the method described above may be administered to a subject in order to treat and/or prevent a disease (for example, cancer, an autoimmune disease, an allergic disease, or the like).

Examples

[0224] Hereinafter, the present invention will be described in more detail with reference to examples, and these examples do not limit the scope of the present invention at all.

[0225] Preparation 1 of Plasmid

A vector for expressing, on membrane of an extracellular vesicle, an MHC class I molecule capable of presenting an antigen outside membrane was prepared using a pCAG-puro vector.

With established cloning techniques, a single chain trimer (sc-Trimer) consisting of a polynucleotide (SEQ ID NO: 2) encoding a signal peptide (amino acids 1 to 20; SEQ ID NO: 1) of β_2 microglobulin, a polynucleotide (SEQ ID NO: 4) encoding an OVA peptide (SEQ ID NO: 3) as a model antigen peptide, a peptide linker (amino acid sequence: SEQ ID NO: 5, polynucleotide: SEQ ID NO: 6), a polynucleotide (SEQ ID NO: 8) encoding a full-length sequence (amino acids 21 to 119; SEQ ID NO: 7) of β_2 microglobulin from which a signal peptide was removed, a polynucleotide (SEQ ID NO: 12) encoding a peptide linker (SEQ ID NO: 11), and a

polynucleotide (SEQ ID NO: 10) encoding a full-length sequence (amino acids 22 to 369; SEQ ID NO: 9) of an MHC class Ia chain from which a signal peptide was removed was prepared (amino acid sequence: SEQ ID NO: 13; polynucleotide: SEQ ID NO: 14). Next, a polynucleotide (SEQ ID NO: 18; corresponding amino acid sequence: SEQ ID NO: 17) in which a sc-Trimer was linked to a polynucleotide (SEQ ID NO: 16) encoding a full-length sequence (amino acids 1 to 236; SEQ ID NO: 15) of CD81 as a tetraspanin was inserted into the pCAG-puro vector (Figs. 1A and 1B: hereinafter, sc-Trimer-CD81).

With the same method, in order to express CD80 as one of T-cell costimulatory molecules on membrane of an extracellular vesicle, a polynucleotide (SEQ ID NO: 24; corresponding amino acid sequence: SEQ ID NO: 23) in which a polynucleotide (SEQ ID NO: 20) encoding a full-length sequence (amino acids 1 to 306; SEQ ID NO: 19) of CD80 was linked to a polynucleotide (SEQ ID NO: 22) encoding a full-length sequence (amino acids 1 to 306; SEQ ID NO: 21) of CD9 as a tetraspanin was inserted into a pCAG-puro or pMX vector (Figs. 1C and 1D: hereinafter, CD80-CD9).

With the same method, in order to express IL-2 as one of T-cell stimulatory cytokines on membrane of an extracellular vesicle, a polynucleotide (SEQ ID NO: 26) encoding a full-length sequence (amino acids 21 to 169; SEQ ID NO: 25) from which a single peptide of IL-2 was removed was inserted between the amino acids 170C and 171I in a large extracellular loop of a mouse CD63 (amino acids 1 to 238; SEQ ID NO: 27; polynucleotide: SEQ ID NO: 28) as a tetraspanin (that is, a sequence of IL-2 was inserted between a polynucleotide (SEQ ID NO: 58) encoding a partial sequence of CD63 of SEQ ID NO: 57 and a polynucleotide (SEQ ID NO: 60) encoding a partial sequence of CD63 of SEQ ID NO: 59). Note that polynucleotides (SEQ ID NO: 30) encoding a peptide linker (amino acid sequence GGGGS: SEQ ID NO: 29) were added to the N-terminus and the C-terminus of IL-2, respectively. The polynucleotide (SEQ ID NO: 32; corresponding amino acid sequence: SEQ ID NO: 31) was inserted into the pCAG-puro vector (Figs. 1E and 1F: hereinafter, CD63-IL-2).

[0226] Preparation 2 of Plasmid:

A vector for expressing, on membrane of an extracellular vesicle, an MHC class II molecule capable of presenting an antigen outside membrane was prepared using a pCAG-puro vector.

With established cloning techniques, a single chain dimer (sc-Dimer) in which a polynucleotide (SEQ ID NO: 34) encoding a signal peptide (amino acids 1 to 27; SEQ ID NO: 33) of an MHC class II β chain, a polynucleotide (SEQ ID NO: 36) encoding an OVA peptide (SEQ ID NO: 35) as a model antigen peptide, and a polynucleotide (SEQ

ID NO: 38) encoding a full-length sequence (amino acids 28 to 265; SEQ ID NO: 37) of an MHC class II β chain from which a signal peptide was removed were linked by a polynucleotide (SEQ ID NO: 40) encoding a peptide linker (SEQ ID NO: 39) was prepared (amino acid sequence: SEQ ID NO: 41; polynucleotide: SEQ ID NO: 42).

- 5 Next, a polynucleotide (SEQ ID NO: 44; corresponding amino acid sequence: SEQ ID NO: 43) in which a sc-Dimer was linked to a polynucleotide (SEQ ID NO: 16) encoding a full-length sequence (amino acids 1 to 236; SEQ ID NO: 15) of CD81 as a tetraspanin was inserted into the pCAG-puro vector (Figs. 1G and 1H: hereinafter, sc-Dimer-CD81).

- 10 A polynucleotide (SEQ ID NO: 46) encoding a full-length sequence (amino acids 1 to 256; SEQ ID NO: 45) of an MHC class II α chain as a constituent element of an MHC class II molecule was inserted into another pCAG-puro vector (Fig. 1I: hereinafter, an MHC class II α chain).

- With the same method, in order to express TGF- β 1 as one of T-cell stimulatory
15 cytokines on membrane of an extracellular vesicle, a polynucleotide (SEQ ID NO: 48) encoding a full-length sequence (amino acids 1 to 390; SEQ ID NO: 47) of TGF- β 1 in which three 33rd, 223rd, and 225th C's of a LAP domain were changed to S's and a polynucleotide (SEQ ID NO: 50) encoding a full-length sequence (amino acids 23 to 463; SEQ ID NO: 49) from which a signal peptide of MFG-E8 in which 89th D was
20 changed to E was removed were linked by a polynucleotide (SEQ ID NO: 30) encoding a peptide linker (SEQ ID NO: 29). The polynucleotide (SEQ ID NO: 52; corresponding amino acid sequence: SEQ ID NO: 51) was inserted into the pCAG-puro vector (Figs. 1J and 1K: hereinafter, TGF- β -MFG-E8).

- With the same method, in order to express IL-4 as one of T-cell stimulatory
25 cytokines on membrane of an extracellular vesicle, a polynucleotide (SEQ ID NO: 54) encoding a full-length sequence (amino acids 21 to 140; SEQ ID NO: 53) from which a single peptide of IL-4 was removed was inserted between the amino acids 177S and 178G in a large extracellular loop of a mouse CD81 (amino acids 1 to 236; SEQ ID NO: 15; polynucleotide: SEQ ID NO: 16) as a tetraspanin (that is, a sequence of IL-4 was
30 inserted between a polynucleotide (SEQ ID NO: 62) encoding a partial sequence of CD81 of SEQ ID NO: 61 and a polynucleotide (SEQ ID NO: 64) encoding a partial sequence of CD81 of SEQ ID NO: 63). Note that polynucleotides (SEQ ID NO: 30) encoding a peptide linker (amino acid sequence GGGGS; SEQ ID NO: 29) were added to the N-terminus and the C-terminus of IL-4, respectively. The polynucleotide (SEQ
35 ID NO: 56; corresponding amino acid sequence: SEQ ID NO: 55) was inserted into the pCAG-puro vector (Figs. 1L and 1M: hereinafter, CD81-IL-4).

[0227] Preparation 3 of Plasmid:

sc-Dimer-CD81-IL-12p40

At the sc-Dimer, a polynucleotide (SEQ ID NO: 92) encoding a protein (SEQ ID NO: 91) obtained by fusing CD81 to IL-12p40 as a subunit of IL-12 as a T-cell stimulatory cytokine was inserted into a pCAG-puro vector, thereby preparing a vector expressing a fusion protein.

IL-12p35

A polynucleotide (SEQ ID NO: 98) encoding IL-12p35 (SEQ ID NO: 97) as one subunit of IL-12 was inserted into a pCAG-puro or pMX vector to prepare a vector expressing IL-12p35.

[0228] CD81-IL-6

In order to express IL-6 as one of T-cell stimulatory cytokines on membrane of an extracellular vesicle, a polynucleotide (SEQ ID NO: 100) encoding a full-length sequence (SEQ ID NO: 99) from which a signal peptide of IL-6 was removed was introduced into a polynucleotide encoding an extracellular loop of CD81 as a tetraspanin, and a polynucleotide (SEQ ID NO: 102) encoding a CD81-IL-6 fusion protein (SEQ ID NO: 101) was inserted into a pCAG-puro or pMX vector, thereby preparing a vector expressing a fusion protein.

[0229] hCD80-hCD9

In order to express human CD80 as one of T-cell costimulatory molecules on membrane of an extracellular vesicle, a polynucleotide (SEQ ID NO: 108) encoding a fusion protein (SEQ ID NO: 107) of human CD80 and human CD9 as a tetraspanin was inserted into a pCAG-puro or pMX vector, thereby preparing a vector expressing a fusion protein.

sc-Trimer-CD81-IL-2

In order to express IL-2 as one of T-cell stimulatory cytokines on membrane of an extracellular vesicle, similar to the CD81-IL-4, a polynucleotide encoding a fusion peptide of CD81-IL2 was prepared, a sequence of the polynucleotide was linked to a nucleotide encoding a sc-Trimer-, and a polynucleotide (SEQ ID NO: 136) encoding sc-Trimer-CD81-IL-2 (SEQ ID NO: 135) was prepared and inserted into a pCAG-puro or pMX vector, thereby preparing a vector expressing a fusion protein.

[0230] hsc-Trimer-hCD81

Using the sc-Trimer-CD81 as a human gene sequence (using HLA-A2402 as a sequence of MHC-I), a polynucleotide (SEQ ID NO: 132) encoding hsc-Trimer-hCD81 (SEQ ID NO: 131) was prepared and inserted into a pCAG-puro or pMX vector to prepare a vector expressing a fusion protein.

SARS-CoV2sc-Trimer-hCD81

Using a SARS-CoV-2 peptide (amino acid sequence: SEQ ID NO: 141; polynucleotide: SEQ ID NO: 142) as an antigen and HLA-A0201 as an MHC molecule, a polynucleotide (SEQ ID NO: 148) encoding an antigen-presenting MHC molecule (SARS-CoV2sc-Trimer; amino acid sequence: SEQ ID NO: 147) was prepared and was further linked to a polynucleotide encoding hCD81, thereby preparing a polynucleotide (SEQ ID NO: 150) encoding SARS-CoV2sc-Trimer-hCD81 (SEQ ID NO: 149). The prepared polynucleotide was inserted into a pCAG-puro or pMX vector to prepare a vector expressing a fusion protein.

10 hCD63-hIL-2

The CD63-IL-2 was prepared using a human gene sequence. A polynucleotide (SEQ ID NO: 116) encoding hCD63-hIL-2 (SEQ ID NO: 115) was prepared and inserted into a pCAG-puro or pMX vector to prepare a vector expressing a fusion protein.

15 [0231] CD63-Akaluc

As a negative control, CD63 and Akaluc luciferase were fused to prepare a polynucleotide (SEQ ID NO: 140) for localizing an AlkaLuc fusion protein (SEQ ID NO: 139) to an extracellular vesicle, and the polynucleotide was inserted into a pCAG-puro or pMX vector, thereby preparing a vector expressing a fusion protein.

20 [0232] The respective sequences used in examples are shown in Tables 1 to 13. Note that the underline portion in each sequence indicates a signal peptide.

[0233]

[Table 1-1]

	Sequence	SEQ ID NO:
Signal peptide of β_2 microglobulin	<u>MARSVTLVFLVLVSLTGLYA</u>	1
	<u>ATGGCTCGCTCGGTGACCCTGGTCTTTCTGGTGCTTGTCTCACTGACCGGCCTGTAT</u>	2
	<u>GCT</u>	
OVA peptide 1 (for MHC class I molecule)	SIINFEL	3
	TCCATTATAAATTTGAAAAGTTG	4
Peptide linker 1	GGGASGGGSGGGGS	5
	GGCGGAGGTGCCTCTGGCGGTGGGGGCAGCGGTGGAGGGGGCAGT	6
β_2 Microglobulin (from which signal peptide is removed)	IQKTPQIQVYSRHPENGKPNILNCYVTQFHPPIEIQMLKNGKKIPKVEMSDMSFS KDWSFYILAHEFTPTETDTYACRVKHASMAEPKTVYWDRDM	7
	ATCCAGAAAACCCCTCAAATTCAAGTATACTCACGCCACCCACCGGAGAATGGGAAG CCGAACATACTGAACTGTACTAGTAACACAGTTCCACCCGCCTCACATTGAAATCCAA ATGCTGAAGAACGGGAAAAAAATTCCTAAAGTAGAGATGTCAGATATGTCCTTCAGC AAGGACTGGTCTTTCTATATCCTGGCTCACACTGAATTCACCCCCACTGAGACTGAT ACATACGCCTGCAGAGTTAAGCATGCCAGTATGGCCGAGCCCAAGACCGTCTACTGG GATCGAGACATG	8
MHC class I α chain (from which signal peptide is removed)	GPHSRLRYFVTAVSRPGLGEPYMEVGYVDDTEFVRFDSDAENPRYEPRARWMEQEGP EYWERETQKAKGNEQSFRVLDRLTLGYYNQSKGGSHTIQVISGCEVSGDRLLRGYQ QYAYDGC DYIALNEDLKTWTAADMAALITKHKEQAGEAERL RAYLEGTCVEWLRRY LKNGNATLLRTDSPKAHVTHSRPEDKVT LRCWALGFYPADITLTWQLNGEELIQDM ELVETRPAGDGT FQKWASVVVPLGKEQYTTCHVYHQGLPEPLTLRWEPPSTVSNMA TVAVLVVLGAAIVTGAVVAFVMKRRRNTGGKGGDYALAPGSQTS DLSLPDCKVMVH DPHSLA	9
	GGCCCACTCGCTGAGGTATTTCTGTCACCGCGTGTCCCGGCCCGGCCTCGGGGAG CCCCGGTACATGGAAGTCGGCTACGTGGACGACACGGAGTTCGTGCGCTTCGACAGC GACGCGGAGAATCCGAGATATGAGCCGCGGGCGGGTGGATGGAGCAGGAGGGGGCC GAGTATTGGGAGCGGGAGACACAGAAAGCCAAGGGCAATGAGCAGAGTTTCCGAGTG GACCTGAGGACCTGCTCGGCTACTACAACAGAGCAAGGGCGGCTCTCACACTATT CAGGTGATCTCTGGCTGTGAAGTGGGGTCCGACGGGCGACTCCTCCGCGGTACCA GAGTACGCCTACGACGGCTGCGATTACATCGCCCTGAACGAAGACCTGAAAACGTGG ACGGCGGCGGACATGGCGGCGCTGATCACCAAACACAAGTGGGAGCAGGCTGGTGAA	10

[Table 1-2]

	GCAGAGAGACTCAGGGCCTACCTGGAGGGCACGTGCGTGGAGTGGCTCCGCAGATAC CTGAAGAACGGGAACGCGACGCTGCTGCGCACAGATTCCCCAAAGGCCCATGTGACC CATCACAGCAGACCTGAAGATAAAGTACCCTGAGGTGCTGGGCCCTGGGCTTCTAC CCTGCTGACATCACCTGACCTGGCAGTTGAATGGGGAGGAGCTGATCCAGGACATG GAGCTTGTGGAGACCAGGCCTGCAGGGGATGGAACCTTCCAGAAGTGGGCATCTGTG GTGGTGCCTCTTGGGAAGGAGCAGTATTACACATGCCATGTGTACCATCAGGGGCTG CCTGAGCCCCCTACCCTGAGATGGGAGCCTCCTCCATCCACTGTCTCCAACATGGCG ACCGTTGCTGTTCTGTTGTCTTGGAGCTGCAATAGTCACTGGAGCTGTGGTGGCT TTTGTGATGAAGATGAGAAGGAGAAACACAGGTGGAAAAGGAGGGGACTATGCTCTG GCTCCAGGCTCCCAGACCTCTGATCTGTCTCTCCAGATTGTAAAGTGATGGTTCAT GACCCTCATTCTCTAGCG	
Peptide linker 2	GGGSGGGSGGGSGGGSGGGS	11
	GGGGGGGAGGCTCCGGTGGAGGGGGTCTGGAGGGGGGGTCTGGTGGAGGCGGA AGT	12
Single chain MHC class I molecule (β_2 microglobulin (from which signal peptide is removed) + peptide linker 2 + MHC class I α chain (from which signal peptide is removed))	IQKTPQIQVYSRHPPENGKPNILNCYVTQFHPPHIEIQMLKNGKKIPKVEMSDMSFS KDWSFYILAHTFTPTETDTYACRVKHASMAEPKTVYWRDMGGGSGGGSGGGGS GGGSGPHSLRYFVTAVSRPGLGEPRYMEVGYYDDTEFVRFDSDAENPRYEPRARWM EQEGPEYWERETQKAKGNEQSFRVDLRTLGGYNNQSKGGSHTIQVISGCEVGS DGRL LRGYQQYAYDGC DYIALNEDLKTWTAADMAALITKHKWEQAGEAERLRLAYLEGT CVE WLRRYLKNGNATLLRTDSPKAHVTHHSRPEDKVT LRCWALGFYPADITLTWQLNGEE LIQDMELVETRPAGDGT FQKWASVVVPLGKEQYYTCHVYHQGLPEPLTLRWEPPST VSNMATVAVLVVLGAAIVTGAVVAFVMKMRRTTGGKGGDYALAPGSQTS DLSLPDC KVMVHDPHSLA	65
	ATCCAGAAAACCCCTCAAATCAAGTATACTCACGCCACCCACCGGAGAATGGGAAG CCGAACATACTGAACTGCTACGTAACACAGTTCCACCCGCCTCACATTGAAATCAA ATGCTGAAGAACGGGAAAAAAATTCCTAAAGTAGAGATGTCAGATATGTCCTTCAGC AAGGACTGGTCTTTCTATATCCTGGCTCACACTGAATTCACCCCCACTGAGACTGAT ACATACGCCTGCAGAGTTAAGCATGCCAGTATGGCCGAGCCCAAGACCGTCTACTGG GATCGAGACATGGGGGGGGGAGGCTCCGGTGGAGGGGGTCTGGAGGGGGGGGTCT GGTGGAGGCGGAAGTGGCCCACTCGCTGAGGTATTTGTCACCGCCGTGTCCCGG CCCGGCCTCGGGAGCCCCGTACATGGAAGTCGGCTACGTGGACGACACGGAGTTC GTGCGCTTCGACAGCGACGCGGAGAATCCGAGATATGAGCCGCGGGCGGGTGGATG GAGCAGGAGGGGCCCCAGTATTGGGAGCGGGAGACACAGAAAGCCAAGGCAATGAG	66

[Table 1-3]

	CAGAGTTTCCGAGTGGACCTGAGGACCCTGCTCGGCTACTACAACCAGAGCAAGGGC GGCTCTCACACTATTACAGGTGATCTCTGGCTGTGAAGTGGGGTCCGACGGGGGACTC CTCCGCGGGTACCAGCAGTACGCCTACGACGGCTGCGATTACATCGCCCTGAACGAA GACCTGAAAACGTGGACGGCGGGGACATGGCGGCGCTGATCACC AAAACACAAGTGG GAGCAGGCTGGTGAAGCAGAGAGACTCAGGGCCTACCTGGAGGGCAGTGCGTGGAG TGGCTCCGAGATACCTGAAGAACGGGAACGCGACGCTGCTGCGCACAGATTCCCCA AAGGCCCATGTGACCCATCACAGCAGACCTGAAGATAAAGTCAACCTGAGGTGCTGG GCCCTGGGCTTCTACCCTGCTGACATCACCTGACCTGGCAGTTGAATGGGGAGGAG CTGATCCAGGACATGGAGCTTGTGGAGACCAGGCCTGCAGGGGATGGAACCTTCCAG AAGTGGGCATCTGTGGTGGTGCCTCTTGGGAAGGAGCAGTATTACACATGCCATGTG TACCATCAGGGGCTGCCTGAGCCCCTCACCTGAGATGGGAGCCTCCTCCATCCACT GTCTCCAACATGGCGACCGTTGCTGTTCTGGTTGTCCTTGGAGCTGCAATAGTCACT GGAGCTGTGGTGGCTTTTGTGATGAAGATGAGAAGGAGAAACACAGGTGAAAAGGA GGGGA CTATGCTCTGGCTCCAGGCTCCAGACCTCTGATCTGTCTCTCCAGATTGT AAAGTGATGGTTCATGACCCCTATTCTCTAGCG	
s c - T r i m e r (OVA peptide 1 + peptide linker 1 + single chain MHC class I molecule)	<u>MARSVTLVFLVLVSLTGLYASI</u>INFEKLGGGASGGGSGGGGSIQKTPQIQVYSRHP PENGKPNILNCYVTQFHPPHIEIQMLKNGKKIPKVMESDMSFSKDW SFYILAHTFT PTETDTYACRVKHASMAEPKTVYWRDMDGGGSGGGGSGGGGSGGGGSGPHSLRYFV TAVSRPGLGEPRYMEVGYYDDTEFVRFDSDAENPRYEPRARWMEQEGPEYWERETQK AKGNEQSFRVDLRTL LGYYNQSKGGSHTIQVISGCEVGS DGRLLRGYQQYAYDGC DY IALNEDLKTWTAADMAALITKHKEQAGEAERL RAYLEGT CVEWLRRYLKNGNATLL RTDSPKAHVTHHSRPEDKVTLR CWALGFYPADITLTWQLNGEELIQDMELVETRPAG DGTFQKWASVVVPLGKEQYTTCHVYHQGLPEPLTLRWEPPPSTVSNMATVAVLVVLG AAIVTGAVVAFVMKMRRRNTGGKGGDYALAPGSQTS DLSLPDCKVMVHDPHSLA	13
	<u>ATGGCTCGCTCGGTGACCTGGTCTTTCTGGTGCTTGTCTCACTGACCGGCTGTAT</u> <u>GCTTCCATTATAAATTTTGAAAAGTTGGGCGGAGGTGCCTCTGGCGGTGGGGG CAGC</u> GGTGGAGGGGGCAGTATCCAGAAAACCCCTCAAATTCAAGTATACTCACGCCACCCA CCGAGAAATGGGAAGCCGAACATACTGAAGTGTACGTAACACAGTTCCACCGCCT CACATTGAAATCCAAATGCTGAAGAACGGGAAAAAAATTCCTAAAGTAGAGATGTCA GATATGTCCTTCAGCAAGGACTGGTCTTTCTATATCCTGGCTCACACTGAATTCACC CCCCTGAGACTGATACATACGCCTGCAGAGTTAAGCATGCCAGTATGGCCGAGCCC AAGACCGTCTACTGGGATCGAGACATGGGGGGGGAGGCTCCGGTGGAGGGGGGTCT GGAGGGGGGGGTCTGGTGGAGGCGGAAGTGGCCCACTCGCTGAGGTATTTCTGTC	14

[Table 1-4]

	ACCGCCGTGTCCCGGCCCGCCTCGGGGAGCCCCGGTACATGGAAGTCGGCTACGTG GACGACACGGAGTTCGTGCGCTTCGACAGCGACGGGAGAATCCGAGATATGAGCCG CGGGCGCGGTGGATGGAGCAGGAGGGGCCGAGTATTGGGAGCGGGAGACACAGAAA GCCAAGGGCAATGAGCAGAGTTTCCGAGTGGACCTGAGGACCCTGCTCGGCTACTAC AACCAGAGCAAGGGCGGCTCTCAGCTATTTCAGGTGATCTCTGGCTGTGAAGTGGGG TCCGACGGGCGACTCCTCCGCGGGTACCAGCAGTACGCCTACGACGGCTGCGATTAC ATCGCCCTGAACGAAGACCTGAAAACGTGGACGGCGGGGACATGGCGGCGCTGATC ACCAAAACAAGTGGGAGCAGGCTGGTGAAGCAGAGAGACTCAGGGCCTACCTGGAG GGCAGCTGCGTGGAGTGGCTCCGCAGATACCTGAAGAACGGGAACGCGACGCTGCTG CGCACAGATTCCCCAAAGGCCCATGTGACCCATCACAGCAGACCTGAAGATAAAGTC ACCCTGAGGTGCTGGGCCCTGGGCTTCTACCCTGCTGACATCACCTGACCTGGCAG TTGAATGGGGAGGAGCTGATCCAGGACATGGAGCTTGTGGAGACCAGGCCTGCAGGG GATGGAACCTTCCAGAAGTGGGCATCTGTGGTGGTGCCTCTTGGAAGGAGCAGTAT TACACATGCCATGTGTACCATCAGGGGCTGCCTGAGCCCTCACCTGAGATGGGAG CCTCCTCCATCCACTGTCTCCAACATGGCGACCGTTGCTGTTCTGGTTGCTCTTGA GCTGCAATAGTCACTGGAGCTGTGGTGGCTTTTGTGATGAAGATGAGAAGGAGAAAC ACAGGTGGAAGGAGGGGACTATGCTCTGGCTCCAGGCTCCAGACCTCTGATCTG TCTCTCCAGATTGTAAAGTGATGGTTTCATGACCCTCATTCTCTAGCG	
C D 8 1	MGVEGCTKCIKYLFFVFNFWLAGGVILGVALWLRHDPQTSLLYLELGNKPAPNT FYVGIYILIAVGAVMMFVGLGCGYGAIQESQCLLGTFFTCLVILFACEVAAGIWGFV NKDQIAKDVKFYDQALQQAVMDDANNAKAVVKTFFHETLNCCGSNALTLTTTILR NSLCPSGGNILTPLLQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEMILSMVLCC GIRNSSVY	15
	ATGGGGGTGGAGGGCTGCACCAATGCATCAAATACCTGCTCTTCGTCTTCAATTC GTCTTCTGGCTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGTCATGAT CCACAGACCACGAGCTGTGTACCTGGAAGTGGGAAACAAACCGGCACCCAACACC TTCTACGTGGGCATCTACATTCTCATTGCTGTGGGAGCTGTGATGATGTTGTAGGC TTCCTGGGGTGCTATGGGGCCATCCAGGAGTCCCAGTGTCTGCTGGGGACGTTCTTC ACCTGCCTTGTGATCCTGTTTGCCTGTGAGGTGGCTGCAGGCATCTGGGGCTTCGTA AACAAAGACCAGATCGCCAAGGATGTGAAGCAGTTCTATGACCAGGCCCTTCAGCAA GCTGTGATGGATGATGATGCCAACAATGCCAAGGCTGTGGTGAAGACTTTCCATGAG ACGCTCAACTGTTGTGGCTCCAACGCACTGACCACACTGACTACCACCATACTGAGG AACAGCCTGTGTCCCTCAGGCGGCAACATACTACCCCCTTACTGCAGCAAGATTGT	16

[Table 1-5]

	CATCAGAAAATCGATGAGCTCTTCTCTGGGAAGCTGTACCTCATTGGAATTGCAGCC ATTGTGGTAGCTGTCATTATGATCTTTGAGATGATTCTGAGCATGGTGCTGTGCTGT GGCATCCGGAACAGCTCCGTGTACTGA	
s c - T r i m e r - C D 8 1 (s c - T r i m e r + C D 8 1)	<u>MARSVTLVFLVLVSLTGLYASI</u> INFEKLGGGASGGGGSGGGGSIQKTPQIQVYSRHP PENGKPNILNCYVTQFHPPHIEIQMLKNGKKIPKVEMSDMSFSKDWFSYILAHTFT PTETDTYACRVKHASMAEPKTVYWRDMGGGGSGGGGSGGGGSGGGSGPHSLRYFV TAVSRPGLGEPYMEVGYVDDTEFVRFDSDAENPRYEPRARWMEQEGPEYWERETQK AKGNEQSFRVLDLRTLLGYYNQSKGGSHTIQVISGCEVGSGRLLRGYQYAYDGC DY IALNEDLKTWTAADMAALITKHKEQAGEAERLRAYLEGTCEWLRRLKNGNATLL RTDSPKAHVTHHSRPEDKVTLRWALGFYPADITLTWQLNGEELIQDMELVETRPAG DGTFAQKVASVVPLGKEQYTTCHVYHQGLPEPLTLRWEPPSTVSNMATVAVLVVLG AAIVTGAVVAFVMKMRRTNTGGKGDYALAPGSQTSDSLSPDKVMVHDPHSLAMGV EGCTKCIKYLFLVFNFVFWLAGGVILGVALWLRHDPQTTSLLYLELGNKPAPNTFYV GIYILIAVGAVMMFVGFLLCCYGAIQESQCLLGTFFTCLVILFACEVAAGIWGFVNKD QIAKDVKQFYDQALQQAVMDDDANNAKAVVKTFFHETLNCCGSNALTTLTTLILNSL CPSGGNLTPLLQQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIR NSSVY	17
	<u>ATGGCTCGCTCGGTGACCCTGGTCTTTCTGGTGCTTGTCTCACTGACCGGCTGTAT</u> <u>GCTTCCATTATAAATTTGAAAAGTTGGGCGGAGGTGCCTCTGGCGGTGGGGGCAGC</u> GGTGGAGGGGGCAGTATCCAGAAAACCCCTCAAATTCAAGTATACTACGCCACCCA CCGGAGAATGGGAAGCCGAACATACTGAACTGCTACGTAACACAGTTCCACCCGCCT CACATTGAAATCCAAATGCTGAAGAACGGGAAAAAATTCCTAAAGTAGAGATGTCA GATATGTCCTTCAGCAAGGACTGGTCTTTCTATATCCTGGCTCACACTGAATTCACC CCCACTGAGACTGATACATACGCCTGCAGAGTTAAGCATGCCAGTATGGCCGAGCCC AAGACCGTCTACTGGGATCGAGACATGGGGGGGGGAGGCTCCGGTGGAGGGGGGTCT GGAGGGGGGGGTCTGGTGGAGGCGGAAGTGGCCCACTCGCTGAGGTATTTTCGTC ACCGCCGTGTCCCGGCCCGGCTCGGGGAGCCCCGGTACATGGAAGTCGGCTACGTG GACGACACGGAGTTCGTGCGCTTCGACAGCGACGCGGAGAATCCGAGATATGAGCCG CGGGCGCGGTGGATGGAGCAGGAGGGGCCGAGTATTGGGAGCGGGAGACACAGAAA GCCAAGGGCAATGAGCAGAGTTTCCGAGTGGACCTGAGGACCCTGCTCGGCTACTAC AACCAGAGCAAGGGCGGCTCTCACACTATTCAAGTGATCTCTGGCTGTGAAGTGGGG TCCGACGGGCGACTCCTCCGCGGTACCAGCAGTACGCCTACGACGGCTGCGATTAC ATCGCCCTGAACGAAGACCTGAAAACGTGGACGGCGGGGACATGGCGGCGCTGATC	18

[Table 1-6]

	ACCAAACACAAGTGGGAGCAGGCTGGTGAAGCAGAGAGACTCAGGGCCTACCTGGAG GGCACGTGCGTGGAGTGGCTCCGCAGATACCTGAAGAACGGGAACGCGACGCTGCTG CGCACAGATTCCCCAAAGGCCCATGTGACCCATCACAGCAGACCTGAAGATAAAGTC ACCCTGAGGTGCTGGGCCCTGGGCTTCTACCCTGCTGACATCACCTGACCTGGCAG TTGAATGGGGAGGAGCTGATCCAGGACATGGAGCTTGTGGAGACCAGGCCTGCAGGG GATGGAACCTTCCAGAAGTGGGCATCTGTGGTGGTGCCTCTTGGAAGGAGCAGTAT TACACATGCCATGTGTACCATCAGGGGCTGCCTGAGCCCCCTACCCTGAGATGGGAG CCTCTCCATCCACTGTCTCCAACATGGCGACCGTTGCTGTTCTGGTTGTCTTGGA GCTGCAATAGTCACTGGAGCTGTGGTGGCTTTTGTGATGAAGATGAGAAGGAGAAAC ACAGGTGGAAGGAGGGGACTATGCTCTGGCTCCAGGCTCCCAGACCTCTGATCTG TCTCTCCAGATTGTAAAGTGATGGTTCATGACCCTCATTCTCTAGCGATGGGGTG GAGGGCTGCACCAAATGCATCAAATACCTGCTCTTCGTCTTCAATTTTCGTCTTCTGG CTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGTCATGATCCACAGACC ACCAGCCTGCTGTACCTGGAACGGGAAACAAACCGGCACCCAACACCTTCTACGTG GGCATCTACATTCTCATTGCTGTGGGAGCTGTGATGATGTTTGTAGGCTTCTGGGG TGCTATGGGGCCATCCAGGAGTCCAGTGTCTGCTGGGGACGTTCTTCACCTGCCTT GTGATCCTGTTTGCTGTGAGGTGGCTGCAGGCATCTGGGGCTTCGTAAACAAAGAC CAGATCGCCAAGGATGTGAAGCAGTTCTATGACCAGGCCCTTCAGCAAGCTGTGATG GATGATGATGCCAACATGCCAAGGCTGTGGTGAAGACTTCCATGAGACGCTCAAC TGTTGTGGCTCCAACGCACTGACCACACTGACTACCACCATACTGAGGAACAGCCTG TGTCCCTCAGGCGGCAACATACTACCCCCTTACTGCAGCAAGATTGTCATCAGAAA ATCGATGAGCTCTTCTCTGGGAAGCTGTACCTCATTGGAATTGCAGCCATTGTGGTA GCTGTCATTATGATCTTTGAGATGATTCTGAGCATGGTGTGCTGTGGCATCCGG AACAGCTCCGTGTACTGA	

[0234]

[Table 2-1]

	Sequence	SEQ ID NO:
C D 8 0	<u>MACNCQLMQDTPLLKFCPRLLILFVLLIRLSQVSSDVDEQLSKSVKDKVLLPCRYN</u> SPHEDESEDRIYWQKHDKVVL SVIAGKLKVWPEYKNRTLYDNTTYSLIILGLVLSDR GTYSCVVQKKERGTYEVKHLALVKLSIKADFSTPNITESGNPSADTKRITCFASGGF PKPRFSWLENGRELPGINTTISQDPESELYTISSQLDFNTRNHTIKCLIKYGDHVS SEDFTWEKPPEDPPDSKNTLVLFAGFGAVITVVVIVVVIKCFCKHRSCFRRNEASR ETNNSLTFGPPEALAEQTVFL	19
	<u>ATGGCTTGCAATTGTCAGTTGATGCAGGATACACCACTCCTCAAGTTTCCATGTCCA</u> <u>AGGCTCATTCTTCTCTTTGTGCTGCTGATTTCGTCTTTCACAAGTGTCTCAGATGTT</u> GATGAACAACGTCCAAGTCAGTGAAAGATAAGGTATTGCTGCCTTGCCGTTACAAC TCTCCTCATGAAGATGAGTCTGAAGACCGAATCTACTGGCAAAAACATGACAAAGTG GTGCTGTCTGTCATTGCTGGGAACTAAAAGTGTGGCCCGAGTATAAGAACCGGACT TTATATGACAACACTACCTACTCTTATCATCTGGGCCTGGTCTTTTCAGACCGG GGCACATACAGCTGTGTCGTTCAAAGAAGGAAAGAGGAACGTATGAAGTTAAACAC TTGGCTTTAGTAAAGTTGCCATCAAAGCTGACTTCTTACCCCCAACATAACTGAG TCTGGAAACCCATCTGCAGACACTAAAAGGATTACCTGCTTTGCTTCCGGGGGTTTC CCAAAGCCTCGCTTCTTGGTTGGAAAAATGGAAGAGAATTACCTGGCATCAATACG ACAATTTCCCAGGATCCTGAATCTGAATTGTACACCATTAGTAGCCAACCTAGATTTC AATACGACTCGCAACCACACCATTAAAGTGTCTCATTAAATATGGAGATGCTCACGTG TCAGAGGACTTCACCTGGGAAAAACCCCCAGAAGACCCTCCTGATAGCAAGAACACA CTTGTGCTCTTTGGGGCAGGATTTCGGCGCAGTAATAACAGTCGTCGTCATCGTTGTC ATCATCAAATGCTTCTGTAAGCACAGAAGCTGTTTCAGAAGAAATGAGGCAAGCAGA GAAACAAACAACAGCCTTACCTTCGGGCCTGAAGAAGCATTAGCTGAACAGACCGTC TTCCTTTAG	20
C D 9	MPVKGGSKCIKYLLFGFNFIFWLAGIAVLAIGLWLRFDSTKSI FEQENNHSSFYTG VYILIGAGALMMLVGFLGCCGAVQESQCM LG LFFGFLLVIFAIEIAAAVWGYTHKDE VIKELQEFYKDTYQKLRSKDEPQRETLKA IHMALDCCGIAGPLEQFISDTCPPKKQLL ESFQVKPCPEAISEVFNNKFHII GAVGIGIAVVMIFGMIFSMILCCAIRRSREMV	21
	ATGCCGGTCAAAGGAGGTAGCAAGTGCATCAAATACCTGCTCTTCGGATTAACTTC ATCTTCTGGCTCGCTGGCATTGCAGTGCTTGCTATTGGACTATGGCTCCGATTTCGAC TCTCAGACCAAGAGCATCTTCGAGCAAGAGAATAACCATTCCAGTTTCTACACAGGA	22

[Table 2-2]

	GTGTACATTCTGATTGGAGCCGGGGCCCTCATGATGCTGGTTGGTTTCCTGGGCTGC TGTGGAGCTGTACAAGAGTCCCAGTGCATGCTGGGATTGTTCTTCGGGTTCTCTTG GTGATATTCGCCATTGAGATAGCCGCCGCCGTCTGGGGCTATACCCACAAGGATGAG GTGATTAAAGAACTCCAGGAGTTTTACAAGGACACCTACCAAAAGTTACGGAGCAAG GATGAACCCAGCGGGAAACACTCAAAGCCATCCATATGGCGTTGGACTGCTGTGGC ATAGCTGGTCCTTTGGAGCAGTTTATCTCGGACACCTGCCCCAAGAAACAGCTTTTG GAAAGTTTCCAGGTTAAGCCCTGCCCTGAAGCCATCAGTGAGGTCTTCAACAACAAG TTCCACATCATTGGAGCAGTGGGTATCGGCATCGCCGTGGTGATGATCTTCGGCATG ATCTTCAGCATGATCCTGTGCTGCGCCATCCGCAGGAGCCGAGAAATGGTCTAG	
	<u>MACNCQLMQDTPLLKFPCPRLILLFVLLIRLSQVSSDVDEQLSKSVKDKVLLPCRYN</u> SPHEDESEDRIYWQKHKVLSVIAGKLKVWPEYKNRTLYDNTTYSLIILGLVLSDR GTYSVVQKKERGTYEVKHLALVKLSIKADFSTPNITESGNPSADTKRITCFASGGF PKPRFSWLENGRELPGINTTISQDPESELYTISSQLDFNTRNHTIKCLIKYGDAHV SEDFTWEKPPEDPPDSKNTLVLFAGFGAVITVVVIVVVIKCFCKHRSCFRNEASR ETNNSLTFGPEEALAEQTVFLMPVKGGSKCIKYLFGFNFIFWLAGIAVLAIGLWLR FDSQTKSIFEQENNHSSFYTGYYILIGAGALMMLVGFLGCCGAVQESQCMLGLFFGF LLVIFAIEIAAAVWGYTHKDEVIKELQEFYKDTYQKLRSKDEPQRET LKA IHMALDC CGIAGPLEQFISDTCPPKKQLLESFQVKPCPEAISEVFNNKFHIIGAVGIGIAVVMIF GMIFSMILCCAIRRSREMV	23
CD 80 - C D 9	<u>ATGGCTTGCAATTGTCAGTTGATGCAGGATACACCACTCCTCAAGTTTCCATGTCCA</u> <u>AGGCTCATTCTTCTCTTTGTGCTGCTGATTCTGCTTTTACAAGTGCTTTCAGATGTT</u> GATGAACAACGTCCAAGTCAGTGAAAGATAAGGTATTGCTGCCTTGCCGTTACAAC TCTCCTCATGAAGATGAGTCTGAAGACCGAATCTACTGGCAAAAACATGACAAAAGTG GTGCTGTCTGTGATTGCTGGGAAACTAAAAGTGTTGGCCCGAGTATAAGAACCGGACT TTATATGACAACACTACCTACTCTCTTATCATCCTGGGCCTGGTCCTTTCAGACCGG GGCACATACAGCTGTGTCGTTCAAAAGAAGGAAAGAGGAACGTATGAAGTTAAACAC TTGGCTTTAGTAAAGTTGTCCATCAAAGCTGACTTCTCTACCCCCAACATAACTGAG TCTGAAAACCCATCTGCAGACACTAAAAGGATTACCTGCTTTGCTTCCGGGGGTTTC CCAAAGCCTCGCTTCTCTTGGTTGGAAAATGGAAGAGAATTACCTGGCATCAATACG ACAATTTCCCAGGATCCTGAATCTGAATTGTACACCATTAGTAGCCAACCTAGATTTTC AATACGACTCGCAACCACACCATTAAAGTGCTCATTAAATATGGAGATGCTCACGTG TCAGAGGACTTCACCTGGGAAAAACCCCCAGAAGACCTCCTGATAGCAAGAACACA CTTGTGCTCTTTGGGGCAGGATTTCGGCGCAGTAATAACAGTCGTCGTCATCGTTGTC	24

[Table 2-3]

	ATCATCAAATGCTTCTGTAAAGCACAGAAGCTGTTTCAGAAGAAATGAGGCAAGCAGA GAAACAAACAACAGCCTTACCTTCGGGCCTGAAGAAGCATTAGCTGAACAGACCGTC TTCCTTATGCCGGTCAAAGGAGGTAGCAAGTGCATCAAATACCTGCTCTTCGGATT AACTTCATCTTCTGGCTCGCTGGCATTGCAGTGCTTGCTATTGGACTATGGCTCCGA TTCGACTCTCAGACCAAGAGCATCTTCGAGCAAGAGAATAACCATTCCAGTTTCTAC ACAGGAGTGTACATTCTGATTGGAGCCGGGGCCCTCATGATGCTGGTTGGTTTCCTG GGCTGCTGTGGAGCTGTACAAGAGTCCCAAGTGCATGCTGGGATTGTTCTTCGGGTTC CTCTTGGTGATATTGCCATTGAGATAGCCGCCGCCGTCTGGGGCTATACCCACAAG GATGAGGTGATTAAAGAACTCCAGGAGTTTTACAAGGACACCTACCAAAAGTTACGG AGCAAGGATGAACCCAGCGGGAACACTCAAAGCCATCCATATGGCGTTGGACTGC TGTGGCATAGCTGGTCCTTTGGAGCAGTTTATCTCGGACACCTGCCCCAAGAAACAG CTTTTGAAAGTTTCCAGGTTAAGCCCTGCCCTGAAGCCATCAGTGAGGTCTTCAAC AACAAGTTCCACATCATTGGAGCAGTGGGTATCGGCATCGCCGTGGTGATGATCTTC GGCATGATCTTCAGCATGATCCTGTGCTGCGCCATCCGCAGGAGCCGAGAAATGGTC TAG	

[0235]

[Table 3-1]

	Sequence	SEQ ID NO:
I L - 2 (from which signal peptide is removed)	APTSSSTSSSTAEEAQQQQQQQQQQHLEQLLMDLQELLSRMENYRNKLPRLMTFK FYLPKQATELKDLDQCLEDELGPLRHVLDLTQSKSFQLEDAENFISNIRVTVVKLKGS DNTFECQFDDESATVVDFLRRWIAFCQSIISTSPQ	25
	GCACCCACTTCAAGCTCCACTCAAGCTCTACAGCGGAAGCACAGCAGCAGCAGCAG CAGCAGCAGCAGCAGCAGCAGCACCTGGAGCAGCTGTTGATGGACCTACAGGAGCTC CTGAGCAGGATGGAGAATTACAGGAACCTGAACTCCCCAGGATGCTCACCTTCAAA TTTTACTTGCCCAAGCAGGCCACAGAATTGAAAGATCTTCAGTGCCTAGAAGATGAA CTTGGACCTCTGCGGCATGTTCTGGATTTGACTCAAAGCAAAAGCTTTCAATTGGAA GATGCTGAGAATTCATCAGCAATATCAGAGTAACTGTTGTAAACTAAAGGGCTCT GACAACACATTTGAGTGCCAATTCGATGATGAGTCAGCAACTGTGGTGGACTTTCTG AGGAGATGGATAGCCTTCTGTCAAAGCATCATCTCAACAAGCCCTCAA	26
C D 6 3	MAVEGGMKCVKFLLYVLLLAFCACAVGLIAIGVAVQVVLKQAITHETTAGSLLPVVI IAVGAFLLVAFVGGCGACKENYCLMITFAIFLSLIMLVEVAVAIAGYVFRDQVKSE FNKSFQQMQNYLKDNTATILDKLQKENNCCGASNYTDWENIPGMAKDRVPDSCCI NITVGCNDFKESTIHTQGCVETIAIWLKRNILLVAAAALGIAFVEVLGIIFSCCLV KSIRSGYEV	27
	ATGGCGGTGGAAGGAGGAATGAAGTGTGTCAAGTTTTTGCTCTACGTTCTCCTGCTG GCCTTCTGCGCTGTGCAGTGGGATTGATCGCCATTGGTGTAGCGGTTACAGTTGTC TTGAAGCAGGCCATTACCATGAGACTACTGCTGGCTCGCTGTTGCCTGTGGTCATC ATTGCAGTGGGTGCCTTCTCTTCTGCTGGCCTTTGTGGGCTGCTGTGGGGCCTGC AAGGAGAACTACTGTCTCATGATTACATTTGCCATCTTCTGTCTCTTATCATGCTT GTGGAGGTGGCTGTGGCCATTGCTGGCTATGTGTTAGAGACCAGGTGAAGTCAGAG TTTAATAAAAGCTTCCAGCAGCAGATGCAGAATTACCTTAAAGACAACAAAACAGCC ACTATTTTGGACAAATTGCAGAAAGAAAATAACTGCTGTGGAGCTTCTAACTACACA GACTGGGAAAACATCCCCGGCATGGCCAAGGACAGAGTCCCCGATTCTTGTGTCATC AACATAACTGTGGGCTGTGGGAATGATTTCAAGGAATCCACTATCCATACCCAGGGC TGGCTGGAGACTATAGCAATATGGCTAAGGAAGAACATACTGCTGGTGGCTGCAGCG GCCCTGGGCATTGCTTTTGTGGAGGTCTTGGGAATTATCTTCTCTGCTGTCTGGTG AAGAGTATTGGAAGTGGCTATGAAGTAATGTAG	28
C D 6 3	MAVEGGMKCVKFLLYVLLLAFCACAVGLIAIGVAVQVVLKQAITHETTAGSLLPVVI	57

[Table 3-2]

(amino acids 1 to 170)	IAVGAFLLVAFVGGCGACKENYCLMITFAIFLSLIMLVEVAVAIAGYVFRDQVKSE FNKSFQQMQNYLKDNKTATILDKLQKENNCCGASNYTDWENIPGMAKDRVPDSCC	
	ATGGCGGTGGAAGGAGGAATGAAGTGTGTCAAGTTTTTGCTCTACGTTCTCCTGCTG GCCTTCTGCGCCTGTGCAGTGGGATTGATCGCCATTGGTGTAGCGGTTCAAGTTGTC TTGAAGCAGGCCATTACCCATGAGACTACTGCTGGCTCGCTGTTGCCTGTGGTCATC ATTGCAGTGGGTGCCTTCCTCTTCCTGGTGGCCTTTGTGGGCTGCTGTGGGGCCTGC AAGGAGAACTACTGTCTCATGATTACATTTGCCATCTTCCTGTCTCTTATCATGCTT GTGGAGGTGGCTGTGGCCATTGCTGGCTATGTGTTTAGAGACCAGGTGAAGTCAGAG TTTAATAAAAGCTTCCAGCAGCAGATGCAGAATTACCTTAAAGACAACAAAACAGCC ACTATTTTGGACAAATTGCAGAAAGAAAATAACTGCTGTGGAGCTTCTAACTACACA GACTGGGAAAACATCCCCGGCATGGCCAAGGACAGAGTCCCCGATTCTTGCTGC	58
C D 6 3 (amino acids 171 to 238)	INITVCGNDFKESTIHTQGCVETIAIWLRKNILLVAAAALGIAFVEVLGIIIFSCCL VKSIRSGYEV	59
	ATCAACATAACTGTGGGCTGTGGGAATGATTCAAGGAATCCACTATCCATACCCAG GGCTGCGTGGAGACTATAGCAATATGGCTAAGGAAGAACATACTGCTGGTGGCTGCA GCGGCCCTGGGCATTGCTTTTGTGGAGGTCTTGGGAATTATCTTCTCCTGCTGTCTG GTGAAGAGTATTCCAAGTGGCTATGAAGTAATGTAG	60
Peptide linker 3	GGGGS	29
	GGAGGAGGAGGAAGC	30
C D 6 3 - I L - 2	MAVEGGMKCVKFLLYVLLLAFCACAVGLIAIGVAVQVVLKQAITHETTAGSLLPVVI IAVGAFLLVAFVGGCGACKENYCLMITFAIFLSLIMLVEVAVAIAGYVFRDQVKSE FNKSFQQMQNYLKDNKTATILDKLQKENNCCGASNYTDWENIPGMAKDRVPDSCCG GGGSAPTSSSTSSSTAEEAQQQQQQQQQQHLEQLLMDLQELLSRMENYRNKLPRM LTFKFYLPKQATELKDLCLEDELGPLRHVLDLTQSKSFQLEDAENFISNIRVTVVK LKGSNTFECQFDDESATVVDLRRWIAFCQSIISTSPQGGGSINITVCGNDFKE STIHTQGCVETIAIWLRKNILLVAAAALGIAFVEVLGIIIFSCCLVKSIRSGYEV	31
	ATGGCGGTGGAAGGAGGAATGAAGTGTGTCAAGTTTTTGCTCTACGTTCTCCTGCTG GCCTTCTGCGCCTGTGCAGTGGGATTGATCGCCATTGGTGTAGCGGTTCAAGTTGTC TTGAAGCAGGCCATTACCCATGAGACTACTGCTGGCTCGCTGTTGCCTGTGGTCATC ATTGCAGTGGGTGCCTTCCTCTTCCTGGTGGCCTTTGTGGGCTGCTGTGGGGCCTGC AAGGAGAACTACTGTCTCATGATTACATTTGCCATCTTCCTGTCTCTTATCATGCTT GTGGAGGTGGCTGTGGCCATTGCTGGCTATGTGTTTAGAGACCAGGTGAAGTCAGAG TTTAATAAAAGCTTCCAGCAGCAGATGCAGAATTACCTTAAAGACAACAAAACAGCC	32

[Table 3-3]

	ACTATTTTGGACAAATTGCAGAAAGAAAATAACTGCTGTGGAGCTTCTAACTACACA GACTGGGAAAACATCCCCGGCATGGCCAAGGACAGAGTCCCCGATTCTTGCTGCGGA GGAGGAGGAAGCGCACCCACTTCAAGCTCCACTTCAAGCTCTACAGCGGAAGCACAG CAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCACCTGGAGCAGCTGTTGATGGAC CTACAGGAGCTCCTGAGCAGGATGGAGAATTACAGGAACCTGAAACTCCCCAGGATG CTCACCTTCAAATTTTACTTGCCCAAGCAGGCCACAGAATTGAAAGATCTTCAGTGC CTAGAAGATGAACTTGGACCTCTGCGGCATGTTCTGGATTTGACTCAAAGCAAAAGC TTTCAATTGGAAGATGCTGAGAATTTTCATCAGCAATATCAGAGTAACTGTTGTA CTAAAGGGCTCTGACAACACATTTGAGTGCCAATTCGATGATGAGTCAGCAACTGTG GTGGACTTTCTGAGGAGATGGATAGCCTTCTGTCAAAGCATCATCTCAACAAGCCCT CAAGGAGGAGGAGGAAGCATCAACATAACTGTGGGCTGTGGGAATGATTTCAAGGAA TCCACTATCCATACCCAGGGCTGCGTGGAGACTATAGCAATATGGCTAAGGAAGAAC ATACTGCTGGTGGCTGCAGCGGCCCTGGGCATTGCTTTTGTGGAGGTCTTGGGAATT ATCTTCTCCTGCTGTCTGGTGAAGAGTATTCGAAGTGGCTATGAAGTAATGTAG	

[0236]

[Table 4-1]

	Sequence	SEQ ID NO:
Signal peptide of MHC class I I β chain	<u>MALQIPSLLLSAAVVLMVLSSPGTEG</u>	33
	<u>ATGGCTCTGCAGATCCCCAGCCTCCTCTCGGCTGCTGTGGTGGTGTGATGGTG</u>	34
	<u>CTGAGCAGCCCAGGGACTGAGGGC</u>	
OVA peptide 2 (for MHC class II molecule)	ISQAVHAAHAEINEAGR	35
	ATATCTCAAGCTGTCCATGCAGCACATGCAGAAATCAATGAAGCAGGCAGA	36
MHC class I I β chain (from which signal peptide is removed)	GDSEHFVYQFMGECYFTNGTQRIRYVTRYIYNREEYVRYDSVGEHRAVTELGRPD AEYWNSQPEILERTRAELDTVCRHNYEGPETHTSLRRLEQPNVVISLSRTEALNHHN TLVCSVTDFYPAKIKVRWFRNGQEETVGVSSQLIRNGDWTQVLVMLEMTPRRGEV YTCHVEHPSLKSPIITVEWRAQSESAWSKMLSGIGGCVLGVIFLGLGLFIRHRSQKGP RGPPPAGLLQ	37
	GGAGACTCCGAAAGGCATTTCTGTACCAAGTTCATGGGCGAGTGCTACTTCACCAAC GGGACGCAGCGCATACGATATGTGACCAGATACATCTACAACCGGGAGGAGTACGTG CGCTACGACAGCGACGTGGGCGAGCACCGCGCGGTGACCGAGCTGGGGCGGCCAGAC GCCGAGTACTGGAACAGCCAGCCGGAGATCCTGGAGCGAACCGGGCCGAGCTGGAC ACGGTGTGCAGACACAACACTACGAGGGCGCGGAGACCCACACCTCCCTGCGGCGGCTT GAACAGCCCAATGTGTCATCTCCCTGTCCAGGACAGAGGCCCTCAACCACCACAAC ACTCTGGTCTGCTCAGTGACAGATTTCTACCCAGCCAAGATCAAAGTGGCTGGTTC CGGAATGGCCAGGAGGAGACGGTGGGGGTCTCATCCACACAGCTTATTAGGAATGGG GACTGGACCTTCCAGGTCTGCTCATGCTGGAGATGACCCCTCGGCGGGGAGAGGTC TACACCTGTCACGTGGAGCATCCCAGCCTGAAGAGCCCCATCACTGTGGAGTGGAGG GCACAGTCTGAGTCTGCCTGGAGCAAGATGTTGAGCGGCATCGGGGGCTGCGTGCTT GGGGTGATCTTCTCGGGCTTGGCCTTTTCATCCGTACAGGAGTCAGAAAGGACCT CGAGGCCCTCCTCCAGCAGGGCTCCTGCAG	38
Peptide linker 4	GGGSGGGGSG	39
	GGAGGAGGAGGAAGCGGAGGAGGAGGAAGCGGA	40
s c - D i m e r (OVA peptide 2 + peptide linker 4 + MHC class II β)	<u>MALQIPSLLLSAAVVLMVLSSPGTEG</u> ISQAVHAAHAEINEAGRGGGGSGGGSGGD SERHFVYQFMGECYFTNGTQRIRYVTRYIYNREEYVRYDSVGEHRAVTELGRPDAE YWNQPEILERTRAELDTVCRHNYEGPETHTSLRRLEQPNVVISLSRTEALNHHNTL VCSVTDFYPAKIKVRWFRNGQEETVGVSSQLIRNGDWTQVLVMLEMTPRRGEVYT	41

[Table 4-2]

chain (from which signal peptide is removed))	CHVEHPSLKSPITVEWRAQSESAWSKMLSGIGGCVLGVIFLGLGLFIRHRSQKGPRG PPPAGLLQ	
	<u>ATGGCTCTGCAGATCCCCAGCCTCCTCCTCTCGGCTGCTGTGGTGGTGTGATGGTG</u> <u>CTGAGCAGCCCAGGGACTGAGGGCATATCTCAAGCTGTCCATGCAGCACATGCAGAA</u> ATCAATGAAGCAGGCAGAGGAGGAGGAGGAAGCGGAGGAGGAGGAAGCGGAGGAGAC TCCGAAAGGCATTTCGTGTACCAGTTCATGGGCGAGTGCTACTTCACCAACGGGACG CAGCGCATACGATATGTGACCAGATACATCTACAACCGGGAGGAGTACGTGCGCTAC GACAGCGACGTGGGCGAGCACCGCGCGGTGACCGAGCTGGGCGGCCAGACGCCGAG TACTGGAACAGCCAGCCGGAGATCCTGGAGCGAACGCGGGCCGAGCTGGACACGGTG TGCAGACACAACCTACGAGGGGCCGGAGACCCACACCTCCCTGCGGCGGCTGAACAG CCCAATGTGTCATCTCCCTGTCCAGGACAGAGGCCCTCAACCACCACAACACTCTG GTCTGCTCAGTGACAGATTTCTACCCAGCCAAGATCAAAGTGCCTGTTCCGGAAT GGCCAGGAGGAGACGGTGGGGGTCTCATCCACACAGCTTATTAGGAATGGGGACTGG ACCTTCCAGGTCCTGGTCATGCTGGAGATGACCCCTCGGCGGGGAGAGGTCTACACC TGTCACGTGGAGCATCCCAGCCTGAAGAGCCCCATCACTGTGGAGTGGAGGGCACAG TCTGAGTCTGCCTGGAGCAAGATGTTGAGCGGCATCGGGGGCTGCGTGCTTGGGGTG ATCTTCCTCGGGCTTGGCCTTTTCATCCGTACAGGAGTCAGAAAGGACCTCGAGGC CCTCCTCCAGCAGGGCTCCTGCAG	42
s c - D i m e r - C D 8 1	<u>MALQIPSLLLSAAVVVLMVLSSPGTEGISQAVHAAHAEINEAGRGGGSGGGSSGDD</u> SERHFVYQFMGECYFTNGTQRIRYVTRYIYNREEYVRYDSVGEHRAVTELGRPDAE YWNSQPEILERTRAEALDTCRHNIEGPEHTSLRRLQPNVVISLSRTEALNHNHNTL VCSVTDFYPAKIKVRWFRNGQEETVGVSSSTQLIRNGDWTQVLVMLEMPRRGEVYT CHVEHPSLKSPITVEWRAQSESAWSKMLSGIGGCVLGVIFLGLGLFIRHRSQKGPRG PPPAGLLQMGVEGCTKCIKYLFLVFNFWLAGGVILGVALWLRHDPQTSLLYLEL GNKPAPNTFYVGIYILIAVGAVMMFVGLGCGYAIQESQCLLGTFFTCVLVIFACEV AAGIWGFVNKDQIAKDVKQFYDQALQQAVMDDDANNAKAVVKTFHETLNCCGSNALT TLTTTILRNSLCPSSGNILTPLLQQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEM ILSMVLCCGIRNSSVY	43
	<u>ATGGCTCTGCAGATCCCCAGCCTCCTCCTCTCGGCTGCTGTGGTGGTGTGATGGTG</u> <u>CTGAGCAGCCCAGGGACTGAGGGCATATCTCAAGCTGTCCATGCAGCACATGCAGAA</u> ATCAATGAAGCAGGCAGAGGAGGAGGAGGAAGCGGAGGAGGAGGAAGCGGAGGAGAC TCCGAAAGGCATTTCGTGTACCAGTTCATGGGCGAGTGCTACTTCACCAACGGGACG CAGCGCATACGATATGTGACCAGATACATCTACAACCGGGAGGAGTACGTGCGCTAC	44

[Table 4-3]

	GACAGCGACGTGGGCGAGCACCGCGCGGTGACCGAGCTGGGGCGGCCAGACGCCGAG TACTGGAACAGCCAGCCGGAGATCCTGGAGCGAACCGGGCCGAGCTGGACACGGTG TGCAGACACAACCTACGAGGGGCCGGAGACCCACACCTCCCTGCGGGCGGCTTGAACAG CCCAATGTCGTCATCTCCCTGTCCAGGACAGAGGCCCTCAACCACCACAACACTCTG GTCTGCTCAGTGACAGATTTCTACCCAGCCAAGATCAAAGTGCCTGGTTCCGGAAT GGCCAGGAGGAGACGGTGGGGGTCTCATCCACACAGCTTATTAGGAATGGGGACTGG ACCTTCCAGGTCCTGGTCATGCTGGAGATGACCCCTCGGGGGGAGAGGTCTACACC TGTCACGTGGAGCATCCCAGCCTGAAGAGCCCCATCACTGTGGAGTGGAGGGCACAG TCTGAGTCTGCCTGGAGCAAGATGTTGAGCGGCATCGGGGGCTGCGTGCTTGGGGTG ATCTTCTCGGGCTTGGCCTTTTCATCCGTACAGGAGTCAGAAAGGACCTCGAGGC CCTCCTCCAGCAGGGCTCCTGCAGATGGGGGTGGAGGGCTGCACCAAATGCATCAAA TACCTGCTCTTCGTCTTCAATTTTCGTCTTCTGGCTGGCTGGAGGCGTGATCCTAGGT GTAGCTCTGTGGTTGCGTCATGATCCACAGACCACCAGCCTGCTGTACCTGGAAGTG GGAAACAAACCGGCACCCAACACCTTCTACGTGGGCATCTACATTCTATTGCTGTG GGAGCTGTGATGATGTTTGTAGGCTTCTGGGGTCTATGGGGCCATCCAGGAGTCC CAGTGTCTGCTGGGGACGTTCTTCACCTGCCTTGTGATCCTGTTTGCCTGTGAGGTG GCTGCAGGCATCTGGGGCTTCGTAAACAAAGACCAGATCGCCAAGGATGTGAAGCAG TTCTATGACCAGGCCCTTCAGCAAGCTGTGATGGATGATGATGCCAACAAATGCCAAG GCTGTGGTGAAGACTTTCCATGAGACGCTCAACTGTTGTGGCTCCAACGCACTGACC ACACTGACTACCACCATACTGAGGAACAGCCTGTGTCCCTCAGGGCGCAACATACTC ACCCCTTACTGCAGCAAGATTGTATCAGAAAAATCGATGAGCTCTTCTCTGGGAAG CTGTACCTCATTGGAATTGCAGCCATTGTGGTAGCTGTCATTATGATCTTTGAGATG ATTCTGAGCATGGTGCTGTGCTGTGGCATCCGGAACAGCTCCGTGTACTGA	
MHC class I I α chain	<u>MPRSRALILGV LALTTMLS LCGGEDD</u> IEADHVGTYGISVYQSPGDIGQYTFEFDGDE LFYVDLDKKETVWMLPEFGQLASFDPPQGLQNIADVVKHNLGVLTGRSNSTPATNEAP QATVFPKSPVLLGQPNTLICFVDNIFPPVINITWLRNSKSVADGVYETSFFVNRDYS FHKLSYLTIFIPSDDDIYDCKVEHWGLEEPVLKHWEPEIPAPMSELTETVVCALGLSV GLVGIVVGTIFIITQGLRSGGTSRHPGPI	45
	<u>ATGCCGCGCAGCAGAGCTCTGATTCTGGGGGTCTCGCCCTGACCACCATGCTCAGC</u> <u>CTCTGTGGAGGTGAAGACGACATTGAGGCCGACCACGTAGGCACCTATGGTATAAGT</u> GTATATCAGTCTCCTGGAGACATTGGCCAGTACACATTTGAATTTGATGGTGATGAG TTGTTCTATGTGGACTTGATAAGAAGGAGACTGTCTGGATGCTTCTGAGTTTGGC CAATTGGCAAGCTTTGACCCCCAAGGTGGACTGCAAAACATAGCTGTAGTAAAACAC	46

[Table 4-4]

	AACTTGGGAGTCTTGACTAAGAGGTCAAATTCCACCCCAGCTACCAATGAGGCTCCT CAAGCGACTGTGTTCCCAAGTCCCCTGTGCTGCTGGGTCAGCCCAACACCCTCATC TGCTTTGTGGACAACATCTTCCCTCCTGTGATCAACATCACATGGCTCAGAAATAGC AAGTCAGTCGCAGACGGTGTATTATGAGACCAGCTTCTTCGTCAACCGTGACTATTCC TTCCACAAGCTGTCTTATCTCACCTTCATCCCTTCTGACGATGACATTTATGACTGC AAGGTGGAACACTGGGGCCTGGAGGAGCCGTTCTGAAACACTGGGAACCTGAGATT CCAGCCCCCATGTCAGAGCTGACAGAGACTGTGGTCTGTGCCCTGGGGTTGTCTGTG GGCCTTGTGGGCATCGTGGTGGGCACCATCTTCATCATTCAAGGCCTGCGATCAGGT GGCACCTCCAGACACCCAGGGCCTTTATGA	

[0237]

[Table 5-1]

	Sequence	SEQ ID NO:
T G F - β 1	MPPSGLRLLPLLLPLPWLLVLTGPRPAAGLSTSKTIDMELVKKRIEAIKQILSKL RLASPPSQGEVPPGGLPEAVLALYNSTRDRVAGESADPEPEPEADYYAKEVTRVLMV DRNNAIYEKTKDISHSIYMFNTSDIREAVPEPPLLSRAELRLQRLKSSVEQHVELY QKYSNNSWRYLGNRLLTPTDTPEWLSFDVTGVVRQWLNQGDGIQGFSAHSSSDSK DNKLHVEINGISPKRRLDGLTIHDMNRPFLLLMATPLERAQHLHSSRHRRALDTNYC FSSTEKNCCVRQLYIDFRKDLGWKWIHEPKGYHANFCLGPCPYIWSLDTQYSKVLAL YNQHNPASASPCVPQALEPLPIVYVGRKPKVEQLSNMIVRSCKCS	47
	<u>ATGCCGCCCTCGGGGCTCGGGCTACTGCCGCTTCTGCTCCCACTCCCGTGGCTTCTA</u> <u>GTGCTGACGCCCGGGAGGCCAGCCGCGGGACTCTCCACCTCTAAGACCATCGACATG</u> GAGCTGGTGAAACGGAAGCGCATCGAAGCCATCCGTGGCCAGATCCTGTCCAACTA AGGCTCGCCAGTCCCCAAGCCAGGGGAGGTACCGCCCGCCCGCTGCCCGAGGCG GTGCTCGCTTTGTACAACAGCACCCGCGACCGGGTGGCAGGCGAGAGCGCCGACCCA GAGCCGGAGCCCGAAGCGGACTACTATGCTAAAGAGGTCACCCGCGTGCTAATGGTG GACCGCAACAACGCCATCTATGAGAAAACAAAGACATCTCACACAGTATATATATG TTCTTCAATACGTCAGACATTGCGGAAGCAGTGCCCGAACCCCATGCTGTCCCGT GCAGAGCTGCGCTTGACAGATTAAAAACAAGTGTGGAGCAACATGTGGAACCTTAC CAGAAATATAGCAACAATCCTGGCGTTACCTTGGTAACCGGCTGCTGACCCCCACT GATACGCCTGAGTGGCTGTCTTTTGACGTCACTGGAGTTGTACGGCAGTGGCTGAAC CAAGGAGACGGAATACAGGGCTTTTCGATTACGCGCTCACTCTTCTTCTGACAGCAAA GATAACAACTCCACGTGGAATCAACGGGATCAGCCCCAACGTCGGGGCGACCTG GGCACCATCCATGACATGAACCGGCCCTTCTGCTCCTCATGGCCACCCCTTGAA AGGGCCAGCACCTGCACAGCTCACGGCACGGGAGGCCCTGGATACCAACTATTGC TTCAGCTCCACAGAGAAGAACTGCTGTGTGCGGCAGCTGTACATTGACTTTAGGAAG GACCTGGGTGGAAGTGATCCACGAGCCCAAGGGCTACCATGCCAACTTCTGTCTG GGACCTGCCCCCTATATTGGAGCCTGGACACACAGTACAGCAAGGTCCTTGCCCTC TACAACCAACACAACCCGGGCGCTTCGGCGTCACCGTGCTGCGTGCCGAGGCTTTG GAGCCACTGCCCATCGTCTACTACGTGGGTGCGAAGCCCAAGGTGGAGCAGTTGTCC AACATGATTGTGCGCTCCTGCAAGTGCAGCTGA	48
M F G - E 8 (from which signal peptide	ASGDFCDSSLCLNGGTCLTGQDNDIYCLCPEGFTGLVCNETERGPCSPNPCYNDAKC LVTLDTQRGEIFTEYICQCPVGYSGIHCETETNYNLDGEYMFHTAVPNTAVPTPAP	49

[Table 5-2]

is removed)	TPDLSNNLASRCSTQLGMEGGAIADSQISASSVYMGFMGLQRWGPELARLYRTGIVN AWTASNYDSKPWIQVNLLRKM RVSGVMTQGASRAGRAEYLKTFKVAYSLDGRKFEFI QDESGGDKEFLGNLDNNSLKVNMFNPTLEAQYIKLYPVSCHRGCTLRFELLGCELHG CSEPLGLKNN TIPDSQMSASSSYKTWNLRAFGWYPHLGRLDNQGKINAWTAQNSAK EWLQVDLGTQRQVTGIITQGARDFGHIQYVASYKVAHSDDG VQWTVYEEQGS SKVPQ GNLDNNSHKKNIFEKPFMARYVRVLPVSWHN RITLRLELLGC	
	GCGTCTGGTGACTTCTGTGACTCCAGCCTGTGCCTGAACGGTGGCACCTGCTTGACG GGCCAAGACAATGACATCTACTGCCTCTGCCCTGAAGGCTTCACAGGCCCTGTGTGC AATGAGACTGAGAGAGGACCATGCTCCCCAAACCCTTGCTACAATGATGCCAAATGT CTGGTGACTTTGGACACACAGCGTGGGGAAATCTTCACCGAATACATCTGCCAGTGC CCTGTGGGCTACTCGGGCATCCACTGTGAAACCGAGACCACTACTACAACCTGGAT GGAGAATACATGTTCAACACAGCCGTCCCCAATACTGCCGTCCCCACCCGGCCCCC ACCCCGATCTTTCCAACAACCTAGCCTCCCGTTGTTCTACACAGCTGGGCATGGAA GGGGCGCCATTGCTGATTCACAGATTTCCGCCTCGTCTGTGTATATGGGTTTCATG GGCTTGACAGCGCTGGGGCCCGAGCTGGCTCGTCTGTACCGCACAGGGATCGTCAAT GCCTGGACAGCCAGCAACTATGATAGCAAGCCCTGGATCCAGGTGAACCTTCTGCGG AAGATGCGGGTATCAGGTGTGATGACGCAGGGTGCCAGCCGTGCCGGGAGGGCGGAG TACCTGAAGACCTTCAAGGTGGCTTACAGCCTCGACGGACGCAAGTTTGAGTTCATC CAGGATGAAAGCGGTGGAGACAAGGAGTTTTTGGGTAACCTGGACAACAACAGCCTG AAGGTTAACATGTTCAACCCGACTCTGGAGGCACAGTACATAAAGCTGTACCCTGTT TCGTGCCACCGCGGCTGCACCTCCGCTTCGAGCTCCTGGGCTGTGAGTTGCACGGA TGTTCTGAGCCCCTGGGCCTGAAGAATAACACAATTCTGACAGCCAGATGTCAGCC TCCAGCAGCTACAAGACATGGAACCTGCGTGCTTTTGGCTGGTACCCCACTTGGGA AGGCTGGATAATCAGGGCAAGATCAATGCCTGGACGGCTCAGAGCAACAGTGCCAAG GAATGGCTGCAGGTTGACCTGGGCACTCAGAGGCAAGTGACAGGAATCATCACCCAG GGGGCCCGTGACTTTGGCCACATCCAGTATGTGGCGTCTACAAGGTAGCCACAGT GATGATGGTGTGAGTGGACTGTATATGAGGAGCAAGGAAGCAGCAAGGTCTTCCAG GGCAACTTGGACAACAACCTCCACAAGAAGAATCTTCGAGAAACCCTTCATGGCT CGCTACGTGCGTGTCTTCCAGTGTCTGGCATAACCGCATCACCTGCGCCTGGAG CTGCTGGGCTGTAA	50
T G F - β 1 - M F G - E 8 (TGF-β 1 +	<u>MPPSGLRLLPLLPLPWL</u>LVLTGPRPAAGLSTSKTIDMELVKRKRIEAI RQILSKL RLASPPSQGEVPPGPLPEAVLALYNSTRDRVAGESADPEPEPEADYYAKEVTRVLMV DRNNAIYEKTKDISHSIYMFNTSDIREAVPEPPLLSRAELRLQRLKSSVEQHVELY	51

[Table 5-3]

peptide linker 3 + MFG-E8 (from which signal peptide is removed))	QKYSNNSWRYLGNRLLTPTDTPEWLSFDVTGVVRQWLNQGDGIQGFRPSAHSSSSDK DNKLHVEINGISPKRRGDLGTIHDNMRPFLLLMATPLERAQHLHSSSRHRRALDTNYC FSSTEKNCCVRQLYIDFRKDLGWKWIHEPKGYHANFCLGPCPYIWSLDTQYSKYLAL YNQHNPASASPCCVPQALEPLPIVYVGRKPKVEQLSNMIVRSCKCSGGGGSASGD FCDSSLCLNGGTCLTGQDNDIYCLCPEGFTGLVCNETERGPCSPNPCYNDACKLVTL DTQRGEIFTEYICQCPVGYSIHCETETNYYNLDGEYMFTTAVPNTAVPTPAPTDL SNNLASRCSTQLGMEGGAIADSQISASSVYMGFMGLQRWGPELARLYRTGIVNAWTA SNYDSKPWIQVNLRLKMRVSGVMTQCASRAGRAEYLKTFKVAYSLDGRKFEFIQDES GGDKFLGNLDNNSLKVNMFNPTLEAQYIKLYPVSCHRGCTLRFELLGCELHGCSEP LGLKNNTIPDSQMSASSSYKTWNLRAFGWYPHLGRLDNQKINAWTAQNSAKEWLQ VDLGTQRQVTGIITQGARDFGHIQYVASYKVAHSDDGVTQVYEEQGSSKVFQGNLD NNSHKKNIFEKPFMARYVRVLPVSWHNRLITLRELLGC	
	<u>ATGCCGCCCTCGGGGCTCGGGCTACTGCCGCTTCTGCTCCCACTCCCGTGGCTTCTA</u> <u>GTGCTGACGCCCGGGAGGCCAGCCGCGGGACTCTCCACCTCTAAGACCATCGACATG</u> GAGCTGGTGAAACGGAAGCGCATCGAAGCCATCCGTGGCCAGATCCTGTCCAAACTA AGGCTCGCCAGTCCCCAAGCCAGGGGAGGTACCGCCCGCCCGCTGCCCGAGGCG GTGCTCGCTTTGTACAACAGCACCCGCGACCGGGTGGCAGGCGAGAGCGCCGACCCA GAGCCGGAGCCCGAAGCGGACTACTATGCTAAAGAGGTACCCGCGTGCTAATGGTG GACCGCAACAACGCCATCTATGAGAAAACCAAAGACATCTCACACAGTATATATATG TTCTTCAATACGTCAGACATTCGGGAAGCAGTGCCCGAACCCCATTTGCTGTCCCGT GCAGAGCTGCGCTTGAGAGATTAAATCAAGTGTGGAGCAACATGTGGAACCTCTAC CAGAAATATAGCAACAATTCCTGGCGTTACCTTGCTAACCGGCTGCTGACCCCACT GATACGCCTGAGTGGCTGTCTTTTACGTCACCTGGAGTTGTACGGCAGTGGCTGAAC CAAGGAGACGGAATACAGGGCTTTGATTACGCGCTCACTCTTCTTCTGACAGCAAA GATAACAACTCCACGTGGAATCAACGGGATCAGCCCCAACGTCGGGGCGACCTG GGCACCATCCATGACATGAACCGGCCCTTCTGCTCCTCATGGCCACCCCTTGAA AGGGCCAGCACCTGCACAGCTCACGGCACCGGAGAGCCCTGGATACCAACTATTGC TTCAGCTCCACAGAGAAGAACTGCTGTGTGCGGCAGCTGTACATTGACTTTAGGAAG GACCTGGGTTGGAAGTGGATCCACGAGCCCAAGGGCTACCATGCCAATTCTGTCTG GGACCTGCCCCTATATTGGAGCCTGGACACACAGTACAGCAAGGTCCTTGCCCTC TACAACCAACACAACCCGGCGCTTCGGCGTCACCGTGCTGCGTGCCGAGGCTTTG GAGCCACTGCCCATCGTCTACTACGTGGGTGCGAAGCCCAAGGTGGAGCAGTTGTCC AACATGATTGTGCGCTCCTGCAAGTGCAGCGGAGGAGGAGGAAGCGCGTCTGGTGAC	52

[Table 5-4]

	TTCTGTGACTCCAGCCTGTGCCTGAACGGTGGCACCTGCTTGACGGGCCAAGACAAT GACATCTACTGCCTCTGCCCTGAAGGCTTCACAGGCCTTGTGTGCAATGAGACTGAG AGAGGACCATGCTCCCCAAACCCTTGCTACAATGATGCCAAATGTCTGGTGACTTTG GACACACAGCGTGGGGAAATCTTCACCGAATACATCTGCCAGTGCCCTGTGGGCTAC TCGGGCATCCACTGTGAAACCGAGACCACTACTACAACCTGGATGGAGAATACATG TTCACCACAGCCGTCCCCAATACTGCCGTCCCCACCCGGCCCCACCCCGATCTT TCCAACAACCTAGCCTCCCGTTGTTCTACACAGCTGGGCATGGAAGGGGGGCCATT GCTGATTCACAGATTTCCGCCTCGTCTGTGTATATGGGTTTCATGGGCTTGACGCGC TGGGGCCCGGAGCTGGCTCGTCTGTACCGCACAGGGATCGTCAATGCCTGGACAGCC AGCAACTATGATAGCAAGCCCTGGATCCAGGTGAACCTTCTGCCGAAGATGCGGGTA TCAGGTGTGATGACGCAGGGTGCCAGCCGTGCCGGGAGGGCGGAGTACCTGAAGACC TTCAAGGTGGCTTACAGCCTCGACGGACGCAAGTTTGAGTTTCATCCAGGATGAAAGC GGTGGAGACAAGGAGTTTTTGGGTAACCTGGACAACAACAGCCTGAAGGTAAACATG TTCAACCCGACTCTGGAGGCACAGTACATAAAGCTGTACCCTGTTTCGTGCCACCGC GGCTGCACCCTCCGCTTCGAGCTCCTGGGCTGTGAGTTGCACGGATGTTCTGAGCCC CTGGGCCTGAAGAATAACACAATTCTGACAGCCAGATGTCAGCCTCCAGCAGCTAC AAGACATGGAACCTGCGTGCTTTTGGCTGGTACCCCACTTGGGAAGGCTGGATAAT CAGGGCAAGATCAATGCCTGGACGGCTCAGAGCAACAGTGCCAAGGAATGGCTGCAG GTTGACCTGGGCACTCAGAGGCAAGTGACAGGAATCATCACCAGGGGGCCCGTGAC TTTGGCCACATCCAGTATGTGGCGTCCTACAAGGTAGCCACAGTGATGATGGTGTG CAGTGGACTGTATATGAGGAGCAAGGAAGCAGCAAGGTCTTCCAGGGCAACTTGGAC AACAACTCCCACAAGAAGAATCTTCGAGAAACCCTTCATGGCTCGCTACGTGCGT GTCCTTCCAGTGTCTGGCATAACCGCATCACCTGCGCCTGGAGCTGCTGGGCTGT TAA	

[0238]

[Table 6-1]

	Sequence	SEQ ID NO:
I L - 4 (from which signal peptide is removed)	HIHGCDKNHLREIIIGILNEVTGEGTPCTEMDVPNVLTATKNTTESELVCRASKVLRI FYLKHGKTPCLKKNSSVLMELQRLFRFRCLDSSISCTMNESKSTSLKDFLESLSKI MQMDYS	53
	CATATCCACGGATGCGACAAAAATCACTTGAGAGAGATCATCGGCATTTGAACGAG GTACAGGAGAAGGGACGCCATGCACGGAGATGGATGTGCCAAACGCTCACAGCA ACGAAGAACACCACAGAGAGTGAGCTCGTCTGTAGGGCTTCCAAGGTGCTTCGCATA TTTTATTTAAACATGGGAAACTCCATGCTTGAAGAAGAACTCTAGTGTTCTCATG GAGCTGCAGAGACTCTTTCGGGCTTTTCGATGCCTGGATTATCGATAAGCTGCACC ATGAATGAGTCCAAGTCCACATCACTGAAAGACTTCCTGGAAAGCCTAAAGAGCATC ATGCAAATGGATTACTCGTAG	54
C D 8 1 (amino acids 1 to 177)	MGVEGCTKCIKYLFFVFNFWLAGGVILGVALWLRHDPQTSLLYLELGNKPAPNT FYVGIYILIAVGAVMMFVGLGCGAIQESQCLLGTFFTCLVILFACEVAAGIWGFV NKDQIAKDVQFYDQALQQAVMDDANNAKAVVKTFFHETLNCCGSNALTTLTITLR NSLCPS	61
	ATGGGGGTGGAGGGCTGCACCAAATGCATCAAATACCTGCTCTTCGTCTTCAATTC GTCTTCTGGCTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGTCATGAT CCACAGACCACCAGCCTGCTGTACCTGGAAGTGGGAAACAAACCGGCACCCAACACC TTCTACGTGGGCATCTACATTCTCATTGCTGTGGGAGCTGTGATGATGTTGTAGGC TTCCTGGGGTGCTATGGGGCCATCCAGGAGTCCCAGTGTCTGCTGGGGACGTTCTTC ACCTGCCTTGTGATCCTGTTGCCTGTGAGGTGGCTGCAGGCATCTGGGGCTTCGTA AACAAAGACCAGATCGCCAAGGATGTGAAGCAGTTCTATGACCAGGCCCTTCAGCAA GCTGTGATGGATGATGATGCCAACAATGCCAAGGCTGTGGTGAAGACTTTCATGAG ACGCTCACTGTTGTGGCTCCAACGCACTGACCACACTGACTACCACCATACTGAGG AACAGCCTGTGTCCCTCA	62
C D 8 1 (amino acids 178 to 236)	GGNILTPLLQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSS VY	63
	GGCGGCAACATACTACCCCTTACTGCAGCAAGATTGTCATCAGAAAATCGATGAG CTCTTCTCTGGGAAGCTGTACCTCATTGGAATTGCAGCCATTGTGGTAGCTGTCATT ATGATCTTTGAGATGATTCTGAGCATGGTGCTGTGCTGTGGCATCCGGAACAGCTCC GTGTACTGA	64

[Table 6-2]

CD 81 - I L - 4	MGVEGCTKCIKYLLFVFNFWLWLAGGVILGVALWLRHDPQTTSLLYLELGNKPAPNT FYVGIYILIAVGAVMMFVGFGLGCGYGAIQESQCLLGTFFTCLVILFACEVAAGIWGFV NKDQIAKDVKQFYDQALQQAVMDDDDANNAKAVVKTFFHETLNCCGSNALTTLTITILR NSLCPSGGGGSHIHGCDKNHLREIIGILNEVTGEGTPCTEMDVPNVLTATKNTTESE LVCRAKSVLRIFYLKHGKTPCLKKNSSVLMELQRLFRAFRCLDSSISCTMNESKSTS LKDFLESLSIMQMDYSGGGGSGGNILTPLLQQDCHQKIDELFSGKLYLIGIAAIVV AVIMIFEMILSMVLCCGIRNSSVY	55
	ATGGGGGTGGAGGGCTGCACCAATGCATCAAATACCTGCTCTTCGTCTTCAATTC GTCTTCTGGCTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGTCATGAT CCACAGACCACCAGCCTGCTGTACCTGGAAGTGGGAAACAAACCGGCACCAACACC TTCTACGTGGGCATCTACATTCTCATTGCTGTGGGAGCTGTGATGATGTTTGTAGGC TTCCTGGGGTGCTATGGGGCCATCCAGGAGTCCCAGTGTCTGCTGGGGACGTTCTTC ACCTGCCTTGTGATCCTGTTTGCTGTGAGGTGGCTGCAGGCATCTGGGGCTTCGTA AACAAAGACCAGATCGCCAAGGATGTGAAGCAGTTCTATGACCAGGCCCTTCAGCAA GCTGTGATGGATGATGATGCCAACAATGCCAAGGCTGTGGTGAAGACTTTCCATGAG ACGCTCAACTGTTGTGGCTCCAACGCACTGACCACACTGACTACCACCATACTGAGG AACAGCCTGTGTCCCTCAGGAGGAGGAGGAAGCCATATCCACGGATGCGACAAAAAT CACTTGAGAGAGATCATCGGCATTTTGAACGAGGTCACAGGAGAAGGGACGCCATGC ACGGAGATGGATGTGCCAAACGTCCTCACAGCAACGAAGAACCACAGAGAGTGAG CTCGTCTGTAGGGCTTCCAAGGTGCTTCGCATATTTTATTTAAACATGGGAAAAC CCATGCTTGAAGAAGAACTCTAGTGTCTCATGGAGCTGCAGAGACTCTTTCGGGCT TTTCGATGCCTGGATTTCATCGATAAGCTGCACCATGAATGAGTCCAAGTCCACATCA CTGAAAGACTTCCTGGAAAGCCTAAAGAGCATCATGCAAATGGATTACTCGGGAGGA GGAGGAAGCGGGGCAACATACTACCCCTTACTGCAGCAAGATTGTCATCAGAAA ATCGATGAGCTCTTCTGTGGGAAGCTGTACCTCATTGGAATTGCAGCCATTGTGGTA GCTGTCATTATGATCTTTGAGATGATTCTGAGCATGGTGTGCTGTGGCATCCGG AACAGCTCCGTGTACTGA	56

[Table 7-1]

	Sequence	SEQ ID NO:
Signal peptide of MHC class I I β chain	<u>MALQIPSLLLSAVVVLMVLSSPGTEG</u>	33
	<u>ATGGCTCTGCAGATCCCCAGCCTCCTCCTCGGCTGCTGTGGTGGTCTGATGGTCTGAGC</u>	34
	<u>AGCCCAGGGACTGAGGGC</u>	
OVA peptide 2 (for MHC class II molecule)	ISQAVHAAHAEINEAGR	35
	ATATCTCAAGCTGTCCATGCAGCACATGCAGAAATCAATGAAGCAGGCAGA	
MHC class I I β chain (from which signal peptide is removed)	GDSEHFVYQFMGECYFTNGTQRIRYVTRYIYNREEYVRYDSVGEHRAVTELGRPDAEYWNS QPEILERTRAELDTVCRHNYEGPETHTSLRRLEQPNVVISLSRTEALNHHNTLVCSVTDFYPA KIKVRWFRNGQEETVGVSSSTQLIRNGDWTQVLVMLEMTPRRGEVYTCHVEHPSLKSPTITVEW RAQSESAWSKMLSGIGGCVLGVIFLGLGLFIRHRSQKGRGPPPPAGLLQ	36
	GGAGACTCCGAAAGGCATTTCTGTACCAAGTTCATGGGCGAGTGCTACTTCACCAACGGGACG CAGCGCATACGATATGTGACCAGATACATCTACAACCGGGAGGAGTACGTGCGCTACGACAGC GACGTGGGCGAGCACCGCGCGGTGACCGAGCTGGGGCGGCCAGACGCCGAGTACTGGAACAGC CAGCCGGAGATCCTGGAGCGAACCGGGCCGAGCTGGACACGGTGTGCAGACAACTACGAG GGGCGGAGACCCACACCTCCCTGCGGCGGCTGAACAGCCCAATGTCGTCTCTCCCTGTCC AGGACAGAGGCCCTCAACCACCACAACACTCTGGTCTGCTCAGTGACAGATTCTACCCAGCC AAGATCAAAGTGCCTGGTTCGGAATGGCCAGGAGGAGACGGTGGGGGTCTCATCCACACAG CTTATTAGGAATGGGACTGGACCTTCCAGGTCTGGTCATGCTGGAGATGACCCCTCGGCGG GGAGAGGTCTACACCTGTACAGTGGAGCATCCCAGCCTGAAGAGCCCCATCACTGTGGAGTGG AGGGCACAGTCTGAGTCTGCCTGGAGCAAGATGTTGAGCGGCATCGGGGCTGCGTCTTGGG GTGATCTTCTCGGCTTGGCCTTTTCATCCGTCACAGGAGTCAGAAAGGACCTCGAGGCCCT CCTCCAGCAGGGCTCCTGCAG	37
Peptide linker 4	GGGSGGGSG	39
	GGAGGAGGAGGAAGCGGAGGAGGAGGAAGCGGA	40
s c - D i m e r (OVA peptide 2 + peptide linker 4 + MHC class II β chain (from which signal peptide is removed))	<u>MALQIPSLLLSAVVVLMVLSSPGTEG</u> ISQAVHAAHAEINEAGRGGGSGGGSGGDSEHFV YQFMGECYFTNGTQRIRYVTRYIYNREEYVRYDSVGEHRAVTELGRPDAEYWNSQPEILERT RAELDTVCRHNYEGPETHTSLRRLEQPNVVISLSRTEALNHHNTLVCSVTDFYPAKIKVRWFR NGQEETVGVSSSTQLIRNGDWTQVLVMLEMTPRRGEVYTCHVEHPSLKSPTITVEWRAQSESAW SKMLSGIGGCVLGVIFLGLGLFIRHRSQKGRGPPPPAGLLQ	41
	<u>ATGGCTCTGCAGATCCCCAGCCTCCTCCTCGGCTGCTGTGGTGGTCTGATGGTCTGAGC</u> <u>AGCCCAGGGACTGAGGGC</u> ATATCTCAAGCTGTCCATGCAGCACATGCAGAAATCAATGAAGCA GGCAGAGGAGGAGGAAGCGGAGGAGGAAGCGGAGGAGACTCCGAAAGGCATTTCTGTG TACCAGTTCATGGGCGAGTGCTACTTCACCAACGGGACGCAGCGCATACGATATGTGACCAGA	42

[Table 7-2]

	TACATCTACAACCGGGAGGAGTACGTGCGCTACGACAGCGACGTGGGCGAGCACCGCGCGGTG ACCGAGCTGGGGCGGCCAGACGCCGAGTACTGGAACAGCCAGCCGAGATCCTGGAGCGAACG CGGGCCGAGCTGGACACGGTGTGCAGACACAACCTACGAGGGGCCGAGACCCACACCTCCCTG CGGCGGCTTGAACAGCCCAATGTCGTCATCTCCCTGTCCAGGACAGAGGCCCTCAACCACCAC AACACTCTGGTCTGCTCAGTGACAGATTCTACCCAGCCAAGATCAAAGTGCCTGGTTCCGG AATGGCCAGGAGGAGACGGTGGGGGTCTCATCCACACAGCTTATTAGGAATGGGGACTGGACC TTCCAGGTCCTGGTCATGCTGGAGATGACCCCTCGGCGGGGAGAGGTCTACACCTGTCACGTG GAGCATCCCAGCCTGAAGAGCCCCATCACTGTGGAGTGGAGGGCACAGTCTGAGTCTGCCTGG AGCAAGATGTTGAGCGGCATCGGGGGCTGCGTGCTTGGGGTGATCTTCTCGGGCTTGGCCTT TTCATCCGTCACAGGAGTCAGAAAGGACCTCGAGGCCCTCCTCCAGCAGGGCTCCTGCAG	
s c - D i m e r - C D 8 1 - I L - 1 2 α	<u>MALQIPSLLLSAVVVLMVLSSPGTEGISQAVHAAHAEINEAGRGGGSGGGSGGDSERHFV</u> YQFMGECYFTNGTQRIRYVTRYIYNREEYVRYDSVGEHRAVTELGRPDAEYWNSQPEILERT RAELDTVCRHNYEGPETHSLRRLQPNVVISLSRTEALNHHNTLVCSVTDYFPAKIKVRWFR NGQEETVGVSSSTQLIRNGDWTQVLVMLEMTPRRGEVYTCHVEHPSLKSPITVEWRAQSESAW SKMLSGIGGCVLGVIFLGLGFIHRHSQKGRGPPPPAGLLQMGVEGCTKCIKYLFFVFNFW LAGGVILGVALWLRHDPQTSLLYLELGNKPAPNTFYVGIYILIAVGAVMMFVFLGCGYAIQ ESQCLLGFTTCLVILFACEVAAGIWGFVNKDQIAKDVQFYDQALQQAUMDDANNAKAVVK TFHETLNCCGSNALTTLTITILRNSLCPSGGGGSRVIPVSGPARCLSQSRNLLKTTDDMVKTA REKLKHYSCTAEDIDHEDITRDQSTLKTCLPLELHKNESCLATRETSSTTRGSCLPPQKTS MMTLCLGSIYEDLKMYQTEFQAINAALQNHNHQQIILDKGMLVAIDELMQSLNHNGETLRQKP PVGEADPYRVKMKLCILLHAFSTRVVTINRVMGYLSSAGGGSGGNILTPLQQDCHQKIDEL FSGKLYLIGIAIVVAVIMIFEMILSMVLCCGIRNSSVY	91
	<u>ATGGCTCTGCAGATCCCCAGCCTCCTCCTCTCGGCTGCTGTGGTGGTGTGATGGTGTGAGC</u> <u>AGCCAGGGACTGAGGGCATATCTCAAGCTGTCCATGCAGCACATGCAGAAATCAATGAAGCA</u> GGCAGAGGAGGAGGAGGAAGCGGAGGAGGAGGAAGCGGAGGAGACTCCGAAAGGCATTTCGTG TACCAGTTCATGGGCGAGTGCTACTTACCAACGGGACGCAGCGCATACGATATGTGACCAGA TACATCTACAACCGGGAGGAGTACGTGCGCTACGACAGCGACGTGGGCGAGCACCGCGCGGTG ACCGAGCTGGGGCGGCCAGACGCCGAGTACTGGAACAGCCAGCCGAGATCCTGGAGCGAACG CGGGCCGAGCTGGACACGGTGTGCAGACACAACCTACGAGGGGCCGAGACCCACACCTCCCTG CGGCGGCTTGAACAGCCCAATGTCGTCATCTCCCTGTCCAGGACAGAGGCCCTCAACCACCAC AACACTCTGGTCTGCTCAGTGACAGATTCTACCCAGCCAAGATCAAAGTGCCTGGTTCCGG AATGGCCAGGAGGAGACGGTGGGGGTCTCATCCACACAGCTTATTAGGAATGGGGACTGGACC TTCCAGGTCCTGGTCATGCTGGAGATGACCCCTCGGCGGGGAGAGGTCTACACCTGTCACGTG GAGCATCCCAGCCTGAAGAGCCCCATCACTGTGGAGTGGAGGGCACAGTCTGAGTCTGCCTGG AGCAAGATGTTGAGCGGCATCGGGGGCTGCGTGCTTGGGGTGATCTTCTCGGGCTTGGCCTT	92

[Table 7-3]

	TTCATCCGTCACAGGAGTCAGAAAGGACCTCGAGGCCCTCCTCCAGCAGGGCTCCTGCAGATG GGGGTGGAGGGCTGCACCAAATGCATCAAATACCTGCTCTTCGTCTTCAATTTCTGCTTCTGG CTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGTCATGATCCACAGACCACCAGC CTGCTGTACCTGGAACCTGGGAAACAAACCGGCACCCAACACCTTCTACGTGGGCATCTACATT CTCATTGCTGTGGGAGCTGTGATGATGTTTGTAGGCTTCTGGGGTCTATGGGGCCATCCAG GAGTCCCACTGTCTGCTGGGGACGTTCTTCACCTGCCTTGTGATCCTGTTTGCCTGTGAGGTG GCTGCAGGCATCTGGGGCTTCGTAAACAAAGACCAGATCGCCAAGGATGTGAAGCAGTTCTAT GACCAGGCCCTTCAGCAAGCTGTGATGGATGATGATGCCAACAATGCCAAGGCTGTGGTGAAG ACTTTCCATGAGACGCTCAACTGTTGTGGCTCCAACGCACTGACCACACTGACTACCACCATA CTGAGGAACAGCCTGTGTCCCTCAGGAGGAGGAGGAAGCAGGGTCATTCCAGTCTCTGGACCT GCCAGGTGTCTTAGCCAGTCCCGAAACCTGCTGAAGACCACAGATGACATGGTGAAGACGGCC AGAGAAAACTGAAACATTATTCCTGCACTGCTGAAGACATCGATCATGAAGACATCACACGG GACCAAACCAGCACATTGAAGACCTGTTTACCACTGGAACACACAAGAACGAGAGTTGCCTG GCTACTAGAGAGACTTCTTCCACAACAAGAGGGAGCTGCCTGCCCCACAGAAGACGCTCTTTG ATGATGACCCTGTGCCTTGGTAGCATCTATGAGGACTTGAAGATGTACCAGACAGAGTTCCAG GCCATCAACGCAGCACTTCAGAATCACAACCATCAGCAGATCATTCTAGACAAGGGCATGCTG GTGGCCATCGATGAGCTGATGCAGTCTCTGAATCATAATGGCGAGACTCTGCGCCAGAAACCT CCTGTGGGAGAAGCAGACCCCTTACAGAGTGAAAAATGAAGCTCTGCATCCTGCTTCACGCCTTC AGCACCCGCGTCTGACCATCAACAGGGTGTGGGCTATCTGAGCTCCGCCGAGGAGGAGGA AGCGGCGGCAACATACTCACCCCTTACTGCAGCAAGATTGTCATCAGAAAATCGATGAGCTC TTCTCTGGGAAGCTGTACCTCATTGGAATTGCAGCCATTGTGGTAGCTGTCTATTATGATCTTT GAGATGATTCTGAGCATGGTGTCTGTCTGTGGCATCCGGAACAGCTCCGTGTACTGA	
MHC class I I α chain	<u>MPRSRALILGVLALTTLMLSLCGGEDDIEADHVGTGYSVYQSPGDIGQYTFEFDGDELFFYVDL</u> DKKETVWMLPEFGQLASFDPPQGLQNIADVKNHNLGVLTKRSNSTPATNEAPQATVFPKSPVLL GQPNTLICFVDNIFPPVINITWLRNSKSVADGVYETSFFVNRDYSFHKLSYLTIFIPSDDDIYD CKVEHWGLEEPVLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTIFI IQGLRSGGTSRH PGPL	45
	<u>ATGCCGCGCAGCAGAGCTCTGATTCTGGGGGTCTCGCCCTGACCACCATGCTCAGCCTCTGT</u> <u>GGAGGTGAAGACGACATTGAGGCCGACCACGTAGGCACCTATGGTATAAGTGATATCAGTCT</u> CCTGGAGACATTGGCCAGTACACATTTGAATTTGATGGTGATGAGTTGTTCTATGTGGACTTG GATAAGAAGGAGACTGTCTGGATGCTTCCTGAGTTTGGCCAATTGGCAAGCTTTGACCCCCAA GGTGGACTGCAAAACATAGCTGTAGTAAACACAACCTGGGAGTCTTGACTAAGAGGTCAAAT TCCACCCAGCTACCAATGAGGCTCCTCAAGCGACTGTGTTCCCAAGTCCCTGTGCTGCTG GGTCAGCCCAACACCTCATCTGCTTTGTGGACAACATCTCCCTCCTGTGATCAACATCACA TGGCTCAGAAATAGCAAGTCAGTCGCAGACGGTGTATGAGACCAGCTTCTTCGTCAACCGT	46

[Table 7-4]

	GACTATTCCTTCCACAAGCTGTCTTATCTCACCTTCATCCCTTCTGACGATGACATTTATGAC TGCAAGGTGGAACACTGGGGCCTGGAGGAGCCGGTTCTGAAACACTGGGAACCTGAGATTCCA GCCCCATGTCAGAGCTGACAGAGACTGTGGTCTGTGCCCTGGGGTTGTCTGTGGGCCTTGTG GGCATCGTGGTGGGCACCATCTTCATCATTCAAGGCCTGCGATCAGGTGGCACCTCCAGACAC CCAGGGCCTTTATGA	

[0240]

[Table 8-1]

	Sequence	SEQ ID NO:
I L - 1 2 α (from which signal peptide is removed)	RVIPVSGPARCLSQSRNLLKTTDDMVKTAREKLKHYSCTAEDIDHEDITRDQTSTLKTCLPLE LHKNESCLATRETSSTTRGSCLPQKTSMMTLCLGSIYEDLKMYQTEFQAINAALQNHNHQQ IILDKGMLVAIDELMQSLNHNGETLRQKPPVGEADPYRVKMKLCILLHAFSTRVVTINRVMGY LSSA	93
	AGGGTCATTCCAGTCTCTGGACCTGCCAGGTGTCTTAGCCAGTCCCGAAACCTGCTGAAGACC ACAGATGACATGGTGAAGACGGCCAGAGAAAACTGAAACATTATTCTGCACTGCTGAAGAC ATCGATCATGAAGACATCACACGGGACCAAACCAGCACATTGAAGACCTGTTTACCACTGGAA CTACACAAGAACGAGAGTTGCCTGGCTACTAGAGAGACTTCTCCACAACAAGAGGGAGCTGC CTGCCCCACAGAAGACGTCTTTGATGATGACCCTGTGCCTTGGTAGCATCTATGAGGACTTG AAGATGTACCAGACAGAGTTCCAGGCCATCAACGCAGCACTTCAGAATCACAACCATCAGCAG ATCATTCTAGACAAGGGCATGCTGGTGGCCATCGATGAGCTGATGCAGTCTCTGAATCATAAT GGCGAGACTCTGCGCCAGAAACCTCCTGTGGGAGAAGCAGACCCCTTACAGAGTGAAAATGAAG CTCTGCATCCTGCTTCACGCCTTCAGCACCCGCGTCGTGACCATCAACAGGGTGATGGGCTAT CTGAGCTCCGCC	94
C D 8 1 (amino acids 1 to 177)	MGVEGCTKCIKYLFFVFNFWLAGGVILGVALWLRHDPQTSLLYLELGNKPAPNTFYVGIY ILIAVGAVMMFVGLGCGYGAIQESQCLLGTFFTCLVILFACEVAAGIWGFVNKDQIAKDVKQF YDQALQQAVMDDDANNAKAVVKTFHETLNCCGSNALTTLTTLILRNSLCPS	61
	ATGGGGGTGGAGGGCTGCACCAATGCATCAAATACCTGCTCTTCGTCTTCAATTCGTCTTC TGGCTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGTCATGATCCACAGACCACC AGCCTGCTGTACCTGGAACCTGGGAAACAAACCGGCACCCAACACCTTCTACGTGGGCATCTAC ATTCTCATTGCTGTGGGAGCTGTGATGATGTTTGTAGGCTTCCTGGGGTGCTATGGGGCCATC CAGGAGTCCCAGTGTCTGCTGGGGACGTTCTTCACTGCCTTGTGATCCTGTTTGCCTGTGAG GTGGCTGCAGGCATCTGGGGCTTCGTAAACAAAGACCAGATCGCCAAGGATGTGAAGCAGTTC TATGACCAGGCCCTTCAGCAAGCTGTGATGGATGATGATGCCAACAATGCCAAGGCTGTGGTG AAGACTTTCATGAGACGCTCAACTGTTGTGGCTCCAACGCACTGACCACACTGACTACCACC ATACTGAGGAACAGCCTGTGTCCCTCA	62
C D 8 1 (amino acids 178 to 236)	GGNLTPLLQQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	63
	GGCGGCAACATACTACCCCTTACTGCAGCAAGATTGTCATCAGAAAATCGATGAGCTCTTC TCTGGGAAGCTGTACCTCATTGGAATTGCAGCCATTGTGGTAGCTGTATTATGATCTTTGAG ATGATTCTGAGCATGGTGTGTGCTGTGGCATCCGGAACAGCTCCGTGTACTGA	64
C D 8 1 - I L - 1 2 α	MGVEGCTKCIKYLFFVFNFWLAGGVILGVALWLRHDPQTSLLYLELGNKPAPNTFYVGIY ILIAVGAVMMFVGLGCGYGAIQESQCLLGTFFTCLVILFACEVAAGIWGFVNKDQIAKDVKQF YDQALQQAVMDDDANNAKAVVKTFHETLNCCGSNALTTLTTLILRNSLCPSGGGGSRVIPVSG	95

[Table 8-2]

	PARCLSQSRNLLKTDDMVKTAREKLKHYSCAEDIDHEDITRDQSTLKTCLPLELHKNESCLATRETSSTTRGSCLPQKTSMLMTLCLGSIYEDLKMYQTEFQAINAALQNNHQIILDKGMLVAIDELMQSLNHNGETLRQKPPVGEADPYRVKMKLCILLHAFSTRVVTINRVMGYLSSAGGGSGGNILTPLLQQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	
	ATGGGGGTGGAGGGCTGCACCAAATGCATCAAATACCTGCTCTTCGTCTTCAATTCGTCTTC TGGCTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGTCATGATCCACAGACCACC AGCCTGCTGTACCTGGAACGGGAAACAAACCGGCACCAACACCTTCTACGTGGGCATCTAC ATTCTCATTGCTGTGGGAGCTGTGATGATGTTTGTAGGCTTCCTGGGGTGCTATGGGGCCATC CAGGAGTCCCAGTGTCTGCTGGGGACGTTCTTCACCTGCCTTGTGATCCTGTTGCTGTGAG GTGGCTGCAGGCATCTGGGGCTTCGTAACAAAGACCAGATCGCCAAGGATGTGAAGCAGTTC TATGACCAGGCCCTTCAGCAAGCTGTGATGGATGATGATGCCAACAATGCCAAGGCTGTGGTG AAGACTTTCCATGAGACGCTCAACTGTTGTGGCTCCAACGCACTGACCACACTGACTACCACC ATACTGAGGAACAGCCTGTGTCCCTCAGGAGGAGGAGGAAGCAGGGTCATTCCAGTCTCTGGA CCTGCCAGGTGTCTTAGCCAGTCCCGAAACCTGCTGAAGACCACAGATGACATGGTGAAGACG GCCAGAGAAAACTGAAACATTATTCCTGCACTGCTGAAGACATCGATCATGAAGACATCACA CGGGACCAAACAGCACATTGAAGACCTGTTTACCACTGGAACCTACACAAGAACGAGAGTTGC CTGGCTACTAGAGAGACTTCTCCACAACAAGAGGGAGCTGCCTGCCCCACAGAAGAGCTCT TTGATGATGACCCTGTGCCTTGGTAGCATCTATGAGGACTTGAAGATGTACCAGACAGAGTTC CAGGCCATCAACGCAGCACTTCAGAATCACAACCATCAGCAGATCATTCTAGACAAGGGCATG CTGGTGGCCATCGATGAGCTGATGCAGTCTCTGAATCATAATGGCGAGACTCTGCGCCAGAAA CCTCCTGTGGGAGAAGCAGACCCTTACAGAGTGAAAATGAAGCTCTGCATCCTGCTTCACGCC TTCAGCACCCGCGTGTGACCATCAACAGGGTGATGGGCTATCTGAGCTCCGCCGAGGAGGA GGAAGCGGCGGCAACATACTACCCCTTACTGCAGCAAGATTGTCATCAGAAAATCGATGAG CTCTTCTCTGGGAAGCTGTACCTCATTGGAATTGCAGCCATTGTGGTAGCTGTCAATTATGATC TTTGAGATGATTCTGAGCATGGTGTGTGTGTGGCATCCGGAACAGCTCCGTGTACTGA	96
IL-12 β	MCPQKLTIWFAIVLLVSPLMAMWELEKDVIYVVEVDWTPDAPGETVNLTCDTPEEDDITWTS QRHGVIGSGKLTITVKEFLDAGQYCHKGGETLSHSHLLLHKKENGIWSTEILKNFKNKTF KCEAPNYSGRFTCSWLVRNMDLKFNKSSSSSPDSRAVTCGMASLSAEKVTLDRDYEKYSV SCQEDVTCPTAEETLPIELALEARQQNKYENYSTSFFIRDI IKPDPPKNLQMKPLKNSQVEVS WEYPDSWSTPHSYFSLKFFVRIQRKKEKMKETEEGCNQKGAFLEKTSSTEVQCKGGNVCVQAQ DRYNNSSCSKWACVPCRVS	97
	ATGTGTCCTCAGAAGCTAACCATCTCCTGGTTTGCCATCGTTTTGCTGGTGTCTCCACTCATG GCCATGTGGGAGCTGGAGAAAGACGTTTATGTTGTAGAGGTGGACTGGACTCCCGATGCCCC GGAGAAACAGTGAACCTCACCTGTGACACGCCTGAAGAAGATGACATCACCTGGACCTCAGAC	98

[Table 8-3]

	CAGAGACATGGAGTCATAGGCTCTGGAAAGACCCTGACCATCACTGTCAAAGAGTTCTAGAT GCTGGCCAGTACACCTGCCACAAAGGAGGCGAGACTCTGAGCCACTCACATCTGCTGCTCCAC AAGAAGGAAAATGGAATTTGGTCCACTGAAATTTAAAAAATTTCAAAAACAAGACTTTCCTG AAGTGTGAAGCACCAAATTACTCCGGACGGTTCACGTGCTCATGGCTGGTGCAAAGAAACATG GACTTGAAGTTCAACATCAAGAGCAGTAGCAGTTCCCCTGACTCTCGGGCAGTGACATGTGGA ATGGCGTCTCTGTCTGCAGAGAAGGTCACACTGGACCAAAGGGACTATGAGAAGTATTCAGTG TCCTGCCAGGAGGATGTCACCTGCCCAACTGCCGAGGAGACCCTGCCCATTTGAAGTGGCGTTG GAAGCACGGCAGCAGAATAAATATGAGAACTACAGCACCAGCTTCTTCATCAGGGACATCATC AAACCAGACCCGCCCAAGAAGTTGCAGATGAAGCCTTTGAAGAACTCACAGGTGGAGGTCAGC TGGGAGTACCCTGACTCCTGGAGCACTCCCCATTCTACTTCTCCCTCAAGTTCTTTGTTTCCA ATCCAGCGCAAGAAAGAAAAGATGAAGGAGACAGAGGAGGGGTGTAACCAGAAAGGTGCGTTC CTCGTAGAGAAGACATCTACCGAAGTCCAATGCAAAGCGGGAATGTCTGCGTGCAAGCTCAG GATCGCTATTACAATTCCTCATGCAGCAAGTGGGCATGTGTTCCCTGCAGGGTCCGATCCTAG	

[0241]

[Table 9-1]

	Sequence	SEQ ID NO:
I L - 6 (from which signal peptide is removed)	FPTSQVRRGDFTEDTTPNRPVYTTSQVGGLITHVLWEIVEMRKELCNGNSDCMNNDALAENN LKLPEIQRNDGQYQTGYNQEICLLKISSGLLEYHSYLEYMKNNLKDNDKDKARVLQRDTETLI HIFNQEVKDLHKIVLPTPISNALLTDKLESQKEWLRTKTIQFILKSLEEFLKVTLRSTRQT	99
	TTCCCTACTTCACAAGTCCGGAGAGGAGACTTCACAGAGGATACCACTCCCAACAGACCTGTC TATACCACTTCACAAGTCCGGAGGCTTAATTACACATGTCTCTGGGAAATCGTGGAATGAGA AAAGAGTTGTGCAATGGCAATTCTGATTGTATGAACAACGATGATGCACTTGCAGAAAAAAT CTGAAACTTCCAGAGATACAAAGAAATGATGGATGCTACCAAACTGGATATAATCAGGAAAT TGCCTATTGAAAATTTCTCTGGTCTTCTGGAGTACCATAGCTACCTGGAGTACATGAAGAAC AACTTAAAGATAACAAGAAAGACAAAGCCAGAGTCTTCAGAGAGATACAGAACTCTAATT CATATCTTCAACCAAGAGGTAAAAGATTTACATAAAATAGTCCTTCTACCCCAATTTCCAAT GCTCTCTAACAGATAAGCTGGAGTACAGAGAGGAGTGGCTAAGGACCAAGACCATCCAATTC ATCTTGAAATCACTTGAAGAATTTCTAAAAGTCACCTTGAGATCTACTCGGCAAACC	100
C D 8 1 (amino acids 1 to 177)	MGVEGCTKCIKYLFFVFNFWFLAGGVILGVALWLRHDPQTSSLYLELGNKPAPNTFYVGIY ILIAVGAVMMFVGLGCGYAIQESQCLLGTFFTCLVILFACEVAAGIWGFVNKQIAKDVQKF YDQALQQAVMDDDANNAKAVVKTFHETLNCCGSNALTTLTTLRNSLCPS	61
	ATGGGGGTGGAGGGCTGCACCAATGCATCAAATACCTGCTCTTCGTCTTCAATTCGTCTTC TGGCTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGTCATGCCAGACCACC AGCCTGCTGTACCTGGAAGTGGGAAACAAACCGGCACCAACACCTTCTACGTGGGCATCTAC ATTCTCATTGCTGTGGAGCTGTGATGATGTTTGTAGGCTTCTGGGGTGCTATGGGCCATC CAGGAGTCCCAGTGTCTGCTGGGACGTTCTTACCTGCCTTGATCCTGTTGCCTGTGAG GTGGCTGCAGGCATCTGGGGCTTCGTAACAAAGACCAGATCGCCAAGGATGTGAAGCAGTTC TATGACCAGGCCCTTCAGCAAGCTGTGATGGATGATGATGCCAACAATGCCAAGGCTGTGGTG AAGACTTTCCATGAGACGCTCAACTGTTGTGGCTCCAACGCACTGACCACACTGACTACCACC ATACTGAGGAACAGCCTGTGTCCCTCA	62
C D 8 1 (amino acids 178 to 236)	GGNLTPLLQQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	63
	GGCGGCAACATACTACCCCCTTACTGCAGCAAGATTGCATCAGAAAAATCGATGAGCTCTTC TCTGGGAAGCTGTACCTCATTGGAATTGCAGCCATTGTGGTAGCTGTCATTATGATCTTTGAG ATGATTCTGAGCATGGTCTGTGCTGTGGCATCCGGAACAGCTCCGTGTACTGA	64
C D 8 1 - I L - 6	MGVEGCTKCIKYLFFVFNFWFLAGGVILGVALWLRHDPQTSSLYLELGNKPAPNTFYVGIY ILIAVGAVMMFVGLGCGYAIQESQCLLGTFFTCLVILFACEVAAGIWGFVNKQIAKDVQKF YDQALQQAVMDDDANNAKAVVKTFHETLNCCGSNALTTLTTLRNSLCPSGGGGSFPTSQVR RGDFTEDTTPNRPVYTTSQVGGLITHVLWEIVEMRKELCNGNSDCMNNDALAENNKLPEIQ RNDGQYQTGYNQEICLLKISSGLLEYHSYLEYMKNNLKDNDKDKARVLQRDTETLIHIFNQEV	101

[Table 9-2]

	KDLHKIVLPTPISNALLTDKLESQKEWLRTKTIQFILKSLEEFKVLRLSTRQTGGGSGGNI LTPLLQQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	
	ATGGGGGTGGAGGGCTGCACCAATGCATCAAATACCTGCTCTTCGTCTTCAATTCGTCTTC TGGCTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGTCATGATCCACAGACCACC AGCCTGCTGTACCTGGAAC TGGGAAACAAACCGGCACCCAACACCTTCTACGTGGGCATCTAC ATTCTCATTGCTGTGGGAGCTGTGATGATGTTTGTAGGCTTCCTGGGGTGCTATGGGGCCATC CAGGAGTCCCAGTGTCTGCTGGGGACGTTCTTCACCTGCCTTGATCCTGTTTGCCTGTGAG GTGGCTGCAGGCATCTGGGGCTTCGTAAACAAAGACCAGATCGCCAAGGATGTGAAGCAGTTC TATGACCAGGCCCTTCAGCAAGCTGTGATGGATGATGATGCCAACAAATGCCAAGGCTGTGGTG AAGACTTCCATGAGACGCTCAACTGTTGTGGCTCCAACGCACTGACCACACTGACTACCACC ATACTGAGGAACAGCCTGTGTCCCTCAGGAGGAGGAGGAAGCTTCCCTACTTACAAGTCCGG AGAGGAGACTTCACAGAGGATACCACTCCCAACAGACCTGTCTATACCACTTACAAGTCGGA GGCTTAATTACACATGTTCTCTGGGAAATCGTGGAAATGAGAAAAGAGTTGTGCAATGGCAAT TCTGATTGTATGAACAACGATGATGCACTTGCAGAAAACAATCTGAAACTTCCAGAGATACAA AGAAATGATGGATGCTACCAAACCTGGATATAATCAGGAAATTTGCCTATTGAAAATTTCTCT GGTCTTCTGGAGTACCATAGCTACCTGGAGTACATGAAGAACAACCTAAAAGATAACAAGAAA GACAAAGCCAGAGTCCTTCAGAGAGATACAGAACTCTAATTCATATCTTCAACCAAGAGGTA AAAGATTTACATAAAATAGTCCTTCTACCCCAATTTCCAATGCTCTCCTAACAGATAAGCTG GAGTCACAGAAGGAGTGGCTAAGGACCAAGACCATCCAATTCATCTTGAAATCACTTGAAGAA TTTCTAAAAGTCACTTTGAGATCTACTCGGCAAACCGGAGGAGGAGGAAGCGGCGGCAACATA CTCACCCCTTACTGCAGCAAGATTGTCATCAGAAAATCGATGAGCTCTTCTCTGGGAAGCTG TACCTCATTTGGAATTGCAGCCATTGTGGTAGCTGTCATTATGATCTTTGAGATGATTCTGAGC ATGGTGCTGTGCTGTGGCATCCGGAACAGCTCCGTGTACTGA	102

[0242]

[Table 10-1]

	Sequence	SEQ ID NO:
h C D 8 0	MGHTRRQGTSPSKCPYLNFFQLLVLAGLSHFCSGVIHVTKEVKEVATLSCGHNVSVEELAQTR IYWQKEKKMVLTMMSGDMNIWPEYKNRTIFDITNNLSIVILALRPSDEGTYESVVLKYEKDAF KREHLAEVTLVKADFPTPSISDFEIPTSNIRRIICSTSGGFPEPHLSWLENGEELNAINTTV SQDPETELYAVSSKLDNMTTNHSFMCLIKYGHRLRVNQTFNWNNTTKQEHFPDNLPSWAITLI SVNGIFVICCLTYCFAPRCRERRRNERLRRESVRPV	103
	ATGGGCCACACACGGAGGCAGGGAACATCACCATCCAAGTGCCATACCTCAATTTCTTTCAG CTCTTGGTGCTGGCTGGTCTTTCTCACTTCTGTTCAAGGTGTTATCCACGTGACCAAGGAAGTG AAAGAAGTGGCAACGCTGTCCTGTGGTCACAATGTTTCTGTTGAAGAGCTGGCACAACCTCGC ATCTACTGGCAAAAGGAGAAGAAAATGGTGCTGACTATGATGTCTGGGACATGAATATATGG CCCAGTACAAGAACCGGACCATCTTTGATATCACTAATAACCTCTCCATTGTGATCCTGGCT CTGCGCCCATCTGACGAGGGCACATACGAGTGTGTTGTTCTGAAGTATGAAAAAGACGCTTTC AAGCGGGAACACCTGGCTGAAGTGACGTTATCAGTCAAAGCTGACTTCCTACACCTAGTATA TCTGACTTTGAAATTCCAACCTCTAATATTAGAAGGATAATTTGCTCAACCTCTGGAGGTTTT CCAGAGCCTCACCTCTCCTGGTTGAAAAATGGAGAAGAATTAAATGCCATCAACACAACAGTT TCCAAGATCCTGAACTGAGCTCTATGCTGTTAGCAGCAAACCTGGATTTCATATGACAACC AACCACAGCTTCATGTGTCTCATCAAGTATGGACATTTAAGAGTGAATCAGACCTTCAACTGG AATACAACCAAGCAAGAGCATTTTCTGATAACCTGCTCCCATCCTGGGCCATTACCTTAATC TCAGTAAATGGAATTTTTGTGATATGCTGCCTGACCTACTGCTTGGCCCAAGATGCAGAGAG AGAAGGAGGAATGAGAGATTGAGAAGGAAAGTGACGCCCTGTA	104
h C D 9	MPVKGGTKCIKYLLFGFNFIWLAGIAVLAIGLWLRFDSTQKSIPEQETNNNNSSFYTGVIIL IGAGALMMLVGFLGCCGAVQESQCMLGLFFGFLLVIFAIEIAAAIWGYSHKDEVIKEVQEFYK DTYNKLTKEDEPQRETLKAIHYALNCCGLAGGVEQFISDIPCCKDVLEFTVKSCPDAIKEVF DNKFHIIGAVGIGIAVVMIFGMIFSMILCCAIRRNREMV	105
	ATGCCGGTCAAAGGAGGCACCAAGTGCATCAAATACCTGCTGTTGCGATTAACTTCATCTTC TGGCTTGCCGGGATTGCTGTCTTGCCATTGGACTATGGCTCCGATTGACTCTCAGACCAAG AGCATCTTCGAGCAAGAACTAATAATAAATTCCAGCTTCTACACAGGAGTCTATATTCTG ATCGGAGCCGGCGCCCTCATGATGCTGGTGGGCTTCTGGGCTGCTGCGGGGCTGTGCAGGAG TCCAGTGCACTGGGACTGTTCTTCGGCTTCTCTTGGTGATATTGCCATTGAAATAGCT GCGGCCATCTGGGGATATTCCACAAGGATGAGGTGATTAAGGAAGTCCAGGAGTTTACAAG GACACCTACAACAAGCTGAAAACCAAGGATGAGCCCCAGCGGGAACGCTGAAAGCCATCCAC TATGCGTTGAACTGCTGTGGTTTGGCTGGGGGCGTGGAACAGTTTATCTCAGACATCTGCCCC AAGAAGGACGTACTCGAAACCTTCACCGTGAAGTCTGCTGCTGATGCCATCAAAGAGGTCTTC GACAATAAATTCCACATCATCGGCGCAGTGGGCATCGGCATTGCCGTGGTCATGATATTGGC	106

[Table 10-2]

	ATGATCTTCAGTATGATCTTGTGCTGTGCTATCCGCAGGAACCGCGAGATGGTCTAG	
h C D 8 0 - h C D 9	MGHTRRQGTSPSKCPYLNFFQLLVLAGLSHFCSGV IHVTKEVKEVATLSCGHNVSEELAQTR IYWQKEKKMVLTMMSGDMNIWPEYKNRTIFDITNNLSIVILALRPSDEGTYESVVLKYEKDAF KREHLAEVTLVKADFPTPSISDFEIPTSNIRRI ICSTSGGFPEPHLSWLENGEELNAINTTV SQDPETELYAVSSKLDNMTTNHSFMCLIKYGLRVNQTFNWNTTKQEHFDPNLLPSWAITLI SVNGIFVICCLTYCFAPRCRERRRRNERLRRESVRPVMVKGKTKCIKYLFGFNFIWFLAGIA VLAIGLWLRFDSTKSIQEETNNNSSFYTGYYILIGAGALMMLVGFLGCCGAVQESQCM LG LFFGFLLVIFAIEIAAAIWGYSHKDEVIKEVQEFYKDTYNKLKTKDEPQRETLKAIHYALNCC GLAGGVEQFISDIPCKKDVLFTFTVKSCPDAIKEVFDNKFHII GAVGIGIAVVMIFGMIFSMI LCCAIRRNREMV	107
	ATGGGCCACACCGGAGGCAGGGAACATCACCATCCAAGTGCCATACCTCAATTTCTTTTCAG CTCTTGGTGCTGGCTGGCTTTTCTCACTTCTGTT CAGGTGTTATCCACGTGACCAAGGAAGTG AAAGAAGTGGCAACGCTGTCCTGTGCTCACAATGTTTCTGTTGAAGAGCTGGCACA AACTCGC ATCTACTGGCAAAAGGAGAAGAAAATGGTGCTGACTATGATGTCTGGGACATGAATATATGG CCCGAGTACAAGAACCGGACCATCTTTGATATCACTAATAACCTCTCCATTGTGATCCTGGCT CTGCGCCCATCTGACGAGGGCACATACGAGTGTGTTGTTCTGAAGTATGAAAAGACGCTTTC AAGCGGGAACACCTGGCTGAAGTGACGTTATCAGTCAAAGCTGACTTCCCTACACCTAGTATA TCTGACTTTGAAATTCAACTTCTAATATTAGAAGGATAATTTGCTCAACCTCTGGAGGTTTT CCAGAGCCTCACCTCTCCTGGTTGGA AATGGAGAAGAATTAAATGCCATCAACACAACAGTT TCCAAGATCCTGAACTGAGCTCTATGCTGTTAGCAGCAAACCTGGATTTC AATATGACAACC AACCACAGCTTCATGTGTCTCATCAAGTATGGACATTTAAGAGTGAATCAGACCTTCAACTGG AATACAACCAAGCAAGAGCATTTCCTGATAACCTGCTCCCATCCTGGGCCATTACCTTAATC TCAGTAAATGGAATTTTGTGATATGCTGCCTGACCTACTGCTTTGCCCAAGATGCAGAGAG AGAAGGAGGAATGAGAGATTGAGAAGGAAAGTGACGCCCTGTAATGCCGGTCAAAGGAGGC ACCAAGTGCATCAAATACCTGCTGTTCCGATTTAACCTCATCTTCTGGCTTGCCGGGATTGCT GTCCTTGCCATTGGACTATGGCTCCGATTGACTCTCAGACCAAGAGCATCTTCGAGCAAGAA ACTAATAATAATAATTCAGCTTCTACACAGGAGTCTATATTCTGATCGGAGCCGGCGCCCTC ATGATGCTGGTGGGCTTCCTGGGCTGCTGCGGGGCTGTGCAGGAGTCCAGTGCATGCTGGGA CTGTTCTTCGGCTTCCTCTTGGTGATATTGCGCATTGAAATAGCTGCGGCCATCTGGGGATAT TCCCACAAGGATGAGGTGATTAAGGAAGTCCAGGAGTTTACAAGGACACCTACAACAAGCTG AAAACCAAGGATGAGCCCCAGCGGAAACGCTGAAAGCCATCCACTATGCGTTGAACTGCTGT GGTTTGGCTGGGGGCGTGGAACAGTTTATCTCAGACATCTGCCCAAGAAGGACGTA CTGAA ACCTTCACCGTGAAGTCTGTCTGATGCCATCAAAGAGGTCTTCGACAATAAATTCACATC ATCGGCGCAGTGGGCATCGGCATTGCCGTGGTCATGATATTTGGCATGATCTTCAGTATGATC TTGTGCTGTGCTATCCGCAGGAACCGCGAGATGGTCTAG	108

[Table 11-1]

	Sequence	SEQ ID NO:
h I L - 2 (from which signal peptide is removed)	APTSSSTKKTQLQLEHLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEL KPLEEVLNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQ SIISTLT	109
	GCACCTACTTCAAGTTCTACAAAGAAAACACAGCTACAACCTGGAGCATTACTGCTGGATTTA CAGATGATTTTGAATGGAATTAATAATTACAAGAATCCCAAACCTACCAGGATGCTCACATTT AAGTTTACATGCCAAGAAGGCCACAGAACTGAAACATCTTCAGTGTCTAGAAGAAGAACTC AAACCTCTGGAGGAAGTCTAAATTTAGCTCAAAGCAAAAACCTTCACTTAAGACCCAGGGAC TTAATCAGCAATATCAACGTAATAGTTCTGGAACATAAGGGATCTGAAACAACATTCATGTGT GAATATGCTGATGAGACAGCAACCATTGTAGAATTTCTGAACAGATGGATTACCTTTTGTCAA AGCATCATCTCAACACTGACT	110
h C D 6 3 (amino acids 1 to 170)	MAVEGGMKCVKFLLYVLLAFACAVGLIAVGVAQLVLSQTIIQGATPGSLLPVVIIAVGVF LFLVAFVGGCGACKENYCLMITFAIFLSLIMLVEVAAAIAGYVFRDKVMSEFNNNFRQQMENY PKNNHTASILDRMQADFKCCGAANYTDWEKIPSMKSNRVPDSCC	111
	ATGGCGGTGGAAGGAGGAATGAAATGTGTGAAGTTCTTGCTCTACGTCCTCCTGCTGGCCTTT TGCGCCTGTGCAGTGGGACTGATTGCCGTGGGTGTCGGGGCACAGCTGTCTGAGTCAGACC ATAATCCAGGGGGCTACCCCTGGCTCTCTGTTGCCAGTGGTCATCATCGCAGTGGGTGTCTTC CTCTTCTGCTGGCTTTTGTGGGCTGCTGCGGGGCTGCAAGGAGAACTATTGTCTTATGATC ACGTTTGCCATCTTTCTGTCTCTTATCATGTTGGTGGAGGTGGCCGAGCCATTGCTGGCTAT GTGTTTAGAGATAAGGTGATGTGAGAGTTAATAACAACTTCCGGCAGCAGATGGAGAATTAC CCGAAAAACAACCACACTGCTTCGATCCTGGACAGGATGCAGGCAGATTTTAAGTGCTGTGGG GCTGCTAACTACACAGATTGGGAGAAAAATCCCTTCCATGTGGAAGAACCGAGTCCCCGACTCC TGCTGC	112
h C D 6 3 (amino acids 171 to 238)	INVTVCGGINFNEKAIHKEGCVKEIGGWLKKNVLVAAAAALGIAFVEVLGIVFACCLVKSIRS GYEVM	113
	ATTAATGTTACTGTGGGCTGTGGGATTAATTTCAACGAGAAGGCGATCCATAAGGAGGGCTGT GTGGAGAAGATTGGGGCTGGCTGAGGAAAAATGTGCTGGTGGTAGCTGCAGCAGCCCTTGGA ATTGCTTTTGTGCGAGGTTTGGGAATTGTCTTTGCCTGCTGCCTCGTGAAGAGTATCAGAAGT GGCTACGAGGTGATGTAG	114
h C D 6 3 - I L - 2	MAVEGGMKCVKFLLYVLLAFACAVGLIAVGVAQLVLSQTIIQGATPGSLLPVVIIAVGVF LFLVAFVGGCGACKENYCLMITFAIFLSLIMLVEVAAAIAGYVFRDKVMSEFNNNFRQQMENY PKNNHTASILDRMQADFKCCGAANYTDWEKIPSMKSNRVPDSCCGGGSAPTSSSTKKTQLQL EHLLEDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLTGGGGSIN	115

[Table 11-2]

	VTVGGGINFNEKAIHKEGCVKEIGGWLRKNVLVAAAAALGIAFVEVLGIVFACCLVKSIRSGY EVM	
	ATGGCGGTGGAAGGAGGAATGAAATGTGTGAAGTTCTTGCTCTACGTCCTCCTGCTGGCCTTT TGCGCCTGTGCAGTGGGACTGATTGCCGTGGGTGTCGGGGCACAGCTTGTCTGAGTCAGACC ATAATCCAGGGGGCTACCCCTGGCTCTCTGTTGCCAGTGGTCATCATCGCAGTGGGTGTCTTC CTCTTCCTGGTGGCTTTTGTGGGCTGCTGCGGGGCCTGCAAGGAGAACTATTGTCTTATGATC ACGTTTGCCATCTTTCTGTCTCTTATCATGTTGGTGGAGGTGGCCGAGCCATTGCTGGCTAT GTGTTTAGAGATAAGGTGATGTCAGAGTTTAATAACAACCTCCGGCAGCAGATGGAGAATTAC CCGAAAAACAACCACACTGCTTCGATCCTGGACAGGATGCAGGCAGATTTTAAGTGCTGTGGG GCTGCTAACTACACAGATTGGGAGAAAATCCCTTCCATGTGAAGAACCGAGTCCCCGACTCC TGCTGCGGAGGAGGAGGAAGCGCACCTACTTCAAGTTCTACAAAGAAAAACAGCTACAACCTG GAGCATTTACTGCTGGATTACAGATGATTTTGAATGGAATTAATAATTACAAGAATCCAAA CTCACCAGGATGCTCACATTTAAGTTTTACATGCCCAAGAAGGCCACAGAACTGAAACATCTT CAGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTAAATTTAGCTCAAAGCAAAAAC TTTCACTTAAGACCCAGGGACTTAATCAGCAATATCAACGTAATAGTTCTGGAACTAAAGGGA TCTGAAACAACATTCATGTGTGAATATGCTGATGAGACAGCAACCATTGTAGAATTTCTGAAC AGATGGATTACCTTTTGTCAAAGCATCATCTCAACACTGACTGGAGGAGGAGGAAGCATTAAAT GTTACTGTGGGCTGTGGGATTAATTTCAACGAGAAGGCGATCCATAAGGAGGGCTGTGTGGAG AAGATTGGGGGCTGGCTGAGGAAAAATGTGCTGGTGGTAGCTGCAGCAGCCCTTGAATTGCT TTTGTGAGGTTTTGGGAATTGTCTTTGCCTGCTGCCTCGTGAAGAGTATCAGAAGTGGCTAC GAGGTGATGTAG	116

[0244]

[Table 12-1]

	Sequence	SEQ ID NO:
Signal peptide of h β_2 microglobulin	<u>MSRSVALAVLALLSLSGLEA</u>	117
	<u>ATGTCTCGCTCCGTGGCCTTAGCTGTGCTCGCGCTACTCTCTCTTTCTGGCCTGGAGGCT</u>	118
WT 1 peptide 1 (for MHC class I molecule)	CYTNQMNL	119
	TGCTACACCTGGAACCAGATGAACCTG	120
Peptide linker 1	GGGASGGGSGGGGS	5
	GGCGGAGGTGCCTCTGGCGGTGGGGGCAGCGGTGGAGGGGGCAGT	6
h β_2 Microglobulin (from which signal peptide is removed)	IQRTPKIQVYSRHPAENGKSNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWFSY LLYTFEFTPEKDEYACRVNHVTLSPKIVKWRDM	121
	ATCCAGCGTACTCCAAAGATTGAGTTTACTCACGTCATCCAGCAGAGAATGAAAAGTCAAAT TTCTGAATTGCTATGTGTCTGGGTTTCATCCATCCGACATTGAAGTTGACTTACTGAAGAAT GGAGAGAGAATTGAAAAAGTGAGCATTGAGACTTGTCTTTCAGCAAGGACTGGTCTTTCTAT CTCTTGACTACTGAATTCACCCCACTGAAAAAGATGAGTATGCCTGCCGTGTGAACCAT GTGACTTTGTCACAGCCCAAGATAGTTAAGTGGGATCGAGACATG	122
h MHC class I α chain (from which signal peptide is removed)	GSHSMRYFSTSVSRPGRGEPRFIAVGYYDDTQFVRFSDAASQRMEPRAPWIEQEGPEYWDEE TGKVKAHSQTDRENLRALRYYNQSEAGSHTLQMMFGCDVGS DGRFLRGYHQYAYDGKDYIAL KEDLRSWTAADMAAQITKRKWEAAHVAEQRAYLEGTCVDGLRRYLENGKETLQRTDPPKTHM THHPISDHEATLRWALGFYPAEITLTWQRDGEDQTQDELVETRPAGDGTQKWA AVVPSG EEQRYTCHVQHEGLPKPLTLRWPSSQPTVPIVGIIAGLVLLGAVITGAVVA VMWRRNSSDR KGGSYSQAASSDSAQGS DVS LTACKV	123
	GGCTCCCACTCCATGAGGTATTTCTCCACATCCGTGTCCCGGCCGGCCGGGGAGCCCCGC TTCATCGCCGTGGGCTACGTGGACGACACGCAGTTTCGTGCGGTTGACAGCGACGCCGCGAGC CAGAGGATGGAGCCGCGGGCGCGGTGATAGAGCAGGAGGGCCGGAGTATTGGGACGAGGAG ACAGGGAAAGTGAAGGCCACTCACAGACTGACCGAGAGAACCTGCGGATCGCGCTCCGCTAC TACAACCAGAGCGAGGCCGTTCTCACACCCTCCAGATGATGTTTGGCTGCGACGTGGGGTCG GACGGGCGCTTCTCCGCGGGTACCACCAGTACGCCTACGACGGCAAGGATTACATCGCCCTG AAAGAGGACCTGCGCTCTTGGACCGCGCGGACATGGCGGCTCAGATACCAAGCGCAAGTGG GAGGCGGCCCATGTGGCGGAGCAGCAGAGAGCCTACCTGGAGGGCACGTGCGTGACGGGCTC CGCAGATACCTGGAGAACGGGAAGGAGACGCTGCAGCGCACGACCCCCCAAGACACATATG ACCCACCACCCATCTCTGACCATGAGGCCACTCTGAGATGCTGGGCCCTGGGCTTCTACCCT GCGGAGATCACACTGACCTGGCAGCGGGATGGGAGGACCAGACCCAGGACACGGAGCTTGTG GAGACCAGGCCTGCAGGGGATGGAACCTTCCAGAAGTGGGCAGCTGTGGTGGTACCTTCTGGA GAGGAGCAGAGATACACCTGCCATGTGCAGCATGAGGGTCTGCCCAAGCCCCTACCCCTGAGA TGGGAGCCATCTCCAGCCACCGTCCCATCGTGGGCATCATTGCTGGCCTGGTTCTCCTT	124

[Table 12-2]

	GGAGCTGTGATCACTGGAGCTGTGGTCGCTGTGATGTGGAGGAGGAACAGCTCAGATAGA AAAGGAGGGAGCTACTCTCAGGCTGCAAGCAGTGACAGTGCCAGGGCTCTGATGTGTCTCTC ACAGCTTGTAAGTG	
Peptide linker 2	GGGGSGGGSGGGSGGGGS	11
	GGGGGGGAGGCTCCGGTGGAGGGGGTCTGGAGGGGGGGTCTGGTGGAGGCGGAAGT	12
h Single chain MHC class I molecule (β_2 microglobulin (from which signal peptide is removed) + peptide linker 2 + MHC class I α chain (from which signal peptide is removed))	IQRTPKIQVYSRHPAENGKSNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWsfy LLYYTEFTPEKDEYACRVNHVTLSPKIVKWDRDMGGGSGGGSGGGSGGGSGSHSMRY FSTSVSRPGRGEPRFIAVGYYDDTQFVRFSDAASQRMEPRAPWIEQEGPEYWDEETGKVKAH SQTDRNLRIALRYYNQSEAGSHTLQMMFGCDVGSGRFLRGYHQYAYDGKDYIALKEDLRsw TAADMAAQITKRKWEAAHVAEQRAYLEGTCDGLRRYLENGKETLQRTDPPKTHMTHHPISD HEATLRCWALGFYPAEITLTWQRDGEDQTQDELVETRPAGDGTfQKWAAVVPSGEEQRYTC HVQHEGLPKPLTLRWEPSQPTVPIVGI IAGLVLLGAVITGAVVAVMWRRNSSDRKGSYSQ AASSDSAQGSVDVSLTACKV	125
	ATCCAGCGTACTCAAAGATTcAGGTTTACTCACGTCATCCAGCAGAGAATGGAAAGTCAAAT TTCTGAATTGCTATGTGTCTGGGTTTcATCCATCCGACATTGAAGTTGACTTACTGAAGAAT GGAGAGAGAATTGAAAAAGTGGAGCATTcAGACTTGTCTTTcAGCAAGGACTGGTCTTTCTAT CTCTTGACTACACTGAATTcACCCCCACTGAAAAAGATGAGTATGCCTGCCGTGTGAACCAT GTGACTTTGTcACAGCCCAAGATAGTTAAGTGGGATCGAGACATGGGGGGGGAGGCTCCGGT GGAGGGGGGTCTGGAGGGGGGGGTCTGGTGGAGGCGGAAGTGGCTCCCACTCCATGAGGTAT TTCTCCACATCCGTGTCCCGGGCCCGCGGGGAGCCCCGTTcATCGCGGTGGGTACGTG GACGACACGCAGTTcGTGCGGTTcGACAGCGACGCCGCGAGCCAGAGGATGGAGCCGCGGGCG CCGTGGATAGAGCAGGAGGGGCCGAGTATTGGGACGAGGAGACAGGGAAAGTGAAGGCCAC TCACAGACTGACCGAGAGAACCTGCGGATCGCGCTCCGCTACTACAACCAGAGCGAGGCCGT TCTCACACCCTCCAGATGATGTTTGGCTGCGACGTGGGGTGGACGGGCGTTCCTCCGCGGG TACCACCAGTACGCTACGACGGCAAGGATTACATCGCCCTGAAAGAGGACCTGCGCTCTTG ACCGCGGCGGACATGGCGGCTCAGATCACCAGCGCAAGTGGGAGGCGGCCATGTGGCGGAG CAGCAGAGAGCTACCTGGAGGGCAGGTGCGTGGACGGGTCCGCAGATACCTGGAGAACGGG AAGGAGACGCTGCAGCGCAGGACCCCCCAAGACACATATGACCCACCACCCATCTCTGAC CATGAGGCCACTCTGAGATGCTGGCCCTGGGCTTCTACCCTGCGGAGATCACACTGACCTGG CAGCGGGATGGGAGGACCAGACCCAGGACACGGAGCTTGTGGAGACCAGGCTGCAGGGGAT GGAACCTTCCAGAAAGTGGGAGCTGTGGTGGTACCTTCTGGAGAGGAGCAGAGATACACCTGC CATGTGCAGCATGAGGGTCTGCCCAAGCCCCCTACCCTGAGATGGGAGCCATCTTCCAGCCC ACCGTCCCCATCGTGGGCATCATTGCTGGCCTGGTTCTCCTTGAGCTGTGATCACTGGAGCT GTGGTCGCTGCTGTGATGTGGAGGAGGAACAGCTCAGATAGAAAAGGAGGGAGCTACTCTCAG GCTGCAAGCAGTGACAGTGCCAGGGCTCTGATGTGTCTCTCACAGCTTGTAAGTG	126

[Table 12-3]

h s c - T r i m e r (WT1 peptide 1 + peptide linker 1 + single chain MHC class I molecule)	<u>MSRSVALAVLALLSLSGLEACYTNQMNLGGGASGGGGSGGGGSIQRTPKIQVYSRHPAENGK</u> SNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWSEFYLLYYTEFTPTTEKDEYACRV NHVTLSQPKIVKWDRDMGGGGSGGGGSGGGGSGGGGSGSHSMRYFSTSVSRPGRGEPRFIAVG YVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWEETGKVKASHQTDRENLRALRYNQSE AGSHTLQMMFGCDVGSDFRFLRGYHQYAYDGKDYIALKEDLRSWTAADMAAQITKRKWEAAHV AEQQRAYLEGTCDVGLRRYLENGKETLQRTDPPKTHMTHHPISDHEATLRCWALGFYPAEITL TWQRDGEDQTQDTELVETRPAGDGTGKWAAVVPSGEEQRYTCHVQHEGLPKPLTLRWEPS QPTVPIVGIIAGLVLLGAVITGAVVAVMWRRNSSDRKGGSYQAASSDSAQGSVDVSLTACKV	127
	<u>ATGTCTCGCTCCGTGGCCTTAGCTGTGCTCGCGCTACTCTCTCTTTCTGGCCTGGAGGCTTGC</u> TACACCTGGAACCAGATGAACCTGGGCGGAGGTGCCTCTGGCGGTGGGGGCAGCGGTGGAGGG GGCAGTATCCAGCGTACTCCAAAGATTAGGTTTACTCACGTATCCAGCAGAGAATGGAAAG TCAAATTTCTGAATTGCTATGTGTCTGGGTTTCATCCATCCGACATTGAAGTTGACTTACTG AAGAATGGAGAGAGAATTGAAAAAGTGGAGCATTGAGCTTGTCTTTCAGCAAGGACTGGTCT TTCTATCTCTTGTACTACACTGAATTCACCCCCACTGAAAAAGATGAGTATGCTTGGCGGTGTG AACCATGTGACTTTGTACAGCCCAAGATAGTTAAGTGGGATCGAGACATGGGGGGGGAGGC TCCGGTGGAGGGGGGTCTGGAGGGGGGGGTCTGGTGGAGGCGGAAGTGGTCCCACTCCATG AGGTATTTCTCCACATCCGTGTCCCGCCCGCCGCGGGGAGCCCCGCTTCATCGCCGTGGGC TACGTGGACGACACGCAGTTCGTGCGTTTCGACAGCGACCCGCGAGCCAGAGGATGGAGCCG CGGGCGCCGTGGATAGAGCAGGAGGGGCCGAGTATTGGGACGAGGAGACAGGAAAGTGAAG GCCCACTCACAGACTGACCGAGAGAACCTGCGGATCGCGCTCCGCTACTACAACCAGAGCGAG GCCGTTCTCACACCTCCAGATGATGTTTGGCTGCGACGTGGGGTCCGACGGGCGCTTCTCTC CGCGGTACCAACAGTACGCTACGACGGCAAGGATTACATCGCCCTGAAAGAGGACCTGCGC TCTTGGACCGCGCGGACATGGCGCTCAGATACCAAGCGCAAGTGGGAGGCGGCCCATGTG GCGGAGCAGCAGAGAGCCTACCTGGAGGGCACGTGCGTGGACGGCTCCGACAGATACCTGGAG AACGGGAAGGAGACGCTGCAGCGCACGGACCCCCCAAGACACATATGACCCACCACCCCATC TCTGACCATGAGGCCACTCTGAGATGCTGGGCCCTGGGCTTCTACCCTGCGGAGATCACACTG ACCTGGCAGCGGATGGGGAGGACCAGACCCAGGACACGGAGCTTGTGGAGACCAGGCCTGCA GGGATGGAACCTTCCAGAAGTGGGCAGCTGTGGTGGTACCTTCTGGAGAGGAGCAGAGATAC ACCTGCCATGTGCAGCATGAGGGTCTGCCAAGCCCCCTACCCTGAGATGGGAGCCATCTTCC CAGCCACCGTCCCATCGTGGGCATCATTGCTGGCCTGGTTCTCTTGGAGCTGTGATCACT GGAGCTGTGGTCTGCTGTGATGTGGAGGAGGAACAGCTCAGATAGAAAAGGAGGGAGCTAC TCTCAGGCTGCAAGCAGTGACAGTGCCAGGGCTCTGATGTGTCTCTCACAGCTTGTAAGTG	128
h C D 8 1	MGVEGCTKCIKYLLFVFNFFVFLAGGVILGVALWLRHDPQTNNLLYLELGDKPAPNTFVVGII ILIAVGAVMMFVGLGCGYGAIQESQCLLGTFFTCVLVILFACEVAAGIWFVFNKDQIAKDVKQF YDQALQQAVVDDDANNAKAVVKTFFHETLDCCGSSTLTALTTSVLKNNLCPSGSNIISNLFKED	129

[Table 12-4]

	CHQKIDDLFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	
	ATGGGAGTGGAGGGCTGCACCAAGTGCATCAAGTACCTGCTCTTCGTCTTCAATTCGTCTTC TGGCTGGCTGGAGGCGTGATCCTGGGTGTGGCCCTGTGGCTCCGCCATGACCCGAGACCACC AACCTCCTGTATCTGGAGCTGGGAGACAAGCCCGCGCCAAACACCTTCTATGTAGGCATCTAC ATCCTCATCGCTGTGGGCGCTGTCATGATGTTCTGTTGGCTTCTGGGCTGTACGGGGCCATC CAGGAATCCCAGTGCCTGCTGGGGACGTTCTTACCTGCCTGGTCATCCTGTTGCCTGTGAG GTGGCCCGCGCATCTGGGGCTTTGTCAACAAGGACCAGATCGCCAAGGATGTGAAGCAGTTC TATGACCAGGCCCTACAGCAGGCCGTGGTGGATGATGACGCCAACACGCCAAGGCTGTGGTG AAGACCTTCCACGAGACGCTTGACTGCTGTGGCTCCAGCACACTGACTGCTTTGACCACCTCA GTGCTCAAGAACAATTTGTGTCCCTCGGGCAGCAACATCATCAGCAACCTCTTCAAGGAGGAC TGCCACCAGAAGATCGATGACCTCTTCTCCGGGAAGCTGTACCTCATCGGCATTGCTGCCATC GTGGTCGCTGTGATCATGATCTTCGAGATGATCCTGAGCATGGTGTGTGCTGTGGCATCCGG AACAGCTCCGTGTACTGA	130
h s c - T r i m e r - C D 8 1 (s c - T r i m e r + C D 8 1)	MSRSVALAVLALLSLSGLEACYTWNQMNLGGGASGGGGSGGGGSIQRTPKIQVYSRHPAENGK SNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWFSYLLYYTEFTPTEKDEYACRV NHVTLSQPKIVKWDRDMGGGGSGGGSGGGSGGGSGGSHSMRYFSTSVSRPGRGEPRFIAVG YVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDEETGKVKAHSQTDRENLRIALRYYNQSE AGSHTLQMMFGCDVGS DGRFLRGYHQYAYDGKDYIALKEDLRSWTAADMAAQITKRKWEAAHV AEQQRAYLEGTCVDGLRRYLENGKETLQRTDPPKTHMTHHPISDHEATLRCWALGFYPAEITL TWQRDGEDQTQDTEL VETRPAGDGTQKWAAVVVPSEEQRYTCHVQHEGLPKPLTLRWEPS QPTVPIVGIIAGLVLLGAVITGAVVAVMWRRNSSDRKGGYSQAASSDSAQGS DVS LTACKV MGVEGCTKCIKYL L FVFN FVFWLAGGVILGVALWLRHDPQTNNLLYLELGDKPAPNTFYVG IY ILIAVGAVMMFVGLGCGYAIQESQCLLGTFFTCLVILFACEVAAGIWGFVNKDQIAKDVKQF YDQALQQAVVDD DANNAKAVKTFHETLDCCGSSTLTALTTSVLKNNLCPSGSNIISNLFKED CHQKIDDLFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	131
	ATGTCTCGCTCCGTGGCCTTAGCTGTGCTCGCGCTACTCTCTCTTCTGGCCTGGAGGCTTGC TACACCTGGAACCAGATGAACCTGGGCGGAGGTGCCTCTGGCGGTGGGGGCAGCGGTGGAGGG GGCAGTATCCAGCGTACTCCAAAGATTGAGTTTACTCACGTATCCAGCAGAGAATGGAAG TCAAATTTCTGAATTGCTATGTGTCTGGGTTTCATCCATCCGACATTGAAGTTGACTTACTG AAGAATGGAGAGAGAATTGAAAAAGTGGAGCATTGAGCTTGTCTTTCAGCAAGGACTGGTCT TTCTATCTCTTGTA CTACACTGAATTCACCCCACTGAAAAAGATGAGTATGCTGCGGTGTG AACCATGTGACTTTGTACAGCCCAAGATAGTTAAGTGGGATCGAGACATGGGGGGGGAGGC TCCGGTGGAGGGGGGTCTGGAGGGGGGGGTCTGGTGGAGGCGGAAGTGGCTCCCACTCCATG AGGTATTTCTCCACATCCGTGTCCCGCCCGCGGGGAGCCCCGTTTCATCGCCGTGGGC TACGTGGACGACACGAGTTTCGTGCGGTTTCGACAGCGACGCCGAGCCAGAGGATGGAGCCG	132

[Table 12-5]

	CGGGCGCCGTGGATAGAGCAGGAGGGGCGGAGTATTGGGACGAGGAGACAGGGAAAGTGAAG GCCCACCTCACAGACTGACCGAGAGAACCTGCGGATCGCGCTCCGCTACTACAACCAGAGCGAG GCCGGTTCTCACACCTCCAGATGATGTTTGGCTGCGACGTGGGGTCGGACGGGCGCTTCCTC CGCGGGTACCACCAGTACGCCTACGACGGCAAGGATTACATCGCCCTGAAAGAGGACCTGCGC TCTTGGACCGCGGCGGACATGGCGGCTCAGATCACCAAGCGCAAGTGGGAGGCGGCCATGTG GCGGAGCAGCAGAGAGCCTACCTGGAGGGCACGTGCGTGGACGGGCTCCGCAGATACCTGGAG AACGGGAAGGAGACGCTGCAGCGCACGGACCCCCCAAGACACATATGACCCACCACCCCATC TCTGACCATGAGGCCACTCTGAGATGCTGGGCCCTGGGCTTCTACCCTGCGGAGATCACACTG ACCTGGCAGCGGGATGGGGAGGACCAGACCCAGGACACGGAGCTTGTGGAGACCAGGCCTGCA GGGGATGGAACCTTCCAGAAGTGGGCAGCTGTGGTGGTACCTTCTGGAGAGGAGCAGAGATAC ACCTGCCATGTGCAGCATGAGGGTCTGCCCAAGCCCCTCACCTGAGATGGGAGCCATCTTCC CAGCCCACCGTCCCCATCGTGGGCATCATTGCTGGCCTGGTTCTCCTTGGAGCTGTGATCACT GGAGCTGTGGTTCGCTGCTGTGATGTGGAGGAGGAACAGCTCAGATAGAAAAGGAGGGAGCTAC TCTCAGGCTGCAAGCAGTGACAGTGCCAGGGCTCTGATGTGTCTCTCACAGCTTGTAAGTG ATGGGAGTGGAGGGCTGCACCAAGTGCATCAAGTACCTGCTCTTCGTCTTCAATTTTCGTCTTC TGGCTGGCTGGAGGCGTGATCCTGGGTGTGGCCCTGTGGCTCCGCCATGACCCGAGACCACC AACCTCCTGTATCTGGAGCTGGGAGACAAGCCCGCGCCCAACACCTTCTATGTAGGCATCTAC ATCCTCATCGCTGTGGGCGCTGTGATGATGTTTCGTTGGCTTCCTGGGCTGCTACGGGGCCATC CAGGAATCCCAGTGCCCTGCTGGGGACGTTCTTCACCTGCCTGGTCATCCTGTTTGCCTGTGAG GTGGCCGCCGGCATCTGGGGCTTTGTCAACAAGGACCAGATCGCCAAGGATGTGAAGCAGTTC TATGACCAGGCCCTACAGCAGGCCGTGGTGGATGATGACGCCAACAACGCCAAGGCTGTGGTG AAGACCTTCCACGAGACGCTTGACTGCTGTGGCTCCAGCACACTGACTGCTTTGACCACCTCA GTGCTCAAGAACAAATTTGTGTCCCTCGGGCAGCAACATCATCAGCAACCTCTTCAAGGAGGAC TGCCACCAGAAGATCGATGACCTCTTCTCCGGAAGCTGTACCTCATCGGCATTGCTGCCATC GTGGTCGCTGTGATCATGATCTTCGAGATGATCCTGAGCATGGTGTGTGCTGTGGCATCCGG AACAGCTCCGTGTACTGA	

[0245]

[Table 13-1]

	Sequence	SEQ ID NO:
Signal peptide of β_2 microglobulin	<u>MARSVTLVFLVLVSLTGLYA</u>	1
	<u>ATGGCTCGCTCGGTGACCCCTGGTCTTCTGGTGCTGTCTCACTGACCGGCTGTATGCT</u>	2
OVA peptide 1 (for MHC class I molecule)	SIINFEKL	3
	TCCATTATAAATTTTAAAAAGTTG	4
Peptide linker 1	GGGASGGGGSGGGGS	5
	GGCGGAGGTGCCTCTGGCGGTGGGGGACCGGTGGAGGGGGCAGT	6
β_2 Microglobulin (from which signal peptide is removed)	IQKTPQIQVYSRHPPENGKPNILNCYVTQFHPHIEIQMLKNGKKIPKVEMSDMSFSKDWSEFY ILAHTFTPTETDITYACRVKHASMAEPKTVVWDRDM	7
	ATCCAGAAAACCCCTCAAATTCAGTATACTACGCCACCCACCGAGAATGGGAAGCCGAAC ATACTGAACTGCTACGTAACACAGTTCCACCCGCCTCACATTGAAATCCAAATGCTGAAGAAC GGGAAAAAATTCCTAAAGTAGAGATGTCAGATATGTCCTTCAGCAAGGACTGGTCTTTCTAT ATCCTGGCTCACACTGAATTCACCCCACTGAGACTGATACATACGCCTGCAGAGTTAAGCAT GCCAGTATGGCCGAGCCCAAGACCGTCTACTGGGATCGAGACATG	8
MHC class I α chain (from which signal peptide is removed)	GPHSLRYFVTAVSRPGLGEPYMEVGYYDDTEFVRFDSDAENPRYEPRARWMEQEGPEYWERE TQKAKGNEQSFRVRLRTLLGYYNQSKGGSHTIQVISGCEVGSGRLLRGYQQYAYDGCYIAL NEDLKTWTAADMAALITKHKWEQAGEAERLRLAYLEGTCVEWLRRLKNGNATLLRTDSPKAHV THHSRPEDKVTLRWCALGFYPADITLTWQLNGEELIQDMELVETRPAGDGTQKQWASVVVPLG KEQYYTCHVYHQGLPEPLTLRWEPPPTVSNMATVAVLVVLGAAIVTGAVVAFVMKMRRTNG GKGGDYALAPGSQTSLSLPDCKVMVHDPHSLA	9
	GGCCCACTCGCTGAGGTATTTCTGTCACCGCGTGTCCCGCCCGGCTCGGGAGCCCCGG TACATGGAAGTCGGCTACGTGGACGACACGGAGTTCTGCGCTTCGACAGCGACCGGAGAAT CCGAGATATGAGCCGCGGCGCGGTGGATGGAGCAGGAGGGCCCGAGTATTGGAGCGGGAG ACACAGAAAGCCAAGGGCAATGAGCAGAGTTCCGAGTGGACCTGAGGACCTGCTCGGCTAC TACAACCAGAGCAAGGGCGGCTCTCACACTATTCAGGTGATCTCTGGCTGTGAAGTGGGGTCC GACGGGCGACTCCTCCGCGGTACCAGCAGTACGCCTACGACGGCTGCGATTACATCGCCCTG AACGAAGACCTGAAAACGTGGACGGCGGCGGACATGGCGGCGCTGATCACCAAAACAAGTGG GAGCAGGCTGGTGAAGCAGAGAGACTCAGGGCCTACCTGGAGGGACGTCGCTGGAGTGGCTC CGCAGATACCTGAAGAACGGGAACGCGACGCTGCTGCGCACAGATCCCCAAAGGCCCATGTG ACCCATCACAGCAGACCTGAAGATAAAGTCACCCCTGAGGTGCTGGGCCCTGGGCTTCTACCT GCTGACATCACCTGACCTGGCAGTTGAATGGGGAGGAGCTGATCCAGGACATGGAGCTTGTG GAGACCAGGCTGCAGGGGATGGAACCTTCAGAAAGTGGGCATCTGTGGTGGTGCCTCTTGGG AAGGAGCAGTATTACACATGCCATGTGTACCATCAGGGGCTGCCTGAGCCCCCTACCCCTGAGA	10

[Table 13-2]

	TGGGAGCCTCCTCCATCCACTGTCTCCAACATGGCGACCGTTGCTGTTCTGGTTGCTCTTGGAGCTGCAATAGTCACTGGAGCTGTGGTGGCTTTTGTGATGAAGATGAGAAGGAGAAACACAGGTGGAAAAGGAGGGGACTATGCTCTGGCTCCAGGCTCCAGACCTCTGATCTGTCTCTCCAGATTGTAAAGTGATGGTTCATGACCCTCATTCTCTAGCG	
Peptide linker 2	GGGGSGGGSGGGSGGGGS	11
	GGGGGGGAGGCTCCGGTGGAGGGGGTCTGGAGGGGGGGTCTGGTGGAGGCGGAAGT	12
Single chain MHC class I molecule (β_2 microglobulin (from which signal peptide is removed) + peptide linker 2 + MHC class I α chain (from which signal peptide is removed))	IQKTPQIQVYSRHPPENGKPNILNCYVTQFHPPIEIQMLKNGKKIPKVEMSDMSFSKDWFSYILAHEFTPTETDTYACRVKHASMAEPTVYWRDMGGGGSGGGSGGGSGGGSGGPHSLRYFVTAVSRPGLGEPRYMEVGIVDDTEFVRFDSDAENPRYEPRARWMEQEGPEYWERETQKAKNGEQSFRVDLRTLGLYYNQSKGGSHTIQVISGCEVGSGRLLRGYQQYAYDGDYIALNEDLKTWTAADMAALITKHKWEQAGEAERLRAYLEGTCVEWLRRLKNGNATLLRTDSPKAHVTHSRPEDKVTLRCWALGFYPADITLTWQLNGEELIQDMELVETRPAGDGTGFKWASVVPLGKEQYYTCHVYHQGLPEPLTLRWEPPSTVSNMATVAVLVVLGAAIVTGAVVAFVMKMRRTNTGGKGGDYALAPGSQTSDSLPLDCKVMVHDPHSLA	65
	ATCCAGAAAACCCCTCAAATTCAGTATACTACGCCACCCACCGAGAATGGGAAGCCGAACATACTGAAGTCTACGTAACACAGTTCACCCCGCTCACATTGAAATCCAAATGCTGAAGAACGGGAAAAAATTCCTAAAGTAGAGATGTCAGATATGTCCTTCAGCAAGGACTGGTCTTTCTATATCCTGGCTCACACTGAATTCACCCCACTGAGACTGATACATACGCCTGCAGAGTTAAGCATGCCAGTATGGCCGAGCCCAAGACCGTCTACTGGGATCGAGACATGGGGGGGGAGGCTCCGGTGGAGGGGGTCTGGAGGGGGGGTCTGGTGGAGGCGGAAGTGGCCCACTCGCTGAGGTATTCTGTACCCGCGTGTCCCGGCCCGGCTCGGGAGCCCCGGTACATGGAAGTCGGCTACGTGACGACACGGAGTTCGTGCGCTTCGACAGCGACGCGGAGAATCCGAGATATGAGCCGCGGGCGCGGTGGATGGAGCAGGAGGGGGCCGAGATTGGGAGCGGAGACACAGAAAGCCAAGGGCAATGAGCAGAGTTTCCGAGTGGACCTGAGGACCCTGCTCGGCTACTACAACCAGAGCAAGGGCGGTCTCACACTATTAGGTGATCTCTGGCTGTGAAGTGGGGTCCGACGGCGACTCCTCCGCGGTACCAGCAGTACGCCTACGACGGCTGCGATTACATCGCCCTGAACGAAGACCTGAAAACGTGGACGGCGGGACATGGCGCGCTGATCACAAACACAAGTGGGAGCAGGCTGGTGAAGCAGAGAGACTCAGGGCCTACCTGGAGGACAGTGCCTGGAGTGGCTCCGAGATACCTGAAGAACGGGAACGCGACGCTGCTGCGCACAGATTCCCCAAAGGCCCATGTACCCATCACAGCAGACCTGAAGATAAAGTCACCTGAGGTGCTGGGCCCTGGGCTTCTACCCTGCTGACATCACCTGACCTGCAGTTGAATGGGAGGAGCTGATCCAGGACATGGAGCTTGTGGAGACCAGGCTGCAGGGGATGGAACTTCCAGAAGTGGGCATCTGTGGTGGTGCCTCTTGGGAAGGAGCAGTATTACACATGCATGTGTACCATCAGGGGCTGCCTGAGCCCCTACCCTGAGATGGGAGCCTCCTCCATCCACTGTCTCCAACATGGCGACCGTTGCTGTTCTGTTGTCTTGGAGCTGCAATAGTCACTGGAGCTGTGGTGGCTTTTGTGATGAAGATGAGAAGGAGAAACACAGGTGGAAAAGGAGGGGACTATGCT	66

[Table 13-3]

	CTGGCTCCAGGCTCCCAGACCTCTGATCTGTCTCTCCAGATTGTAAAGTGATGGTTCATGAC CCTCATTCTCTAGCG	
s c - T r i m e r (OVA peptide 1 + peptide linker 1 + single chain MHC class I molecule)	MARSVTLVFLVLVSLTGLYASINFEKLGGASGGGGSGGGGSIQKTPQIQVYSRHPPENGKP NILNCYVTQFHPPIEIQMLKNGKKIPKVEMSDMSFSKDWISFYILAHEFTPTETDTYACRVK HASMAEPKTVYWRDMGGGSGGGGSGGGGSGGGSGPHSLRYFVTAVSRPGLGEPRYMEVGY VDDTEFVRFDSDAENPRYEPRARWMEQEGPEYWERETQKAKGNEQSFRVDLRTLGLYNNQSKG GSHTIQVISGCEVGSGRLLRGYQYAYDGCYIALNEDLKTWTAADMAALITKHKWEQAGEA ERLRAYLEGTCEWLRRLKNGNATLLRTDSPKAHVTHSRPEDKVTLRWALGFYPADITLT WQLNGEELIQDMELVETRPAGDGTQKQWASVVVPLGKEQYYTCHVYHQGLPEPLTLRWEPPPS TVSNMATVAVLVVLGAAIVTGAVVAFVMKRRRNTGGKGGDYALAPGSQTSDSLSPDCKVMVH DPHSLA	13
	ATGGCTCGCTCGGTGACCTGGTCTTTCTGGTGCTTGTCTCACTGACCGGCTGTATGCTTCC ATTATAAATTTGAAAAGTTGGGCGGAGGTGCCTCTGGCGGTGGGGGCGAGCGGTGGAGGGGGC AGTATCCAGAAAACCCCTCAAATTCAGTATACTACGCCACCCACCGGAGAATGGGAAGCCG AACATACTGAAGTGTACGTAACACAGTTCCACCCGCCTCACATTGAAATCCAAATGCTGAAG AACGGGAAAAAAATTCCTAAAGTAGAGATGTCAGATATGTCCTTCAGCAAGGACTGGTCTTTC TATATCCTGGCTCACACTGAATTCACCCCACTGAGACTGATACATACGCCTGCAGAGTTAAG CATGCCAGTATGGCCGAGCCCAAGACCGTCTACTGGGATCGAGACATGGGGGGGGAGGCTCC GGTGGAGGGGGTCTGGAGGGGGGGGTCTGGTGGAGGCGGAAGTGCCCACTCGCTGAGG TATTTTCGTACCGCCGTGTCCCGGCCCGCCTCGGGGAGCCCGGTACATGGAAGTCGGCTAC GTGGACGACACGGAGTTCTGTGCGCTTCGACAGCGACGCGGAGAATCCGAGATATGAGCCGCGG GCCGCGTGGATGGAGCAGGAGGGGCCGAGTATTGGGAGCGGGAGACACAGAAAGCCAAGGGC AATGAGCAGAGTTTCCGAGTGGACCTGAGGACCTGTCTCGGCTACTACAACCAGAGCAAGGGC GGCTCTCACACTATTACGGTGATCTCTGGCTGTGAAGTGGGTCCGACGGGCGACTCCTCCGC GGGTACCAGCAGTACGCCTACGACGGCTGCGATTACATCGCCCTGAACGAAGACCTGAAAACG TGGACGGCGGCGACATGGCGGCGCTGATCACAAACACAAGTGGGAGCAGGCTGGTGAAGCA GAGAGACTCAGGGCCTACCTGGAGGGCAGTGCCTGGAGTGGCTCCGAGATACCTGAAGAAC GGGAACGCGACGCTGCTGCGCACAGATTCCCCAAGGCCATGTGACCCATCACAGCAGACCT GAAGATAAAGTCACCTGAGGTGCTGGGCCCTGGGCTTCTACCCTGTGACATCACCTGACC TGGCAGTTGAATGGGAGGAGCTGATCCAGGACATGGAGCTTGTGGAGACCAGGCCTGCAGGG GATGGAACCTTCCAGAAGTGGGCATCTGTGGTGGTGCCTCTTGGGAAGGAGCAGTATTACACA TGCCATGTGTACCATCAGGGGCTGCCTGAGCCCCCTACCTGAGATGGGAGCCTCCTCCATCC ACTGTCTCCAACATGGCGACCGTTGCTGTTCTGGTTGTCCTTGGAGCTGCAATAGTCACTGGA GCTGTGGTGGCTTTTGTGATGAAGATGAGAAGGAGAAACACAGGTGGAAAAGGAGGGGACTAT GCTCTGGCTCCAGGCTCCCAGACCTCTGATCTGTCTCTCCAGATTGTAAAGTGATGGTTCAT	14

[Table 13-4]

	GACCCCTATTCTCTAGCG	
I L - 2 (from which signal peptide is removed)	APTSSTSSSTAEAAQQQQQQQQQQHLEQLLMDLQELLSRMENYRNKLPRMLTFKFYLPKQ ATELKDLCLEDELGPLRHVLDLTQSKSFQLEDAENFISNIRVTVVKLKGSNTFECQFDDDES ATVVDFLRRWIAFCQSIISTSPQ	25
	GCACCCACTTCAAGCTCCACTTCAAGCTCTACAGCGGAAGCACAGCAGCAGCAGCAGCAGCAG CAGCAGCAGCAGCAGCAGCAGCTGGAGCAGCTGTTGATGGACCTACAGGAGCTCCTGAGCAGGATG GAGAATTACAGGAACCTGAACTCCCCAGGATGCTCACCTTCAAATTTTACTTGCCCAAGCAG GCCACAGAATTGAAAGATCTTCAGTGCCTAGAAGATGAACTTGACCTCTGCGGCATGTTCTG GATTTGACTCAAAGCAAAAGCTTCAATTGGAAGATGCTGAGAATTCATCAGCAATATCAGA GTAAGTGTGTAATACTAAAGGGCTCTGACAACACATTTGAGTGCCAATTCGATGATGAGTCA GCAACTGTGGTGGACTTTCTGAGGAGATGGATAGCCTTCTGTCAAAGCATCATCTCAACAAGC CCTCAA	26
C D 8 1 (amino acids 1 to 177)	MGVEGCTKCIKYLFFVFNFFVFWLAGGVILGVALWLRHDPQTTSLLYLELGNKPAPNTFYVGIY ILIAVGAVMMFVGFLGCGYAIQESQCLLGTTFFTCVLVILFACEVAAGIWGFVNKDQIAKDVKQF YDQALQQAVMDDANNAKAVVKTFFHETLNCCGSNALTTLTTLILRNSLCPS	61
	ATGGGGGTGGAGGGCTGCACCAATGCATCAAATACCTGCTCTTCGTCTTCAATTCGTCTTC TGGCTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGTCATGATCCACAGACCACC AGCCTGCTGTACCTGGAAGTGGGAAACAAACCGGCACCAACACCTTCTACGTGGGCATCTAC ATTCTCATTGCTGTGGGAGCTGTGATGATGTTTGTAGGCTTCCTGGGGTGTATGGGGCCATC CAGGAGTCCCAGTGTCTGCTGGGACGTTCTTCACCTGCCTTGTGATCCTGTTTGCCTGTGAG GTGGCTGCAGGCATCTGGGGCTTCGTAAACAAAGACCAGATCGCCAAGGATGTGAAGCAGTTC TATGACCAGGCCCTTCAGCAAGCTGTGATGGATGATGATGCCAACAATGCCAAGGCTGTGGTG AAGACTTTCCATGAGACGCTCAACTGTTGTGGCTCCAACGCACTGACCACACTGACTACCACC ATACTGAGGAACAGCCTGTGTCCCTCA	62
C D 8 1 (amino acids 178 to 236)	GGNLTPLQQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	63
	GGCGGCAACATACTACCCCTTACTGCAGCAAGATTGTCATCAGAAAATCGATGAGCTCTTC TCTGGGAAGCTGTACCTCATTGGAATTGCAGCCATTGTGGTAGCTGTCATTATGATCTTTGAG ATGATTCTGAGCATGGTGTGTGCTGTGGCATCCGGAACAGCTCCGTGTACTGA	64
C D 8 1 - I L - 2	MGVEGCTKCIKYLFFVFNFFVFWLAGGVILGVALWLRHDPQTTSLLYLELGNKPAPNTFYVGIY ILIAVGAVMMFVGFLGCGYAIQESQCLLGTTFFTCVLVILFACEVAAGIWGFVNKDQIAKDVKQF YDQALQQAVMDDANNAKAVVKTFFHETLNCCGSNALTTLTTLILRNSLCPSGGGGSAPTSST SSSTAEAAQQQQQQQQQQHLEQLLMDLQELLSRMENYRNKLPRMLTFKFYLPKQATELKDLCLEDELGPLRHVLDLTQSKSFQLEDAENFISNIRVTVVKLKGSNTFECQFDDDESATVVDFLRRWIAFCQSIISTSPQGGGGSGGNLTPLQQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	133
	ATGGGGGTGGAGGGCTGCACCAATGCATCAAATACCTGCTCTTCGTCTTCAATTCGTCTTC TGGCTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGTCATGATCCACAGACCACC AGCCTGCTGTACCTGGAAGTGGGAAACAAACCGGCACCAACACCTTCTACGTGGGCATCTAC ATTCTCATTGCTGTGGGAGCTGTGATGATGTTTGTAGGCTTCCTGGGGTGTATGGGGCCATC	134

[Table 13-5]

[illegible]

[Table 13-6]

	TGCCATGTGTACCATCAGGGGCTGCCTGAGCCCCTACCCCTGAGATGGGAGCCTCCTCCATCC ACTGTCTCCAACATGGCGACCGTTGCTGTTCTGCTTGGAGCTGCAATAGTCACTGGA GCTGTGGTGGCTTTTGTGATGAAGATGAGAAGGAGAAAACACAGGTGGAAAAGGAGGGGACTAT GCTCTGGCTCCAGGCTCCAGACCTCTGATCTGTCTCTCCAGATTGTAAGTGATGGTTTCAT GACCCTCATTCTCTAGCGATGGGGGTGGAGGGCTGCACCAAATGCATCAAATACCTGCTCTTC GTCTTCAATTTCTGCTTCTGGCTGGCTGGAGGCGTGATCCTAGGTGTAGCTCTGTGGTTGCGT CATGATCCACAGACCACCAGCCTGCTGTACCTGGAACCTGGGAAACAAACCGGCACCCAAACACC TTCTACGTGGGCATCTACATTCTCATTGCTGTGGGAGCTGTGATGATGTTTGTAGGCTTCCTG GGGTGCTATGGGGCCATCCAGGAGTCCAGTGTCTGCTGGGGACGTTCTTACCTGCCTTGTG ATCCTGTTTGCCTGTGAGGTGGCTGCAGGCATCTGGGGCTTCGTAACAAAGACCAGATCGCC AAGGATGTGAAGCAGTTCTATGACCAGGCCCTTCAGCAAGCTGTGATGGATGATGATGCCAAC AATGCCAAGGCTGTGGTGAAGACTTTCATGAGACGCTCAACTGTTGTGGCTCCAACGCACTG ACCACACTGACTACCACCATACTGAGGAACAGCCTGTGTCCCTCAGGAGGAGGAGGAAGCGCA CCCCTTCAAGCTCCACTTCAAGCTCTACAGCGGAAGCACAGCAGCAGCAGCAGCAGCAGCAG CAGCAGCAGCAGCAGCTGGAGCAGCTGTTGATGGACCTACAGGAGCTCCTGAGCAGGATGGAG AATTACAGGAACCTGAAACTCCCAGGATGCTCACCTTCAAATTTTACTTGCCCAAGCAGGCC ACAGAATTGAAAGATCTTCAGTGCCTAGAAGATGAACTTGGACCTCTCGGCATGTTCTGGAT TTGACTCAAAGCAAAAGCTTCAATTGGAAGATGCTGAGAATTCATCAGCAATATCAGAGTA ACTGTTGTAAACTAAAGGGCTCTGACAAACACATTTGAGTGCCAAATTCGATGATGAGTCAGCA ACTGTGGTGGACTTTCTGAGGAGATGGATAGCCTTCTGTCAAAGCATCATCTCAACAAGCCCT CAAGGAGGAGGAGGAAGCGGGGCAACATACTACCCCTTACTGCAGCAAGATTGTATCAG AAAATCGATGAGCTCTTCTCTGGGAAGCTGTACCTCATTGGAATTGCAGCCATTGTGGTAGCT GTCATTATGATCTTTGAGATGATTCTGAGCATGGTGTGTGTGTGGCATCCGGAACAGCTCC GTGTACTGA	
Aka-Luc	MEDAKNIKKGPAPFYPLEDGTAGEQLHKAMKRYALVPGAIAFTDAHIQVDVTYAEYFEMSVRL AEAMRRYGLNTHRIVVCSENSSQFFMPVLGALFIGVAVAPANDIYNERELLSMGIQPTVV FVSKKGLRKVLNVQKLP IIRKIIIMDSKTDYQGFQSMYTFVTSHLPPSFNEYDFVPESFDRD KTIALIMNSSGSTGLPKGVALPHRTACVRFSHARDPIFGYQNPDTAILSVVPFHHGFGMFTT LGYLICGFRVVLMYRFEEELFLRSLQDYKIQSALLVPTLFSCLAKSTLIDKYDLSSLREIASG GAPLSKEVGEAVAKRFRLPGRQGYGLTETTNVMITPEGDRKPGSVGVVPPFEAKVVDLVT GKTLGVNQRGELCVRGPMIMSGYVNNPEATNALIDKDWLHSGDIAWDEDEHFFIVDRLSL IKYKGYQVAPAELEGILLQHPYIFDAGVAGLPDDAGELPAAVVLEHGKTMTEKEIVDYVAS QVTTAKKL RGGVVFVDEVPRSGKLDARKIREILTKAKKDGKIAV	137
	ATGGAAGATGCCAAAAACATTAAGAAGGGCCCAGCGCGTTCTACCCACTCGAAGACGGGACC GCCGGCGAGCAGCTGCACAAAGCCATGAAGCGCTACGCCCTGGTGCCCGGCCATCGCCTTT ACCGACGCACATATTACGGTGGACGTTACCTACGCCGAGTACTTCGAGATGAGCGTTCCGGCTG GCAGAAGCTATGAGGCGCTATGGGCTGAATACAAACCATCGGATCGTGGTGTGCAGCGAGAAT AGCTCGCAGTTCTTCATGCCCGTGTGGGTGCCCTGTTTCATCGGTGTGGCTGTGGCCCCAGCT AACGACATCTACAACGAGCGCGAGCTGCTGAACAGCATGGGCATCAGCCAGCCCACCGTCGTA TTCGTGAGCAAGAAAGGGCTGCCAAAGGTCTCAACGTGCAAAAGAAGCTACCGATCATACGA AAGATCATCATCATGGATAGCAAGACCGACTACCAGGGCTTCCAAAGCATGTACACCTTCGTG ACTTCCCATTTGCCACCCAGCTTCAACGAGTACGACTTCGTGCCGAGAGCTTCGACCGGGAC AAAACCATCGCCCTGATCATGAACAGTAGTGGTAGTACAGGATTACCCAAGGGCGTAGCCCTA CCGACCGCACCCTTGTGTCCGATTCACTCATGCCCCGACCCCATCTTCGGCTACCAGAAC ATCCCCGACACCGCTATCCTCAGCGTGGTGCCATTTACCACGGCTTCGGCATGTTACCACG CTGGGCTACTTGATCTGCGGCTTTCGGGTCGTGCTCATGTACCGCTTCGAGGAGGAGCTATTTC TTGCGCAGCTTGCAAGACTATAAGATTCAATCTGCCCTGCTGGTGCCACACTATTAGCTGC CTCGCTAAGAGCACTCTCATCGACAAGTACGACCTAAGCAGCTTGCGCGAGATCGCCAGCGGC GGGGCGCCGCTCAGCAAGGAGGTAGGTGAGGCCGTGGCCAAACGCTTCGCGCTACCAGGCATC CGCCAGGGCTATGGCTGACAGAAACAACCAACGCCGTGATGATACCCCCGAGGGGACCGT AAGCCTGGCTCAGTAGGAAGGTGGTGCCCTTCTTCGAGGCTAAGGTGGTAGACTTGGTCACC GGTAAGACACTGGGTGTGAACAGCGCGTGAGCTGTGCGTCCGTGGCCCCATGATCATGAGC	138

[Table 13-7]

	GGCTACGTTAACAACCCCGAGGCTACGAACGCTCTCATCGACAAGGACGGCTGGCTGCACAGC GGCGACATCGCCTACTGGGACGAGGACGAGCACTTCTTCATCGTGGACCGGCTGAAGAGCCTG ATCAAATACAAGGGCTACCAGGTAGCCCCAGCCGAAGTGGAGGGCATCCTGCTGCAACACCCC TACATCTTCGACGCCGAGTCGCCGGCTGCCGACGACGATGCCGGCGAGCTGCCCGCCCA GTCGTCGTGTTGGAACACGGTAAAACCATGACCGAGAAAGAGATCGTGGACTATGTGGCCAGC CAGGTTACAACCGCCAAGAAGCTGCGCGGTGGTGTGTTGTGTTGTGGATGAAGTCCCTAGAGGA TCGACCGGCAAGTTAGACGCCCGCAAGATCCGCGAGATTCTCACTAAGGCCAAGAAGGACGGC AAGATCGCCGTG	
	MAVEGGMKCVKFLLYVLLAFCAVGLIAIGVAVQVVLKQAITHETTAGSLLPVVIIAVGAF LFLVAFVGGCGACKENYCLMITFAIFLSLIMLVEVAVAIAGYVFRDQVKSEFNKSFQQMQNY LKDNKTATILDKLQKENNCCGASNYTDWENIPGMAKDRVPDSCCINITVGCNDFKESTIHTQ GCVETIAIWLKRNILLVAAAALGIAFVEVLGIIFSCCLVKSIRSGYEV	27
CD 6 3	ATGGCGGTGGAAGGAGGAATGAAGTGTGTCAAGTTTTTGCTCTACGTTCTCCTGCTGGCCTTC TGCGCCTGTGCAGTGGGATTGATCGCCATTGGTGTAGCGGTCAGGTTGTCTGAAGCAGGCC ATTACCCATGAGACTACTGCTGGCTCGCTGTTGCCTGTGGTCATCATTGCAGTGGGTGCCTTC CTCTTCCTGGTGGCCTTTGTGGGCTGCTGTGGGGCCTGCAAGGAGAACTACTGTCTCATGATT ACATTTGCCATCTTCCTGTCTCTTATCATGCTTGTGGAGGTGGCTGTGGCCATTGCTGGCTAT GTGTTTAGAGACCAGGTGAAGTCAGAGTTAATAAAAAGCTCCAGCAGCAGATGCAGAATTAC CTTAAAGACAACAAAACAGCCACTATTTTGGACAAATTGCAGAAAGAAAATAACTGCTGTGGA GCTTCTAACTACACAGACTGGGAAAACATCCCCGGCATGGCCAAGGACAGAGTCCCCGATTCT TGCTGCATCAACATAACTGTGGGCTGTGGGAATGATTTCAAGGAATCCACTATCCATACCCAG GGCTGCGTGGAGACTATAGCAATATGGCTAAGGAAGAACATACTGCTGGTGGCTGCAGCGGCC CTGGGCATTGCTTTTGTGGAGGTCTTGGGAATTATCTTCTCCTGCTGTCTGGTGAAGAGTATT CGAAGTGGCTATGAAGTAATGTAG	28
	MAVEGGMKCVKFLLYVLLAFCAVGLIAIGVAVQVVLKQAITHETTAGSLLPVVIIAVGAF LFLVAFVGGCGACKENYCLMITFAIFLSLIMLVEVAVAIAGYVFRDQVKSEFNKSFQQMQNY LKDNKTATILDKLQKENNCCGASNYTDWENIPGMAKDRVPDSCC	57
CD 6 3 (amino acids 1 to 170)	ATGGCGGTGGAAGGAGGAATGAAGTGTGTCAAGTTTTTGCTCTACGTTCTCCTGCTGGCCTTC TGCGCCTGTGCAGTGGGATTGATCGCCATTGGTGTAGCGGTCAGGTTGTCTGAAGCAGGCC ATTACCCATGAGACTACTGCTGGCTCGCTGTTGCCTGTGGTCATCATTGCAGTGGGTGCCTTC CTCTTCCTGGTGGCCTTTGTGGGCTGCTGTGGGGCCTGCAAGGAGAACTACTGTCTCATGATT ACATTTGCCATCTTCCTGTCTCTTATCATGCTTGTGGAGGTGGCTGTGGCCATTGCTGGCTAT GTGTTTAGAGACCAGGTGAAGTCAGAGTTAATAAAAAGCTCCAGCAGCAGATGCAGAATTAC CTTAAAGACAACAAAACAGCCACTATTTTGGACAAATTGCAGAAAGAAAATAACTGCTGTGGA GCTTCTAACTACACAGACTGGGAAAACATCCCCGGCATGGCCAAGGACAGAGTCCCCGATTCT TGCTGC	58
CD 6 3 (amino acids 171 to 238)	INITVGCNDFKESTIHTQGCVETIAIWLKRNILLVAAAALGIAFVEVLGIIFSCCLVKSIRS GYEVM	59

[Table 13-8]

	ATCAACATAACTGTGGGCTGTGGGAATGATTTCAAGGAATCCACTATCCATACCCAGGGCTGC GTGGAGACTATAGCAATATGGCTAAGGAAGAACATACTGCTGGTGGCTGCAGCGGCCCTGGGC ATTGCTTTTGTGGAGGTCTTGGGAATTATCTTCTCCTGCTGTCTGGTGAAGAGTATTGGAAGT GGCTATGAAGTAATGTAG	60
Peptide linker 3	GGGGS	29
	GGAGGAGGAGGAAGC	30
C D 6 3 -Aka- Luc	MAVEGGMKCVKFLLYVLLAFACAVGLIAIGVAVQVVLKQAITHETTAGSLLPVV I IAVGAF LFLVAFVGGCCGACKENYCLMITFAIFLSLIMLVEVAVAIAGYVFRDQVKSEFNKSFQQMQNY LKDNKTATILDKLQKENNCCGASNYTDWENIPGMAKDRVPDSCCGGGGSMEDAKNIKKGPAPF YPLEDGTAGEQLHKAMKRYALVPGAIAFTDAHIQVDVTYAEYFEMSURLAEAMRRYGLNTNHR IVVCSSENSQFFMPVLGALFIGVAVAPANDIYNERELLSMGI SQPTVVVFSKGLRKVLNVQ KKLP IIRK I IIMDSKTDYQGFQSMYTFVTSHLPPSFNEYDFVPESFDRDKTIALIMNSSGSTG LPKGVALPHRTACVRFSHARDPIFGYQNIPTAILSVVPFHGFGMFTTLGYLICGFRVVL MY RFEELFLRSLQDYKIQSALLVPTLFSCLAKSTLIDKYDLSSLREIASGGAPLSKEVGEAVAK RFRLPGIRQGYGLTETTNVMI TPEGDRKPGSVGKVVPFFFEAKVVDLVTGKTLGVNQRGELCV RGPIMIMSGYVNNPEATNALIDKDGWLHSGDIAYWDEDEHFFIVDRKSLIKYKGYQVAPAELE GILLQHPYIFDAGVAGLPDDAGELPAAVVVLEHGKTMTEKEIVDYVASQVTTAKKLRGGVVF VDEVPRGSTGKLDARKIREILTAKKDKGKIAVGGGGSINITVGCNDFKESTIHTQGCVETIA IWLKRNILLVAAAALGIAFVEVLGIIFSCCLVKSIIRSGYEV M	139
	ATGGCGGTGGAAGGAGGAATGAAGTGTGTCAAGTTTTTGTCTACGTTCTCCTGCTGGCCTTC TGCGCCTGTGCAGTGGGATTGATCGCCATTGGTGTAGCGGTTCAAGTTGTCTTGAAGCAGGCC ATTACCCATGAGACTACTGCTGGCTCGCTGTTGCCTGTGGTCATCATTGCAGTGGGTGCCTTC CTCTTCTGCTGGCCTTTGTGGGCTGCTGTGGGGCCTGCAAGGAGAACTACTGTCTCATGATT ACATTTGCCATCTTCTGTCTCTTATCATGCTTGTGGAGGTGGCTGTGGCCATTGTGCTGCTAT GTGTTTAGAGACCAGGTGAAGTCAGAGTTAATAAAAGCTTCCAGCAGCAGATGCAGAATTAC CTAAAGACAACAAAACAGCCACTATTTTGGACAAATTGCAGAAAGAAAATAACTGTGTGGA GCTTCTAACTACACAGACTGGGAAAACATCCCCGGCATGGCCAAGGACAGATCCCCGATTCT TGCTGCGGTGGTGGTGTCTATGGAAGATGCCAAAACATTAAGAAGGGCCAGCGCCGCTTC TACCCACTCGAAGACGGGACCGCGCGAGCAGCTGCACAAAGCCATGAAGCGCTACGCCCTG GTGCCCGCGCCATCGCCTTTACCGACGCACATATTAGGTGGACGTTACCTACGCCGAGTAC TTCGAGATGAGCGTTTCGGCTGGCAGAAGCTATGAGGCGCTATGGGCTGAATACAAACCATCGG ATCGTGGTGTGCAGCGAGAATAGCTCGCAGTTCTTCATGCCCGTGTGGGTGCCCTGTTTCATC GGTGTGGCTGTGGCCCCAGCTAACGACATCTACAACGAGCGCGAGCTGCTGAACAGCATGGGC ATCAGCCAGCCACCGTCGTATTTCGTGAGCAAGAAAGGGCTGCGAAAGGTCCTCAACGTGCAA AAGAAGCTACCGATCATACGAAAGATCATCATGATAGCAAGACCGACTACCAGGGCTTC CAAAGCATGTACACCTTCGTGACTTCCCATTTGCCACCCAGCTTCAACGAGTACGACTTCGTG CCCGAGAGCTTCGACCGGGACAAAACCATCGCCCTGATCATGAACAGTAGTGGTAGTACAGGA TTACCCAAGGGCGTAGCCCTACCGCACCGCACCGCTTGTGTCCGATTCAATCATGCCCGGAC CCCATCTTCGGCTACGAGAATCCCCGACACCGCTATCCTCAGCGTGGTGCCATTTACCCAC GGCTTCGGCATGTTACACAGCTGGGCTACTTGATCTGCGGCTTTCGGGTGCTGCTCATGTAC CGCTTCGAGGAGGAGCTATTCTTGGCAGCTTGCAAGACTATAAGATTCAATCTGCCCTGCTG GTGCCCACACTATTTAGCTGCCTCGCTAAGAGCACTCTCATCGACAAGTACGACCTAAGCAGC TTGCGCGAGATCGCCAGCGCGGGCGCGCTCAGCAAGGAGGTAGGTGAGGCGGTGGCCAAA CGCTTCCGCTTACCAGGCATCCGCCAGGGCTATGGCCTGACAGAAACAACACCGCGTCATG ATCACCCCGAGGGGGACCGTAAGCCTGGCTCAGTAGCAAGGTGGTGCCCTTCTTCGAGGCT AAGGTGGTAGACTTGGTCACCGGTAAGACACTGGGTGTGAACAGCGCGGTGAGCTGTGCGTC CGTGCCCCATGATCATGAGCGGCTACGTTAACAACCCCGAGGCTACGAACGCTCTCATCGAC AAGGACGGCTGGCTGCACAGCGGCACATCGCCTACTGGGACGAGGACGAGCACTTCTTCATC GTGGACCGGCTGAAGAGCCTGATCAAATACAAGGGCTACCAGGTAGCCCCAGCCGAAGTGGAG GGCATCCTGCTGCAACACCCCTACATCTTCGACGCGGAGTCGCGGCGCTGCCCGACGACGAT	140

[Table 13-9]

	GCCGGCGAGCTGCCCGCCGAGTCGTCGTGTTGGAACACGGTAAAACCATGACCGAGAAAGAG ATCGTGGACTATGTGGCCAGCCAGGTTACAACCGCCAAGAAGCTGCGCGGTGGTGTGTGTTT GTGGATGAAGTCCCTAGAGGATCGACCGGCAAGTTAGACGCCCGCAAGATCCGCGAGATTCTC ACTAAGGCCAAGAAGGACGGCAAGATCGCCGTGGGTGGTGGTGGTTCTATCAACATAACTGTG GGCTGTGGGAATGATTTC AAGGAATCCACTATCCATACCCAGGGCTGCGTGGAGACTATAGCA ATATGGCTAAGGAAGAACATACTGCTGGTGGCTGCAGCGGCCCTGGGCATTGCTTTTGTGGAG GTCTTGGGAATTATCTTCTCCTGCTGTCTGGTGAAGAGTATTCGAAGTGGCTATGAAGTAATG TAG	

[0246]

[Table 14-1]

	Sequence	SEQ ID NO:
Signal peptide of h β_2 microglobulin	<u>MSRSVALAVLALLSLSGLEA</u>	121
	<u>ATGTCTCGCTCCGTGGCCTTAGCTGTGCTCGCGCTACTCTCTCTTTCTGGCCTGGAGGCT</u>	122
SARS-CoV2 peptide 1 (for MHC class I molecule)	KLWAQCVQL	141
	AAACTGTGGGCCAGTGTGTGCAGCTG	142
Peptide linker 1	GGGASGGGSGGGGS	5
	GGCGGAGGTGCCTCTGGCGGTGGGGGCAGCGGTGGAGGGGGCAGT	6
h β_2 Microglobulin (from which signal peptide is removed)	IQRTPKIQVYSRHPAENGKSNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWFSY LLYTEFTPTKEDEYACRVNHVTLSPKIVKWDRDM	121
	ATCCAGCGTACTCCAAAGATTCAAGTTTACTCACGTCATCCAGCAGAGAATGGAAAGTCAAAT TTCCTGAATTGCTATGTGTCTGGGTTTCATCCATCCGACATTGAAGTTGACTTACTGAAGAAT GGAGAGAGAATTGAAAAAGTGGAGCATTCAAGCTTGTCTTTCAGCAAGGACTGGTCTTTCTAT CTCTTGACTACACTGAATTCACCCCCACTGAAAAAGATGAGTATGCCTGCCGTGTGAACCAT GTGACTTTGTCACAGCCCAAGATAGTTAAGTGGGATCGAGACATG	122
h MHC class I (HLA-A0201) α chain (from which signal peptide is removed)	GSHSMRYFFTSVSRPGRGEPRFIAVGYYDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGE TRKVKAHSQTHRVDLGLRGYYNQSEAGSHTVQRMYGCDVGSWDRFLRGYHQAAYDGDYIAL KEDLRSWTAADMAAQTTHKHWEAAHVAEQLRAYLEGTCVEWLRRLYLENGKETLQRTDAPKTHM THHAVSDHEATLRWALSFYPAEITLTWQRDGEDQTQDELVETRPAGDGTQKWAAVVPSG QEQRYTCHVQHEGLPKPLTLRWPSSQPTIPIVGIIAGLVLFGAVITGAVVAAMWRRKSSDR KGGSYSQAASSDSAQGSVDVSLTACKV	143
	GGCTCTCACTCCATGAGGTATTCTTCACATCCGTGTCCCGGCCCGCGCGGGAGCCCCGC TTCATCGCAGTGGGCTACGTGGACGACACGCAGTTTCGTGCGGTTTCGACAGCGACGCCGCGAGC CAGAGGATGGAGCCGCGGGCGCGCTGGATAGAGCAGGAGGGTCCGGAGTATTGGGACGGGGAG ACACGGAAGTGAAGGCCACTCACAGACTCACCGAGTGGACCTGGGACCCCTGCGCGGCTAC TACAACCAGAGCGAGGCGGTTCTCACACCGTCCAGAGGATGTATGGCTGCGACGTGGGGTCG GACTGGCGCTTCTCCGCGGTACACCAAGTACGCCTACGACGGCAAGGATTACATCGCCCTG AAAGAGGACCTGCGCTCTTGACCGCGGGGACATGGCAGCTCAGACCACCAAGCACAAAGTGG GAGGCGGCCCATGTGGCGGAGCAGTTGAGAGCCTACCTGGAGGGCAGCTGCGTGGAGTGGCTC CGCAGATACCTGGAGAACGGGAAGGAGACGCTGCAGCGCACGGACGCCCCAAAACGCATATG ACTCACACGCTGTCTCTGACCATGAAGCCACCCTGAGGTGCTGGGCCCTGAGCTTCTACCT GCGGAGATCACACTGACCTGGCAGCGGGATGGGGAGGACCAGACCCAGGACACGGAGCTCGTG GAGACCAGGCTGCAGGGGATGGAACCTTCCAGAAGTGGGCGGCTGTGGTGGTGCCTTCTGGA CAGGAGCAGAGATACACCTGCCATGTGCAGCATGAGGGTTTGCCCAAGCCCTCACCTTGAGA TGGGAGCCGTCTTCCAGCCACCATCCCATCGTGGGCATCATTGCTGGCCTGGTTCTCTTT GGAGCTGTGATCACTGGAGCTGTGGTCTGCTGTGATGTGGAGGAGGAAGAGCTCAGATAGA AAAGGAGGAGCTACTCTCAGGCTGCAAGCAGTGACAGTGCCAGGGCTCTGATGTGTCTCTC ACAGCTTGTAAGTG	144
Peptide linker 2	GGGGSGGGSGGGSGGGGS	11
	GGGGGGGAGGCTCCGTGGAGGGGGTCTGGAGGGGGGGTCTGGTGGAGGCGGAAGT	12
	IQRTPKIQVYSRHPAENGKSNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWFSY	145

[Table 14-2]

h single chain MHC class I molecule (β_2 microglobulin (from which signal peptide is removed) + peptide linker 2 + MHC class I (HLA-A0201) α chain (from which signal peptide is removed))	LLYYTEFTPTEKDEYACRVNHVTLSPKIVKWDRDMGGGGSGGGSGGGSGGGSGSHSMRY FFTSVSRPGRGEPRFIAVGYYDDTQFVRFSDAASQRMEPRAPWIEQEGPEYWDGETRKKVAH SQTHRVDLGLRGYYNQSEAGSHTVQRMYGCDVGSWDRFLRGYHQYAYDGK DYIALKEDLRSWTAADMAAQTTHKWEAAHVAEQLRAYLEGTCVEWLRRLYLENGKETLQRTDA PKTHMTHHAVSDHEATLRWALSFPYPAEITLTWQRDGEDQTQDTELVETRPAGDGTGFKWAAV VVPSSGQEQRYTCHVQHEGLPKPLTLRWEPSQPTIPVGI IAGLVLFGAVITGAVVAAMWRR KSSDRKGGSYSQAASSDSAQGSVDVSLTACKV ATCCAGCGTACTCCAAAGATTGAGTTTACTCACGTCATCCAGCAGAGAATGGAAAGTCAAAT TTCTGAATTGCTATGTGTCTGGGTTTCATCCATCCGACATTGAAGTTGACTTACTGAAGAAT GGAGAGAGAATTGAAAAAGTGGAGCATTGAGACTTGTCTTTCAGCAAGGACTGGTCTTTCTAT CTCTTGTACTACACTGAATTCACCCCACTGAAAAAGATGAGTATGCCTGCCGTGTGAACCAT GTGACTTTGTACAGCCCAAGATAGTTAAGTGGGATCGAGACATGGGAGCGCGGGCTCTGGC GGCGGCGGAGTGGCGGTGGCGGTAGCGGCGGAGGTGGATCTGGCTCTCACTCCATGAGGTAT TTCTTCACATCCGTGTCCCGGCGGCGGCGGAGCGGCGGCTTCATCGCAGTGGGTACGTG GACGACACGCAGTTCGTGCGGTTCGACAGCGACGCGCGGAGCCAGAGGATGGAGCCGCGGGC CCGTGGATAGAGCAGGAGGTCCGAGTATTGGGACGGGAGACAGGAAAGTGAAGGCCAC TCACAGACTCACGAGTGGACCTGGGAGCCCTGCGCGGCTACTACAACAGAGCGAGCCGCT TCTCACACCGTCCAGAGGATGTATGGCTGCGACGTGGGTGCGACTGGCGCTTCTCCGCGGG TACCACAGTACGCCTACGACGGCAAGGATTACATCGCCCTGAAAGAGGACCTGCGCTCTTGG ACCGCGGCGGACATGGCAGCTCAGACCACCAAGCACAAAGTGGGAGGCGGCCATGTGGCGGAG CAGTTGAGAGCCTACCTGGAGGCGACGTGCGTGGAGTGGCTCCGAGATACCTGGAGAACGGG AAGGAGACGCTGCAGCGCACGGACGCCCCAAAACGCATATGACTACACGCTGTCTCTGAC CATGAAGCCACCCTGAGGTGCTGGGCCCTGAGCTTCTACCCTGGGAGATCACACTGACCTGG CAGCGGGATGGGGAGGACCAGACCCAGGACACGGAGCTCGTGGAGACCAGGCTGCAGGGGAT GGAACCTTCCAGAAGTGGGCGCTGTGGTGGTGCCTTCTGGACAGGAGCAGAGATACACCTGC CATGTGCAGCATGAGGGTTTGGCCAGCCCTCACCTGAGATGGGAGCCGCTTCCCAGCCC ACCATCCCATCGTGGGCATATTGCTGGCCTGGTTCTTTGGAGCTGTGATCACTGGAGCT GTGGTCGCTGCTGTGATGTGGAGGAGGAGAGCTCAGATAGAAAAGGAGGGAGCTACTCTCAG GCTGCAAGCAGTGACAGTGGCCAGGGCTGTATGTGTCTCTCACAGCTTGAAAAGTG	146
h s c - T r i m e r (SARS-CoV2 peptide 1 + peptide linker 1 + single chain MHC class I (HLA-A0201) molecule)	MSRSVALAVLALLSLSGLEAKLWAQCVQLGGGASGGGGSGGGSIQRTPKIQVYSRHPAENGK SNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWSYLLYYTEFTPTEKDEYACRV NHVTLSPKIVKWDRDMGGGGSGGGSGGGSGGGSGGGSGSHSMRYFFTSVSRPGRGEPRFIAVG YVDDTQFVRFSDAASQRMEPRAPWIEQEGPEYWDGETRKKVAHSQTHRVDLGLRGYYNQSE AGSHTVQRMYGCDVGSWDRFLRGYHQYAYDGKDYIALKEDLRSWTAADMAAQTTHKWEAAHV AEQLRAYLEGTCVEWLRRLYLENGKETLQRTDAPKTHMTHHAVSDHEATLRWALSFPYPAEITL TWQRDGEDQTQDTELVETRPAGDGTGFKWAAVVVPSSGQEQRYTCHVQHEGLPKPLTLRWEPS QPTIPVGI IAGLVLFGAVITGAVVAAMWRRKSSDRKGGSYSQAASSDSAQGSVDVSLTACKV ATGTCTCGCTCCGTGGCCTTAGCTGTGCTCGCGCTACTCTCTCTTTCTGGCCTGGAGGCTAAA CTGTGGGCCAGTGTGTGCAGCTGGGCGGAGGGGCATCAGGCGCGGTGGGTGAGGTGAGGT GGGAGTATCCAGCGTACTCCAAAGATTGAGTTTACTCACGTCATCCAGCAGAGAATGGAAAG TCAAATTTCTGAATTGCTATGTGTCTGGGTTTCATCCATCCGACATTGAAGTTGACTTACTG AAGAATGGAGAGAGAATTGAAAAAGTGGAGCATTGAGACTTGTCTTTCAGCAAGGACTGGTCT TTCTATCTCTTGTACTACACTGAATTCACCCCACTGAAAAAGATGAGTATGCCTGCCGTGTG AACCATGTGACTTTGTACAGCCCAAGATAGTTAAGTGGGATCGAGACATGGGAGCGCGGG TCTGGCGGCGGCGGAGTGGCGGTGGCGGTAGCGGCGGAGGTGGATCTGGCTCTCACTCCATG AGGTATTCTTCACATCCGTGTCCCGGCGGCGGCGGAGCGGCGGCTTCATCGCAGTGGGC TACGTGGACGACACGCAGTTCGTGCGGTTTCGACAGCGACGCGCGGAGCCAGAGGATGGAGCCG CGGGCGCGGTGGATAGAGCAGGAGGTCCGGAGTATTGGGACGGGAGACACGAAAGTGAAG GCCCCTCACAGACTCACGAGTGGACCTGGGAGCCCTGCGCGGCTACTACAACAGAGCGAG GCCGTTCTCACACCGTCCAGAGGATGTATGGCTGCGACGTGGGTGCGACTGGCGCTTCTC CGCGGTACCACAGTACGCCTACGACGGCAAGGATTACATCGCCCTGAAAGAGGACCTGCGC TCTTGACCGCGGCGGACATGGCAGCTCAGACCACCAAGCACAAAGTGGGAGGCGGCCATGTG CGGAGCAGTTGAGAGCCTACCTGGAGGCGACGTGCGTGGAGTGGCTCCGAGATACCTGGAG	147 148

[Table 14-3]

	AACGGGAAGGAGACGCTGCAGCGCACGGACGCCCCAAAACGCATATGACTCACCACGCTGTC TCTGACCATGAAGCCACCCTGAGGTGCTGGGCCCTGAGCTTCTACCCTGCGGAGATCACACTG ACCTGGCAGCGGGATGGGAGGACCAGACCCAGGACACGGAGCTCGTGGAGACCAGGCCTGCA GGGGATGGAACCTTCCAGAAGTGGGCGGCTGTGGTGGTGCCTTCTGGACAGGAGCAGAGATAC ACCTGCCATGTGCAGCATGAGGGTTTGCCCAAGCCCCCTACCCTGAGATGGGAGCCGTCTTCC CAGCCCACCATCCCCATCGTGGGCATCATTGCTGGCCTGGTTCTCTTTGGAGCTGTGATCACT GGAGCTGTGGTGGTGTGATGTGGAGGAGGAAGAGCTCAGATAGAAAAGGAGGGAGCTAC TCTCAGGCTGCAAGCAGTGACAGTGCCAGGGCTCTGATGTGTCTCTCACAGCTTGTAAAGTG	
hCD81	MGVEGCTKCIKYLFFVFNFWLWLAGGVILGVALWLRHDPQTTNLLYLELGDKPAPNTFYVGIY ILIAVGAVMMFVGLGCGYGAIQESQCLLGTFFTCLVILFACEVAAGIWGFVNKQIAKDVKQF YDQALQQAVVDDANNAKAVVKTFFHETLDCCGSSTLTALTTSVLKNNLCPSGSNIISNLFKED CHQKIDDLFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	129
	ATGGGAGTGGAGGGCTGCACCAAGTGCATCAAGTACCTGCTCTTCGTCTTCAATTTCTGCTTC TGGCTGGCTGGAGGCGTGATCCTGGGTGTGGCCCTGTGGCTCCGCCATGACCCGCAGACCACC AACCTCCTGTATCTGGAGCTGGGAGACAAGCCCGCGCCCAACACCTTCTATGTAGGCATCTAC ATCCTCATCGCTGTGGGCGCTGTGATGATGTTTGGTTTCTGGGCTGTACGGGGCCATC CAGGAATCCCAGTGCCTGTGGGACGTTCTTACCTGCCTGGTTCATCTGTTTGCCTGTGAG GTGGCCGCCGGCATCTGGGGCTTTGTCAACAAGGACCAGATCGCCAAGGATGTGAAGCAGTTC TATGACCAGGCCCTACAGCAGGCCGTGGTGGATGATGACGCCAACAACGCCAAGGCTGTGGTG AAGACCTTCCACGAGACGCTTGACTGCTGTGGCTCCAGCACACTGACTGCTTTGACCACCTCA GTGCTCAAGAACAATTTGTGTCCCTCGGGCAGCAACATCATCAGCAACCTCTTCAAGGAGGAC TGCCACCAGAAGATCGATGACCTCTTCTCCGGAAGCTGTACCTCATCGGCATTGCTGCCATC GTGGTGGCTGTGATCATGATCTTCGAGATGATCTGAGCATGGTGTGTGTGTGGCATCCGG AACAGCTCCGTGTACTGA	130
hsc-Trim er-CD8 1 (SARS-CoV2 s c-Trim er + CD81)	MSRSVALAVLALLSLSGLEAKLWQCVQLGGGASGGGGSGGGGSIQRTPKIQVYSRHPAENGK SNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWSFYLLYYTEFTPEKDEYACRV NHVTLSPKIVKWRDMGGGGSGGGGSGGGGSGGGGSGSHSMRYFTSVSRPGRGEPRFIAVG YVDDTQFVRFDSDAASQRMERAPWIEQEGPEYWDGETRKVKKAHSQTHRVLDLTLRGYNNQSE AGSHTVQRMYGCDVGSWRFLRGYHYAYDGKDYIALKEDLRSWTAADMAAQTTHKHWAAHV AEQLRAYLEGTCEWLRRLRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRWALSFPYAEITL TWQRDGEDQTQDELVETRPAGDGTGKWAAVVVPSCGEQRYTCHVQHEGLPKPLTLRWEPS QPTPIVIGIIAGLVFGAVITGAVVAVMWRRKSSDRKGSYSQAASSDSAQGSVDVSLTACKV MGVEGCTKCIKYLFFVFNFWLWLAGGVILGVALWLRHDPQTTNLLYLELGDKPAPNTFYVGIY ILIAVGAVMMFVGLGCGYGAIQESQCLLGTFFTCLVILFACEVAAGIWGFVNKQIAKDVKQF YDQALQQAVVDDANNAKAVVKTFFHETLDCCGSSTLTALTTSVLKNNLCPSGSNIISNLFKED CHQKIDDLFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	149
	ATGTCTCGCTCCGTGGCCTTAGCTGTGCTCGCGCTACTCTCTCTTTCTGGCCTGGAGGCTAAA CTGTGGGGCCAGTGTGTGCAGCTGGGCGGAGGGGCATCAGGCGGCGGTGGGTGGAGGT GGGAGTATCCAGCGTACTCCAAAGATTAGGTTTACTACGTCTCCAGCAGAGAATGGAAAG TCAAATTTCTGAATTGCTATGTGTCTGGGTTTCATCCATCCGACATTGAAGTTGACTTACTG AAGAATGGAGAGAGAATTGAAAAAGTGGAGCATTGAGACTTGTCTTTACGAAGGACTGGTCT TTCTATCTCTGTACTACACTGAATTCACCCCACTGAAAAAGATGAGTATGCGCTGCCGTGTG AACCATGTGACTTTGTACAGCCCAAGATAGTTAAGTGGGATCGAGACATGGGAGCGGGCGGG TCTGGCGGGCGGGCAGTGGCGGTGGCGGTAGCGGGGAGGTTGGATCTGGCTCTCACTCCATG AGGTATTTCTTACATCCGTGTCCCGGCCGGCGGGGAGCCCCGCTTCATCGCAGTGGGC	150

[Table 14-4]

	TACGTGGACGACACGCAGTTTCGTGCGGTTTCGACAGCGACGCCGCGAGCCAGAGGATGGAGCCG CGGGCGCCGTGGATAGAGCAGGAGGGTCCGGAGTATTGGGACGGGGAGACACGGAAAGTGAAG GCCCACTCACAGACTCACCGAGTGGACCTGGGGACCCTGCGCGGCTACTACAACCAGAGCGAG GCCGTTCTCACACCGTCCAGAGGATGTATGGCTGCGACGTGGGGTCGGACTGGCGCTTCCTC CGCGGTACCAACAGTACGCCCTACGACGGCAAGGATTACATCGCCCTGAAAGAGGACCTGCGC TCTTGGACCGCGGGGACATGGCAGCTCAGACCACCAAGCACAAAGTGGGAGGCGGCCATGTG GCGGAGCAGTTGAGAGCCTACCTGGAGGGCACGTGCGTGGAGTGGCTCCGCAGATACCTGGAG AACGGGAAGGAGACGCTGCAGCGCACGGACGCCCCAAAACGCATATGACTCACCACGCTGTC TCTGACCATGAAGCCACCTGAGGTGCTGGGCCCTGAGCTTCTACCTGCGGAGATCACACTG ACCTGGCAGCGGGATGGGGAGGACCAGACCCAGGACACGGAGCTCGTGGAGACCAGGCTGCA GGGGATGGAACCTTCCAGAAGTGGGCGGCTGTGGTGGTGCCTTCTGGACAGGAGCAGAGATAC ACCTGCCATGTGCAGCATGAGGTTTGTCCCAAGCCCCCTACCTGAGATGGGAGCCGTCTTCC CAGCCCCACCATCCCCATCGTGGGCATCATTGCTGGCCTGGTTCTCTTGGAGCTGTGATCACT GGAGCTGTGGTGGTGTGTGTGTGTGGAGGAGGAAGAGCTCAGATAGAAAAGAGGGAGCTAC TCTCAGGCTGCAAGCAGTGACAGTGCCAGGGCTCTGATGTGTCTCTCACAGCTTGTAAAGTG ATGGGAGTGGAGGGCTGCACCAAGTGCATCAAGTACCTGCTCTTCGTCTTCAATTCGTCTTC TGGCTGGCTGGAGGCGTGATCCTGGGTGTGGCCCTGTGGCTCCGCCATGACCCGAGACCACC AACCTCCTGTATCTGGAGCTGGGAGACAAGCCCGCGCCCAACACCTTCTATGTAGGCATCTAC ATCCTCATCGCTGTGGGCGCTGTCATGATGTTGCTTGGCTTCTGGGCTGCTACGGGGCCATC CAGGAATCCCAGTGCCTGCTGGGGACGTTCTTCACTGCCTGGTTCATCCTGTTTGCTGTGAG GTGGCCGCGGCATCTGGGGCTTGTCAACAAGGACCAGATCGCCAAGGATGTGAAGCAGTTC TATGACCAGGCCCTACAGCAGGCCGTGGTGGATGATGACGCCAACAACGCCAAGGCTGTGGTG AAGACCTTCCACGAGACGCTTGACTGCTGTGGCTCCAGCACACTGACTGCTTTGACCACCTCA GTGCTCAAGAACAATTTGTGTCCTCGGGCAGCAACATCATCAGCAACCTCTTCAAGGAGGAC TGCCACCAGAAGATCGATGACCTCTTCTCCGGGAAGCTGTACCTCATCGGCATTGCTGCCATC GTGGTGGTGTGATCATGATCTTCGAGATGATCCTGAGCATGCTGCTGTGCTGTGGCATCCGG AACAGCTCCGTGTACTGA	

[0247] Preparation of Fetal Bovine Serum from which Exosomes Are Removed

After 10 mL of inactivated FBS and 2 mL of a 50% poly(ethylene glycol)
5 10,000 solution (manufactured by Sigma-Aldrich, #81280) were stirred at 4°C for 2
hours, exosomes were precipitated under centrifugation conditions of 1,500 × g, 4°C,
and 30 minutes, and supernatant was collected to obtain fetal bovine serum from which
the exosomes were removed.

10 [0248] [Example 1] Antigen-Presenting Extracellular Vesicles Containing MHC Class
I Molecules and T-Cell Stimulatory Cytokines in Membrane

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's
modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin
were added. Cells at about 50% confluence were transfected with two plasmids
(pCAG vectors encoding sc-Trimer-CD81 and CD63-IL-2, respectively) at the same
15 time using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to
the manufacturer's instructions. The medium was replaced 3 hours after the
transfection, and 24 hours after the transfection, the medium was replaced with a
Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed

serum and penicillin/streptomycin were added. 72 hours after the transfection, supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 μ m filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. A supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. Then the supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 μ L of PBS were used as antigen-presenting extracellular vesicles of Example 1 (Fig. 2A). The concentration of the extracellular vesicles was measured according to the manufacturer's instructions using a BCA protein assay kit (manufactured by Thermo Fisher Scientific Inc.).

[0249] [Example 2] Antigen-Presenting Extracellular Vesicles Containing MHC Class I Molecules, T-Cell Costimulatory Molecules, and T-Cell Stimulatory Cytokines in Membrane

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with the three plasmids (pCAG vectors encoding sc-Trimer-CD81, CD80-CD9, and CD63-IL-2, respectively) prepared above at the same time using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to the manufacturer's instructions. The medium was replaced 3 hours after the transfection, and 24 hours after the transfection, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed serum and penicillin/streptomycin were added. 72 hours after the transfection, a supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 μ m filter. A supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. A supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After supernatant was collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 μ L of PBS were used as antigen-presenting extracellular vesicles of Example 2 (Fig. 2B). The concentration of the antigen-presenting extracellular vesicles was measured according to the manufacturer's instructions using a BCA protein assay kit (manufactured by Thermo Fisher Scientific Inc.).

[0250] [Example 3] Antigen-Presenting Extracellular Vesicles 1 Containing MHC

Class II Molecules, T-Cell Costimulatory Molecules, and T-Cell Stimulatory Cytokines in Membrane

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with the four plasmids (pCAG vectors encoding sc-Dimer-CD81, an MHC class II α chain, CD80-CD9, and CD63-IL-2, respectively) prepared above at the same time using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to the manufacturer's instructions. The medium was replaced 3 hours after the transfection, and 24 hours after the transfection, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine serum from which exosomes were removed and penicillin/streptomycin were added. 72 hours after the transfection, a supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 μ m filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. Then, supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 μ L of PBS were used as antigen-presenting extracellular vesicles of Example 3 (Fig. 2C). The concentration of the antigen-presenting extracellular vesicles was measured according to the manufacturer's instructions using a BCA protein assay kit (manufactured by Thermo Fisher Scientific Inc.).

[0251] [Example 4] Antigen-Presenting Extracellular Vesicles 2 Containing MHC Class II Molecules, T-Cell Costimulatory Molecules, and T-Cell Stimulatory Cytokines in Membrane

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with five plasmids (pCAG vectors encoding sc-Dimer-CD81, an MHC class II α chain, CD80-CD9, TGF- β -MFGE8, and CD63-IL-2, respectively) at the same time using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to the manufacturer's instructions. The medium was replaced 3 hours after the transfection, and 24 hours after the transfection, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed serum and penicillin/streptomycin were added. 72 hours after the transfection, supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 μ m filter.

Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After a supernatant was collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 μ L of PBS were used as antigen-presenting extracellular vesicles of Example 4 (Fig. 2D). The concentration of the antigen-presenting extracellular vesicles was measured according to the manufacturer's instructions using a BCA protein assay kit (manufactured by Thermo Fisher Scientific Inc.).

[0252] [Example 5] Antigen-Presenting Extracellular Vesicles 3 Containing MHC Class II Molecules, T-Cell Costimulatory Molecules, and T-Cell Stimulatory Cytokines in Membrane

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with the four plasmids (pCAG vectors encoding sc-Dimer-CD81, an MHC class II α chain, CD80-CD9, and CD81-IL-4, respectively) prepared above at the same time using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to the manufacturer's instructions. The medium was replaced 3 hours after the transfection, and 24 hours after the transfection, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed serum and penicillin/streptomycin were added. 72 hours after the transfection, supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 μ m filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After supernatant was collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, a supernatant was removed, and the pellets suspended in 100 μ L of PBS were used as antigen-presenting extracellular vesicles of Example 5 (Fig. 2E). The concentration of the antigen-presenting extracellular vesicles was measured according to the manufacturer's instructions using a BCA protein assay kit (manufactured by Thermo Fisher Scientific Inc.).

[0253] [Reference Example 1] Control Extracellular Vesicles

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's

modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. The medium was replaced with cells at about 50% confluence, and after 24 hours, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed serum and penicillin/streptomycin were added. 48 hours after the replacement with the medium from which exosomes were removed, supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 µm filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After a supernatant was collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, a supernatant was removed, and the pellets suspended in 100 µL of PBS were used as extracellular vesicles of Reference Example 1. The concentration of the antigen-presenting extracellular vesicles was measured according to the manufacturer's instructions using a BCA protein assay kit (manufactured by Thermo Fisher Scientific Inc.).

[0254] [Reference Example 2] Extracellular Vesicles Containing MHC Class I Molecules in Membrane

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with a plasmid (a pCAG vector encoding sc-Trimer-CD81) using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to manufacturer's instructions. The medium was replaced 3 hours after the transfection, and 24 hours after the transfection, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed serum and penicillin/streptomycin were added. .72 hours after the transfection, supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 µm filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After a supernatant was collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 µL of PBS were used as extracellular vesicles of Reference Example 2. The concentration of the extracellular vesicles was measured according to the manufacturer's instructions using a BCA

protein assay kit (manufactured by Thermo Fisher Scientific Inc.).

[0255] [Reference Example 3] Extracellular Vesicles Containing T-Cell Costimulatory Molecules in Membrane

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with a plasmid (a pCAG vector encoding CD80-CD9) using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to manufacturer's instructions. The medium was replaced 3 hours after the transfection, and 24 hours after the transfection, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed serum and penicillin/streptomycin were added. 72 hours after the transfection, supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 µm filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After supernatant was collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 µL of PBS were used as extracellular vesicles of Reference Example 3. The concentration of the extracellular vesicles was measured according to the manufacturer's instructions using a BCA protein assay kit (manufactured by Thermo Fisher Scientific Inc.).

[Reference Example 4] Extracellular Vesicles Containing T-Cell Stimulatory Cytokines in Membrane

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with a plasmid (a pCAG vector encoding CD63-IL-2) using polyethylenimine "Max" (Polysciences Inc.) according to manufacturer's instructions. The medium was replaced 3 hours after the transfection, and 24 hours after the transfection, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed serum and penicillin/streptomycin were added. 72 hours after the transfection, supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 µm filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After supernatant was

collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 µL of PBS were used as extracellular vesicles of Reference Example 4. The concentration of the extracellular vesicles was measured according to the manufacturer's instructions using a BCA protein assay kit (manufactured by Thermo Fisher Scientific Inc.).

[0256] [Reference Example 5] Extracellular Vesicles Containing MHC Class I Molecules and T-Cell Costimulatory Molecules in Membrane

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with two plasmids (pCAG vectors encoding sc-Trimer-CD81 and CD80-CD9, respectively) at the same time using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to the manufacturer's instructions. The medium was replaced 3 hours after the transfection, and 24 hours after the transfection, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed serum and penicillin/streptomycin were added. 72 hours after the transfection, supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 µm filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After a supernatant was collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 µL of PBS were used as extracellular vesicles of Reference Example 5. The concentration of the extracellular vesicles was measured according to the manufacturer's instructions using a BCA protein assay kit (manufactured by Thermo Fisher Scientific Inc.).

[0257] Test Example 1-1: Flow Cytometry Analysis of Fusion Protein Contained in Membrane of Extracellular Vesicle

The antigen-presenting extracellular vesicles of Example 2 were immunostained by a PS Capture (trademark) exosome flow cytometry kit (manufactured by FUJIFILM Wako Pure Chemical Corporation) according to the manufacturer's instruction. Antibodies used for staining are as follows (staining time: 15 minutes, temperature: 4°C). After the staining, expression of each fusion protein

was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- APC-conjugated anti-mouse H-2KbOVA complex antibody (25-D1.16, manufactured by Biolegend, Inc.)

- PE-conjugated anti-mouse CD80 antibody (16-10A1, manufactured by Biolegend, Inc.)

- Brilliant Violet421-conjugated anti-mouse IL-2 antibody (JES6-5H4, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 3A.

[0258] [Results]

From the results of Test Example 1-1, it could be seen that MHC class I molecules presenting OVA antigens, CD80, and IL-2 were contained in the membrane of the antigen-presenting extracellular vesicle of Example 2 (Fig. 3A).

[0259] Test Example 1-2: Flow Cytometry Analysis of Fusion Protein Contained in Membrane of Extracellular Vesicle

The antigen-presenting extracellular vesicles of Example 3 were immunostained by a PS Capture (trademark) exosome flow cytometry kit (manufactured by FUJIFILM Wako Pure Chemical Corporation) according to the manufacturer's instruction. The antibodies used for the staining are as follows. After the staining, expression of each fusion protein was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- APC-conjugated anti-mouse IL-2 antibody (JES6-5H4, manufactured by Biolegend, Inc.)

- PE-conjugated anti-mouse CD80 antibody (16-10A1, manufactured by Biolegend, Inc.)

- APC-Cy7-conjugated anti-mouse I-A/I-E antibody (M5/114.15.2, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 3B.

[0260] [Results]

From the results of Test Example 1-2, it could be seen that MHC class II molecules presenting OVA antigens, CD80, and IL-2 were contained in the membrane of the antigen-presenting extracellular vesicle of Example 3 (Fig. 3B).

[0261] Test Example 1-3: Flow Cytometry Analysis of Fusion Protein Contained in Membrane of Extracellular Vesicle

The antigen-presenting extracellular vesicles of Example 4 were immunostained by a PS Capture (trademark) exosome flow cytometry kit (manufactured by FUJIFILM Wako Pure Chemical Corporation) according to the

manufacturer's instruction. The antibodies used for the staining are as follows. After the staining, expression of each fusion protein was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- APC-conjugated anti-mouse IL-2 antibody (JES6-5H4, manufactured by Biolegend, Inc.)
- PE-conjugated anti-mouse CD80 antibody (16-10A1, manufactured by Biolegend, Inc.)
- APC-Cy7-conjugated anti-mouse I-A/I-E antibody (M5/114.15.2, manufactured by Biolegend, Inc.)
- APC-conjugated anti-mouse LAP (TGF- β 1) antibody (TW7-16B4, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 3C.

[0262] [Results]

From the results of Test Example 1-3, it could be seen that MHC class II molecules presenting OVA antigens, CD80, IL-2, and TGF- β 1 were contained in the membrane of the antigen-presenting extracellular vesicle of Example 4 (Fig. 3C).

[0263] Test Example 1-4: Flow Cytometry Analysis of Fusion Protein Contained in Membrane of Extracellular Vesicle

The antigen-presenting extracellular vesicles of Example 5 were immunostained by a PS Capture (trademark) exosome flow cytometry kit (manufactured by FUJIFILM Wako Pure Chemical Corporation) according to the manufacturer's instruction. The antibodies used for the staining are as follows. After the staining, expression of each fusion protein was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- Alexa Fluor 488-conjugated anti-mouse IL-4 antibody (11B11, manufactured by Biolegend, Inc.)
- PE-conjugated anti-mouse CD80 antibody (16-10A1, manufactured by Biolegend, Inc.)
- APC-Cy7-conjugated anti-mouse I-A/I-E antibody (M5/114.15.2, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 3D.

[0264] [Results]

From the results of Test Example 1-4, it could be seen that MHC class II molecules presenting OVA antigens, CD80, and IL-4 were contained in the membrane of the antigen-presenting extracellular vesicle of Example 5 (Fig. 3D).

[0265] Test Example 2: Experiment on Activation of OVA-Specific CD8-Positive T

Cells (OT-1 T Cells) In Vitro by Antigen-Presenting Extracellular Vesicles

The following test was conducted in vitro to determine whether the antigen-presenting extracellular vesicles activate antigen-specific CD8-positive T cells.

Lymph nodes extracted from an OT-1 mouse, which was an OVA-reactive
5 TCR transgenic mouse, were disrupted on a 100 µm filter to obtain a lymph node cell suspension. The cell suspension was stained using CellTrace Violet (manufactured by Thermo Fisher Scientific Inc.) as a cell proliferation assay reagent according to the manufacturer's instructions. 2×10^5 stained lymph node cells were suspended in 200 µL of an RPMI1640 medium to which 10% fetal bovine serum, 50 µM 2-
10 mercaptoethanol, and penicillin/streptomycin were added, the antigen-presenting extracellular vesicles of Example 1 or 2 (final concentration: 3 µg/mL), a mixture of three types of the extracellular vesicles of Reference Examples 2 to 4 (final concentration of each of the three types of the extracellular vesicles: 3 µg/mL), or the extracellular vesicles of Reference Examples 1, 2, or 5 (final concentration: 3 µg/mL)
15 were added, culture was performed in a 96 well round bottom plate for 3 days, and then, immunostaining was performed. Antibodies used for staining are as follows (staining time: 15 minutes, temperature: 4°C). After the staining, a luminescence intensity of CellTrace Violet as a cell proliferation assay reagent in the OT-1 T cells was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- 20 • APC-conjugated anti-mouse CD8 antibody (53-6.7, manufactured by Biolegend, Inc.)
 • PE-conjugated anti-mouse TCR Vb5.1,5.2 antibody (MR9-4, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 4.

25 [0266] [Results]

From the results of Test Example 2, it was confirmed that the antigen-presenting extracellular vesicles of Examples 1 and 2 remarkably differentiated and/or proliferated antigen-specific CD8-positive T cells in comparison with the mixture of the three types of the extracellular vesicles of Reference Examples 2 to 4 or the
30 extracellular vesicles of Reference Examples 1, 2, and 5 (Fig. 4).

[0267] Test Example 3: Experiment on Activation of OVA-Specific CD8-Positive T Cells (OT-1 T Cells) In Vivo by Antigen-Presenting Extracellular Vesicles

The following test was conducted in vivo to determine whether the antigen-presenting extracellular vesicles activate antigen-specific CD8-positive T cells.

35 Lymph nodes were extracted from an OT-1 mouse, which was OVA-reactive TCR transgenic mouse, and the same lymphocyte suspension as that of Test Example 2

was prepared. Lymph nodes were similarly extracted from a CD45.1 congenic mouse, and a lymphocyte suspension was prepared. The respective lymphocyte suspensions were mixed at a ratio of 1:1, and the mixture was stained using CellTrace Violet as a cell proliferation assay reagent. 1×10^7 CellTrace Violet-stained mixed lymphocyte suspension suspended in PBS was transferred from the tail vein of the CD45.1/CD45.2 congenic mouse. The next day, a mixture (IL-2/anti-IL-2 antibody complex) of 50 μ g of the antigen-presenting extracellular vesicles of Example 2 or the extracellular vesicles of Reference Example 1, or 1.5 μ g of IL-2 (manufactured by Biolegend, Inc.) and 50 μ g of anti-mouse IL-2 antibodies (S4B6-1, manufactured by Bio X Cell) was transferred to from the tail vein into a CD45.1/CD45.2 congenic mouse. 4 days after cell transfer, lymph nodes were extracted from the recipient mouse, and a lymphocyte suspension was prepared and immunostained. Antibodies used for staining are as follows (staining time: 15 minutes, temperature: 4°C). After the staining, a luminescence intensity of CellTrace Violet as a cell proliferation assay reagent in the transferred OT-1 T cells and wild-type CD8T cells was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- PE-Cy7-conjugated anti-mouse CD8 antibody (53-6.7, manufactured by Biolegend, Inc.)
- PE-conjugated anti-mouse TCR Vb5.1,5.2 antibody (MR9-4, manufactured by Biolegend, Inc.)
- FITC-conjugated anti-mouse CD45.1 antibody (A20, manufactured by Biolegend, Inc.)
- APC-conjugated anti-mouse CD45.2 antibody (104, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 5.

[0268] [Results]

From the results of Test Example 3, it could be seen that the antigen-presenting extracellular vesicles of Example 2 hardly activated other CD8-positive T cells (antigen-non-specific CD8-positive T cells) and remarkably differentiated and/or proliferated antigen-specific CD8-positive T cells in vivo in comparison with the extracellular vesicles of Reference Example 1 (Fig. 5). In addition, it is possible that serious side effects such as cytokine storm are low because the antigen-presenting extracellular vesicles of Example 2 hardly activate other CD8-positive T cells (antigen-non-specific CD8-positive T cells) in comparison with the IL-2/anti-IL-2 antibody complex (Fig. 5).

[0269] Test Example 4: Experiment on Activation of OVA-Specific CD4-Positive T

Cells (OT-2 T Cells) In Vitro by Antigen-Presenting Extracellular Vesicles

The following test was conducted in vitro to determine whether the antigen-presenting extracellular vesicles activate antigen-specific CD4-positive T cells.

Lymph nodes extracted from an OT-2 mouse, which was an OVA-reactive CD4TCR transgenic mouse, were disrupted on a 100 µm filter to obtain a lymph node cell suspension. The cell suspension was stained using CellTrace Violet (manufactured by Thermo Fisher Scientific Inc.) as a cell proliferation assay reagent according to the manufacturer's instructions. 2×10^5 stained lymph node cells were suspended in 200 µL of an RPMI1640 medium to which 10% fetal bovine serum, 50 µM 2-mercaptoethanol, and penicillin/streptomycin were added, the antigen-presenting extracellular vesicles of Example 3 or the extracellular vesicles of Reference Example 1 were added so that the final concentration was 10 µg/mL, and culture was performed in a 96 well round bottom plate for 4 days. After 4 days, the cells were recovered and immunostained. Antibodies used for staining are as follows (staining time: 15 minutes, temperature: 4°C). After the staining, a luminescence intensity of CellTrace Violet as a cell proliferation assay reagent in the OT-2 T cells was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- PE-Cy7-conjugated anti-mouse CD4 antibody (RM4-5, manufactured by Biolegend, Inc.)
- APC-conjugated anti-mouse TCR Vb5.1,5.2 antibody (MR9-4, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 6.

[0270] [Results]

From the results of Test Example 4, it was confirmed that the antigen-presenting extracellular vesicles of Example 3 remarkably differentiated and/or proliferated antigen-specific CD4 T cells in comparison with the extracellular vesicles of Reference Example 1 (Fig. 6).

[0271] Test Example 5: Experiment on Differentiation Induction of OVA-Specific CD4-Positive T Cells (OT-2 T Cells) In Vitro into Regulatory T Cells by Antigen-Presenting Extracellular Vesicles

The following test was conducted in vitro to determine whether the antigen-presenting extracellular vesicles induce antigen-specific CD4-positive T cells into regulatory T cells (Treg).

Lymph nodes extracted from an OT-2 mouse, which was an OVA-reactive CD4TCR transgenic mouse, were disrupted on a 100 µm filter to obtain a lymph node cell suspension. The cell suspension was stained using CellTrace Violet

(manufactured by Thermo Fisher Scientific Inc.) as a cell proliferation assay reagent according to the manufacturer's instructions. 2×10^5 stained lymph node cells were suspended in 200 μ L of an RPMI1640 medium to which 10% fetal bovine serum, 50 μ M 2-mercaptoethanol, and penicillin/streptomycin were added, the antigen-presenting
5 extracellular vesicles of Example 4 or the extracellular vesicles of Reference Example 1 were added so that the final concentration was 10 μ g/mL, and culture was performed in a 96 well round bottom plate for 4 days. After 4 days, the cells were recovered, and extracellular immunostaining was performed. Antibodies used for staining are as follows (staining time: 15 minutes, temperature: 4°C). After the extracellular staining,
10 intracellular immunostaining was performed using True-Nuclear Transcription Factor Buffer Set (manufactured by Biolegend, Inc.) and anti-mouse FOXP3 antibodies according to the manufacturer's instructions. After the intracellular staining, expression of CD25 molecules and FOXP3 molecules as markers of regulatory T cells on the OT-2 T cells was detected with a flow cytometer FACSCantoII (manufactured by
15 BD Biosciences).

- PE-conjugated anti-mouse CD25 antibody (PC61, manufactured by Biolegend, Inc.)
- PE-Cy7-conjugated anti-mouse CD4 antibody (RM4-5, manufactured by Biolegend, Inc.)
- 20 • APC-conjugated anti-mouse TCR Vb5.1,5.2 antibody (MR9-4, manufactured by Biolegend, Inc.)
- Alexa Fluor 488-conjugated anti-mouse FOXP3 antibody (MF-14, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 7.
25 [0272] [Results]

From the results of Test Example 5, it could be seen that the antigen-presenting extracellular vesicles of Example 4 induced differentiation of the antigen-specific CD4-positive T cells into regulatory T cells (preferably, regulatory T cells expressing Foxp3) in comparison with the extracellular vesicles of Reference Example 1 (Fig. 7).

30 [0273] Test Example 6: Experiment on Differentiation Induction of OVA-Specific CD4-Positive T Cells (OT-2 T Cells) In Vitro into Th2T Cells by Antigen-Presenting Extracellular Vesicles

The following test was conducted in vitro to determine whether antigen-presenting extracellular vesicles induce differentiation of antigen-specific CD4-positive
35 T cells into Th2T cells.

Lymph nodes extracted from an OT-2 mouse, which was an OVA-reactive

CD4TCR transgenic mouse, were disrupted on a 100 µm filter to obtain a lymph node cell suspension. The cell suspension was stained using CellTrace Violet (manufactured by Thermo Fisher Scientific Inc.) as a cell proliferation assay reagent according to the manufacturer's instructions. 2×10^5 stained lymph node cells were
5 suspended in 200 µL of an RPMI1640 medium to which 10% fetal bovine serum, 50 µM 2-mercaptoethanol, and penicillin/streptomycin were added, the antigen-presenting extracellular vesicles of Example 3 or 5 or the extracellular vesicles of Reference Example 1 were added so that the final concentration was 10 µg/mL, and culture was performed in a 96 well round bottom plate for 4 days. After 4 days, the cells were
10 recovered, and extracellular immunostaining was performed. Antibodies used for staining are as follows (staining time: 15 minutes, temperature: 4°C). After the extracellular staining, intracellular immunostaining was performed using True-Nuclear Transcription Factor Buffer Set (manufactured by Biolegend, Inc.) and anti-GATA3 antibodies according to the manufacturer's instructions. After the intracellular
15 staining, a luminescence intensity of CellTrace Violet as a cell proliferation assay reagent in the OT-2 T cells and expression of GATA3 as a marker of Th2T cells were detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- PE-conjugated anti-mouse TCR Vb5.1,5.2 antibody (MR9-4, manufactured by Biolegend, Inc.)
- 20 • PE-Cy7-conjugated anti-mouse CD4 antibody (RM4-5, manufactured by Biolegend, Inc.)
- APC-conjugated anti-GATA3 antibody (16E10A23, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 8.

25 [0274] [Results]

From the results of Test Example 6, it could be seen that the antigen-presenting extracellular vesicles of Examples 3 and 5 induced differentiation of antigen-specific CD4-positive T cells into Th2 cells in vitro in comparison with the extracellular vesicles of Reference Example 1 (Fig. 8). The Th2 cells secrete cytokines such as IL-4 or IL-5,
30 activate differentiation of naive B cells that recognize the same antigen, and promote induction of antigen-specific IgE production (that is, activation of humoral immunity).

[0275] [Example 6] Antigen-Presenting Extracellular Vesicles 4 Containing MHC Class II Molecules, T-Cell Costimulatory Molecules, and T-Cell Stimulatory Cytokines in Membrane

35 HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin

were added. Cells at about 50% confluence were transfected with the four plasmids (pCAG vectors encoding sc-Dimer-CD81-IL-12p40, an MHC class II α chain, CD80-CD9, and IL-12p35, respectively) prepared above at the same time using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to the
5 manufacturer's instructions. 3 to 12 hours after the transfection, the medium was replaced, and 24 hours after the transfection, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed serum and penicillin/streptomycin were added. 72 hours after the transfection, a supernatant was collected, and then the supernatant was centrifuged at 300 g for 5
10 minutes after being passed through a 0.22 μ m filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After supernatant was collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets
15 and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 μ L of PBS were used as antigen-presenting extracellular vesicles of Example 6. The concentration of the antigen-presenting extracellular vesicles was measured according to the manufacturer's instructions using a BCA protein assay kit (manufactured by Thermo Fisher Scientific Inc.).
20 [0276] Test Example 1-5: Flow Cytometry Analysis of Fusion Protein Contained in Membrane of Extracellular Vesicle

The antigen-presenting extracellular vesicles of Example 6 were immunostained by a PS Capture (trademark) exosome flow cytometry kit (manufactured by FUJIFILM Wako Pure Chemical Corporation) according to the
25 manufacturer's instruction. The antibodies used for the staining are as follows. After the staining, expression of each fusion protein was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- Alexa Fluor 488-conjugated anti-mouse I-A/I-E antibody M5/114.15.2, manufactured by Biolegend, Inc.)
- 30 • PE-conjugated anti-mouse IL-12 antibody (C15.6, manufactured by Biolegend, Inc.)
- The results of APC-conjugated anti-mouse CD80 antibody (16-10A1, manufactured by Biolegend, Inc.) are illustrated in Fig. 3E.

[0277] [Results]

35 From the results of Test Example 1-5, it could be confirmed that MHC class II molecules presenting OVA antigens, CD80, and functional IL-12 were contained in the

membrane of the antigen-presenting extracellular vesicle of Example 6 (Fig. 3E).

[0278] [Example 7] Antigen-Presenting Extracellular Vesicles 5 Containing MHC Class II Molecules, T-Cell Costimulatory Molecules, and T-Cell Stimulatory Cytokines in Membrane

5 HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with the five plasmids (pCAG vectors encoding sc-Dimer-CD81, an MHC class II α chain, CD80-CD9, CD81-IL-6, and TGF- β -MFGE8, respectively) prepared above at the same time using
10 polyethylenimine "Max" (manufactured by Polysciences Inc.) according to the manufacturer's instructions. 3 to 12 hours after the transfection, the medium was replaced, and 24 hours after the transfection, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed serum and penicillin/streptomycin were added. 72 hours after the transfection, a
15 supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 μ m filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After supernatant was collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant
20 was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 μ L of PBS were used as antigen-presenting extracellular vesicles of Example 7. The concentration of the antigen-presenting extracellular vesicles was measured according to the manufacturer's instructions using a BCA
25 protein assay kit (manufactured by Thermo Fisher Scientific Inc.).

[0279] Test Example 1-6: Flow Cytometry Analysis of Fusion Protein Contained in Membrane of Extracellular Vesicle

The antigen-presenting extracellular vesicles of Example 7 were immunostained by a PS Capture (trademark) exosome flow cytometry kit
30 (manufactured by FUJIFILM Wako Pure Chemical Corporation) according to the manufacturer's instruction. The antibodies used for the staining are as follows. After the staining, expression of each fusion protein was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- FITC-conjugated anti-mouse CD80 antibody (16-10A1, manufactured by
35 Biolegend, Inc.)
- PE-conjugated anti-mouse IL-6 antibody (MP5-20F3, manufactured by

Biolegend, Inc.)

- APC-Cy7-conjugated anti-mouse I-A/I-E antibody (M5/114.15.2, manufactured by Biolegend, Inc.)

- APC-conjugated anti-mouse LAP (TGF- β 1) antibody (TW7-16B4, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 3F.

[0280] [Results]

From the results of Test Example 1-6, it could be seen that MHC class II molecules presenting OVA antigens, CD80, IL-6, and TGF β were contained in the membrane of the antigen-presenting extracellular vesicle of Example 7 (Fig. 3F).

[0281] [Example 8] Establishment of Cell Strain Stably Expressing MHC Class I Molecules, T-Cell Costimulatory Molecules, and T-Cell Stimulatory Cytokines and Preparation of Antigen-Presenting Extracellular Vesicles

PLAT-A cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with a pMX vector encoding CD80-CD9 or sc-Trimer-CD81-IL-2 using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to manufacturer's instructions. 12 hours after the transfection, the medium was replaced, and 60 hours after the transfection, a supernatant was collected and centrifuged at 300 g for 5 minutes. The collected supernatant was used as virus particles. HEK293 cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. A DOTAP transfection reagent (Roche) was added to viral particles in which the CD80-CD9 adjusted above was incorporated into the cells at about 50% confluence according to the manufacturer's instructions, and the mixture was added to HEK293 cells. The cells to which the viral particles were added were centrifuged at 2,500 rpm for 3 minutes. 24 hours after the transfection, the medium was replaced, and 1 week after the transfection, CD80-positive cells were sorted with FACSMelody (manufactured by BD Biosciences). The sorted CD80-positive cells were cultured for 1 week, and the cultured cells were seeded in a dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. A DOTAP transfection reagent was added to viral particles in which the sc-Trimer-CD81-IL-2 prepared above was incorporated into the cells at about 50% confluence according to the manufacturer's instructions, and the mixture was added to CD80-positive HEK293 cells. The cells to which the viral particles were added were centrifuged at 2,500 rpm for 3 minutes. 24

hours after the transfection, the medium was replaced, and 1 week after the transfection, CD80-positive and MHCI-positive cells were sorted with FACSMelody (manufactured by BD Biosciences). The sorted cells were used as stable expression cells. The stable expression cells were seeded in a dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. The supernatant of the cells at about 50% confluence was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed and penicillin/streptomycin were added. 72 hours after the medium replacement, supernatant was collected, and then the supernatant was centrifuged at 300 g for 5 minutes after being passed through a 0.22 µm filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After supernatant was collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant was removed, and pellets were washed with PBS. After PBS was added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 µL of PBS were used as antigen-presenting extracellular vesicles of Example 8.

[0282] Test Example 1-7: Flow Cytometry Analysis of Fusion Protein Contained in Membrane of Extracellular Vesicle

The antigen-presenting extracellular vesicles of Example 8 were immunostained by a PS Capture (trademark) exosome flow cytometry kit (manufactured by FUJIFILM Wako Pure Chemical Corporation) according to the manufacturer's instruction. Antibodies used for staining are as follows (staining time: 15 minutes, temperature: 4°C). After the staining, expression of each fusion protein was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- PE-conjugated anti-mouse H-2KbOVA complex antibody (25-D1.16, manufactured by Biolegend, Inc.)

- FITC-conjugated anti-mouse CD80 antibody (16-10A1, manufactured by Biolegend, Inc.)

- APC-conjugated anti-mouse IL-2 antibody (JES6-5H4, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 3G.

[0283] [Results]

From the results of Test Example 1-7, it could be confirmed that MHC class I molecules presenting OVA antigens, CD80, and IL-2 were contained in the membrane of the antigen-presenting extracellular vesicle of Example 8 (Fig. 3G).

[0284] [Example 9] Antigen-Presenting Extracellular Vesicles Containing HLA Class I Molecules, Human T-Cell Costimulatory Molecules, and Human T-Cell Stimulatory Cytokines in Membrane

HEK293T cells in which B2m was deleted were seeded in a cell culture dish
5 and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with the two plasmids (pCAG vectors encoding HLA_{sc}-Trimer-human CD81, human CD80-human CD9, and CD63-IL2, respectively) prepared above at the same time using polyethylenimine "Max" (manufactured by Polysciences Inc.)
10 according to the manufacturer's instructions. 3 to 12 hours after the transfection, the medium was replaced, and 24 hours after the transfection, the medium was replaced with a Dulbecco's modified Eagle medium to which 2% fetal bovine exosomes-removed serum and penicillin/streptomycin were added. 72 hours after the transfection, supernatant was collected, and then the supernatant was centrifuged at 300
15 g for 5 minutes after being passed through a 0.22 µm filter. Supernatant was collected, and the supernatant was centrifuged at 2,000 g for 20 minutes. Supernatant was collected, and the supernatant was centrifuged at 10,000 g for 30 minutes. After supernatant was collected and the supernatant was centrifuged at 100,000 g for 2 hours, the supernatant was removed, and pellets were washed with PBS. After PBS was
20 added to the pellets and the pellets were centrifuged at 100,000 g for 2 hours, supernatant was removed, and the pellets suspended in 100 µL of PBS were used as human antigen-presenting extracellular vesicles of Example 9. The concentration of the antigen-presenting extracellular vesicles was measured according to the manufacturer's instructions using a BCA protein assay kit (manufactured by Thermo
25 Fisher Scientific Inc.).

By using SARS-CoV2_{sc}-Trimer-hCD81 instead of hsc-Trimer-hCD81, it is possible to prepare human antigen-presenting extracellular vesicles presenting antigen-presenting MHC molecules presenting SARS-CoV2 peptides as antigens, hCD80, and hIL-2 on a surface thereof.

30 [0285] Test Example 1-8: Flow Cytometry Analysis of Fusion Protein Contained in Membrane of Extracellular Vesicle

The antigen-presenting extracellular vesicles of Example 9 were immunostained by a PS Capture (trademark) exosome flow cytometry kit (manufactured by FUJIFILM Wako Pure Chemical Corporation) according to the
35 manufacturer's instruction. Antibodies used for staining are as follows (staining time: 15 minutes, temperature: 4°C). After the staining, expression of each fusion protein

was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- APC-conjugated anti-human IL-2 antibody (MQ1-17H12, manufactured by Biolegend, Inc.)

- PE-conjugated anti-human CD80 antibody (2D10, manufactured by Biolegend, Inc.)

- APC-conjugated anti-human β 2m antibody (2M2, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 3H.

[0286] [Results]

From the results of Test Example 1-8, it could be confirmed that MHC class I molecules presenting WT1 antigens, hCD80, and hIL-2 were contained in the membrane of the antigen-presenting extracellular vesicle of Example 9 (Fig. 3H).

[0287] Test Example 7: Experiment on Differentiation Induction of OVA-Specific CD4-Positive T Cells (OT-2 T Cells) In Vitro into Th1 T Cells by Antigen-Presenting Extracellular Vesicles

The following test was conducted in vitro to determine whether the antigen-presenting extracellular vesicles induce differentiation of antigen-specific CD4-positive T cells into Th1 T cells.

Lymph nodes extracted from an OT-2 mouse, which was an OVA-reactive CD4TCR transgenic mouse, were disrupted on a 100 μ m filter to obtain a lymph node cell suspension. The cell suspension was stained using CellTrace Violet (manufactured by Thermo Fisher Scientific Inc.) as a cell proliferation assay reagent according to the manufacturer's instructions. 2×10^5 stained lymph node cells were suspended in 200 μ L of an RPMI1640 medium to which 10% fetal bovine serum, 50 μ M 2-mercaptoethanol, and penicillin/streptomycin were added, the antigen-presenting extracellular vesicles of Example 3 or 6 or the extracellular vesicles of Reference Example 1 were added so that the final concentration was 10 μ g/mL, and culture was performed in a 96 well round bottom plate for 4 days. After 4 days, the cells were recovered, and extracellular immunostaining was performed. Antibodies used for staining are as follows (staining time: 15 minutes, temperature: 4°C). After the extracellular staining, intracellular immunostaining was performed using True-Nuclear Transcription Factor Buffer Set (manufactured by Biolegend, Inc.) and anti-T-bet antibodies according to the manufacturer's instructions. After the intracellular staining, a luminescence intensity of CellTrace Violet as a cell proliferation assay reagent in the OT-2 T cells and expression of T-bet as a marker of Th1 T cells were detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- PerCP/Cy5.5-conjugated anti-mouse TCRVa2 antibody (B20.1, manufactured by Biolegend, Inc.)

- APC-Cy7-conjugated anti-mouse CD4 antibody (RM4-5, manufactured by Biolegend, Inc.)

- 5 • PE-conjugated anti-T-bet antibody (4B10, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 9.

[0288] [Results]

From the results of Test Example 7, it was confirmed that the antigen-presenting extracellular vesicles of Example 6 induced differentiation of antigen-specific CD4-positive T cells into Th1 cells in vitro in comparison with the extracellular vesicles of Reference Example 1 (Fig. 9). The Th1 cells produce IFN- γ , IL-2, or the like, and promote activation of macrophages and cytotoxic T cells that destroy pathogen cells, virus-infected cells, cancer cells, and the like (that is, activation of cellular immunity).

15 [0289] Test Example 8: Experiment on Differentiation Induction of OVA-Specific CD4-Positive T Cells (OT-2 T Cells) In Vitro into Th17T Cells by Antigen-Presenting Extracellular Vesicles

The following test was conducted in vitro to determine whether the antigen-presenting extracellular vesicles induce differentiation of antigen-specific CD4-positive T cells into Th17T cells.

Lymph nodes extracted from a mouse obtained by mating an OVA-reactive CD4TCR transgenic mouse and an RORrt-GFP mouse were disrupted on a 100 μ m filter to obtain a lymph node cell suspension. The cell suspension was stained using CellTrace Violet (manufactured by Thermo Fisher Scientific Inc.) as a cell proliferation assay reagent according to the manufacturer's instructions. 2×10^5 stained lymph node cells were suspended in 200 μ L of an RPMI1640 medium to which 10% fetal bovine serum, 50 μ M 2-mercaptoethanol, and penicillin/streptomycin were added, the antigen-presenting vesicles of Example 7 or the extracellular vesicles of Reference Example 1 were added so that the final concentration was 10 μ g/mL, and culture was performed in a 96 well round bottom plate for 4 days. After 4 days, the cells were recovered, and extracellular immunostaining was performed. Antibodies used for staining are as follows (staining time: 15 minutes, temperature: 4°C). After the intracellular staining, a luminescence intensity of CellTrace Violet as a cell proliferation assay reagent in the OT-2 T cells and expression of RORrt as a marker of Th17T cells were detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- APC-conjugated anti-mouse TCRVa2 antibody (B20.1, manufactured by

Biolegend, Inc.)

- PE-Cy7-conjugated anti-mouse CD4 antibody (RM4-5, manufactured by Biolegend, Inc.)

- PE-conjugated anti-mouse TCR Vb5.1,5.2 antibody (MR9-4, manufactured by Biolegend, Inc.)

The results are illustrated in Fig. 10.

[0290] [Results]

From the results of Test Example 8, it could be seen that the antigen-presenting extracellular vesicles of Example 7 induced differentiation of antigen-specific CD4-positive T cells into Th17 cells in vitro in comparison with the extracellular vesicles of Reference Example 1 (Fig. 10). Unlike the Th1 or Th2 cells, the Th17 cells produce inflammatory cytokines such as IL-17, IL-21, IL-22, and TNF- α to induce inflammation, promote recruitment and proliferation of neutrophils and monocytes, and contribute to infection defense of fungi (including pathogenic fungi such as candida, *Staphylococcus aureus*, and *Streptococcus pyogenes*).

[0291] Test Example 9: Experiment on Activation of OVA-Specific CD8-Positive T Cells (OT-1 T Cells) In Vitro by Antigen-Presenting Extracellular Vesicles Obtained by Purification of Stable Cell Strain

The following test was conducted in vitro to determine whether the antigen-presenting extracellular vesicles obtained by purification of a stable cell line activate antigen-specific CD8-positive T cells.

Lymph nodes extracted from an OT-1 mouse, which was an OVA-reactive TCR transgenic mouse, were disrupted on a 100 μ m filter to obtain a lymph node cell suspension. The cell suspension was stained using CellTrace Violet (manufactured by Thermo Fisher Scientific Inc.) as a cell proliferation assay reagent according to the manufacturer's instructions. 2×10^5 stained lymph node cells were suspended in 200 μ L of an RPMI1640 medium to which 10% fetal bovine serum, 50 μ M 2-mercaptoethanol, and penicillin/streptomycin were added, the antigen-presenting extracellular vesicles of Example 1 or 8 or the extracellular vesicles of Reference Example 1 were added so that the final concentration was 9 μ g/mL, and culture was performed in a 96 well round bottom plate for 4 days. After the culture in the 96 well round bottom plate for 3 days, immunostaining was performed. Antibodies used for staining are as follows (staining time: 15 minutes, temperature: 4°C). After the staining, a luminescence intensity of CellTrace Violet as a cell proliferation assay reagent in the OT-1 T cells was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- APC-conjugated anti-mouse CD8 antibody (53-6.7, manufactured by Biolegend, Inc.)
- PE-conjugated anti-mouse TCR Vb5.1,5.2 antibody (MR9-4, manufactured by Biolegend, Inc.)

5 The results are illustrated in Fig. 11.

[0292] [Results]

From the results of Test Example 9, it was confirmed that the antigen-presenting extracellular vesicles of Examples 1 and 8 remarkably proliferated antigen-specific CD8-positive T cells in comparison with the extracellular vesicles of Reference
10 Example 1 (Fig. 11). This indicates that not only the extracellular vesicles in which the constitutional requirement (A) exemplified by sc-Trimer-CD81 and the constitutional requirement (B) exemplified by CD81-IL-2 are present as different proteins, but also the extracellular vesicles in which a fusion protein having both functions, which is exemplified by sc-Trimer-CD81-IL-2, is present, exhibit equivalent
15 effects on T cells.

[0293] Test Example 10: Experiment for Evaluating Anti-Tumor Effect by Antigen-Presenting Extracellular Vesicles

In order to determine whether the antigen-presenting extracellular vesicles obtained by purification of a stable cell strain have an anti-tumor effect, 1×10^5 B16
20 melanoma cells expressing OVA were subcutaneously ingested in a CD45.1/CD45.2 congenic mouse, and 1×10^5 OT-1T cells were transferred after 3 days. After 1 day, 4 days, and 7 days after the OT-1T cell transfer, 50 μ g of the antigen-presenting extracellular vesicles of Example 8 or the extracellular vesicles of Reference Example 1 were transferred from the tail vein of the recipient mouse, and the size of the B16
25 melanoma cells was observed.

[0294] [Results]

From the results of Test Example 10, it was confirmed that the antigen-presenting extracellular vesicles of Example 8 remarkably suppressed proliferation of B16 melanoma cells in comparison with the extracellular vesicles of Reference
30 Example 1 (Fig. 12). This indicates that not only the extracellular vesicles in which the constitutional requirement (A) exemplified by sc-Trimer-CD81 and the constitutional requirement (B) exemplified by CD81-IL-2 are present as different proteins, but also the extracellular vesicles in which a fusion protein having both functions, which is exemplified by sc-Trimer-CD81-IL-2, is present, exhibit equivalent
35 medicinal effects.

[0295] [Example 10] Antigen-Presenting Extracellular Vesicles Containing sc-Trimer-

CD81-IL-2 Fusion Protein in Membrane

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with the plasmid (an expression vector expressing sc-Trimer-CD81-IL-2) prepared above using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to manufacturer's instructions. Antigen-presenting extracellular vesicles were prepared from the cells after the transfection by the method described above.

[0296] Reference Example 6: Antigen-Presenting Extracellular Vesicles Containing

CD63-AkaLuc Fusion Protein in Membrane

HEK293T cells were seeded in a cell culture dish and cultured in a Dulbecco's modified Eagle medium to which 2% fetal bovine serum and penicillin/streptomycin were added. Cells at about 50% confluence were transfected with the plasmid (an expression vector expressing CD63-AkaLuc) prepared above using polyethylenimine "Max" (manufactured by Polysciences Inc.) according to manufacturer's instructions. Antigen-presenting extracellular vesicles were prepared from the cells after the transfection by the method described above.

[0297] Test Example 11: Experiment on Activation of OVA-Specific CD8-Positive T Cells (OT-1 T Cells) In Vivo by Antigen-Presenting Extracellular Vesicles Containing

sc-Trimer-CD81-IL-2 Fusion Protein in Membrane

Lymph nodes extracted from an OT-1 mouse, which was an OVA-reactive TCR transgenic mouse, were disrupted on a 100 µm filter to obtain a lymph node cell suspension. Lymph nodes were similarly extracted from a CD45.1 congenic mouse, and a lymphocyte suspension was prepared. The respective lymphocyte suspensions were mixed at a ratio of 1:1, and the mixture was stained using CellTrace Violet as a cell proliferation assay reagent. 1×10^7 CellTrace Violet-stained mixed lymphocyte suspension suspended in PBS was transferred from the tail vein of the CD45.1/CD45.2 congenic mouse. The next day, 50 µg of the extracellular vesicles of Example 11 or Reference Example 6 were transferred from the tail vein to a CD45.1/CD45.2 congenic mouse. 4 days after cell transfer, the spleen was extracted from the recipient mouse, and a lymphocyte suspension was prepared and immunostained. The following antibodies were used for the staining (staining time: 15 minutes, temperature: 4°C). After the staining, a luminescence intensity of CellTrace Violet as a cell proliferation assay reagent in the transferred OT-1 T cells and wild-type CD8T cells was detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- PE-Cy7-conjugated anti-mouse CD8 antibody (53-6.7, manufactured by

Biolegend, Inc.)

- PE-conjugated anti-mouse TCR Vb5.1,5.2 antibody (MR9-4, manufactured by Biolegend, Inc.)

- FITC-conjugated anti-mouse CD45.1 antibody (A20, manufactured by Biolegend, Inc.)

- APC-conjugated anti-mouse CD45.2 antibody (104, manufactured by Biolegend, Inc.)

[0298] The extracellular vesicles of Example 10 hardly activate other CD8-positive T cells (antigen-non-specific CD8-positive T cells) and can remarkably differentiate and/or proliferate antigen-specific CD8-positive T cells in vivo in comparison with the extracellular vesicles of Reference Example 6.

[0299] Test Example 12: Experiment on Activation of Intrinsic OVA-Reactive T Cells by Extracellular Vesicles Expressing sc-Trimer-CD81-IL-2 Fusion Protein

50 µg of the extracellular vesicles of Example 10 or Reference Example 6 were transferred from a tail vein of a C57BL/6 mouse. 4 days after transfer, the spleen was extracted from the recipient mouse, a lymphocyte suspension was prepared, and OVA-reactive T cells were immunostained with a tetramer according to the manufacturer's instructions. The following antibodies were used for the staining. After the staining, tetramer-positive cells were detected with a flow cytometer FACSCantoII (manufactured by BD Biosciences).

- APC-conjugated H-2Kb OVA Tetramer (Tetramer Shop ApS)
- PE-conjugated H-2Kb OVA Tetramer (Tetramer Shop ApS)
- Brilliant Violet421-conjugated anti-mouse CD8 antibody (53-6.7, manufactured by Biolegend, Inc.)

[0300] The extracellular vesicles of Example 10 can proliferate OVA-reactive CD8T cells that are remarkably intrinsically present, in comparison with the extracellular vesicles of Reference Example 6.

[0301] Hereinabove, as described in the examples, the antigen-presenting extracellular vesicles and polynucleotides described in the present specification can satisfactorily activate, proliferate, and/or differentiate antigen-specific T cells (for example, antigen-specific CD8-positive T cells, antigen-specific CD4-positive cells, and the like).

[0302] Hereinafter, a summary of the sequences included in the sequence listing will be described.

[0303] [Table 15]

	SEQ ID NO:	
	Amino acid sequence	Polynucleotide
Signal peptide of β_2 microglobulin	1	2
β_2 Microglobulin (from which signal peptide is removed)	7	8
MHC class I α chain (from which signal peptide is removed)	9	10
Signal peptide of MHC class I I β chain	33	34
MHC class I I β chain (from which signal peptide is removed)	37	38
MHC class I I α chain (full length)	45	46
MHC class I I α chain (from which signal peptide is removed)	71	72

[0304] [Table 16]

	SEQ ID NO:	
	Amino acid sequence	Polynucleotide
O V A PEPTIDE 1 (for MHC class I molecule)	3	4
O V A PEPTIDE 2 (for MHC class I I molecule)	35	36

[0305] [Table 17]

	SEQ ID NO:	
	Amino acid sequence	Polynucleotide
CD 9 (full length)	2 1	2 2
CD 6 3 (full length)	2 7	2 8
CD 6 3 (partial sequence containing TM 1 to TM 3)	5 7	5 8
CD 6 3 (partial sequence containing TM 4)	5 9	6 0
CD 8 1 (full length)	1 5	1 6
CD 8 1 (partial sequence containing TM 1 to TM 3)	6 1	6 2
CD 8 1 (partial sequence containing TM 4)	6 3	6 4
MFG - E 8 (from which signal peptide is removed)	4 9	5 0

[0306] [Table 18]

	SEQ ID NO:	
	Amino acid sequence	Polynucleotide
IL - 2 (from which signal peptide is removed)	2 5	2 6
IL - 4 (from which signal peptide is removed)	5 3	5 4
TGF - β 1 (full length)	4 7	4 8
TGF - β 1 (from which signal peptide is removed)	7 3	7 4

[0307] [Table 19]

	SEQ ID NO:	
	Amino acid sequence	Polynucleotide
CD 8 0 (full length)	1 9	2 0
CD 8 0 (from which signal peptide is removed)	6 7	6 8

5

[0308] [Table 20]

	SEQ ID NO:	
	Amino acid sequence	Polynucleotide
Peptide linker 1	5	6
Peptide linker 2	1 1	1 2
Peptide linker 3	2 9	3 0
Peptide linker 4	3 9	4 0
Peptide linker 5	7 7	7 8

[0309] [Table 21]

	SEQ ID NO:	
	Amino acid sequence	Polynucleotide
Single chain MHC class I molecule (β_2 microglobulin + MHC class I α chain)	6 5	6 6
s c - T r i m e r (OVA peptide 1 + single chain MHC class I molecule)	1 3	1 4
s c - T r i m e r + C D 8 1 (full length)	1 7	1 8
s c - D i m e r (OVA peptide 2 + MHC class I I β chain)	4 1	4 2
s c - D i m e r + C D 8 1 (full length)	4 3	4 4
C D 6 3 - I L - 2	3 1	3 2
C D 8 1 - I L - 4	5 5	5 6
T G F - β 1 (full length) + M G F - E 8 (from which signal peptide is removed)	5 1	5 2
T G F - β 1 (from which signal peptide is removed) + M G F - E 8 (from which signal peptide is removed)	7 5	7 6
C D 8 0 (full length) + C D 9 (full length)	2 3	2 4
C D 8 0 (from which signal peptide is removed) + C D 9 (full length)	6 9	7 0

[0310] [Table 22]

	SEQ ID NO:	
	Amino acid sequence	Polynucleotide
P N E tag	7 9	8 0
Anti-P N E tag nanobody (full length)	8 1	8 2
Anti-P N E tag nanobody (from which signal peptide is removed)	8 3	8 4
C D 8 a	8 5	8 6
Anti-P N E tag nanobody (full length) + C D 8 a + C D 8 1 (full length)	8 7	8 8
Anti-P N E tag nanobody (from which signal peptide is removed) + C D 8 a + C D 8 1 (full length)	8 9	9 0

[0311]

[Table 23-1]

	SEQ ID NO:	
	Amino acid sequence	Polynucleotide
s c - D i m e r - C D 8 1 - I L - 1 2 α	91	92
I L - 1 2 α (from which signal peptide is removed)	93	94
C D 8 1 - I L - 1 2 α	95	96
I L - 1 2 β	97	98
I L - 6 (from which signal peptide is removed)	99	100
C D 8 1 - I L - 6	101	102
h C D 8 0	103	104
h C D 9	105	106
h C D 8 0 - h C D 9	107	108
h I L - 2 (from which signal peptide is removed)	109	110
h C D 6 3 (amino acids 1 to 170)	111	112
h C D 6 3 (amino acids 171 to 238)	113	114
h C D 6 3 - I L - 2	115	116
Signal peptide of h β 2 microglobulin	117	118
W T 1 P E P T I D E 1 (for M H C class I molecule)	119	120
h β 2 Microglobulin (from which signal peptide is removed)	121	122
h M H C class I α chain (from which signal peptide is removed)	123	124
h single chain M H C class I molecule (β 2 microglobulin (from which signal peptide is removed) + peptide linker 2 + M H C class I α chain (from which signal peptide is removed))	125	126
h s c - T r i m e r (W T 1 peptide 1 + peptide linker 1 + single chain M H C class I molecule)	127	128

[Table 23-2]

hCD81	129	130
hsc-Trimer-CD81 (sc-Trimer+CD81)	131	132
CD81-IL-2	133	134
sc-Trimer-CD81-IL-2 (sc-Trimer+CD81)	135	136
Aka-Luc	137	138
CD63-Aka-Luc	139	140
SARS-CoV2 peptide 1	141	142
hMHC class I (HLA-A0201) α chain (from which signal peptide is removed)	143	144
h single chain MHC class I molecule (β 2 microglobulin (from which signal peptide is removed) + peptide linker 2 + MHC class I (HLA-A0201) α chain (from which signal peptide is removed))	145	146
hsc-Trimer (SARS-CoV2 peptide 1 + peptide linker 1 + single chain MHC class I (HLA-A0201) molecule)	147	148
hsc-Trimer-CD81 (SARS-CoV2sc-Trimer+CD81)	149	150

CLAIMS

1. An antigen-presenting extracellular vesicle presenting an antigen-presenting MHC molecule and a T-cell stimulatory cytokine outside membrane.
- 5 2. The antigen-presenting extracellular vesicle according to claim 1, the membrane of which contains:
 - (A) a protein which contains the antigen-presenting MHC molecule and is capable of presenting the antigen outside membrane; and
 - (B) a protein which contains a first T-cell stimulatory cytokine or a subunit
 - 10 thereof and is capable of presenting the first T-cell stimulatory cytokine outside membrane.
3. The antigen-presenting extracellular vesicle according to claim 2, the membrane of which contains:
 - (A) a fusion protein or a protein complex which contains an antigen-presenting
 - 15 MHC molecule, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof, and is capable of presenting the antigen outside membrane; and
 - (B) a fusion protein which comprises a first T-cell stimulatory cytokine or a
 - 20 subunit thereof, and membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof, and is capable of presenting the first T-cell stimulatory cytokine outside membrane.
4. The antigen-presenting extracellular vesicle according to claim 2, the
- 25 membrane of which contains:
 - (A) a fusion protein or a protein complex which comprises an antigen-presenting MHC molecule and a tetraspanin or a transmembrane domain thereof or MFG-E8 or a domain thereof, and is capable of presenting the antigen outside
 - 30 membrane; and
 - (B) a fusion protein which comprises a first T-cell stimulatory cytokine or a subunit thereof and a partial sequence of a tetraspanin, and is capable of presenting the first T-cell stimulatory cytokine outside membrane, wherein the partial sequence of the tetraspanin contains at least two transmembrane domains, and the first T-cell
 - stimulatory cytokine is disposed between the two transmembrane domains, or
 - 35 (B) a fusion protein which comprises a first T-cell stimulatory cytokine or a subunit thereof and MFG-E8 or a domain thereof, and is capable of presenting the first

T-cell stimulatory cytokine outside membrane.

5. The antigen-presenting extracellular vesicle according to claim 2, the membrane of which contains:

(A) a fusion protein capable of presenting an antigen peptide outside
5 membrane, in which the fusion protein comprises an amino acid sequence consisting of, from an N-terminal side,

(A) a protein complex capable of presenting an antigen peptide outside
membrane, wherein the protein complex contains,

10 a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

(A-1) an MHC molecule-restricted antigen peptide,

(A-2) a spacer sequence which may be optionally present,

(A-3) an MHC class I α chain, β_2 microglobulin, an MHC class II α chain, or
an MHC class II β chain,

15 (A-4) a spacer sequence which may be optionally present, and

(A-5) a tetraspanin,

and

(A-6) a protein comprising an amino acid sequence of β_2 microglobulin, an
MHC class I α chain, an MHC class II β chain, or an MHC class II α chain; and

20 (B) a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

(B-1) a partial sequence of a tetraspanin containing, from an N-terminal side,
a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a
small intracellular loop, and a transmembrane domain 3,

25 (B-2) a spacer sequence which may be optionally present,

(B-3) a first T-cell stimulatory cytokine or a subunit thereof,

(B-4) a spacer sequence which may be optionally present, and

(B-5) a partial sequence of a tetraspanin containing a transmembrane domain
4,

30 the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane, or

(B) a fusion protein comprising an amino acid sequence consisting of, from an
N-terminal side thereof,

(B-3) a first T-cell stimulatory cytokine or a subunit thereof,

35 (B-4) a spacer sequence which may be optionally present, and

(B-5) MFG-E8,

the fusion protein being capable of presenting the first T-cell stimulatory cytokine outside membrane.

6. The antigen-presenting extracellular vesicle according to claim 5, the membrane of which contains:

5 (A) a fusion protein capable of presenting an antigen peptide outside membrane, in which the fusion protein comprises an amino acid sequence consisting of, from an N-terminal side thereof,

(A-1) an MHC class I molecule-restricted antigen peptide,

(A-2) a spacer sequence which may be optionally present,

10 (A-3) a single chain MHC class I molecule,

(A-4) a spacer sequence which may be optionally present, and

(A-5) a tetraspanin.

7. The antigen-presenting extracellular vesicle according to claim 5, the membrane of which contains,

15 (A) a protein complex capable of presenting an antigen peptide outside membrane, in which the protein complex contains:

a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

(A-1) an MHC class II molecule-restricted antigen peptide,

20 (A-2) a spacer sequence which may be optionally present,

(A-3) an MHC class II β chain,

(A-4) a spacer sequence which may be optionally present, and

(A-5) a tetraspanin; and

25 (A-6) a protein comprising an amino acid sequence of an MHC class II α chain.

8. The antigen-presenting extracellular vesicle according to any one of claims 1 to 7, wherein the T-cell stimulatory cytokine is IL-2, IL-4, IL-6, IL-12, or TGF- β , or a subunit thereof.

9. The antigen-presenting extracellular vesicle according to any one of claims 1 to 30 8, the membrane of which contains,

(C) a protein which contains a T-cell costimulatory molecule and is capable of allowing the T-cell costimulatory molecule to interact with T cells.

10. The antigen-presenting extracellular vesicle according to any one of claims 1 to 9, the membrane of which contains,

35 (C) a fusion protein which contains a T-cell costimulatory molecule, and a membrane protein capable of being expressed in membrane of an extracellular vesicle

or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof, and is capable of allowing the T-cell costimulatory molecule to interact with T cells.

11. The antigen-presenting extracellular vesicle according to any one of claims 1 to 5 9, the membrane of which contains,

(C) a fusion protein which contains a T-cell costimulatory molecule, and a tetraspanin or a transmembrane domain thereof or MFG-E8 or a domain thereof, and is capable of allowing the T-cell costimulatory molecule to interact with T cells.

12. The antigen-presenting extracellular vesicle according to any one of claims 1 to 10 9, the membrane of which contains,

(C) a fusion protein comprising an amino acid sequence consisting of, from an N-terminal side thereof,

(C-1) a T-cell costimulatory molecule,

(C-2) a spacer sequence which may be optionally present, and

15 (C-3) a tetraspanin,

the fusion protein being capable of allowing the T-cell costimulatory molecule to interact with T cells.

13. The antigen-presenting extracellular vesicle according to any one of claims 2 to 8, wherein the protein or the protein complex defined in (A) and the protein or the 20 protein complex defined in (B) are fused to each other.

14. The antigen-presenting extracellular vesicle according to any one of claims 9 to 12, wherein the protein or the protein complex defined in (A) and the protein or the protein complex defined in (C) are fused to each other.

15. The antigen-presenting extracellular vesicle according to any one of claims 9 to 25 12, wherein the protein or the protein complex defined in (B) and the protein or the protein complex defined in (C) are fused to each other.

16. The antigen-presenting extracellular vesicle according to any one of claims 9 to 12, wherein the protein or the protein complex defined in (A), the protein or the protein complex defined in (B), and the protein or the protein complex defined in (C) are fused 30 to each other.

17. The antigen-presenting extracellular vesicle according to claim 1, the membrane of which contains,

(D) a fusion protein which contains the antigen-presenting MHC molecule, and at least one of the T-cell stimulatory cytokines or subunits thereof, and is capable of 35 presenting the antigen and the T-cell stimulatory cytokine outside membrane.

18. The antigen-presenting extracellular vesicle according to claim 17, wherein the

fusion protein contains the antigen-presenting MHC molecule, the at least one T-cell stimulatory cytokine or subunit thereof, and a membrane protein capable of being localized to membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a membrane-binding domain thereof.

19. The antigen-presenting extracellular vesicle according to claim 18, wherein the membrane protein capable of being localized to membrane of an extracellular vesicle or the protein capable of binding to membrane of an extracellular vesicle is a tetraspanin or MFG-E8.

20. The antigen-presenting extracellular vesicle according to claim 19, wherein the fusion protein contains an amino acid sequence encoding, from an N-terminal side thereof,

(D-1) an MHC molecule-restricted antigen peptide,

(D-2) a spacer sequence which may be optionally present,

(D-3) a single chain MHC molecule,

(D-4) a spacer sequence which may be optionally present, and

(D-5) a fusion peptide comprising a tetraspanin or a transmembrane domain thereof or MFG-E8 or a transmembrane domain thereof, and the at least one T-cell stimulatory cytokine or subunit thereof, in this order.

21. The antigen-presenting extracellular vesicle according to claim 19, wherein the fusion protein comprises an amino acid sequence encoding, from an N-terminal side,

(D-1) a fusion peptide comprising a tetraspanin or a transmembrane domain thereof or MFG-E8 or a transmembrane domain thereof, and the at least one T-cell stimulatory cytokine or subunit thereof,

(D-2) a spacer sequence which may be optionally present,

(D-3) a single chain MHC molecule,

(D-4) a spacer sequence which may be optionally present, and

(D-5) an MHC molecule-restricted antigen peptide, in this order.

22. The antigen-presenting extracellular vesicle according to claim 20 or 21, wherein the fusion peptide comprises an amino acid sequence encoding, from an N-terminal side thereof,

(1) a partial sequence of a tetraspanin containing a transmembrane domain 1, a small extracellular loop, a transmembrane domain 2, a small intracellular loop, and a transmembrane domain 3,

(2) a spacer sequence which may be optionally present,

(3) the at least one T-cell stimulatory cytokine or subunit thereof,

(4) a spacer sequence which may be optionally present, and

(5) a partial sequence of a tetraspanin containing a transmembrane domain 4, in this order.

23. The antigen-presenting extracellular vesicle according to claim 20 or 21,
5 wherein the fusion peptide comprises an amino acid sequence encoding, from an N-terminal side thereof,

(1) the at least one T-cell stimulatory cytokine or subunit thereof,

(2) a spacer sequence which may be optionally present, and

(3) MFG-E8, in this order.

10 24. The antigen-presenting extracellular vesicle according to claim 20 or 21,
wherein the MHC molecule-restricted antigen peptide is an MHC class I molecule-restricted antigen peptide, and the single chain MHC molecule contains an extracellular domain of an MHC class I α chain.

25. The antigen-presenting extracellular vesicle according to claim 20 or 21,
15 wherein the MHC molecule-restricted antigen peptide is an MHC class II molecule-restricted antigen peptide, and the single chain MHC molecule contains an extracellular domain of an MHC class II α chain and/or an extracellular domain of an MHC class II β chain.

26. The antigen-presenting extracellular vesicle according to any one of claims 17
20 to 25, wherein the antigen-presenting extracellular vesicle further contains, in the membrane thereof, (C) a protein which contains at least one T-cell costimulatory molecule and is capable of allowing the T-cell costimulatory molecule to interact with T cells.

27. The antigen-presenting extracellular vesicle according to claim 26, wherein the
25 protein capable of interacting with T cells contains the at least one T-cell costimulatory molecule, and a membrane protein capable of being expressed in membrane of an extracellular vesicle or a transmembrane domain thereof or a protein capable of binding to membrane of an extracellular vesicle or a domain thereof.

28. The antigen-presenting extracellular vesicle according to claim 26, wherein the
30 protein capable of interacting with T cells contains the at least one T-cell costimulatory molecule, and a tetraspanin or a transmembrane domain thereof or MFG-E8 or a domain thereof.

29. The antigen-presenting extracellular vesicle according to claim 26, wherein the
protein capable of interacting with T cells comprises,

35 (C) an amino acid sequence encoding, from an N-terminal side,

(C-1) the at least one T-cell costimulatory molecule,

(C-2) a spacer sequence which may be optionally present, and

(C-3) a tetraspanin, in this order.

30. The antigen-presenting extracellular vesicle according to any one of claims 26 to 29, wherein the fusion protein (D) is fused to the protein (C) capable of interacting with T cells.

31. The antigen-presenting extracellular vesicle according to any one of claims 1 to 30, wherein the extracellular vesicle is an exosome.

32. Polynucleotide encoding any one of:

(i) the fusion protein or the protein complex of (A) defined in any one of claims 3 to 7;

(ii) the fusion protein of (B) defined in any one of claims 3 to 5;

(iii) the fusion protein of (C) defined in any one of claims 10 to 12; and

(iv) the fusion protein of (D) defined in any one of claims 18 to 25.

33. A vector comprising at least one polynucleotide selected from the polynucleotides according to claim 32.

34. A cell transformed with a single vector or a combination of two or more vectors, the vector comprising:

(i) a polynucleotide encoding the fusion protein or the protein complex of (A) defined in any one of claims 2 to 6;

(ii) a polynucleotide encoding the fusion protein of (B) defined in any one of claims 2 to 4; and optionally,

(iii) a polynucleotide encoding the fusion protein of (C) defined in any one of claims 9 to 11.

35. A cell transformed with a single vector or a combination of two or more vectors, the vector comprising:

(iv) a polynucleotide encoding the fusion protein of (D) defined in any one of claims 18 to 25; and optionally,

(iii) a polynucleotide encoding the fusion protein of (C) defined in any one of claims 10 to 12.

36. A culture supernatant obtained by culturing the cell according to claim 34 or 35.

37. An antigen-presenting extracellular vesicle obtained from the culture supernatant according to claim 36.

38. A method for preparing the antigen-presenting extracellular vesicle according to any one of claims 1 to 12, the method comprising a step of collecting a culture supernatant obtained by culturing the cell according to claim 15.

39. A pharmaceutical composition comprising the antigen-presenting extracellular vesicle according to any one of claims 1 to 31 and 37 or the culture supernatant according to claim 36.

5 40. A pharmaceutical composition for treating or preventing an infectious disease comprising the antigen-presenting extracellular vesicle according to any one of claims 1 to 31 and 37 or the culture supernatant according to claim 36.

41. A pharmaceutical composition for treating or preventing cancer comprising the antigen-presenting extracellular vesicle according to any one of claims 1 to 31 and 37 or the culture supernatant according to claim 36.

10 42. The pharmaceutical composition according to claim 41, further comprising an immune checkpoint inhibitor.

43. The pharmaceutical composition according to claim 42, wherein the immune checkpoint inhibitor is present on the membrane of the antigen-presenting extracellular vesicle.

15 44. The pharmaceutical composition according to claim 42 or 43, wherein the immune checkpoint inhibitor is selected from the group consisting of an anti-PD-1 antibody or an active fragment thereof, an anti-CTLA-4 antibody or an active fragment thereof, and a PD-L1 antibody or an active fragment thereof.

20 45. A pharmaceutical composition for treating or preventing an autoimmune disease comprising the antigen-presenting extracellular vesicle according to any one of claims 1 to 31 and 37 or the culture supernatant according to claim 36.

46. A pharmaceutical composition for treating or preventing an allergic disease comprising the antigen-presenting extracellular vesicle according to any one of claims 1 to 31 and 37 or the culture supernatant according to claim 36.

25 47. A method for activating and/or proliferating T cells against a specific antigen, the method comprising contacting the antigen-presenting extracellular vesicle according to any one of claims 1 to 31 and 37 with T cells in vitro or ex vivo.

Fig. 1A

MODEL DIAGRAM OF sc-Trimer-CD81 FUSION PROTEIN

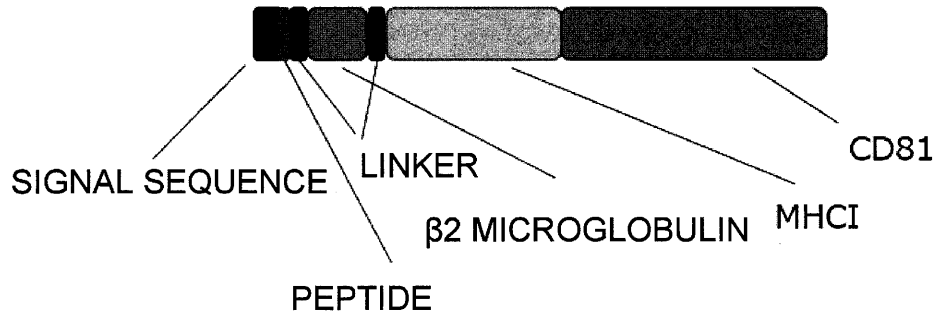


Fig. 1B

AMINO ACID SEQUENCE OF sc-Trimer-CD81 FUSION PROTEIN

MARSVTLVFLVLVSLTGLYASIINFELKGGGASGGGGSGGGGSIQKTPQIQVYSRHPPENGKPNILNCYVTQFHP
 PHIEIQMLKNGKKIPKVMSDMSFSKDWSFYILAHTFTPTETDTYACRVKHASMAEPKTVYWDRDMGGGGG
 GGGGSGGGGSGGGGSGPHSLRYFVTAVSRPGLGEPRYMEVGYYDDTEFVRFDSDAENPRYEPRARWMEQEG
 PEYWERETQKAKGNEQSFRVDLRTLGGYNNQSKGGSHTIQVISGCEVGSDGRLLRGYQQYAYDGCYIALNED
 LKTWTAADMAALITKHKWEQAGEAERLRLAYLEGTCVEWLRRLKNGNATLLRTDSPKAHVTHHSRPEDKVT
 RCWALGFYPADITLTWQLNGEELIQDMELVETRPAGDGTQKWASVVVPLGKEQYYTCHVYHQGLPEPLTLR
 WEPPPSTVSNMATVAVLVVLGAAIVTGAVVAFVMKMRRRNTGGKGGDYALAPGSQTSDLSPDCKVMVHDPH
 SLAMGVEGCTKCIKYLFFVNFVFWLAGGVILGVALWLRHDPQTSLLYLELGKNKPAPNTFYVGIYILIAVGAVM
 MFVGFGLGCYGAIQESQCLLTGTTFTCLVILFACEVAAGIWGFVNKDQIAKDVKQFYDQALQQAVMDDANNAKA
 VVKTFHETLNCCGSNALTTLTTILRNSLCPSGGNILTPLLQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEMIL
 SMVLCCGIRNSSVY

Fig. 1C

MODEL DIAGRAM OF CD80-CD9 FUSION PROTEIN

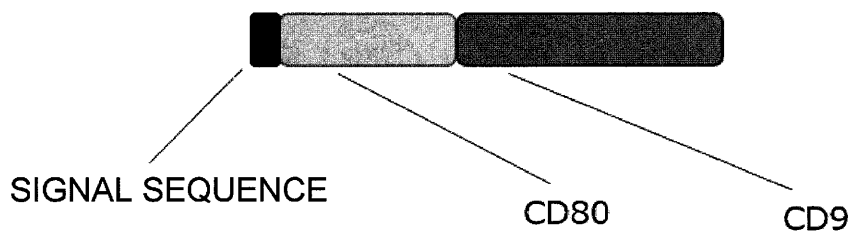


Fig. 1D

AMINO ACID SEQUENCE OF CD80-CD9 FUSION PROTEIN

MACNCQLMQDTPLLKFPCPRLILLFVLLIRLSQVSSDVDEQLSKSVKDKVLLPCRYNSPHEDESEDRIYWQKHDK
 VVLSVIAGKLKVVWPEYKNRTLYDNTTYSLLILGLVLSDRGTYSVQKKERGTYEVKHLALVKLSIKADFSTPNITE
 SGNPSADTKRITCFASGGFPKPRFSWLENGRELPGINTTISQDPESELYTISSQLDFNTTRNHTIKCLIKYGDHVS
 EDFTWEKPPEDPPDSKNTLVLFAGAGFVITVVVIVVVIKCFCKHRSCFRRNEASRETNNSLTFGPEEALAEQTVFL
 MPVKGGSKCIKYLFGFNFIWLAGIAVLAIGLWLRFDSTKTSIFEQENNHSSFYTGYYILIGALMMLVGFLGCC
 GAVQESQCMLGLFFGFLLVIFAIEIAAAVWGYYTHKDEVIKELQEFYKDTYQKLRSKDEPQRETLLKATHMALDCCGI
 AGPLEQFISDTCPPKQLLESFQVKPCPEAISEVFNNKFHII GAVGIGIAVVMIFGMIFSMILCCAIRRSREMV

Fig. 1E

MODEL DIAGRAM OF CD63-IL-2 FUSION PROTEIN

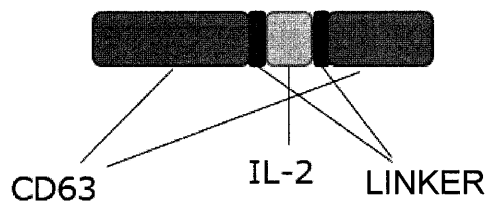


Fig. 1F

AMINO ACID SEQUENCE OF CD63-IL-2 FUSION PROTEIN

MAVEGGMKCVKFLLYVLLLAFCACAVGLIAIGVAVQVVLKQAITHETTAGSLLPVVIIAVGAFLFLVAFVGGCGAC
 KENYCLMITFAIFLSLIMLVEVAIAIAGYVFRDQVKSEFNKSFQQQMQLKDNKTATILDKLQKENNCCGASN
 YTDWENIPGMAKDRVPDSCCGGGGSAPTSSSTSSSTAEAAQQQQQQQQQQHLEQLLMDLQELLSRMENY
 RNLKLPRMLTFKFYLPKQATELKDLCLEDELGPLRHVLDLTQSKSFQLEDAENFISNIRVTVVKLGSDNTFEC
 QFDDSATVVDLRRWIAFCQSIISTSPQGGGGSINTVGCNDKFESTIHTQGCVETIAIWLKKNILLVAAAAL
 GIAFVEVLGIIFSCCLVKISIRSGYEV

Fig. 1G

MODEL DIAGRAM OF sc-Dimer-CD81 FUSION PROTEIN

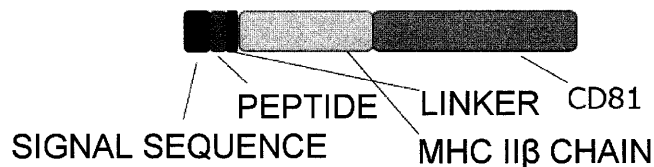


Fig. 1H

AMINO ACID SEQUENCE OF sc-Dimer-CD81 FUSION PROTEIN

MALQIPSLLLSAVVLMVLSSPGTEGISQAVHAAHAEINEAGRGSGGGSGGGSDSERHFVYQFMGECYFTNGTQIRIRYVTRYIY
 NREEYVRYDSVDGEHRAVTELGRPDAEYWNSQPEILERTRAELDTVCRHNYEGPETHSLRRLEQPNVVISLSRTEALNHHTLVCSV
 TDFYPAKIKVRWFRNGQEETVGSSTQLIRNGDWTQVLVLMLEMTPRRGEVYTCHVEHPSLKSPITVEWRAQSESASWSKMLSGIGG
 CVLGVIFLGLGFIRHRSQKGRGPPAGLLQMGVEGCTKCIKYLFFVFNFWLAGGVILGVALWLRHDPQTTSLLYLELGNKPAPNTF
 YVGIYILIAVGAVMMFVGLGCGYAIQESQCLLGTFFTCVLVFACEVAAGIWFVFNKQIAKDVKQFYDQALQQAVMDDDANNAKAV
 VKTFHETLNCCGSNALTTLTTLIRNSLCPSSGNILTPLLQQDCHQKIDELFSGKLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY

Fig. 1I

AMINO ACID SEQUENCE OF MHC CLASS II α CHAIN

MPRSRALILGVLAALTMLSLCGGEDDIEADHVGTYGISVYQSPGDIGQYTFEFDGDELFFVDLDKKETVWMLPEFGQLASFDPQGGLO
 NIAVVKHNLGLVTKRSNSTPATNEAPQATVFPKSPVLLGQPNLTLCFVDNIFPPVINITWLRNSKSVADGVYETSFFVNRDYSFHKLSYL
 TFIPTDDDIYDCKVEHWGLEEPVLKHWEPEIPAPMSELTETVVCALGLSVGLVGIWGTIFIIQGLRSGGTSRHPGPL

Fig. 1J

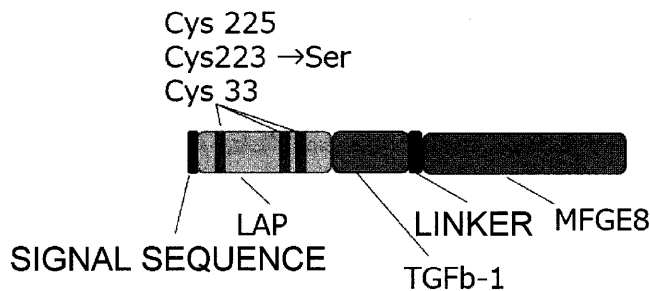
MODEL DIAGRAM OF TGF- β -MFG-E8 FUSION PROTEIN

Fig. 1K

AMINO ACID SEQUENCE OF TGF- β -MFG-E8 FUSION PROTEIN

MPPSGRLRLPLLLPLPWLLVLTGPRPAAGLSTSKTIDMELVKKRKRIEAIKQILSKLRLASPPSQGEVPPGGLPEAVL
 ALYNSTRDRVAGESADPEPEPEADYYAKEVTRVLMVDRNNAIYEKTKDISHSIYMFNTSDIREAVPEPPLLSRAE
 LRLQRLKSSVEQHVELYQKYSNNSWRYLGNRLTPTDTPWLSFDVTGVVRQWLNQGDGIQGRFSAHSSSDS
 KDNKLHVEINGISPKRRGDLGTIHDNMRPFLMATPLERAQHLSRRHRRALDTNYCFSSTEKNCCVRQLYIDF
 RKDLGWKWIHEPKGYHANFCLGPCPYIWSLDTQYSKVLALYNQHNPASASPCCVPQALEPLPIVYVGRKPKV
 EQLSNMIVRSCKCSGGGGSASGDFCDSSLCLNGGTCLTGQDNDIYCLCEGFTGLVCNETERGPCSPNCPYNDA
 KCLVTLDTQRGEIFTEYICQCPVGYSGIHCEETETNYNLDGEYMFETAVPNTAVPTPAPTDLNNSNLASRCSTQLG
 MEGGAIADSQISASSVYMGFMGLQRWGPALARLYRTGIVNAWTASNYDSKPWIQVNLRLKMRVSGVMTQGAS
 RAGRAEYLKTFKVAYSLDGRKFEFIQDESGGDKFLGNLDNNSLKVNMFNPTLEAQYIKLYPVSCHRGCTLRFL
 LGCELHGCSEPLGLKNNTIPDSQMSASSYKTNWNLRAFGWYPHLGRLDNQKINAWTAQNSAKEWLQVDLG
 TQRQVTGIITQGARDFGHIQYVASYKVAHSDDGWQVTVYEEQGSSKVFQGNLDNNSHKKNIKEKPFMARYVRV
 LPVSWHNRLRLLELLGC

Fig. 1L

MODEL DIAGRAM OF CD81-IL-4 FUSION PROTEIN

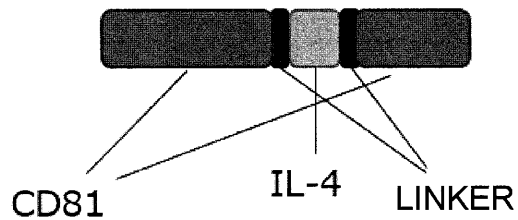


Fig. 1M

AMINO ACID SEQUENCE OF CD81-IL-4 FUSION PROTEIN

MGVEGCTKCIKYLFFVFNFWLGGVILGVALWLRHDPQTTSLLYLELGNKPA PNTFYVGIYILIAV
 GAVMMFVGFLGCGYGAIQESQCLLGTFFTCLVILFACEVAAGIWGFVNKDQIAKDVKQFYDQALQQA
 VMDDDANNAKAVVKTFFHETLNCCGSNALTTLTTTILRNSLCPSGGGGSHIHGCDKNHLREIIGILNE
 VTGEGTPCTEMDVPNVLTATKNTTESELVCRASKVLRIFYLKHGKTPCLKKNSSVLMELQRLFRAFR
 CLDSSISCTMNESKSTSLKDFLESLSIMQMDYSGGGGSGGNILTPLLQQDCHQKIDELFSGKLYLI
 GIAAIVVAVIMIFEMILSMVLCCGIRNSSVY

Fig. 2A

MODEL DIAGRAM OF ANTIGEN-PRESENTING EXTRACELLULAR VESICLE OF EXAMPLE 1

ANTIGEN

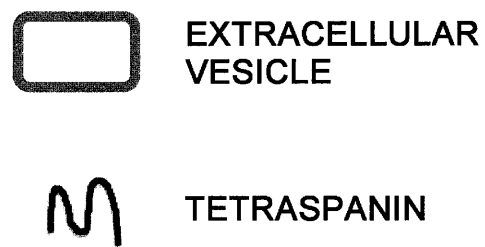
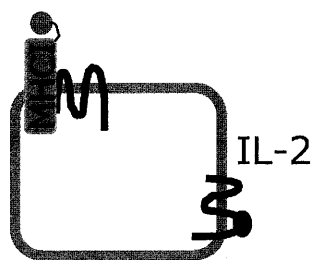


Fig. 2B

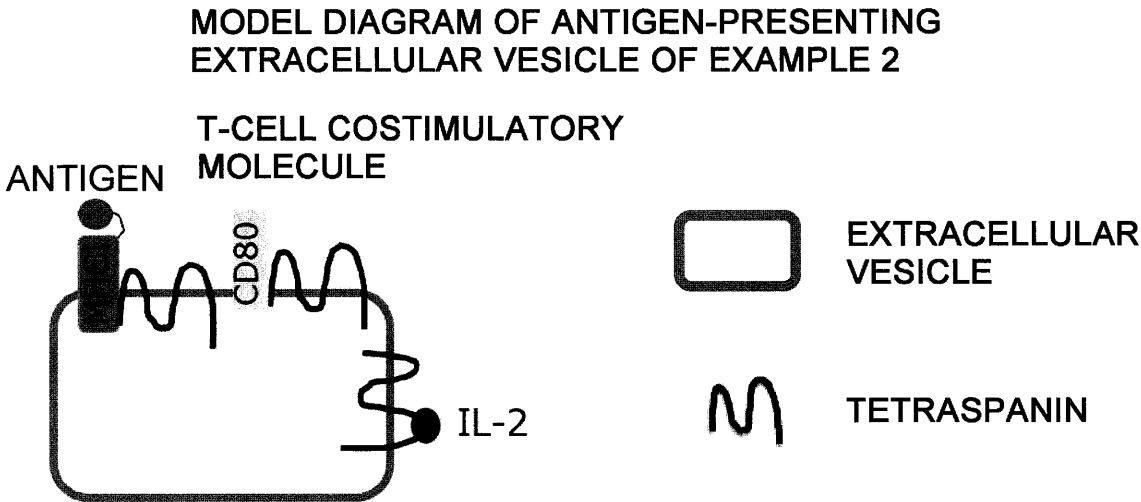


Fig. 2C

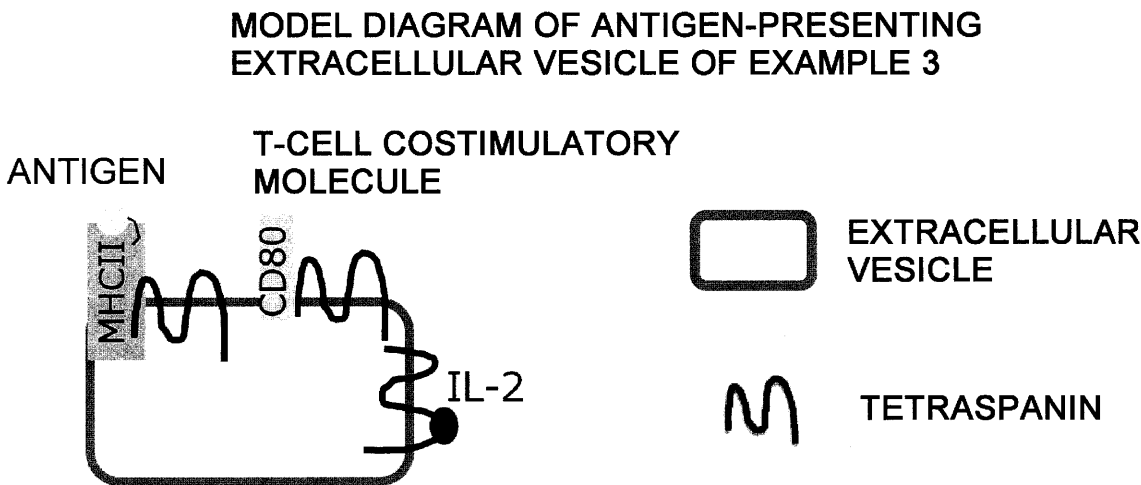


Fig. 2D

**MODEL DIAGRAM OF ANTIGEN-PRESENTING
EXTRACELLULAR VESICLE OF EXAMPLE 4**

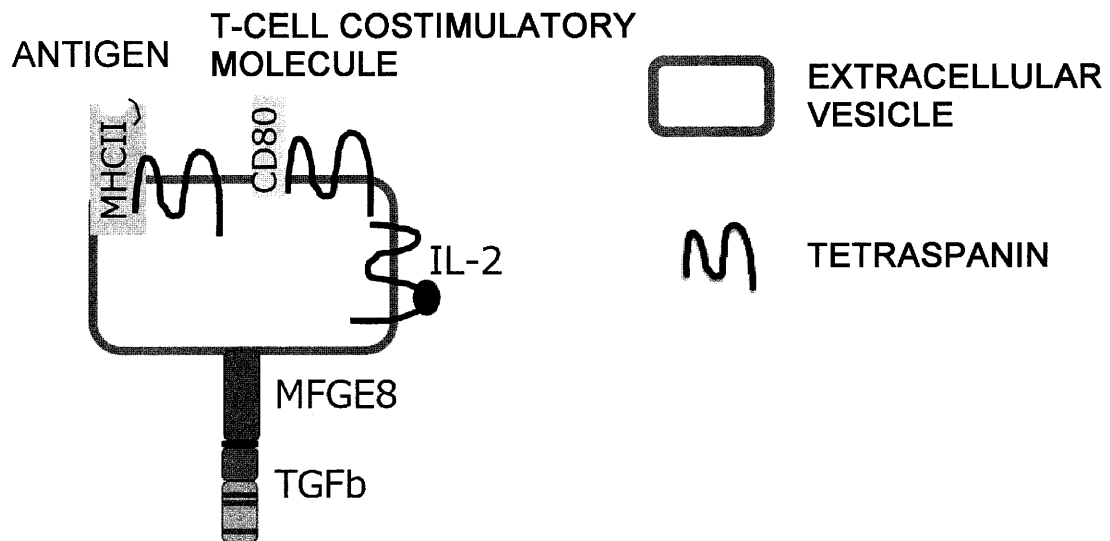


Fig. 2E

**MODEL DIAGRAM OF ANTIGEN-PRESENTING
EXTRACELLULAR VESICLE OF EXAMPLE 5**

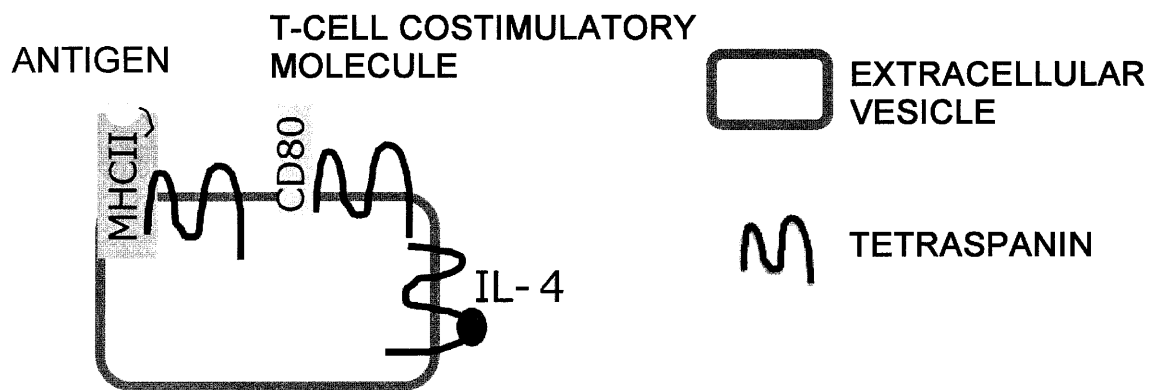


Fig. 2F

MODEL DIAGRAM OF ANTIGEN-PRESENTING
EXTRACELLULAR VESICLE OF EXAMPLE 6

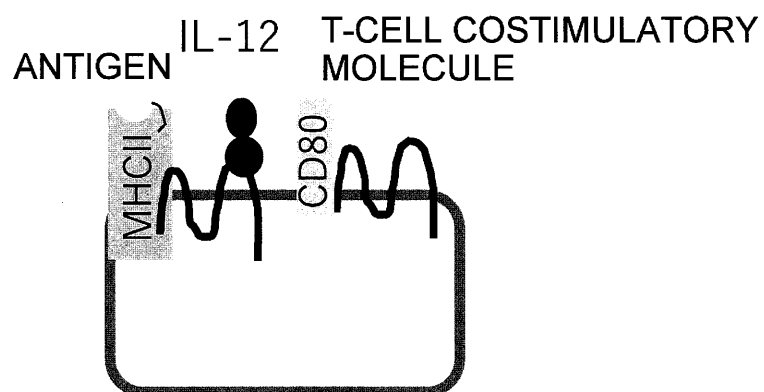


Fig. 2G

MODEL DIAGRAM OF ANTIGEN-PRESENTING
EXTRACELLULAR VESICLE OF EXAMPLE 7

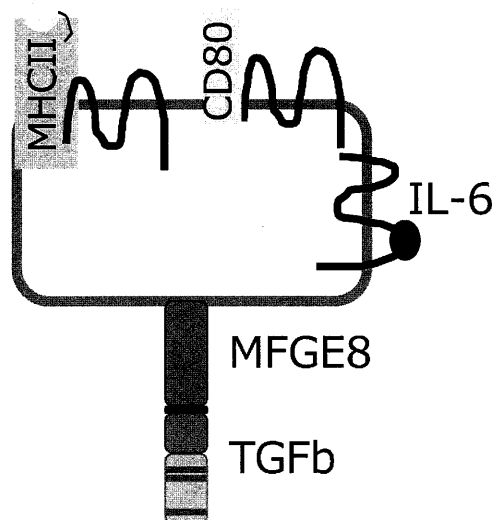


Fig. 2H

MODEL DIAGRAM OF ANTIGEN-PRESENTING
EXTRACELLULAR VESICLE OF EXAMPLE 8

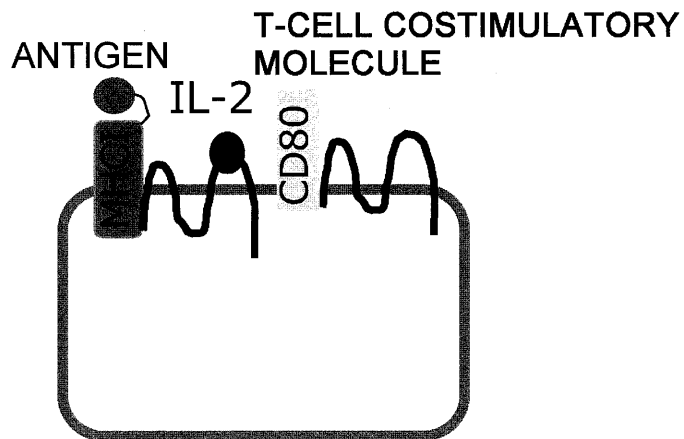


Fig. 2I

MODEL DIAGRAM OF ANTIGEN-PRESENTING
VESICLE OF EXAMPLE 9

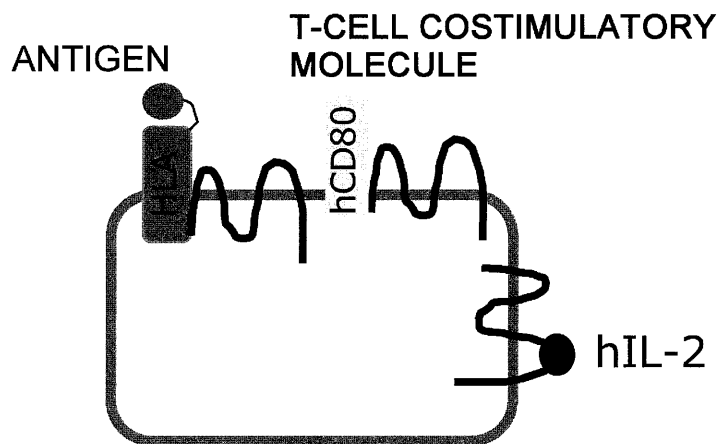


Fig. 2J

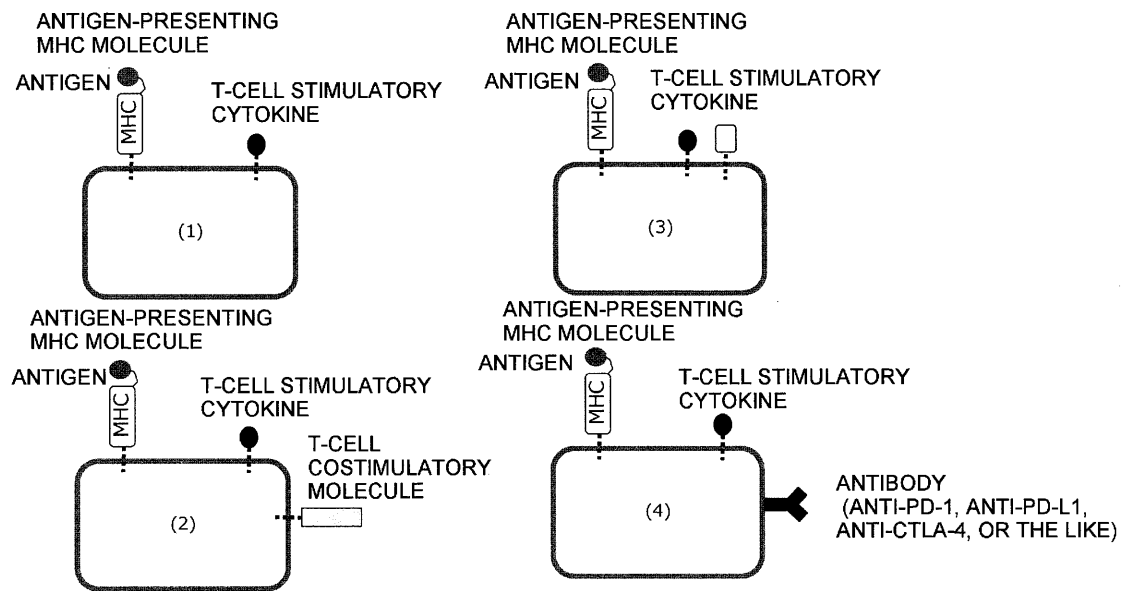


Fig. 3A

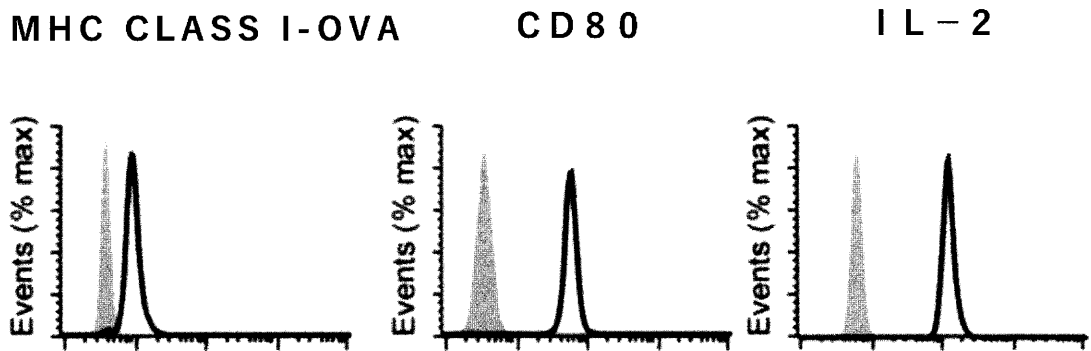


Fig. 3B

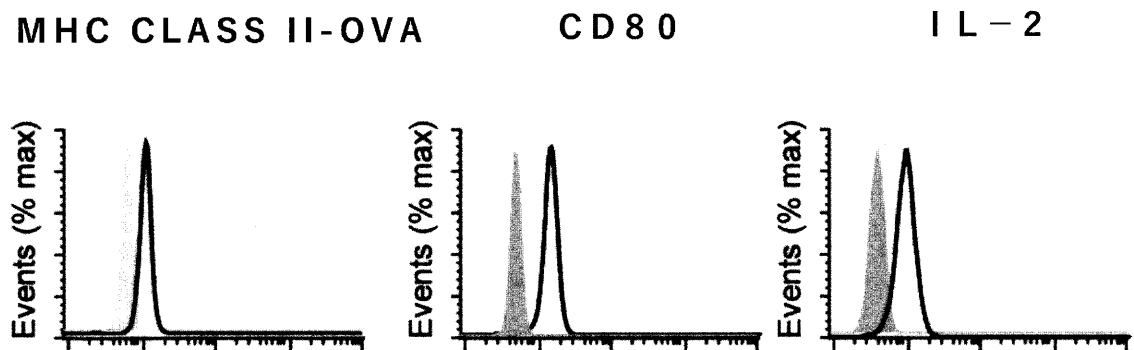


Fig. 3C

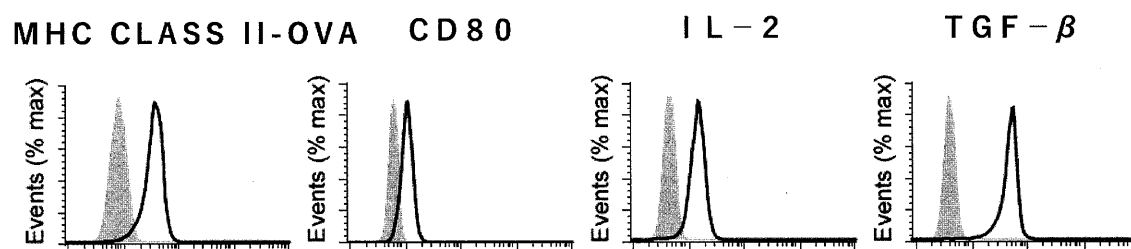


Fig. 3D

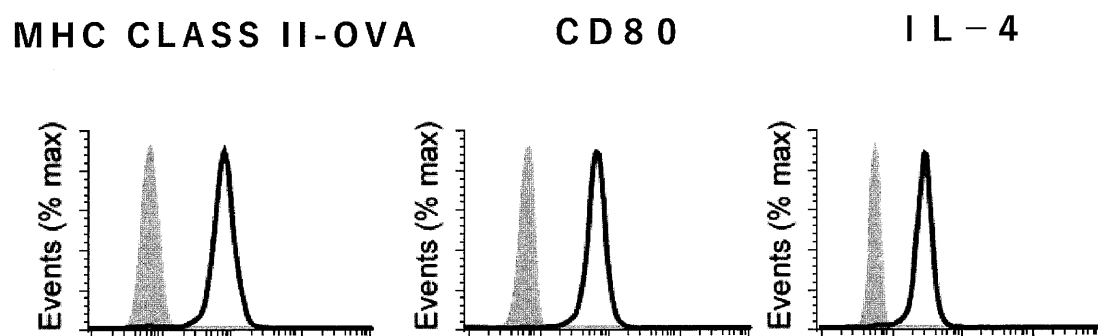


Fig. 3E

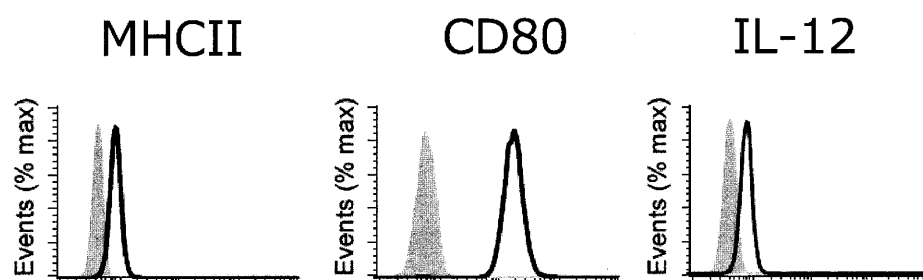


Fig. 3F

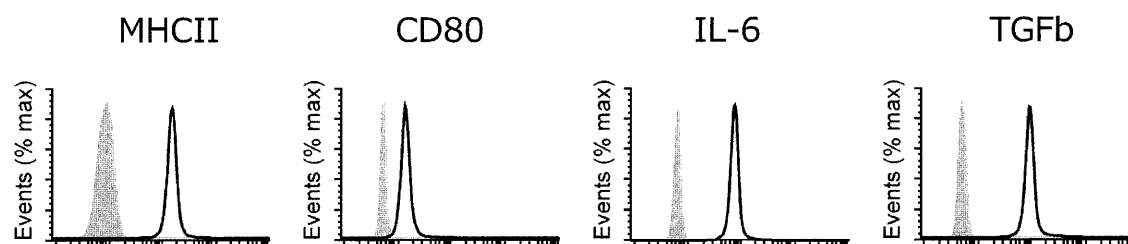


Fig. 3G

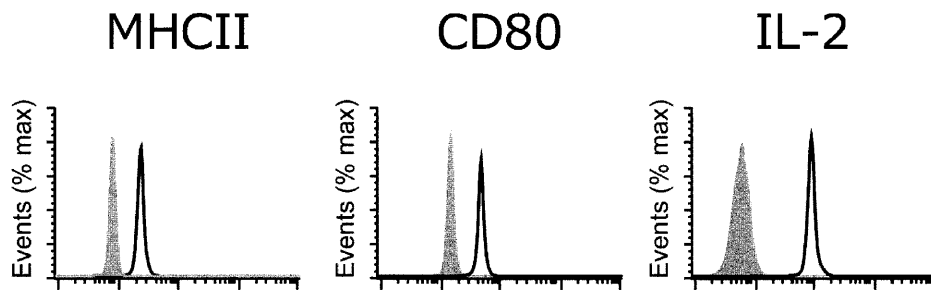


Fig. 3H

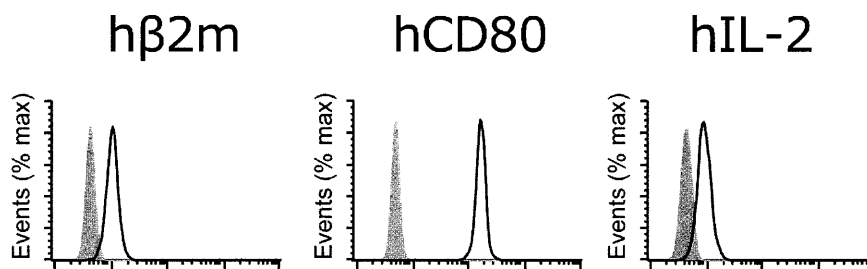


Fig. 4

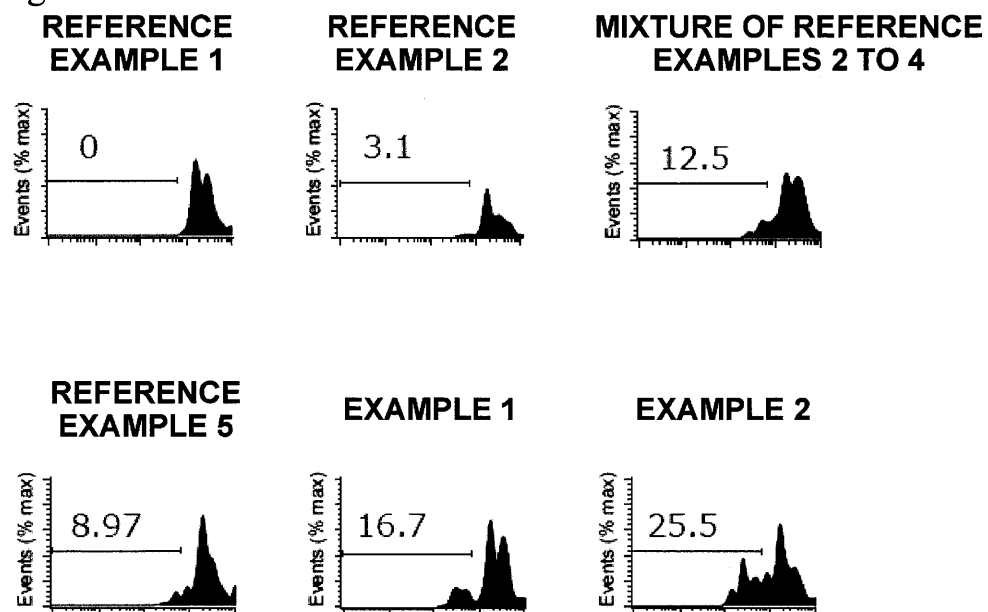


Fig. 5

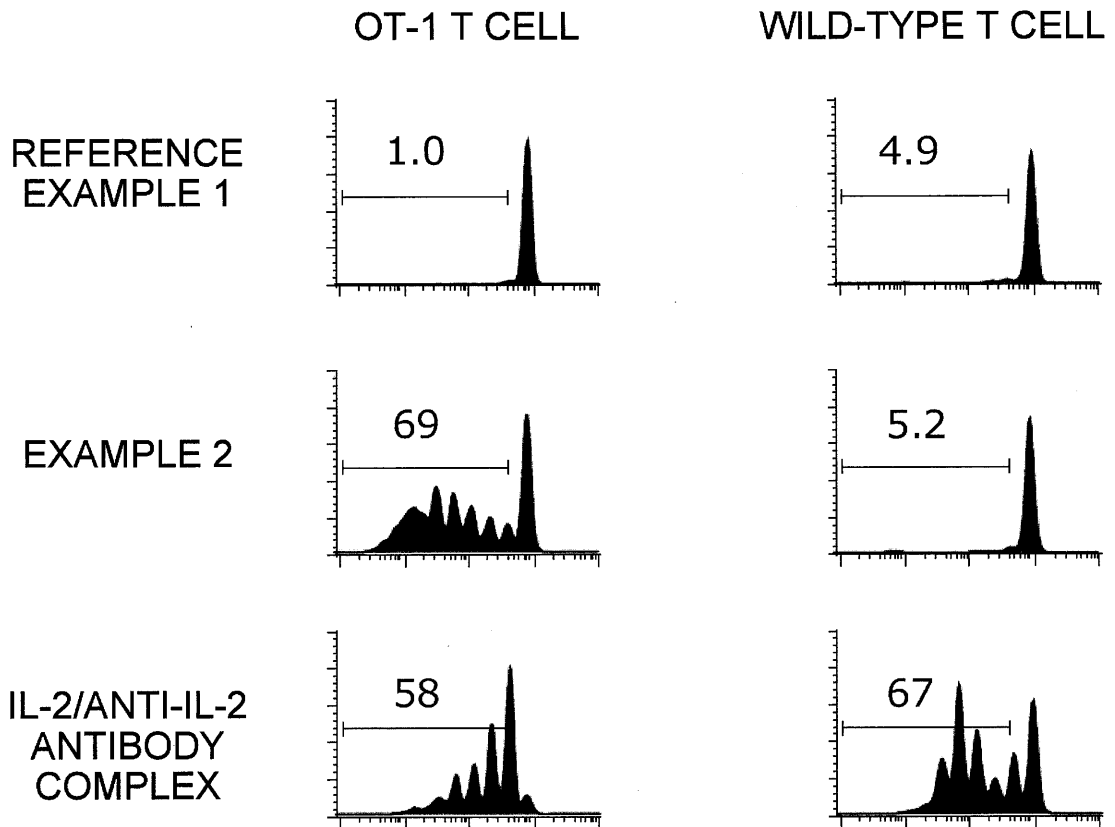


FIG. 6

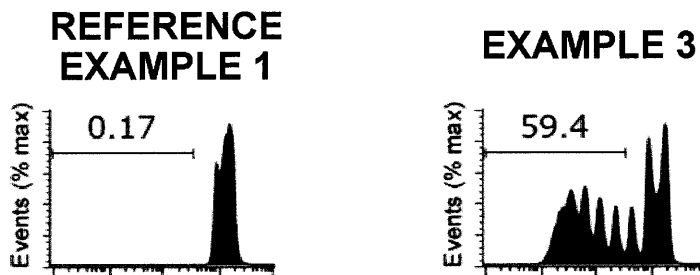


FIG. 7

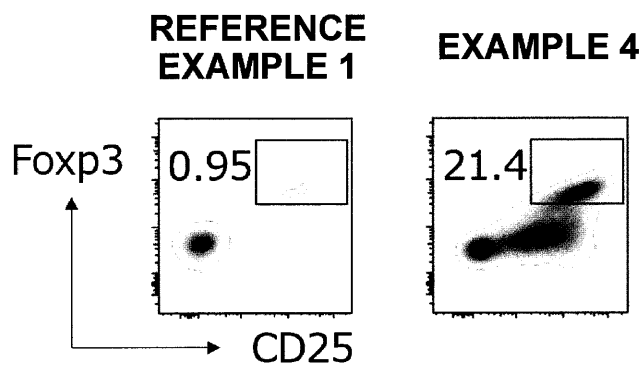


FIG. 8

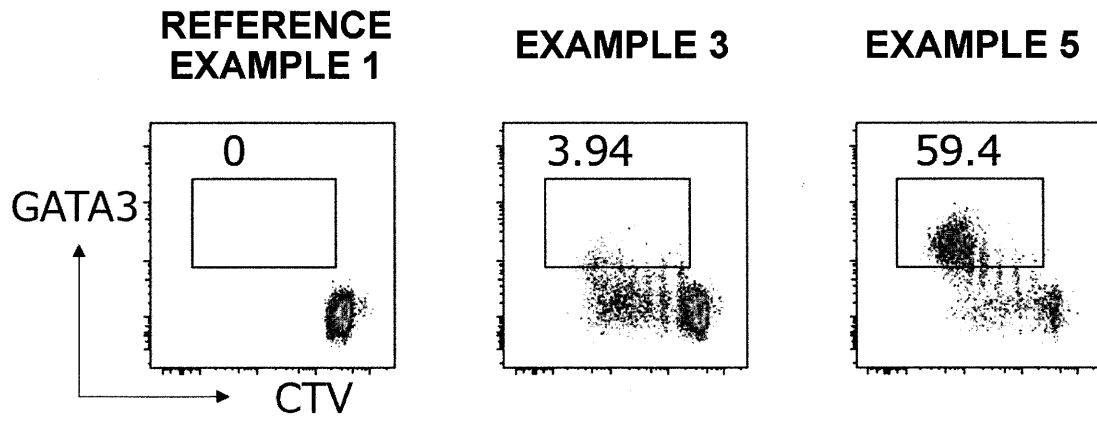


FIG. 9

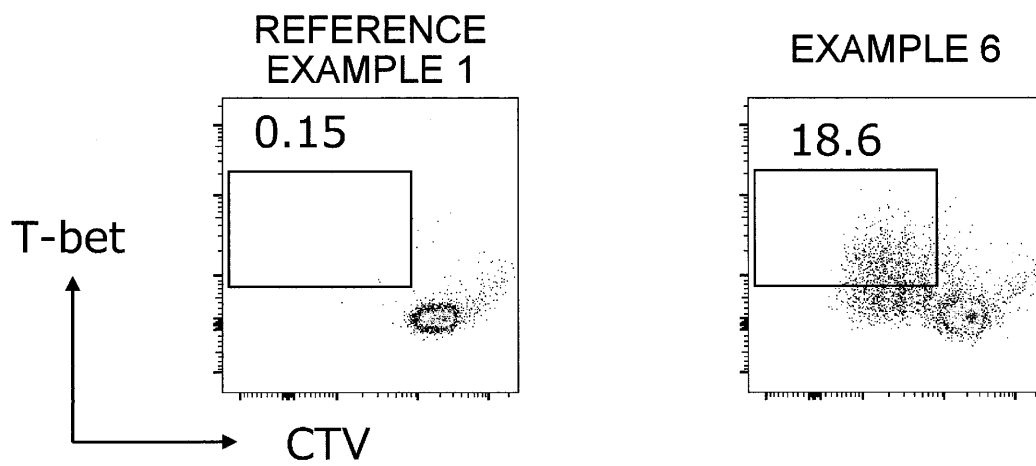


FIG. 10

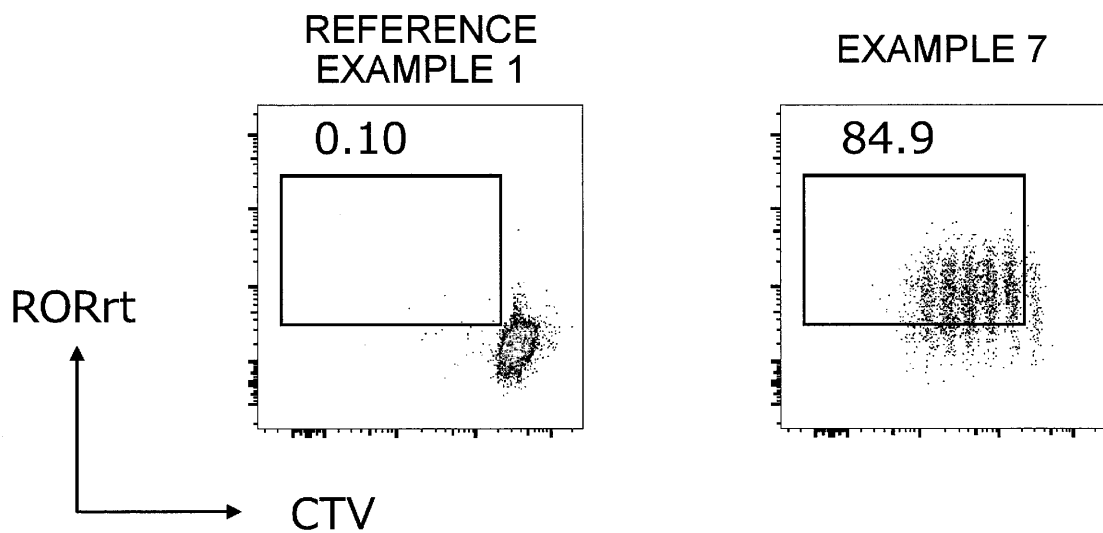


FIG. 11

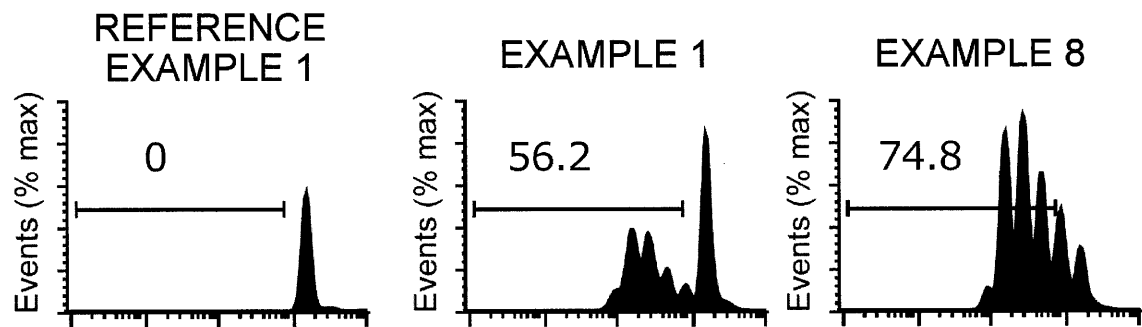
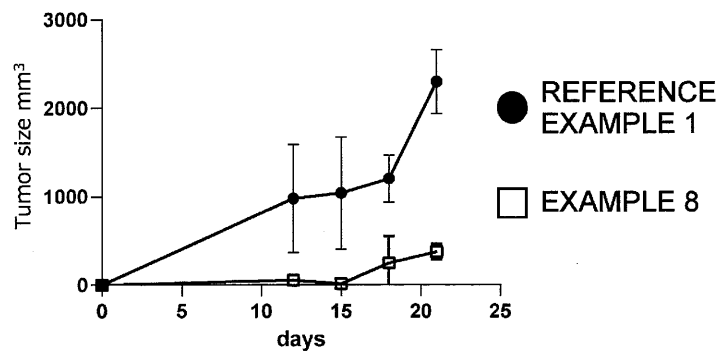


FIG. 12



SEQUENCE LISTING

<110> NATIONAL UNIVERSITY CORPORATION KANAZAWA UNIVERSITY
NISSAN CHEMICAL CORPORATION

<120> ANTIGEN PRESENTING EXTRACELLULAR VESICLES, COMPOSITIONS COMPRISING
THEREOF, AND METHODS FOR MANUFACTURING THEREOF

<130> FP4630PCT

<150> JP 2020-033331

<151> 2020-02-28

<160> 150

<170> PatentIn version 3.5

<210> 1

<211> 20

<212> PRT

<213> Mus musculus

<400> 1

Met	Ala	Arg	Ser	Val	Thr	Leu	Val	Phe	Leu	Val	Leu	Val	Ser	Leu	Thr
1				5				10					15		

Gly	Leu	Tyr	Ala
			20

<210> 2

<211> 60

<212> DNA

<213> Mus musculus

<400> 2

atggctcgct	cggtgaccct	ggctcttctg	gtgcttgcct	cactgaccgg	cctgtatgct	60

<210> 3

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> peptide sequence derived from OVA

<400> 3

Ser	Ile	Ile	Asn	Phe	Glu	Lys	Leu
1			5				

<210> 4
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence derived from OVA

<400> 4
tccattataa attttgaaaa gttg

24

<210> 5
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> synthesized peptide sequence

<400> 5
Gly Gly Gly Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 6
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<223> synthesized DNA sequence

<400> 6
ggcggagggtg cctctggcgg tgggggcagc ggtggagggg gcagt

45

<210> 7
<211> 99
<212> PRT
<213> Mus musculus

<400> 7

Ile Gln Lys Thr Pro Gln Ile Gln Val Tyr Ser Arg His Pro Pro Glu
1 5 10 15

Asn Gly Lys Pro Asn Ile Leu Asn Cys Tyr Val Thr Gln Phe His Pro
20 25 30

Pro His Ile Glu Ile Gln Met Leu Lys Asn Gly Lys Lys Ile Pro Lys
35 40 45

Val Glu Met Ser Asp Met Ser Phe Ser Lys Asp Trp Ser Phe Tyr Ile
50 55 60

Leu Ala His Thr Glu Phe Thr Pro Thr Glu Thr Asp Thr Tyr Ala Cys
65 70 75 80

Arg Val Lys His Ala Ser Met Ala Glu Pro Lys Thr Val Tyr Trp Asp
85 90 95

Arg Asp Met

<210> 8
<211> 297
<212> DNA
<213> Mus musculus

<400> 8
atccagaaaa cccctcaaat tcaagtatac tcacgccacc caccggagaa tgggaagccg 60
aacataactga actgctacgt aacacagttc caccgcctc acattgaaat ccaaattgctg 120
aagaacggga aaaaaattcc taaagtagag atgtcagata tgtccttcag caaggactgg 180
tctttctata tcctggctca cactgaattc acccccactg agactgatac atacgcctgc 240
agagttaagc atgccagtat ggccgagccc aagaccgtct actgggatcg agacatg 297

<210> 9
<211> 348
<212> PRT
<213> Mus musculus

<400> 9

Gly Pro His Ser Leu Arg Tyr Phe Val Thr Ala Val Ser Arg Pro Gly
1 5 10 15

Leu Gly Glu Pro Arg Tyr Met Glu Val Gly Tyr Val Asp Asp Thr Glu
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Glu Asn Pro Arg Tyr Glu Pro Arg
35 40 45

Ala Arg Trp Met Glu Gln Glu Gly Pro Glu Tyr Trp Glu Arg Glu Thr
50 55 60

Gln Lys Ala Lys Gly Asn Glu Gln Ser Phe Arg Val Asp Leu Arg Thr
65 70 75 80

Leu Leu Gly Tyr Tyr Asn Gln Ser Lys Gly Gly Ser His Thr Ile Gln
85 90 95

Val Ile Ser Gly Cys Glu Val Gly Ser Asp Gly Arg Leu Leu Arg Gly
100 105 110

Tyr Gln Gln Tyr Ala Tyr Asp Gly Cys Asp Tyr Ile Ala Leu Asn Glu
115 120 125

Asp Leu Lys Thr Trp Thr Ala Ala Asp Met Ala Ala Leu Ile Thr Lys
130 135 140

His Lys Trp Glu Gln Ala Gly Glu Ala Glu Arg Leu Arg Ala Tyr Leu
145 150 155 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Lys Asn Gly Asn
165 170 175

Ala Thr Leu Leu Arg Thr Asp Ser Pro Lys Ala His Val Thr His His
180 185 190

Ser Arg Pro Glu Asp Lys Val Thr Leu Arg Cys Trp Ala Leu Gly Phe
195 200 205

Tyr Pro Ala Asp Ile Thr Leu Thr Trp Gln Leu Asn Gly Glu Glu Leu
210 215 220

Ile Gln Asp Met Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ser Val Val Val Pro Leu Gly Lys Glu Gln Tyr
245 250 255

Tyr Thr Cys His Val Tyr His Gln Gly Leu Pro Glu Pro Leu Thr Leu
260 265 270

Arg Trp Glu Pro Pro Pro Ser Thr Val Ser Asn Met Ala Thr Val Ala
275 280 285

Val Leu Val Val Leu Gly Ala Ala Ile Val Thr Gly Ala Val Val Ala
290 295 300

Phe Val Met Lys Met Arg Arg Arg Asn Thr Gly Gly Lys Gly Gly Asp
305 310 315 320

Tyr Ala Leu Ala Pro Gly Ser Gln Thr Ser Asp Leu Ser Leu Pro Asp
325 330 335

Cys Lys Val Met Val His Asp Pro His Ser Leu Ala
340 345

<210> 10
<211> 1044
<212> DNA
<213> Mus musculus

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cggtacatgg aagtcggcta cgtggacgac acggagttcg tgcgcttcga cagcgacgcg 120
gagaatccga gatatgagcc gcggggcgcg tggatggagc aggagggggcc cgagtattgg 180
gagcggggaga cacagaaagc caagggcaat gagcagagtt tccgagtgga cctgaggacc 240
ctgctcggct actacaacca gagcaagggc ggctctcaca ctattcaggt gatctctggc 300
tgtgaagtgg ggtccgacgg gcgactcctc cgcggggtacc agcagtacgc ctacgacggc 360
tgcgattaca tcgccctgaa cgaagacctg aaaacgtgga cggcggcgga catggcggcg 420
ctgatcacca aacacaagtg ggagcaggct ggtgaagcag agagactcag ggcctacctg 480
gagggcacgt gcgtggagtg gctccgcaga tacctgaaga acgggaacgc gacgctgctg 540
cgcacagatt ccccaaaggc ccatgtgacc catcacagca gacctgaaga taaagtcacc 600
ctgaggtgct gggccctggg cttctaccct gctgacatca ccctgacctg gcagttgaat 660
ggggaggagc tgatccagga catggagctt gtggagacca ggcctgcagg ggatggaacc 720

ttccagaagt gggcatctgt ggtggtgcct cttgggaagg agcagtatta cacatgccat	780
gtgtaccatc aggggctgcc tgagcccctc accctgagat gggagcctcc tccatccact	840
gtctccaaca tggcgaccgt tgctgttctg gttgtccttg gagctgcaat agtcactgga	900
gctgtggtgg cttttgtgat gaagatgaga aggagaaaca caggtggaaa aggaggggac	960
tatgctctgg ctccaggctc ccagacctct gatctgtctc tcccagattg taaagtgatg	1020
gttcatgacc ctcatctct agcg	1044

<210> 11
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthesized peptide sequence

<400> 11

Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly
1				5					10					15	

Gly	Gly	Gly	Ser
			20

<210> 12
 <211> 60
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> synthesized DNA sequence

gggggggggag gctccggtgg aggggggtct ggaggggggg ggtctggtgg aggcggaagt	60

<210> 13
 <211> 510
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> peptide sequence derived from OVA, mus musculus

<400> 13

Met Ala Arg Ser Val Thr Leu Val Phe Leu Val Leu Val Ser Leu Thr

1	5	10	15
Gly	Leu	Tyr	Ala
	20		25
Ser	Ile	Ile	Asn
			30
Gly	Gly	Gly	Ala
Ser	Gly	Gly	Gly
	35		40
Ser	Ile	Gln	Lys
			45
Thr	Pro		
Gln	Ile	Gln	Val
	50		55
Tyr	Ser	Arg	His
			60
Pro	Pro	Glu	Asn
Gly	Lys	Pro	Asn
Ile	Leu	Asn	Cys
	65		70
Tyr	Val	Thr	Gln
			75
Phe	His	Pro	Pro
			80
His	Ile	Glu	Ile
Gln	Met	Leu	Lys
			85
Asn	Gly	Lys	Lys
			90
Ile	Pro	Lys	Val
Glu	Met	Ser	Asp
			95
Met	Ser	Phe	Ser
			100
Lys	Asp	Trp	Ser
			105
Phe	Tyr	Ile	Leu
Ala	His	Thr	Glu
			110
Phe	Thr	Pro	Thr
			115
Glu	Thr	Asp	Thr
			120
Tyr	Ala	Cys	Arg
			125
Val	Lys	His	Ala
Ser	Met	Ala	Glu
			130
Pro	Lys	Thr	Val
			135
Tyr	Trp	Asp	Arg
			140
Asp	Met	Gly	Gly
Gly	Gly	Ser	Gly
			145
Gly	Gly	Gly	Gly
			150
Ser	Gly	Gly	Gly
			155
Ser	Gly	Gly	Gly
			160
Gly	Ser	Gly	Gly
Gly	Ser	Gly	Pro
			165
His	Ser	Leu	Arg
			170
Tyr	Phe	Val	Thr
Ala	Val	Ser	Arg
			175
Pro	Gly	Leu	Gly
			180
Glu	Pro	Arg	Tyr
			185
Met	Glu	Val	Gly
			190
Tyr	Val	Asp	Asp
Thr	Glu	Phe	Val
			195
Arg	Phe	Asp	Ser
			200
Asp	Ala	Glu	Asn
			205
Pro	Arg	Tyr	Trp
Glu	Tyr	Trp	Glu
			210
Arg	Pro	Glu	Tyr
			215
Pro	Arg	Ala	Arg
			220
Trp	Glu	Arg	

Glu Thr Gln Lys Ala Lys Gly Asn Glu Gln Ser Phe Arg Val Asp Leu
225 230 235 240

Arg Thr Leu Leu Gly Tyr Tyr Asn Gln Ser Lys Gly Gly Ser His Thr
245 250 255

Ile Gln Val Ile Ser Gly Cys Glu Val Gly Ser Asp Gly Arg Leu Leu
260 265 270

Arg Gly Tyr Gln Gln Tyr Ala Tyr Asp Gly Cys Asp Tyr Ile Ala Leu
275 280 285

Asn Glu Asp Leu Lys Thr Trp Thr Ala Ala Asp Met Ala Ala Leu Ile
290 295 300

Thr Lys His Lys Trp Glu Gln Ala Gly Glu Ala Glu Arg Leu Arg Ala
305 310 315 320

Tyr Leu Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Lys Asn
325 330 335

Gly Asn Ala Thr Leu Leu Arg Thr Asp Ser Pro Lys Ala His Val Thr
340 345 350

His His Ser Arg Pro Glu Asp Lys Val Thr Leu Arg Cys Trp Ala Leu
355 360 365

Gly Phe Tyr Pro Ala Asp Ile Thr Leu Thr Trp Gln Leu Asn Gly Glu
370 375 380

Glu Leu Ile Gln Asp Met Glu Leu Val Glu Thr Arg Pro Ala Gly Asp
385 390 395 400

Gly Thr Phe Gln Lys Trp Ala Ser Val Val Val Pro Leu Gly Lys Glu
405 410 415

Gln Tyr Tyr Thr Cys His Val Tyr His Gln Gly Leu Pro Glu Pro Leu
420 425 430

Thr Leu Arg Trp Glu Pro Pro Pro Ser Thr Val Ser Asn Met Ala Thr

435

440

445

Val Ala Val Leu Val Val Leu Gly Ala Ala Ile Val Thr Gly Ala Val
 450 455 460

Val Ala Phe Val Met Lys Met Arg Arg Arg Asn Thr Gly Gly Lys Gly
 465 470 475 480

Gly Asp Tyr Ala Leu Ala Pro Gly Ser Gln Thr Ser Asp Leu Ser Leu
 485 490 495

Pro Asp Cys Lys Val Met Val His Asp Pro His Ser Leu Ala
 500 505 510

<210> 14
 <211> 1530
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> DNA sequence derived from OVA, mus musculus

<400> 14
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 tccattataa attttgaaaa gttgggcgga ggtgcctctg gcggtggggg cagcgggtgga 120
 gggggcagta tccagaaaac ccctcaaatt caagtatact cacgccaccc accggagaat 180
 gggaagccga acatactgaa ctgctacgta acacagttcc accgcctca cattgaaatc 240
 caaatgctga agaacgggaa aaaaattcct aaagtagaga tgtcagatat gtccttcagc 300
 aaggactggc ctttctatat cctggctcac actgaattca cccccactga gactgataca 360
 tacgcctgca gaggtaagca tgccagtatg gccgagccca agaccgtcta ctgggatcga 420
 gacatggggg ggggaggctc cggtggaggg gggctctggag gggggggggtc tgggtggaggc 480
 ggaagtggcc cacactcgct gaggtatttc gtcaccgccg tgtcccggcc cggcctcggg 540
 gagccccggc acatggaagt cggctacgtg gacgacacgg agttcgtgcg cttcgacagc 600
 gacgcggaga atccgagata tgagccgcgg gcgcgggtgga tggagcagga ggggcccagag 660
 tattgggagc gggagacaca gaaagccaag ggcaatgagc agagtttccg agtggacctg 720
 aggaccctgc tcggctacta caaccagagc aagggcggct ctcacactat tcaggtgatc 780

tctggctgtg aagtggggtc cgacgggcga ctcctccgcg ggtaccagca gtacgcctac	840
gacggctgcg attacatcgc cctgaacgaa gacctgaaaa cgtggacggc ggcggacatg	900
gcggcgctga tcaccaaaca caagtgggag caggctgggtg aagcagagag actcagggcc	960
tacctggagg gcacgtgcgt ggagtggctc cgcagatacc tgaagaacgg gaacgcgacg	1020
ctgctgcgca cagattcccc aaaggcccat gtgaccatc acagcagacc tgaagataaa	1080
gtcaccctga ggtgctgggc cctgggcttc taccctgctg acatcacct gacctggcag	1140
ttgaatgggg aggagctgat ccaggacatg gagcttgtgg agaccaggcc tgcaggggat	1200
ggaaccttcc agaagtgggc atctgtggtg gtgcctcttg ggaaggagca gtattacaca	1260
tgccatgtgt accatcaggg gctgcctgag cccctcacc tgagatggga gcctcctcca	1320
tccactgtct ccaacatggc gaccgttgct gttctggttg tccttgagc tgcaatagtc	1380
actggagctg tgggtggcttt tgtgatgaag atgagaagga gaaacacagg tggaaaagga	1440
ggggactatg ctctggctcc aggctcccag acctctgatc tgtctctccc agattgtaaa	1500
gtgatggttc atgaccctca ttctctagcg	1530

<210> 15
 <211> 236
 <212> PRT
 <213> Mus musculus

<400> 15

Met	Gly	Val	Glu	Gly	Cys	Thr	Lys	Cys	Ile	Lys	Tyr	Leu	Leu	Phe	Val
1				5					10					15	

Phe	Asn	Phe	Val	Phe	Trp	Leu	Ala	Gly	Gly	Val	Ile	Leu	Gly	Val	Ala
			20					25					30		

Leu	Trp	Leu	Arg	His	Asp	Pro	Gln	Thr	Thr	Ser	Leu	Leu	Tyr	Leu	Glu
		35					40					45			

Leu	Gly	Asn	Lys	Pro	Ala	Pro	Asn	Thr	Phe	Tyr	Val	Gly	Ile	Tyr	Ile
	50					55					60				

Leu	Ile	Ala	Val	Gly	Ala	Val	Met	Met	Phe	Val	Gly	Phe	Leu	Gly	Cys
65					70					75					80

Tyr Gly Ala Ile Gln Glu Ser Gln Cys Leu Leu Gly Thr Phe Phe Thr
85 90 95

Cys Leu Val Ile Leu Phe Ala Cys Glu Val Ala Ala Gly Ile Trp Gly
100 105 110

Phe Val Asn Lys Asp Gln Ile Ala Lys Asp Val Lys Gln Phe Tyr Asp
115 120 125

Gln Ala Leu Gln Gln Ala Val Met Asp Asp Asp Ala Asn Asn Ala Lys
130 135 140

Ala Val Val Lys Thr Phe His Glu Thr Leu Asn Cys Cys Gly Ser Asn
145 150 155 160

Ala Leu Thr Thr Leu Thr Thr Thr Ile Leu Arg Asn Ser Leu Cys Pro
165 170 175

Ser Gly Gly Asn Ile Leu Thr Pro Leu Leu Gln Gln Asp Cys His Gln
180 185 190

Lys Ile Asp Glu Leu Phe Ser Gly Lys Leu Tyr Leu Ile Gly Ile Ala
195 200 205

Ala Ile Val Val Ala Val Ile Met Ile Phe Glu Met Ile Leu Ser Met
210 215 220

Val Leu Cys Cys Gly Ile Arg Asn Ser Ser Val Tyr
225 230 235

<210> 16
<211> 711
<212> DNA
<213> Mus musculus

<400> 16
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ttctggctgg ctggaggcgt gatcctaggt gtagctctgt ggttgcgtca tgatccacag 120
accaccagcc tgctgtacct ggaactggga aacaaaccgg cacccaacac cttctacgtg 180
ggcatctaca ttctcattgc tgtgggagct gtgatgatgt ttgtaggctt cctgggggtgc 240

tatggggcca tccaggagtc ccagtgtctg ctggggacgt tcttcacctg ctttgtgatc	300
ctgtttgcct gtgaggtggc tgcaggcatc tggggcttcg taaacaaaga ccagatcgcc	360
aaggatgtga agcagttcta tgaccaggcc cttcagcaag ctgtgatgga tgatgatgcc	420
aacaatgcca aggctgtggt gaagactttc catgagacgc tcaactgttg tggctccaac	480
gcactgacca cactgactac caccatactg aggaacagcc tgtgtccctc aggcggcaac	540
atactcaccc ctttactgca gcaagattgt catcagaaaa tcgatgagct cttctctggg	600
aagctgtacc tcattggaat tgcagccatt gtggtagctg tcattatgat ctttgagatg	660
attctgagca tgggtgctgtg ctgtggcatc cggaacagct ccgtgtactg a	711

<210> 17
 <211> 746
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> peptide sequence derived from OVA, mus musculus

<400> 17

Met	Ala	Arg	Ser	Val	Thr	Leu	Val	Phe	Leu	Val	Leu	Val	Ser	Leu	Thr
1				5				10					15		

Gly	Leu	Tyr	Ala	Ser	Ile	Ile	Asn	Phe	Glu	Lys	Leu	Gly	Gly	Gly	Ala
			20				25					30			

Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ile	Gln	Lys	Thr	Pro
	35					40						45			

Gln	Ile	Gln	Val	Tyr	Ser	Arg	His	Pro	Pro	Glu	Asn	Gly	Lys	Pro	Asn
50						55					60				

Ile	Leu	Asn	Cys	Tyr	Val	Thr	Gln	Phe	His	Pro	Pro	His	Ile	Glu	Ile
65					70					75				80	

Gln	Met	Leu	Lys	Asn	Gly	Lys	Lys	Ile	Pro	Lys	Val	Glu	Met	Ser	Asp
			85					90						95	

Met	Ser	Phe	Ser	Lys	Asp	Trp	Ser	Phe	Tyr	Ile	Leu	Ala	His	Thr	Glu
			100					105					110		

Phe Thr Pro Thr Glu Thr Asp Thr Tyr Ala Cys Arg Val Lys His Ala
115 120 125

Ser Met Ala Glu Pro Lys Thr Val Tyr Trp Asp Arg Asp Met Gly Gly
130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Pro His Ser Leu Arg Tyr Phe Val Thr Ala Val Ser Arg
165 170 175

Pro Gly Leu Gly Glu Pro Arg Tyr Met Glu Val Gly Tyr Val Asp Asp
180 185 190

Thr Glu Phe Val Arg Phe Asp Ser Asp Ala Glu Asn Pro Arg Tyr Glu
195 200 205

Pro Arg Ala Arg Trp Met Glu Gln Glu Gly Pro Glu Tyr Trp Glu Arg
210 215 220

Glu Thr Gln Lys Ala Lys Gly Asn Glu Gln Ser Phe Arg Val Asp Leu
225 230 235 240

Arg Thr Leu Leu Gly Tyr Tyr Asn Gln Ser Lys Gly Gly Ser His Thr
245 250 255

Ile Gln Val Ile Ser Gly Cys Glu Val Gly Ser Asp Gly Arg Leu Leu
260 265 270

Arg Gly Tyr Gln Gln Tyr Ala Tyr Asp Gly Cys Asp Tyr Ile Ala Leu
275 280 285

Asn Glu Asp Leu Lys Thr Trp Thr Ala Ala Asp Met Ala Ala Leu Ile
290 295 300

Thr Lys His Lys Trp Glu Gln Ala Gly Glu Ala Glu Arg Leu Arg Ala
305 310 315 320

Tyr Leu Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Lys Asn

325

330

335

Gly Asn Ala Thr Leu Leu Arg Thr Asp Ser Pro Lys Ala His Val Thr
 340 345 350

His His Ser Arg Pro Glu Asp Lys Val Thr Leu Arg Cys Trp Ala Leu
 355 360 365

Gly Phe Tyr Pro Ala Asp Ile Thr Leu Thr Trp Gln Leu Asn Gly Glu
 370 375 380

Glu Leu Ile Gln Asp Met Glu Leu Val Glu Thr Arg Pro Ala Gly Asp
 385 390 395 400

Gly Thr Phe Gln Lys Trp Ala Ser Val Val Val Pro Leu Gly Lys Glu
 405 410 415

Gln Tyr Tyr Thr Cys His Val Tyr His Gln Gly Leu Pro Glu Pro Leu
 420 425 430

Thr Leu Arg Trp Glu Pro Pro Pro Ser Thr Val Ser Asn Met Ala Thr
 435 440 445

Val Ala Val Leu Val Val Leu Gly Ala Ala Ile Val Thr Gly Ala Val
 450 455 460

Val Ala Phe Val Met Lys Met Arg Arg Arg Asn Thr Gly Gly Lys Gly
 465 470 475 480

Gly Asp Tyr Ala Leu Ala Pro Gly Ser Gln Thr Ser Asp Leu Ser Leu
 485 490 495

Pro Asp Cys Lys Val Met Val His Asp Pro His Ser Leu Ala Met Gly
 500 505 510

Val Glu Gly Cys Thr Lys Cys Ile Lys Tyr Leu Leu Phe Val Phe Asn
 515 520 525

Phe Val Phe Trp Leu Ala Gly Gly Val Ile Leu Gly Val Ala Leu Trp
 530 535 540

Leu Arg His Asp Pro Gln Thr Thr Ser Leu Leu Tyr Leu Glu Leu Gly
545 550 555 560

Asn Lys Pro Ala Pro Asn Thr Phe Tyr Val Gly Ile Tyr Ile Leu Ile
565 570 575

Ala Val Gly Ala Val Met Met Phe Val Gly Phe Leu Gly Cys Tyr Gly
580 585 590

Ala Ile Gln Glu Ser Gln Cys Leu Leu Gly Thr Phe Phe Thr Cys Leu
595 600 605

Val Ile Leu Phe Ala Cys Glu Val Ala Ala Gly Ile Trp Gly Phe Val
610 615 620

Asn Lys Asp Gln Ile Ala Lys Asp Val Lys Gln Phe Tyr Asp Gln Ala
625 630 635 640

Leu Gln Gln Ala Val Met Asp Asp Asp Ala Asn Asn Ala Lys Ala Val
645 650 655

Val Lys Thr Phe His Glu Thr Leu Asn Cys Cys Gly Ser Asn Ala Leu
660 665 670

Thr Thr Leu Thr Thr Thr Ile Leu Arg Asn Ser Leu Cys Pro Ser Gly
675 680 685

Gly Asn Ile Leu Thr Pro Leu Leu Gln Gln Asp Cys His Gln Lys Ile
690 695 700

Asp Glu Leu Phe Ser Gly Lys Leu Tyr Leu Ile Gly Ile Ala Ala Ile
705 710 715 720

Val Val Ala Val Ile Met Ile Phe Glu Met Ile Leu Ser Met Val Leu
725 730 735

Cys Cys Gly Ile Arg Asn Ser Ser Val Tyr
740 745

<211> 2241
<212> DNA
<213> Artificial Sequence

<220>

<223> DNA sequence derived from OVA, mus musculus

<400> 18

atggctcgct cggtgaccct ggtctttctg gtgcttgtct cactgaccgg cctgtatgct	60
tccattataa attttgaaaa gttgggcgga ggtgcctctg gcggtggggg cagcgggtgga	120
gggggcagta tccagaaaac ccctcaaatt caagtatact cacgccaccc accggagaat	180
gggaagccga acatactgaa ctgctacgta acacagttcc accgcctca cattgaaatc	240
caaatgctga agaacgggaa aaaaattcct aaagtagaga tgtcagatat gtccttcagc	300
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ggaagtggcc cacactcgct gaggtatttc gtcaccgccg tgtcccggcc cggcctcggg	540
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gacgcggaga atccgagata tgagccgcgg gcgcgggtgga tggagcagga ggggcccag	660
tattgggagc gggagacaca gaaagccaag ggcaatgagc agagtttccg agtggacctg	720
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gacggctgcg attacatcg cctgaacgaa gacctgaaaa cgtggacggc ggcggacatg	900
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catgagacgc tcaactgttg tggctccaac gcactgacca cactgactac caccatactg	2040
aggaacagcc tgtgtccctc aggcggcaac atactcacc cttactgca gcaagattgt	2100
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cggaacagct ccgtgtactg a	2241

<210> 19
 <211> 306
 <212> PRT
 <213> Mus musculus

<400> 19

Met	Ala	Cys	Asn	Cys	Gln	Leu	Met	Gln	Asp	Thr	Pro	Leu	Leu	Lys	Phe
1				5					10					15	

Pro	Cys	Pro	Arg	Leu	Ile	Leu	Leu	Phe	Val	Leu	Leu	Ile	Arg	Leu	Ser
			20					25					30		

Gln	Val	Ser	Ser	Asp	Val	Asp	Glu	Gln	Leu	Ser	Lys	Ser	Val	Lys	Asp
		35					40					45			

Lys	Val	Leu	Leu	Pro	Cys	Arg	Tyr	Asn	Ser	Pro	His	Glu	Asp	Glu	Ser
	50					55					60				

Glu Asp Arg Ile Tyr Trp Gln Lys His Asp Lys Val Val Leu Ser Val
65 70 75 80

Ile Ala Gly Lys Leu Lys Val Trp Pro Glu Tyr Lys Asn Arg Thr Leu
85 90 95

Tyr Asp Asn Thr Thr Tyr Ser Leu Ile Ile Leu Gly Leu Val Leu Ser
100 105 110

Asp Arg Gly Thr Tyr Ser Cys Val Val Gln Lys Lys Glu Arg Gly Thr
115 120 125

Tyr Glu Val Lys His Leu Ala Leu Val Lys Leu Ser Ile Lys Ala Asp
130 135 140

Phe Ser Thr Pro Asn Ile Thr Glu Ser Gly Asn Pro Ser Ala Asp Thr
145 150 155 160

Lys Arg Ile Thr Cys Phe Ala Ser Gly Gly Phe Pro Lys Pro Arg Phe
165 170 175

Ser Trp Leu Glu Asn Gly Arg Glu Leu Pro Gly Ile Asn Thr Thr Ile
180 185 190

Ser Gln Asp Pro Glu Ser Glu Leu Tyr Thr Ile Ser Ser Gln Leu Asp
195 200 205

Phe Asn Thr Thr Arg Asn His Thr Ile Lys Cys Leu Ile Lys Tyr Gly
210 215 220

Asp Ala His Val Ser Glu Asp Phe Thr Trp Glu Lys Pro Pro Glu Asp
225 230 235 240

Pro Pro Asp Ser Lys Asn Thr Leu Val Leu Phe Gly Ala Gly Phe Gly
245 250 255

Ala Val Ile Thr Val Val Val Ile Val Val Ile Ile Lys Cys Phe Cys
260 265 270

Lys His Arg Ser Cys Phe Arg Arg Asn Glu Ala Ser Arg Glu Thr Asn
275 280 285

Asn Ser Leu Thr Phe Gly Pro Glu Glu Ala Leu Ala Glu Gln Thr Val
 290 295 300

Phe Leu
 305

<210> 20
 <211> 921
 <212> DNA
 <213> Mus musculus

<400> 20
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 caactgtcca agtcagtgaag agataaggta ttgctgcctt gccgttataa ctctcctcat 180
 gaagatgagt ctgaagaccg aatctactgg caaaaacatg acaaagtggg gctgtctgtc 240
 attgctggga aactaaaagt gtggcccgag tataagaacc ggactttata tgacaacact 300
 acctactctc ttatcatcct gggcctgggc ctttcagacc ggggcacata cagctgtgtc 360
 gttcaaaaga aggaaagagg aacgtatgaa gttaaactact tggctttagt aaagttgtcc 420
 atcaaagctg acttctctac ccccaacata actgagtctg gaaacccatc tgcagacact 480
 aaaaggatta cctgctttgc ttccgggggt ttcccaaagc ctcgcttctc ttggttggaa 540
 aatggaagag aattacctgg catcaatacg acaatttccc aggatcctga atctgaattg 600
 tacaccatta gtagccaact agatttcaat acgactcgca accacaccat taagtgtctc 660
 attaaatatg gagatgctca cgtgtcagag gacttcacct gggaaaaacc cccagaagac 720
 cctcctgata gcaagaacac acttgtgctc tttggggcag gattcggcgc agtaataaca 780
 gtcgtcgtca tcgttgcatt catcaaagtc ttctgtaagc acagaagctg tttcagaaga 840
 aatgaggcaa gcagagaaac aaacaacagc cttaccttcg ggcctgaaga agcattagct 900
 gaacagaccg tcttccttta g 921

<210> 21
 <211> 226
 <212> PRT
 <213> Mus musculus

<400> 21

Met Pro Val Lys Gly Gly Ser Lys Cys Ile Lys Tyr Leu Leu Phe Gly
1 5 10 15

Phe Asn Phe Ile Phe Trp Leu Ala Gly Ile Ala Val Leu Ala Ile Gly
20 25 30

Leu Trp Leu Arg Phe Asp Ser Gln Thr Lys Ser Ile Phe Glu Gln Glu
35 40 45

Asn Asn His Ser Ser Phe Tyr Thr Gly Val Tyr Ile Leu Ile Gly Ala
50 55 60

Gly Ala Leu Met Met Leu Val Gly Phe Leu Gly Cys Cys Gly Ala Val
65 70 75 80

Gln Glu Ser Gln Cys Met Leu Gly Leu Phe Phe Gly Phe Leu Leu Val
85 90 95

Ile Phe Ala Ile Glu Ile Ala Ala Ala Val Trp Gly Tyr Thr His Lys
100 105 110

Asp Glu Val Ile Lys Glu Leu Gln Glu Phe Tyr Lys Asp Thr Tyr Gln
115 120 125

Lys Leu Arg Ser Lys Asp Glu Pro Gln Arg Glu Thr Leu Lys Ala Ile
130 135 140

His Met Ala Leu Asp Cys Cys Gly Ile Ala Gly Pro Leu Glu Gln Phe
145 150 155 160

Ile Ser Asp Thr Cys Pro Lys Lys Gln Leu Leu Glu Ser Phe Gln Val
165 170 175

Lys Pro Cys Pro Glu Ala Ile Ser Glu Val Phe Asn Asn Lys Phe His
180 185 190

Ile Ile Gly Ala Val Gly Ile Gly Ile Ala Val Val Met Ile Phe Gly
195 200 205

Met Ile Phe Ser Met Ile Leu Cys Cys Ala Ile Arg Arg Ser Arg Glu
 210 215 220

Met Val
 225

<210> 22
 <211> 681
 <212> DNA
 <213> Mus musculus

<400> 22
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 accaagagca tcttcgagca agagaataac cattccagtt tctacacagg agtgtacatt 180
 ctgattggag ccggggccct catgatgctg gttggtttcc tgggctgctg tggagctgta 240
 caagagtccc agtgcacgct gggattgttc ttcgggttcc tcttggtgat attcgccatt 300
 gagatagccg ccgccgtctg gggctatacc cacaaggatg aggtgattaa agaactccag 360
 gagttttaca aggacaccta ccaaaagtta cggagcaagg atgaaccca gcgggaaaca 420
 ctcaaagcca tccatatggc gttggactgc tgtggcatag ctggtccttt ggagcagttt 480
 atctcggaca cctgccccaa gaaacagctt ttggaaagt tccaggttaa gccctgccct 540
 gaagccatca gtgaggtctt caacaacaag ttccacatca ttggagcagt gggatatcggc 600
 atcgccgtgg tgatgatctt cggcatgatc ttcagcatga tcctgtgctg cgccatccgc 660
 aggagccgag aaatggtcta g 681

<210> 23
 <211> 532
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> peptide sequence derived from mus musculus

<400> 23

Met Ala Cys Asn Cys Gln Leu Met Gln Asp Thr Pro Leu Leu Lys Phe
 1 5 10 15

Pro Cys Pro Arg Leu Ile Leu Leu Phe Val Leu Leu Ile Arg Leu Ser

20

25

30

Gln Val Ser Ser Asp Val Asp Glu Gln Leu Ser Lys Ser Val Lys Asp
 35 40 45

Lys Val Leu Leu Pro Cys Arg Tyr Asn Ser Pro His Glu Asp Glu Ser
 50 55 60

Glu Asp Arg Ile Tyr Trp Gln Lys His Asp Lys Val Val Leu Ser Val
 65 70 75 80

Ile Ala Gly Lys Leu Lys Val Trp Pro Glu Tyr Lys Asn Arg Thr Leu
 85 90 95

Tyr Asp Asn Thr Thr Tyr Ser Leu Ile Ile Leu Gly Leu Val Leu Ser
 100 105 110

Asp Arg Gly Thr Tyr Ser Cys Val Val Gln Lys Lys Glu Arg Gly Thr
 115 120 125

Tyr Glu Val Lys His Leu Ala Leu Val Lys Leu Ser Ile Lys Ala Asp
 130 135 140

Phe Ser Thr Pro Asn Ile Thr Glu Ser Gly Asn Pro Ser Ala Asp Thr
 145 150 155 160

Lys Arg Ile Thr Cys Phe Ala Ser Gly Gly Phe Pro Lys Pro Arg Phe
 165 170 175

Ser Trp Leu Glu Asn Gly Arg Glu Leu Pro Gly Ile Asn Thr Thr Ile
 180 185 190

Ser Gln Asp Pro Glu Ser Glu Leu Tyr Thr Ile Ser Ser Gln Leu Asp
 195 200 205

Phe Asn Thr Thr Arg Asn His Thr Ile Lys Cys Leu Ile Lys Tyr Gly
 210 215 220

Asp Ala His Val Ser Glu Asp Phe Thr Trp Glu Lys Pro Pro Glu Asp
 225 230 235 240

Pro Pro Asp Ser Lys Asn Thr Leu Val Leu Phe Gly Ala Gly Phe Gly
245 250 255

Ala Val Ile Thr Val Val Val Ile Val Val Ile Ile Lys Cys Phe Cys
260 265 270

Lys His Arg Ser Cys Phe Arg Arg Asn Glu Ala Ser Arg Glu Thr Asn
275 280 285

Asn Ser Leu Thr Phe Gly Pro Glu Glu Ala Leu Ala Glu Gln Thr Val
290 295 300

Phe Leu Met Pro Val Lys Gly Gly Ser Lys Cys Ile Lys Tyr Leu Leu
305 310 315 320

Phe Gly Phe Asn Phe Ile Phe Trp Leu Ala Gly Ile Ala Val Leu Ala
325 330 335

Ile Gly Leu Trp Leu Arg Phe Asp Ser Gln Thr Lys Ser Ile Phe Glu
340 345 350

Gln Glu Asn Asn His Ser Ser Phe Tyr Thr Gly Val Tyr Ile Leu Ile
355 360 365

Gly Ala Gly Ala Leu Met Met Leu Val Gly Phe Leu Gly Cys Cys Gly
370 375 380

Ala Val Gln Glu Ser Gln Cys Met Leu Gly Leu Phe Phe Gly Phe Leu
385 390 395 400

Leu Val Ile Phe Ala Ile Glu Ile Ala Ala Ala Val Trp Gly Tyr Thr
405 410 415

His Lys Asp Glu Val Ile Lys Glu Leu Gln Glu Phe Tyr Lys Asp Thr
420 425 430

Tyr Gln Lys Leu Arg Ser Lys Asp Glu Pro Gln Arg Glu Thr Leu Lys
435 440 445

Ala Ile His Met Ala Leu Asp Cys Cys Gly Ile Ala Gly Pro Leu Glu

450

455

460

Gln Phe Ile Ser Asp Thr Cys Pro Lys Lys Gln Leu Leu Glu Ser Phe
 465 470 475 480

Gln Val Lys Pro Cys Pro Glu Ala Ile Ser Glu Val Phe Asn Asn Lys
 485 490 495

Phe His Ile Ile Gly Ala Val Gly Ile Gly Ile Ala Val Val Met Ile
 500 505 510

Phe Gly Met Ile Phe Ser Met Ile Leu Cys Cys Ala Ile Arg Arg Ser
 515 520 525

Arg Glu Met Val
 530

<210> 24
 <211> 1599
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> DNA sequence derived from mus musculus

<400> 24
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 ctcatcttc tctttgtgct gctgattcgt ctttcacaag tgtcttcaga tgttgatgaa 120
 caactgtcca agtcagtgaag agataaggta ttgctgcctt gccgttataa ctctcctcat 180
 gaagatgagt ctgaagaccg aatctactgg caaaaacatg acaaagtggg gctgtctgtc 240
 attgctggga aactaaaagt gtggcccgag tataagaacc ggactttata tgacaacact 300
 acctactctc ttatcatcct gggcctgggc ctttcagacc ggggcacata cagctgtgtc 360
 gttcaaaaga aggaaagagg aacgtatgaa gttaaact tggctttagt aaagttgtcc 420
 atcaaagctg acttctctac cccaacata actgagtctg gaaacccatc tgcagacact 480
 aaaaggatta cctgctttgc ttccgggggt ttcccaaagc ctcgcttctc ttggttggaa 540
 aatggaagag aattacctgg catcaatacg acaatttccc aggatcctga atctgaattg 600
 tacaccatta gtagccaact agatttcaat acgactcgca accacaccat taagtgtctc 660

attaaatatg gagatgctca cgtgtcagag gacttcacct gggaaaaacc cccagaagac	720
cctcctgata gcaagaacac acttgtgctc tttggggcag gattcggcgc agtaataaca	780
gtcgtcgtca tcgttgtcat catcaaatgc ttctgtaagc acagaagctg tttcagaaga	840
aatgaggcaa gcagagaaac aaacaacagc cttaccttcg ggcctgaaga agcattagct	900
gaacagaccg tcttccttat gccgggtcaaa ggaggtagca agtgcacaa atacctgctc	960
ttcggattta acttcatctt ctggctcgct ggcatcgcag tgcttgctat tggactatgg	1020
ctccgattcg actctcagac caagagcatc ttcgagcaag agaataacca ttccagtttc	1080
tacacaggag tgtacattct gattggagcc ggggccctca tgatgctggt tggtttcctg	1140
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ttggtgatat tcgccattga gatagccgcc gccgtctggg gctataacca caaggatgag	1260
gtgattaaag aactccagga gttttacaag gacacctacc aaaagttacg gagcaaggat	1320
gaaccccagc gggaaacact caaagccatc catatggcgt tggactgctg tggcatagct	1380
ggtccttttg agcagtttat ctcggacacc tgccccaaga aacagctttt ggaaagtttc	1440
caggttaagc cctgccctga agccatcagt gaggtcttca acaacaagtt ccacatcatt	1500
ggagcagtgg gtatcggcat cgccgtgggtg atgatcttcg gcatgatctt cagcatgac	1560
ctgtgctgcg ccatccgcag gagccgagaa atgggtctag	1599

<210> 25
 <211> 149
 <212> PRT
 <213> Mus musculus

<400> 25

Ala	Pro	Thr	Ser	Ser	Ser	Thr	Ser	Ser	Ser	Thr	Ala	Glu	Ala	Gln	Gln
1			5					10					15		

Gln	Gln	Gln	Gln	Gln	Gln	Gln	Gln	Gln	Gln	His	Leu	Glu	Gln	Leu	Leu
			20					25					30		

Met	Asp	Leu	Gln	Glu	Leu	Leu	Ser	Arg	Met	Glu	Asn	Tyr	Arg	Asn	Leu
		35					40					45			

Lys	Leu	Pro	Arg	Met	Leu	Thr	Phe	Lys	Phe	Tyr	Leu	Pro	Lys	Gln	Ala
	50					55					60				

Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu Leu Gly Pro Leu
65 70 75 80

Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe Gln Leu Glu Asp
85 90 95

Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val Val Lys Leu Lys
100 105 110

Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp Glu Ser Ala Thr
115 120 125

Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys Gln Ser Ile Ile
130 135 140

Ser Thr Ser Pro Gln
145

<210> 26
<211> 447
<212> DNA
<213> Mus musculus

<400> 26
gcaccactt caagctccac ttcaagctct acagcggaag cacagcagca gcagcagcag 60
cagcagcagc agcagcagca cctggagcag ctgttgatgg acctacagga gctcctgagc 120
aggatggaga attacaggaa cctgaaactc cccaggatgc tcaccttcaa attttacttg 180
cccaagcagg ccacagaatt gaaagatctt cagtgcctag aagatgaact tggacctctg 240
cggcatgttc tggatttgac tcaaagcaaa agctttcaat tggaagatgc tgagaatttc 300
atcagcaata tcagagtaac tgttgtaaaa ctaaagggtc ctgacaacac atttgagtgc 360
caattcgatg atgagtcagc aactgtggtg gactttctga ggagatggat agccttctgt 420
caaagcatca tctcaacaag ccctcaa 447

<210> 27
<211> 238
<212> PRT
<213> Mus musculus

<400> 27

Met Ala Val Glu Gly Gly Met Lys Cys Val Lys Phe Leu Leu Tyr Val
1 5 10 15

Leu Leu Leu Ala Phe Cys Ala Cys Ala Val Gly Leu Ile Ala Ile Gly
20 25 30

Val Ala Val Gln Val Val Leu Lys Gln Ala Ile Thr His Glu Thr Thr
35 40 45

Ala Gly Ser Leu Leu Pro Val Val Ile Ile Ala Val Gly Ala Phe Leu
50 55 60

Phe Leu Val Ala Phe Val Gly Cys Cys Gly Ala Cys Lys Glu Asn Tyr
65 70 75 80

Cys Leu Met Ile Thr Phe Ala Ile Phe Leu Ser Leu Ile Met Leu Val
85 90 95

Glu Val Ala Val Ala Ile Ala Gly Tyr Val Phe Arg Asp Gln Val Lys
100 105 110

Ser Glu Phe Asn Lys Ser Phe Gln Gln Gln Met Gln Asn Tyr Leu Lys
115 120 125

Asp Asn Lys Thr Ala Thr Ile Leu Asp Lys Leu Gln Lys Glu Asn Asn
130 135 140

Cys Cys Gly Ala Ser Asn Tyr Thr Asp Trp Glu Asn Ile Pro Gly Met
145 150 155 160

Ala Lys Asp Arg Val Pro Asp Ser Cys Cys Ile Asn Ile Thr Val Gly
165 170 175

Cys Gly Asn Asp Phe Lys Glu Ser Thr Ile His Thr Gln Gly Cys Val
180 185 190

Glu Thr Ile Ala Ile Trp Leu Arg Lys Asn Ile Leu Leu Val Ala Ala
195 200 205

Ala Ala Leu Gly Ile Ala Phe Val Glu Val Leu Gly Ile Ile Phe Ser
210 215 220

Cys Cys Leu Val Lys Ser Ile Arg Ser Gly Tyr Glu Val Met
225 230 235

<210> 28
<211> 717
<212> DNA
<213> Mus musculus

<400> 28
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ttctgcgctt gtgcagtggg attgatcgcc attggtgtag cggttcaggt tgtcttgaag 120
caggccatta cccatgagac tactgctggc tcgctgttgc ctgtgggtcat cattgcagtg 180
ggcgccttcc tcttcctggg ggcctttgtg ggctgctgtg gggcctgcaa ggagaactac 240
tgtctcatga ttacatttgc catcttcctg tctcttatca tgcttgtgga ggtggctgtg 300
gccattgctg gctatgtgtt tagagaccag gtgaagtcag agtttaataa aagcttccag 360
cagcagatgc agaattacct taaagacaac aaaacagcca ctattttgga caaattgcag 420
aaagaaaata actgctgtgg agcttctaac tacacagact gggaaaacat ccccgcatg 480
gccaaggaca gagtccccga ttcttgctgc atcaacataa ctgtgggctg tgggaatgat 540
ttcaaggaat ccactatcca taccagggc tgcgtggaga ctatagcaat atggctaagg 600
aagaacatac tgctgggtggc tgcagcggcc ctgggcattg cttttgtgga ggtcttggga 660
attatcttct cctgctgtct ggtgaagagt attcgaagtg gctatgaagt aatgtag 717

<210> 29
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> synthesized peptide sequence

<400> 29

Gly Gly Gly Gly Ser
1 5

<210> 30

<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<223> synthesized DNA sequence

<400> 30
ggaggaggag gaagc

15

<210> 31
<211> 397
<212> PRT
<213> Artificial Sequence

<220>
<223> peptide sequence derived from mus musculus

<400> 31

Met Ala Val Glu Gly Gly Met Lys Cys Val Lys Phe Leu Leu Tyr Val
1 5 10 15

Leu Leu Leu Ala Phe Cys Ala Cys Ala Val Gly Leu Ile Ala Ile Gly
20 25 30

Val Ala Val Gln Val Val Leu Lys Gln Ala Ile Thr His Glu Thr Thr
35 40 45

Ala Gly Ser Leu Leu Pro Val Val Ile Ile Ala Val Gly Ala Phe Leu
50 55 60

Phe Leu Val Ala Phe Val Gly Cys Cys Gly Ala Cys Lys Glu Asn Tyr
65 70 75 80

Cys Leu Met Ile Thr Phe Ala Ile Phe Leu Ser Leu Ile Met Leu Val
85 90 95

Glu Val Ala Val Ala Ile Ala Gly Tyr Val Phe Arg Asp Gln Val Lys
100 105 110

Ser Glu Phe Asn Lys Ser Phe Gln Gln Gln Met Gln Asn Tyr Leu Lys
115 120 125

Asp Asn Lys Thr Ala Thr Ile Leu Asp Lys Leu Gln Lys Glu Asn Asn

130

135

140

Cys Cys Gly Ala Ser Asn Tyr Thr Asp Trp Glu Asn Ile Pro Gly Met
 145 150 155 160

Ala Lys Asp Arg Val Pro Asp Ser Cys Cys Gly Gly Gly Gly Ser Ala
 165 170 175

Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala Glu Ala Gln Gln Gln
 180 185 190

Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu Glu Gln Leu Leu Met
 195 200 205

Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn Tyr Arg Asn Leu Lys
 210 215 220

Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu Pro Lys Gln Ala Thr
 225 230 235 240

Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu Leu Gly Pro Leu Arg
 245 250 255

His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe Gln Leu Glu Asp Ala
 260 265 270

Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val Val Lys Leu Lys Gly
 275 280 285

Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp Glu Ser Ala Thr Val
 290 295 300

Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys Gln Ser Ile Ile Ser
 305 310 315 320

Thr Ser Pro Gln Gly Gly Gly Gly Ser Ile Asn Ile Thr Val Gly Cys
 325 330 335

Gly Asn Asp Phe Lys Glu Ser Thr Ile His Thr Gln Gly Cys Val Glu
 340 345 350

Thr Ile Ala Ile Trp Leu Arg Lys Asn Ile Leu Leu Val Ala Ala Ala
355 360 365

Ala Leu Gly Ile Ala Phe Val Glu Val Leu Gly Ile Ile Phe Ser Cys
370 375 380

Cys Leu Val Lys Ser Ile Arg Ser Gly Tyr Glu Val Met
385 390 395

<210> 32
<211> 1194
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence derived from mus musculus

<400> 32
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ttctgcgctt gtgcagtggg attgatcgcc attggtgtag cggttcaggt tgtcttgaag 120
caggccatta cccatgagac tactgctggc tcgctgttgc ctgtgggtcat cattgcagtg 180
ggcgccttcc tcttcctggt ggcctttgtg ggctgctgtg gggcctgcaa ggagaactac 240
tgtctcatga ttacatttgc catcttcctg tctcttatca tgcttgtgga ggtggctgtg 300
gccattgctg gctatgtgtt tagagaccag gtgaagtcag agtttaataa aagcttccag 360
cagcagatgc agaattacct taaagacaac aaaacagcca ctattttgga caaattgcag 420
aaagaaaata actgctgtgg agcttctaac tacacagact gggaaaacat ccccgcatg 480
gccaaggaca gagtccccga ttcttgctgc ggaggaggag gaagcgcacc cacttcaagc 540
tccacttcaa gctctacagc ggaagcacag cagcagcagc agcagcagca gcagcagcag 600
cagcacctgg agcagctggt gatggacctc caggagctcc tgagcaggat ggagaattac 660
aggaacctga aactccccag gatgctcacc ttcaaatttt acttgcccaa gcaggccaca 720
gaattgaaag atcttcagtg cctagaagat gaacttggac ctctgctggca tgttctggat 780
ttgactcaaa gcaaaagctt tcaattggaa gatgctgaga atttcatcag caatatcaga 840
gtaactgttg taaaactaaa gggctctgac aacacatttg agtgccaatt cgatgatgag 900
tcagcaactg tgggtggactt tctgaggaga tggatagcct tctgtcaaag catcatctca 960

acaagccctc aaggaggagg aggaagcatc aacataactg tgggctgtgg gaatgatttc	1020
aaggaatcca ctatccatac ccagggtctgc gtggagacta tagcaatatg gctaaggaag	1080
aacatactgc tgggtggctgc agcggccctg ggcattgctt ttgtggaggt cttgggaatt	1140
atcttctcct gctgtctggg gaagagtatt cgaagtggct atgaagtaat gtag	1194

<210> 33
 <211> 27
 <212> PRT
 <213> Mus musculus

<400> 33

Met	Ala	Leu	Gln	Ile	Pro	Ser	Leu	Leu	Leu	Ser	Ala	Ala	Val	Val	Val
1			5					10					15		

Leu	Met	Val	Leu	Ser	Ser	Pro	Gly	Thr	Glu	Gly
		20						25		

<210> 34
 <211> 81
 <212> DNA
 <213> Mus musculus

<400> 34

atggctctgc agatccccag cctcctcctc tcggctgctg tgggtggtgct gatggtgctg	60
agcagcccag ggactgaggg c	81

<210> 35
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> peptide sequence derived from OVA

<400> 35

Ile	Ser	Gln	Ala	Val	His	Ala	Ala	His	Ala	Glu	Ile	Asn	Glu	Ala	Gly
1				5					10					15	

Arg

<210> 36

<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence derived from OVA

<400> 36
atatctcaag ctgtccatgc agcacatgca gaaatcaatg aagcaggcag a

51

<210> 37
<211> 238
<212> PRT
<213> Mus musculus

<400> 37

Gly Asp Ser Glu Arg His Phe Val Tyr Gln Phe Met Gly Glu Cys Tyr
1 5 10 15

Phe Thr Asn Gly Thr Gln Arg Ile Arg Tyr Val Thr Arg Tyr Ile Tyr
20 25 30

Asn Arg Glu Glu Tyr Val Arg Tyr Asp Ser Asp Val Gly Glu His Arg
35 40 45

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
50 55 60

Pro Glu Ile Leu Glu Arg Thr Arg Ala Glu Leu Asp Thr Val Cys Arg
65 70 75 80

His Asn Tyr Glu Gly Pro Glu Thr His Thr Ser Leu Arg Arg Leu Glu
85 90 95

Gln Pro Asn Val Val Ile Ser Leu Ser Arg Thr Glu Ala Leu Asn His
100 105 110

His Asn Thr Leu Val Cys Ser Val Thr Asp Phe Tyr Pro Ala Lys Ile
115 120 125

Lys Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Thr Val Gly Val Ser
130 135 140

Ser Thr Gln Leu Ile Arg Asn Gly Asp Trp Thr Phe Gln Val Leu Val
145 150 155 160

Met Leu Glu Met Thr Pro Arg Arg Gly Glu Val Tyr Thr Cys His Val
165 170 175

Glu His Pro Ser Leu Lys Ser Pro Ile Thr Val Glu Trp Arg Ala Gln
180 185 190

Ser Glu Ser Ala Trp Ser Lys Met Leu Ser Gly Ile Gly Gly Cys Val
195 200 205

Leu Gly Val Ile Phe Leu Gly Leu Gly Leu Phe Ile Arg His Arg Ser
210 215 220

Gln Lys Gly Pro Arg Gly Pro Pro Pro Ala Gly Leu Leu Gln
225 230 235

<210> 38
<211> 714
<212> DNA
<213> Mus musculus

<400> 38
ggagactccg aaaggcattt cgtgtaccag ttcattgggag agtgctactt caccaacggg 60
acgcagcgca tacgatattg gaccagatac atctacaacc gggaggagta cgtgcgctac 120
gacagcgacg tgggagcgca ccgcgcggtg accgagctgg ggcggccaga cgccgagtac 180
tggaacagcc agccggagat cctggagcga acgcggggccg agctggacac ggtgtgcaga 240
cacaactacg agggggccga gaccacacc tccctgcggc ggcttgaaca gccaatgtc 300
gtcatctccc tgtccaggac agaggccctc aaccaccaca acactctggt ctgctcagtg 360
acagatttct acccagccaa gatcaaagtg cgctgggttc ggaatggcca ggaggagacg 420
gtgggggtct catccacaca gcttattagg aatggggact ggaccttcca ggtcctggtc 480
atgctggaga tgaccctcg gcggggagag gtctacacct gtcacgtgga gcatcccagc 540
ctgaagagcc ccatcactgt ggagtggagg gcacagtctg agtctgcctg gagcaagatg 600
ttgagcggca tcgggggctg cgtgcttggg gtgatcttcc tcgggcttgg ctttttcac 660
cgtcacagga gtcagaaagg acctcgaggc cctcctccag cagggtcct gcag 714

<210> 39
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> synthesized peptide sequence

<400> 39

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10

<210> 40
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> synthesized DNA sequence

<400> 40

ggaggaggag gaagcggagg aggaggaagc gga

33

<210> 41
<211> 293
<212> PRT
<213> Artificial Sequence

<220>
<223> peptide sequence derived from OVA, mus musculus

<400> 41

Met Ala Leu Gln Ile Pro Ser Leu Leu Leu Ser Ala Ala Val Val Val
1 5 10 15

Leu Met Val Leu Ser Ser Pro Gly Thr Glu Gly Ile Ser Gln Ala Val
20 25 30

His Ala Ala His Ala Glu Ile Asn Glu Ala Gly Arg Gly Gly Gly Gly
35 40 45

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ser Glu Arg His Phe Val Tyr
50 55 60

Gln Phe Met Gly Glu Cys Tyr Phe Thr Asn Gly Thr Gln Arg Ile Arg

65

70

75

80

Tyr Val Thr Arg Tyr Ile Tyr Asn Arg Glu Glu Tyr Val Arg Tyr Asp
85 90 95

Ser Asp Val Gly Glu His Arg Ala Val Thr Glu Leu Gly Arg Pro Asp
100 105 110

Ala Glu Tyr Trp Asn Ser Gln Pro Glu Ile Leu Glu Arg Thr Arg Ala
115 120 125

Glu Leu Asp Thr Val Cys Arg His Asn Tyr Glu Gly Pro Glu Thr His
130 135 140

Thr Ser Leu Arg Arg Leu Glu Gln Pro Asn Val Val Ile Ser Leu Ser
145 150 155 160

Arg Thr Glu Ala Leu Asn His His Asn Thr Leu Val Cys Ser Val Thr
165 170 175

Asp Phe Tyr Pro Ala Lys Ile Lys Val Arg Trp Phe Arg Asn Gly Gln
180 185 190

Glu Glu Thr Val Gly Val Ser Ser Thr Gln Leu Ile Arg Asn Gly Asp
195 200 205

Trp Thr Phe Gln Val Leu Val Met Leu Glu Met Thr Pro Arg Arg Gly
210 215 220

Glu Val Tyr Thr Cys His Val Glu His Pro Ser Leu Lys Ser Pro Ile
225 230 235 240

Thr Val Glu Trp Arg Ala Gln Ser Glu Ser Ala Trp Ser Lys Met Leu
245 250 255

Ser Gly Ile Gly Gly Cys Val Leu Gly Val Ile Phe Leu Gly Leu Gly
260 265 270

Leu Phe Ile Arg His Arg Ser Gln Lys Gly Pro Arg Gly Pro Pro Pro
275 280 285

Ala Gly Leu Leu Gln
290

<210> 42
<211> 879
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence derived from OVA, mus musculus

<400> 42
atggctctgc agatccccag cctcctcctc tcggctgctg tgggtggtgct gatggtgctg 60
agcagcccag ggactgaggg catatctcaa gctgtccatg cagcacatgc agaaatcaat 120
gaagcaggca gaggaggagg aggaagcggg ggaggaggaa gcggaggaga ctccgaaagg 180
catttcgtgt accagttcat gggcgagtgc tacttcacca acgggacgca gcgcatacga 240
tatgtgacca gatacatcta caaccgggag gagtacgtgc gctacgacag cgacgtgggc 300
gagcaccgcg cggtgaccga gctggggcgg ccagacgccg agtactggaa cagccagccg 360
gagatcctgg agcgaacgcg ggccgagctg gacacggtgt gcagacacaa ctacgagggg 420
ccggagaccc acacctccct gcggcggttt gaacagccca atgtcgtcat ctccctgtcc 480
aggacagagg ccctcaacca ccacaacact ctggtctgct cagtgcacaga tttctaccca 540
gccaagatca aagtgcgctg gttccggaat ggccaggagg agacggtggg ggtctcatcc 600
acacagctta ttaggaatgg ggactggacc ttccaggtcc tggatcatgct ggagatgacc 660
cctcggcggg gagaggctta cacctgtcac gtggagcatc ccagcctgaa gagccccatc 720
actgtggagt ggagggcaca gtctgagtct gcctggagca agatgttgag cggcatcggg 780
ggctgcgtgc ttgggggtgat cttcctcggg cttggccttt tcatccgtca caggagtcag 840
aaaggacctc gaggccctcc tccagcaggg ctctgcag 879

<210> 43
<211> 529
<212> PRT
<213> Artificial Sequence

<220>
<223> peptide sequence derived from OVA, mus musculus

<400> 43

Met Ala Leu Gln Ile Pro Ser Leu Leu Leu Ser Ala Ala Val Val Val
1 5 10 15

Leu Met Val Leu Ser Ser Pro Gly Thr Glu Gly Ile Ser Gln Ala Val
20 25 30

His Ala Ala His Ala Glu Ile Asn Glu Ala Gly Arg Gly Gly Gly Gly
35 40 45

Ser Gly Gly Gly Gly Ser Gly Gly Asp Ser Glu Arg His Phe Val Tyr
50 55 60

Gln Phe Met Gly Glu Cys Tyr Phe Thr Asn Gly Thr Gln Arg Ile Arg
65 70 75 80

Tyr Val Thr Arg Tyr Ile Tyr Asn Arg Glu Glu Tyr Val Arg Tyr Asp
85 90 95

Ser Asp Val Gly Glu His Arg Ala Val Thr Glu Leu Gly Arg Pro Asp
100 105 110

Ala Glu Tyr Trp Asn Ser Gln Pro Glu Ile Leu Glu Arg Thr Arg Ala
115 120 125

Glu Leu Asp Thr Val Cys Arg His Asn Tyr Glu Gly Pro Glu Thr His
130 135 140

Thr Ser Leu Arg Arg Leu Glu Gln Pro Asn Val Val Ile Ser Leu Ser
145 150 155 160

Arg Thr Glu Ala Leu Asn His His Asn Thr Leu Val Cys Ser Val Thr
165 170 175

Asp Phe Tyr Pro Ala Lys Ile Lys Val Arg Trp Phe Arg Asn Gly Gln
180 185 190

Glu Glu Thr Val Gly Val Ser Ser Thr Gln Leu Ile Arg Asn Gly Asp
195 200 205

Trp Thr Phe Gln Val Leu Val Met Leu Glu Met Thr Pro Arg Arg Gly

210

215

220

Glu Val Tyr Thr Cys His Val Glu His Pro Ser Leu Lys Ser Pro Ile
 225 230 235 240

Thr Val Glu Trp Arg Ala Gln Ser Glu Ser Ala Trp Ser Lys Met Leu
 245 250 255

Ser Gly Ile Gly Gly Cys Val Leu Gly Val Ile Phe Leu Gly Leu Gly
 260 265 270

Leu Phe Ile Arg His Arg Ser Gln Lys Gly Pro Arg Gly Pro Pro Pro
 275 280 285

Ala Gly Leu Leu Gln Met Gly Val Glu Gly Cys Thr Lys Cys Ile Lys
 290 295 300

Tyr Leu Leu Phe Val Phe Asn Phe Val Phe Trp Leu Ala Gly Gly Val
 305 310 315 320

Ile Leu Gly Val Ala Leu Trp Leu Arg His Asp Pro Gln Thr Thr Ser
 325 330 335

Leu Leu Tyr Leu Glu Leu Gly Asn Lys Pro Ala Pro Asn Thr Phe Tyr
 340 345 350

Val Gly Ile Tyr Ile Leu Ile Ala Val Gly Ala Val Met Met Phe Val
 355 360 365

Gly Phe Leu Gly Cys Tyr Gly Ala Ile Gln Glu Ser Gln Cys Leu Leu
 370 375 380

Gly Thr Phe Phe Thr Cys Leu Val Ile Leu Phe Ala Cys Glu Val Ala
 385 390 395 400

Ala Gly Ile Trp Gly Phe Val Asn Lys Asp Gln Ile Ala Lys Asp Val
 405 410 415

Lys Gln Phe Tyr Asp Gln Ala Leu Gln Gln Ala Val Met Asp Asp Asp
 420 425 430

Ala Asn Asn Ala Lys Ala Val Val Lys Thr Phe His Glu Thr Leu Asn
435 440 445

Cys Cys Gly Ser Asn Ala Leu Thr Thr Leu Thr Thr Thr Ile Leu Arg
450 455 460

Asn Ser Leu Cys Pro Ser Gly Gly Asn Ile Leu Thr Pro Leu Leu Gln
465 470 475 480

Gln Asp Cys His Gln Lys Ile Asp Glu Leu Phe Ser Gly Lys Leu Tyr
485 490 495

Leu Ile Gly Ile Ala Ala Ile Val Val Ala Val Ile Met Ile Phe Glu
500 505 510

Met Ile Leu Ser Met Val Leu Cys Cys Gly Ile Arg Asn Ser Ser Val
515 520 525

Tyr

<210> 44
<211> 1590
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence derived from OVA, mus musculus

<400> 44
atggctctgc agatccccag cctcctcctc tcggctgctg tgggtggtgct gatggtgctg 60
agcagcccag ggactgaggg catatctcaa gctgtccatg cagcacatgc agaaatcaat 120
gaagcaggca gaggaggagg aggaagcgga ggaggaggaa gcggaggaga ctccgaaagg 180
catttcgtgt accagttcat gggcgagtgc tacttcacca acgggacgca gcgcatacga 240
tatgtgacca gatacatcta caaccgggag gagtacgtgc gctacgacag cgacgtgggc 300
gagcaccgcg cggtgaccga gctggggcgg ccagacgccg agtactggaa cagccagccg 360
gagatcctgg agcgaacgcg ggccgagctg gacacggtgt gcagacacaa ctacgagggg 420
ccggagaccc acacctccct gcggcggctt gaacagccca atgtcgtcat ctccctgtcc 480

aggacagagg ccctcaacca ccacaacact ctggtctgct cagtgacaga tttctaccca	540
gccaagatca aagtgcgctg gttccggaat ggccaggagg agacggtggg ggtctcatcc	600
acacagctta ttaggaatgg ggactggacc ttccagggtcc tggatcatgct ggagatgacc	660
cctcggcggg gagaggctta cacctgtcac gtggagcatc ccagcctgaa gagccccatc	720
actgtggagt ggagggcaca gtctgagtct gcctggagca agatgttgag cggcatcggg	780
ggctgcgtgc ttgggggtgat cttcctcggg cttggccttt tcatccgtca caggagtcag	840
aaaggacctc gaggccctcc tccagcaggg ctctgcaga tgggggtgga gggctgcacc	900
aaatgcatca aatacctgct cttcgtcttc aatttcgtct tctggctggc tggaggcgtg	960
atcctaggtg tagctctgtg gttgcgtcat gatccacaga ccaccagcct gctgtacctg	1020
gaactgggaa acaaaccggc acccaacacc ttctacgtgg gcatctacat tctcattgct	1080
gtgggagctg tgatgatggt ttaggcttc ctgggggtgct atggggccat ccaggagtcc	1140
cagtgtctgc tggggacgtt cttcacctgc cttgtgatcc tgtttgcctg tgaggtggct	1200
gcaggcatct ggggcttcgt aaacaaagac cagatcgcca aggatgtgaa gcagttctat	1260
gaccaggccc ttcagcaagc tgtgatggat gatgatgcca acaatgcca ggctgtggtg	1320
aagactttcc atgagacgct caactgttgt ggctccaacg cactgaccac actgactacc	1380
accatactga ggaacagcct gtgtccctca ggcggcaaca tactcacccc cttactgcag	1440
caagattgtc atcagaaaat cgatgagctc ttctctggga agctgtacct cattggaatt	1500
gcagccattg tggtagctgt cattatgatc tttagatga ttctgagcat ggtgctgtgc	1560
tgtggcatcc ggaacagctc cgtgtactga	1590

<210> 45
 <211> 256
 <212> PRT
 <213> Mus musculus

<400> 45

Met	Pro	Arg	Ser	Arg	Ala	Leu	Ile	Leu	Gly	Val	Leu	Ala	Leu	Thr	Thr
1				5					10					15	

Met	Leu	Ser	Leu	Cys	Gly	Gly	Glu	Asp	Asp	Ile	Glu	Ala	Asp	His	Val
			20					25					30		

Gly Thr Tyr Gly Ile Ser Val Tyr Gln Ser Pro Gly Asp Ile Gly Gln
35 40 45

Tyr Thr Phe Glu Phe Asp Gly Asp Glu Leu Phe Tyr Val Asp Leu Asp
50 55 60

Lys Lys Glu Thr Val Trp Met Leu Pro Glu Phe Gly Gln Leu Ala Ser
65 70 75 80

Phe Asp Pro Gln Gly Gly Leu Gln Asn Ile Ala Val Val Lys His Asn
85 90 95

Leu Gly Val Leu Thr Lys Arg Ser Asn Ser Thr Pro Ala Thr Asn Glu
100 105 110

Ala Pro Gln Ala Thr Val Phe Pro Lys Ser Pro Val Leu Leu Gly Gln
115 120 125

Pro Asn Thr Leu Ile Cys Phe Val Asp Asn Ile Phe Pro Pro Val Ile
130 135 140

Asn Ile Thr Trp Leu Arg Asn Ser Lys Ser Val Ala Asp Gly Val Tyr
145 150 155 160

Glu Thr Ser Phe Phe Val Asn Arg Asp Tyr Ser Phe His Lys Leu Ser
165 170 175

Tyr Leu Thr Phe Ile Pro Ser Asp Asp Asp Ile Tyr Asp Cys Lys Val
180 185 190

Glu His Trp Gly Leu Glu Glu Pro Val Leu Lys His Trp Glu Pro Glu
195 200 205

Ile Pro Ala Pro Met Ser Glu Leu Thr Glu Thr Val Val Cys Ala Leu
210 215 220

Gly Leu Ser Val Gly Leu Val Gly Ile Val Val Gly Thr Ile Phe Ile
225 230 235 240

Ile Gln Gly Leu Arg Ser Gly Gly Thr Ser Arg His Pro Gly Pro Leu
245 250 255

<210> 46
<211> 771
<212> DNA
<213> Mus musculus

<400> 46
atgccgcgca gcagagctct gattctgggg gtcctcgccc tgaccaccat gctcagcctc 60
tgtggaggtg aagacgacat tgaggccgac cacgtaggca cctatggtat aagtgtatat 120
cagtctcctg gagacattgg ccagtacaca tttgaatttg atggtgatga gttgttctat 180
gtggacttgg ataagaagga gactgtctgg atgcttcctg agtttggcca attggcaagc 240
tttgaccccc aaggtggact gcaaaacata gctgtagtaa aacacaactt gggagtcttg 300
actaagaggt caaattccac ccagctacc aatgaggctc ctcaagcgac tgtgttcccc 360
aagtcccctg tgctgctggg tcagcccaac accctcatct gctttgtgga caacatcttc 420
cctcctgtga tcaacatcac atggctcaga aatagcaagt cagtcgcaga cggtgtttat 480
gagaccagct tcttcgtcaa ccgtgactat tccttcaca agctgtctta tctcaccttc 540
atcccttctg acgatgacat ttatgactgc aaggtggaac actggggcct ggaggagccg 600
gttctgaaac actgggaacc tgagattcca gccccatgt cagagctgac agagactgtg 660
gtctgtgccc tggggttgtc tgtgggcctt gtgggcatcg tgggtgggcac catcttcac 720
attcaaggcc tgcgatcagg tggcacctcc agacaccag ggcctttatg a 771

<210> 47
<211> 390
<212> PRT
<213> Artificial Sequence

<220>
<223> peptide sequence derived from mus musculus

<400> 47

Met Pro Pro Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Pro
1 5 10 15

Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr
20 25 30

Ser Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala

35

40

45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser
 50 55 60

Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu
 65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu
 85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu
 100 105 110

Met Val Asp Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser
 115 120 125

His Ser Ile Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val
 130 135 140

Pro Glu Pro Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu
 145 150 155 160

Lys Ser Ser Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn
 165 170 175

Asn Ser Trp Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr
 180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu
 195 200 205

Asn Gln Gly Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala His Ser Ser
 210 215 220

Ser Asp Ser Lys Asp Asn Lys Leu His Val Glu Ile Asn Gly Ile Ser
 225 230 235 240

Pro Lys Arg Arg Gly Asp Leu Gly Thr Ile His Asp Met Asn Arg Pro
 245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser
275 280 285

Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys
290 295 300

Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn
305 310 315 320

Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr
325 330 335

Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala
340 345 350

Ser Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr
355 360 365

Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val
370 375 380

Arg Ser Cys Lys Cys Ser
385 390

<210> 48
<211> 1173
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence derived from mus musculus

<400> 48
atgccgccct cggggctgcg gctactgccg cttctgctcc cactcccgtagt 60
ctgacgcccc ggaggccagc cgcgggactc tccacctcta agaccatcga catggagctg 120
gtgaaacgga agcgcacga agccatccgt ggccagatcc tgtccaaact aaggctcgcc 180
agtcccccaa gccaggggga ggtaccgccc ggcccgtgc cagaggcggt gctcgctttg 240

tacaacagca cccgcgaccg ggtggcaggc gagagcgccg acccagagcc ggagcccgaa	300
gcggaactact atgctaaaga ggtcacccgc gtgctaattg tggaccgcaa caacgccatc	360
tatgagaaaa ccaaagacat ctcacacagt atatatatgt tcttcaatac gtcagacatt	420
cgggaagcag tgcccgaacc cccattgctg tcccgtgcag agctgcgctt gcagagatta	480
aatcaagtg tggagcaaca tgtggaactc taccagaaat atagcaacaa ttcctggcgt	540
taccttggtg accggctgct gacccccact gatacgcctg agtggctgtc ttttgacgtc	600
actggagttg tacggcagtg gctgaaccaa ggagacggaa tacagggctt tcgattcagc	660
gctcactctt cttctgacag caaagataac aaactccacg tggaatatcaa cgggatcagc	720
cccaaacgtc ggggcgacct gggcaccatc catgacatga accggccctt cctgctcctc	780
atggccaccc ccctggaaag ggcccagcac ctgcacagct cacggcaccg gagagccctg	840
gataccaact attgcttcag ctccacagag aagaactgct gtgtgcggca gctgtacatt	900
gacttttagga aggacctggg ttggaagtgg atccacgagc ccaagggcta ccatgccaac	960
ttctgtctgg gaccctgccc ctatatattg agcctggaca cacagtacag caaggtcctt	1020
gccctctaca accaacacaa cccgggcgct tcggcgtcac cgtgctgcgt gccgcaggct	1080
ttggagccac tgcccatcgt ctactacgtg ggtcgcaagc ccaaggtgga gcagttgtcc	1140
aacatgattg tgcgctcctg caagtgcagc tga	1173

<210> 49
 <211> 441
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> peptide sequence derived from mus musculus

<400> 49

Ala	Ser	Gly	Asp	Phe	Cys	Asp	Ser	Ser	Leu	Cys	Leu	Asn	Gly	Gly	Thr
1				5					10					15	

Cys	Leu	Thr	Gly	Gln	Asp	Asn	Asp	Ile	Tyr	Cys	Leu	Cys	Pro	Glu	Gly
			20					25					30		

Phe	Thr	Gly	Leu	Val	Cys	Asn	Glu	Thr	Glu	Arg	Gly	Pro	Cys	Ser	Pro
		35					40					45			

Asn Pro Cys Tyr Asn Asp Ala Lys Cys Leu Val Thr Leu Asp Thr Gln
50 55 60

Arg Gly Glu Ile Phe Thr Glu Tyr Ile Cys Gln Cys Pro Val Gly Tyr
65 70 75 80

Ser Gly Ile His Cys Glu Thr Glu Thr Asn Tyr Tyr Asn Leu Asp Gly
85 90 95

Glu Tyr Met Phe Thr Thr Ala Val Pro Asn Thr Ala Val Pro Thr Pro
100 105 110

Ala Pro Thr Pro Asp Leu Ser Asn Asn Leu Ala Ser Arg Cys Ser Thr
115 120 125

Gln Leu Gly Met Glu Gly Gly Ala Ile Ala Asp Ser Gln Ile Ser Ala
130 135 140

Ser Ser Val Tyr Met Gly Phe Met Gly Leu Gln Arg Trp Gly Pro Glu
145 150 155 160

Leu Ala Arg Leu Tyr Arg Thr Gly Ile Val Asn Ala Trp Thr Ala Ser
165 170 175

Asn Tyr Asp Ser Lys Pro Trp Ile Gln Val Asn Leu Leu Arg Lys Met
180 185 190

Arg Val Ser Gly Val Met Thr Gln Gly Ala Ser Arg Ala Gly Arg Ala
195 200 205

Glu Tyr Leu Lys Thr Phe Lys Val Ala Tyr Ser Leu Asp Gly Arg Lys
210 215 220

Phe Glu Phe Ile Gln Asp Glu Ser Gly Gly Asp Lys Glu Phe Leu Gly
225 230 235 240

Asn Leu Asp Asn Asn Ser Leu Lys Val Asn Met Phe Asn Pro Thr Leu
245 250 255

Glu Ala Gln Tyr Ile Lys Leu Tyr Pro Val Ser Cys His Arg Gly Cys

260

265

270

Thr Leu Arg Phe Glu Leu Leu Gly Cys Glu Leu His Gly Cys Ser Glu
 275 280 285

Pro Leu Gly Leu Lys Asn Asn Thr Ile Pro Asp Ser Gln Met Ser Ala
 290 295 300

Ser Ser Ser Tyr Lys Thr Trp Asn Leu Arg Ala Phe Gly Trp Tyr Pro
 305 310 315 320

His Leu Gly Arg Leu Asp Asn Gln Gly Lys Ile Asn Ala Trp Thr Ala
 325 330 335

Gln Ser Asn Ser Ala Lys Glu Trp Leu Gln Val Asp Leu Gly Thr Gln
 340 345 350

Arg Gln Val Thr Gly Ile Ile Thr Gln Gly Ala Arg Asp Phe Gly His
 355 360 365

Ile Gln Tyr Val Ala Ser Tyr Lys Val Ala His Ser Asp Asp Gly Val
 370 375 380

Gln Trp Thr Val Tyr Glu Glu Gln Gly Ser Ser Lys Val Phe Gln Gly
 385 390 395 400

Asn Leu Asp Asn Asn Ser His Lys Lys Asn Ile Phe Glu Lys Pro Phe
 405 410 415

Met Ala Arg Tyr Val Arg Val Leu Pro Val Ser Trp His Asn Arg Ile
 420 425 430

Thr Leu Arg Leu Glu Leu Leu Gly Cys
 435 440

<210> 50

<211> 1326

<212> DNA

<213> Artificial Sequence

<220>

<223> DNA sequence derived from mus musculus

<400> 50

gcgtctggtg acttctgtga ctccagcctg tgcctgaacg gtggcacctg cttgacgggc	60
caagacaatg acatctactg cctctgccct gaaggcttca caggccttgt gtgcaatgag	120
actgagagag gaccatgctc cccaaaccct tgctacaatg atgccaaatg tctggtgact	180
ttggacacac agcgtgggga aatcttcacc gaatacatct gccagtgcc tgtgggctac	240
tcgggcatcc actgtgaaac cgagaccaac tactacaacc tggatggaga atacatgttc	300
accacagccg tccccaatac tgccgtcccc accccggccc ccacccccga tctttccaac	360
aacctagcct cccgttggtc tacacagctg ggcatggaag ggggcgccat tgctgattca	420
cagatttccg cctcgtctgt gtatatgggt ttcatgggct tgcagcgtg gggcccggag	480
ctggctcgtc tgtaccgcac agggatcgtc aatgcctgga cagccagcaa ctatgatagc	540
aagccctgga tccaggtgaa ctttctgcgg aagatgcggg tatcaggtgt gatgacgcag	600
ggtgccagcc gtgccgggag ggcggagtac ctgaagacct tcaaggtggc ttacagcctc	660
gacggacgca agtttgagtt catccaggat gaaagcgggt gagacaagga gtttttgggt	720
aacctggaca acaacagcct gaaggttaac atgttcaacc cgactctgga ggcacagtac	780
ataaagctgt accctgtttc gtgccaccgc ggctgcaccc tccgcttcga gctcctgggc	840
tgtgagttgc acggatgttc tgagcccctg ggcctgaaga ataacacaat tcctgacagc	900
cagatgtcag cctccagcag ctacaagaca tggaacctgc gtgcttttgg ctggtacccc	960
cacttgggaa ggctggataa tcagggaag atcaatgcct ggacggctca gagcaacagt	1020
gccaaggaat ggctgcaggt tgacctgggc actcagaggc aagtgcagg aatcatcacc	1080
cagggggccc gtgactttgg ccacatccag tatgtggcgt cctacaaggt agcccacagt	1140
gatgatggtg tgcagtggac tgtatatgag gagcaaggaa gcagcaaggt cttccagggc	1200
aacttggaca acaactccca caagaagaac atcttcgaga aacccttcac ggctcgttac	1260
gtgcgtgtcc ttccagtgtc ctggcataac cgcatacccc tgcgcctgga gctgctgggc	1320
tgtaa	1326

<210> 51
 <211> 836
 <212> PRT
 <213> Artificial Sequence

<220>

<223> peptide sequence derived from mus musculus

<400> 51

Met Pro Pro Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Pro
1 5 10 15

Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr
20 25 30

Ser Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala
35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser
50 55 60

Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu
65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu
85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu
100 105 110

Met Val Asp Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser
115 120 125

His Ser Ile Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val
130 135 140

Pro Glu Pro Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu
145 150 155 160

Lys Ser Ser Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn
165 170 175

Asn Ser Trp Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu

195

200

205

Asn Gln Gly Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala His Ser Ser
 210 215 220

Ser Asp Ser Lys Asp Asn Lys Leu His Val Glu Ile Asn Gly Ile Ser
 225 230 235 240

Pro Lys Arg Arg Gly Asp Leu Gly Thr Ile His Asp Met Asn Arg Pro
 245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His
 260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser
 275 280 285

Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys
 290 295 300

Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn
 305 310 315 320

Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr
 325 330 335

Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala
 340 345 350

Ser Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr
 355 360 365

Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val
 370 375 380

Arg Ser Cys Lys Cys Ser Gly Gly Gly Gly Ser Ala Ser Gly Asp Phe
 385 390 395 400

Cys Asp Ser Ser Leu Cys Leu Asn Gly Gly Thr Cys Leu Thr Gly Gln
 405 410 415

Asp Asn Asp Ile Tyr Cys Leu Cys Pro Glu Gly Phe Thr Gly Leu Val
420 425 430

Cys Asn Glu Thr Glu Arg Gly Pro Cys Ser Pro Asn Pro Cys Tyr Asn
435 440 445

Asp Ala Lys Cys Leu Val Thr Leu Asp Thr Gln Arg Gly Glu Ile Phe
450 455 460

Thr Glu Tyr Ile Cys Gln Cys Pro Val Gly Tyr Ser Gly Ile His Cys
465 470 475 480

Glu Thr Glu Thr Asn Tyr Tyr Asn Leu Asp Gly Glu Tyr Met Phe Thr
485 490 495

Thr Ala Val Pro Asn Thr Ala Val Pro Thr Pro Ala Pro Thr Pro Asp
500 505 510

Leu Ser Asn Asn Leu Ala Ser Arg Cys Ser Thr Gln Leu Gly Met Glu
515 520 525

Gly Gly Ala Ile Ala Asp Ser Gln Ile Ser Ala Ser Ser Val Tyr Met
530 535 540

Gly Phe Met Gly Leu Gln Arg Trp Gly Pro Glu Leu Ala Arg Leu Tyr
545 550 555 560

Arg Thr Gly Ile Val Asn Ala Trp Thr Ala Ser Asn Tyr Asp Ser Lys
565 570 575

Pro Trp Ile Gln Val Asn Leu Leu Arg Lys Met Arg Val Ser Gly Val
580 585 590

Met Thr Gln Gly Ala Ser Arg Ala Gly Arg Ala Glu Tyr Leu Lys Thr
595 600 605

Phe Lys Val Ala Tyr Ser Leu Asp Gly Arg Lys Phe Glu Phe Ile Gln
610 615 620

Asp Glu Ser Gly Gly Asp Lys Glu Phe Leu Gly Asn Leu Asp Asn Asn

[illegible]

<210> 52
<211> 2511
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence derived from mus musculus

<400> 52
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ctgacgcccg ggaggccagc cgcgggactc tccacctcta agaccatcga catggagctg 120
gtgaaacgga agcgcacga agccatccgt ggccagatcc tgtccaaact aaggctcgcc 180
agtcccccaa gccaggggga ggtaccgccc ggcccgtgc cagaggcggt gctcgctttg 240
tacaacagca cccgcgaccg ggtggcaggc gagagcgccg acccagagcc ggagcccga 300
gcggtactat atgctaaaga ggtcaccgc gtgctaattg tggaccgcaa caacgccatc 360
tatgagaaaa ccaaagacat ctacacagt atatatatgt tcttcaatac gtcagacatt 420
cgggaagcag tgcccgaacc cccattgctg tcccgtgcag agctgcgctt gcagagatta 480
aatcaagtg tggagcaaca tgtggaactc taccagaaat atagcaacaa ttcctggcgt 540
taccttggtg accggctgct gacccccact gatagcctg agtggctgtc ttttgacgtc 600
actggagttg tacggcagt gctgaaccaa ggagacggaa tacagggtt tcgattcagc 660
gctcactctt cttctgacag caaagataac aaactccacg tggaaatcaa cgggatcagc 720
cccaaacgtc ggggcgacct gggcaccatc catgacatga accggccctt cctgctcctc 780
atggccaccc ccctggaaag ggcccagcac ctgcacagct cacggcaccg gagagccctg 840
gataccaact attgcttcag ctccacagag aagaactgct gtgtgcggca gctgtacatt 900
gacttttagga aggacctggg ttggaagtgg atccacgagc ccaagggtta ccatgccaac 960
ttctgtctgg gaccctgccc ctatatgttg agcctggaca cacagtacag caaggtcctt 1020
gccctctaca accaacacaa cccgggcgct tcggcgctcac cgtgctgcgt gccgcaggct 1080
ttggagccac tgcccatcgt ctactacgtg ggtcgcaagc ccaagggtga gcagttgtcc 1140
aacatgattg tgcgctcctg caagtgcagc ggaggaggag gaagcgcgtc tggtgacttc 1200
tgtgactcca gcctgtgcct gaacggtggc acctgcttga cgggccaaga caatgacatc 1260
tactgcctct gccctgaagg cttcacaggc cttgtgtgca atgagactga gagaggacca 1320

tgctcccca	acccttgcta	caatgatgcc	aaatgtctgg	tgactttgga	cacacagcgt	1380
ggggaaatct	tcaccgaata	catctgccag	tgccctgtgg	gctactcggg	catccactgt	1440
gaaaccgaga	ccaactacta	caacctggat	ggagaataca	tgttcaccac	agccgtcccc	1500
aatactgccg	tccccacccc	ggccccacc	cccgatcttt	ccaacaacct	agcctcccgt	1560
tgttctacac	agctgggcat	ggaagggggc	gccattgctg	attcacagat	ttccgcctcg	1620
tctgtgtata	tgggtttcat	gggcttgtag	cgctggggcc	cggagctggc	tcgtctgtac	1680
cgcacaggga	tcgtcaatgc	ctggacagcc	agcaactatg	atagcaagcc	ctggatccag	1740
gtgaaccttc	tgcggaagat	gcgggtatca	ggtgtgatga	cgcagggtgc	cagccgtgcc	1800
gggagggcgg	agtacctgaa	gaccttcaag	gtggcttaca	gcctcgacgg	acgcaagttt	1860
gagttcatcc	aggatgaaag	cgggtggagac	aaggagtttt	tgggtaacct	ggacaacaac	1920
agcctgaagg	ttaacatggt	caacccgact	ctggaggcac	agtacataaa	gctgtaccct	1980
gtttcgtgcc	accgcggctg	caccctccgc	ttcgagctcc	tgggctgtga	gttgacagga	2040
tgttctgagc	ccctgggcct	gaagaataac	acaattcctg	acagccagat	gtcagcctcc	2100
agcagctaca	agacatggaa	cctgcgtgct	tttggctggg	acccccactt	gggaaggctg	2160
gataatcagg	gcaagatcaa	tgcctggacg	gctcagagca	acagtgccaa	ggaatggctg	2220
caggttgacc	tgggcactca	gaggcaagtg	acaggaatca	tcaccagagg	ggcccgtgac	2280
tttggccaca	tccagtatgt	ggcgtcctac	aaggtagccc	acagtgatga	tggtgtgcag	2340
tggactgtat	atgaggagca	aggaagcagc	aaggtcttcc	agggcaactt	ggacaacaac	2400
tcccacaaga	agaacatctt	cgagaaacct	ttcatggctc	gctacgtgcg	tgtccttcca	2460
gtgtcctggc	ataaccgcat	caccctgcgc	ctggagctgc	tgggctgtta	a	2511

<210> 53
 <211> 120
 <212> PRT
 <213> Mus musculus

<400> 53

His	Ile	His	Gly	Cys	Asp	Lys	Asn	His	Leu	Arg	Glu	Ile	Ile	Gly	Ile
1				5					10					15	

Leu	Asn	Glu	Val	Thr	Gly	Glu	Gly	Thr	Pro	Cys	Thr	Glu	Met	Asp	Val
			20					25					30		

Pro Asn Val Leu Thr Ala Thr Lys Asn Thr Thr Glu Ser Glu Leu Val
 35 40 45

Cys Arg Ala Ser Lys Val Leu Arg Ile Phe Tyr Leu Lys His Gly Lys
 50 55 60

Thr Pro Cys Leu Lys Lys Asn Ser Ser Val Leu Met Glu Leu Gln Arg
 65 70 75 80

Leu Phe Arg Ala Phe Arg Cys Leu Asp Ser Ser Ile Ser Cys Thr Met
 85 90 95

Asn Glu Ser Lys Ser Thr Ser Leu Lys Asp Phe Leu Glu Ser Leu Lys
 100 105 110

Ser Ile Met Gln Met Asp Tyr Ser
 115 120

<210> 54
 <211> 363
 <212> DNA
 <213> Mus musculus

<400> 54
 catatccacg gatgcgacaa aaatcacttg agagagatca tcggcatttt gaacgaggtc 60
 acaggagaag ggacgccatg cacggagatg gatgtgccaa acgtcctcac agcaacgaag 120
 aacaccacag agagtgaact cgtctgtagg gcttccaagg tgcttcgcat attttattta 180
 aaacatggga aaactccatg cttgaagaag aactctagtg ttctcatgga gctgcagaga 240
 ctcttttcggg cttttcgatg cctggattca tcgataagct gcacccatgaa tgagtccaag 300
 tccacatcac tgaaagactt cctggaaagc ctaaagagca tcatgcaaat ggattactcg 360
 tag 363

<210> 55
 <211> 366
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> peptide sequence derived from mus musculus

<400> 55

Met Gly Val Glu Gly Cys Thr Lys Cys Ile Lys Tyr Leu Leu Phe Val
1 5 10 15

Phe Asn Phe Val Phe Trp Leu Ala Gly Gly Val Ile Leu Gly Val Ala
20 25 30

Leu Trp Leu Arg His Asp Pro Gln Thr Thr Ser Leu Leu Tyr Leu Glu
35 40 45

Leu Gly Asn Lys Pro Ala Pro Asn Thr Phe Tyr Val Gly Ile Tyr Ile
50 55 60

Leu Ile Ala Val Gly Ala Val Met Met Phe Val Gly Phe Leu Gly Cys
65 70 75 80

Tyr Gly Ala Ile Gln Glu Ser Gln Cys Leu Leu Gly Thr Phe Phe Thr
85 90 95

Cys Leu Val Ile Leu Phe Ala Cys Glu Val Ala Ala Gly Ile Trp Gly
100 105 110

Phe Val Asn Lys Asp Gln Ile Ala Lys Asp Val Lys Gln Phe Tyr Asp
115 120 125

Gln Ala Leu Gln Gln Ala Val Met Asp Asp Asp Ala Asn Asn Ala Lys
130 135 140

Ala Val Val Lys Thr Phe His Glu Thr Leu Asn Cys Cys Gly Ser Asn
145 150 155 160

Ala Leu Thr Thr Leu Thr Thr Thr Ile Leu Arg Asn Ser Leu Cys Pro
165 170 175

Ser Gly Gly Gly Gly Ser His Ile His Gly Cys Asp Lys Asn His Leu
180 185 190

Arg Glu Ile Ile Gly Ile Leu Asn Glu Val Thr Gly Glu Gly Thr Pro
195 200 205

Cys Thr Glu Met Asp Val Pro Asn Val Leu Thr Ala Thr Lys Asn Thr
210 215 220

Thr Glu Ser Glu Leu Val Cys Arg Ala Ser Lys Val Leu Arg Ile Phe
225 230 235 240

Tyr Leu Lys His Gly Lys Thr Pro Cys Leu Lys Lys Asn Ser Ser Val
245 250 255

Leu Met Glu Leu Gln Arg Leu Phe Arg Ala Phe Arg Cys Leu Asp Ser
260 265 270

Ser Ile Ser Cys Thr Met Asn Glu Ser Lys Ser Thr Ser Leu Lys Asp
275 280 285

Phe Leu Glu Ser Leu Lys Ser Ile Met Gln Met Asp Tyr Ser Gly Gly
290 295 300

Gly Gly Ser Gly Gly Asn Ile Leu Thr Pro Leu Leu Gln Gln Asp Cys
305 310 315 320

His Gln Lys Ile Asp Glu Leu Phe Ser Gly Lys Leu Tyr Leu Ile Gly
325 330 335

Ile Ala Ala Ile Val Val Ala Val Ile Met Ile Phe Glu Met Ile Leu
340 345 350

Ser Met Val Leu Cys Cys Gly Ile Arg Asn Ser Ser Val Tyr
355 360 365

<210> 56
<211> 1101
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence derived from mus musculus

<400> 56
atgggggtgg agggctgcac caaatgcatc aaatacctgc tcttcgtctt caatttcgtc 60
ttctggctgg ctggaggcgt gatcctaggt gtagctctgt ggttgcgtca tgatccacag 120

accaccagcc tgctgtacct ggaactggga aacaaaccgg cacccaacac cttctacgtg	180
ggcatctaca ttctcattgc tgtgggagct gtgatgatgt ttgtaggctt cctgggggtgc	240
tatggggcca tccaggagtc ccagtgtctg ctggggacgt tcttcacctg ctttgtgac	300
ctgtttgcct gtgagggtggc tgcaggcatc tggggcttcg taaacaaaga ccagatcgcc	360
aaggatgtga agcagttcta tgaccaggcc cttcagcaag ctgtgatgga tgatgatgcc	420
aacaatgcca aggctgtggt gaagactttc catgagacgc tcaactgttg tggctccaac	480
gcactgacca cactgactac caccatactg aggaacagcc tgtgtccctc aggaggagga	540
ggaagccata tccacggatg cgacaaaaat cacttgagag agatcatcgg cattttgaac	600
gaggtcacag gagaaggac gccatgcacg gagatggatg tgccaaacgt cctcacagca	660
acgaagaaca ccacagagag tgagctcgtc tgtagggctt ccaaggtgct tcgcatat	720
tatttaaaac atgggaaaac tccatgcttg aagaagaact ctagtgttct catggagctg	780
cagagactct ttcgggcttt tcgatgcctg gattcatcga taagctgcac catgaatgag	840
tccaagtcca catcactgaa agacttcctg gaaagcctaa agagcatcat gcaa	900
tactcgggag gaggaggaag cggcggcaac atactcacc cttactgca gcaagattgt	960
catcagaaaa tcgatgagct cttctctggg aagctgtacc tcattggaat tgcagccatt	1020
gtggtagctg tcattatgat ctttgagatg attctgagca tgggtgctgtg ctgtggcatc	1080
cggaacagct ccgtgtactg a	1101

<210> 57
 <211> 170
 <212> PRT
 <213> Mus musculus

<400> 57

Met	Ala	Val	Glu	Gly	Gly	Met	Lys	Cys	Val	Lys	Phe	Leu	Leu	Tyr	Val
1				5					10					15	

Leu	Leu	Leu	Ala	Phe	Cys	Ala	Cys	Ala	Val	Gly	Leu	Ile	Ala	Ile	Gly
			20					25					30		

Val	Ala	Val	Gln	Val	Val	Leu	Lys	Gln	Ala	Ile	Thr	His	Glu	Thr	Thr
		35					40					45			

Ala Gly Ser Leu Leu Pro Val Val Ile Ile Ala Val Gly Ala Phe Leu
50 55 60

Phe Leu Val Ala Phe Val Gly Cys Cys Gly Ala Cys Lys Glu Asn Tyr
65 70 75 80

Cys Leu Met Ile Thr Phe Ala Ile Phe Leu Ser Leu Ile Met Leu Val
85 90 95

Glu Val Ala Val Ala Ile Ala Gly Tyr Val Phe Arg Asp Gln Val Lys
100 105 110

Ser Glu Phe Asn Lys Ser Phe Gln Gln Gln Met Gln Asn Tyr Leu Lys
115 120 125

Asp Asn Lys Thr Ala Thr Ile Leu Asp Lys Leu Gln Lys Glu Asn Asn
130 135 140

Cys Cys Gly Ala Ser Asn Tyr Thr Asp Trp Glu Asn Ile Pro Gly Met
145 150 155 160

Ala Lys Asp Arg Val Pro Asp Ser Cys Cys
165 170

<210> 58
<211> 510
<212> DNA
<213> Mus musculus

<400> 58
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ttctgcgctt gtgcagtggg attgatcgcc attggtgtag cggttcaggt tgtcttgaag 120
caggccatta cccatgagac tactgctggc tcgctgttgc ctgtgggtcat cattgcagtg 180
ggcgcccttc tcttcctggg ggcctttgtg ggctgctgtg gggcctgcaa ggagaactac 240
tgtctcatga ttacatttgc catcttcctg tctcttatca tgcttgtgga ggtggctgtg 300
gccattgctg gctatgtgtt tagagaccag gtgaagtcag agtttaataa aagcttccag 360
cagcagatgc agaattacct taaagacaac aaaacagcca ctattttgga caaattgcag 420
aaagaaaata actgctgtgg agcttctaac tacacagact gggaaaacat ccccgcatg 480

gccaaaggaca gaggccccga ttcttgctgc

510

<210> 59
<211> 68
<212> PRT
<213> Mus musculus

<400> 59

Ile Asn Ile Thr Val Gly Cys Gly Asn Asp Phe Lys Glu Ser Thr Ile
1 5 10 15

His Thr Gln Gly Cys Val Glu Thr Ile Ala Ile Trp Leu Arg Lys Asn
20 25 30

Ile Leu Leu Val Ala Ala Ala Ala Leu Gly Ile Ala Phe Val Glu Val
35 40 45

Leu Gly Ile Ile Phe Ser Cys Cys Leu Val Lys Ser Ile Arg Ser Gly
50 55 60

Tyr Glu Val Met
65

<210> 60
<211> 207
<212> DNA
<213> Mus musculus

<400> 60

atcaacataa ctgtgggctg tgggaatgat ttcaaggaat ccactatcca taccagggc 60

tgcgtggaga ctatagcaat atggctaagg aagaacatac tgctggtggc tgcagcggcc 120

ctgggcattg cttttgtgga ggtcttggga attatcttct cctgctgtct ggtgaagagt 180

attcgaagtg gctatgaagt aatgtag 207

<210> 61
<211> 177
<212> PRT
<213> Mus musculus

<400> 61

Met Gly Val Glu Gly Cys Thr Lys Cys Ile Lys Tyr Leu Leu Phe Val
1 5 10 15

Phe Asn Phe Val Phe Trp Leu Ala Gly Gly Val Ile Leu Gly Val Ala
20 25 30

Leu Trp Leu Arg His Asp Pro Gln Thr Thr Ser Leu Leu Tyr Leu Glu
35 40 45

Leu Gly Asn Lys Pro Ala Pro Asn Thr Phe Tyr Val Gly Ile Tyr Ile
50 55 60

Leu Ile Ala Val Gly Ala Val Met Met Phe Val Gly Phe Leu Gly Cys
65 70 75 80

Tyr Gly Ala Ile Gln Glu Ser Gln Cys Leu Leu Gly Thr Phe Phe Thr
85 90 95

Cys Leu Val Ile Leu Phe Ala Cys Glu Val Ala Ala Gly Ile Trp Gly
100 105 110

Phe Val Asn Lys Asp Gln Ile Ala Lys Asp Val Lys Gln Phe Tyr Asp
115 120 125

Gln Ala Leu Gln Gln Ala Val Met Asp Asp Asp Ala Asn Asn Ala Lys
130 135 140

Ala Val Val Lys Thr Phe His Glu Thr Leu Asn Cys Cys Gly Ser Asn
145 150 155 160

Ala Leu Thr Thr Leu Thr Thr Thr Ile Leu Arg Asn Ser Leu Cys Pro
165 170 175

Ser

<210> 62

<211> 531

<212> DNA

<213> Mus musculus

<400> 62

atgggggtgg agggctgcac caaatgcac aaatacctgc tcttcgtctt caatttcgtc

60

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accaccagcc tgctgtacct ggaactggga aacaaaccgg cacccaacac cttctacgtg	180
ggcatctaca ttctcattgc tgtggggagct gtgatgatgt ttgtaggctt cctgggggtgc	240
tatggggcca tccaggagtc ccagtgtctg ctggggacgt tcttcacctg ctttgtgatc	300
ctgtttgcct gtgaggtggc tgcaggcatc tggggcttcg taaacaaaga ccagatcgcc	360
aaggatgtga agcagttcta tgaccaggcc cttcagcaag ctgtgatgga tgatgatgcc	420
aacaatgcca aggctgtggt gaagactttc catgagacgc tcaactgttg tggctccaac	480
gcactgacca cactgactac caccatactg aggaacagcc tgtgtccctc a	531

<210> 63
 <211> 59
 <212> PRT
 <213> Mus musculus

<400> 63

Gly	Gly	Asn	Ile	Leu	Thr	Pro	Leu	Leu	Gln	Gln	Asp	Cys	His	Gln	Lys
1				5					10					15	

Ile	Asp	Glu	Leu	Phe	Ser	Gly	Lys	Leu	Tyr	Leu	Ile	Gly	Ile	Ala	Ala
		20						25					30		

Ile	Val	Val	Ala	Val	Ile	Met	Ile	Phe	Glu	Met	Ile	Leu	Ser	Met	Val
		35				40						45			

Leu	Cys	Cys	Gly	Ile	Arg	Asn	Ser	Ser	Val	Tyr
	50					55				

<210> 64
 <211> 180
 <212> DNA
 <213> Mus musculus

<400> 64

ggcggcaaca tactcacccc cttactgcag caagattgtc atcagaaaat cgatgagctc	60
ttctctggga agctgtacct cattggaatt gcagccattg tggtagctgt cattatgatc	120
tttgagatga ttctgagcat ggtgctgtgc tgtggcatcc ggaacagctc cgtgtactga	180

<210> 65

<211> 467
<212> PRT
<213> Artificial Sequence

<220>
<223> peptide sequence derived from mus musculus

<400> 65

Ile Gln Lys Thr Pro Gln Ile Gln Val Tyr Ser Arg His Pro Pro Glu
1 5 10 15

Asn Gly Lys Pro Asn Ile Leu Asn Cys Tyr Val Thr Gln Phe His Pro
20 25 30

Pro His Ile Glu Ile Gln Met Leu Lys Asn Gly Lys Lys Ile Pro Lys
35 40 45

Val Glu Met Ser Asp Met Ser Phe Ser Lys Asp Trp Ser Phe Tyr Ile
50 55 60

Leu Ala His Thr Glu Phe Thr Pro Thr Glu Thr Asp Thr Tyr Ala Cys
65 70 75 80

Arg Val Lys His Ala Ser Met Ala Glu Pro Lys Thr Val Tyr Trp Asp
85 90 95

Arg Asp Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
100 105 110

Gly Ser Gly Gly Gly Gly Ser Gly Pro His Ser Leu Arg Tyr Phe Val
115 120 125

Thr Ala Val Ser Arg Pro Gly Leu Gly Glu Pro Arg Tyr Met Glu Val
130 135 140

Gly Tyr Val Asp Asp Thr Glu Phe Val Arg Phe Asp Ser Asp Ala Glu
145 150 155 160

Asn Pro Arg Tyr Glu Pro Arg Ala Arg Trp Met Glu Gln Glu Gly Pro
165 170 175

Glu Tyr Trp Glu Arg Glu Thr Gln Lys Ala Lys Gly Asn Glu Gln Ser

180

185

190

Phe Arg Val Asp Leu Arg Thr Leu Leu Gly Tyr Tyr Asn Gln Ser Lys
 195 200 205

Gly Gly Ser His Thr Ile Gln Val Ile Ser Gly Cys Glu Val Gly Ser
 210 215 220

Asp Gly Arg Leu Leu Arg Gly Tyr Gln Gln Tyr Ala Tyr Asp Gly Cys
 225 230 235 240

Asp Tyr Ile Ala Leu Asn Glu Asp Leu Lys Thr Trp Thr Ala Ala Asp
 245 250 255

Met Ala Ala Leu Ile Thr Lys His Lys Trp Glu Gln Ala Gly Glu Ala
 260 265 270

Glu Arg Leu Arg Ala Tyr Leu Glu Gly Thr Cys Val Glu Trp Leu Arg
 275 280 285

Arg Tyr Leu Lys Asn Gly Asn Ala Thr Leu Leu Arg Thr Asp Ser Pro
 290 295 300

Lys Ala His Val Thr His His Ser Arg Pro Glu Asp Lys Val Thr Leu
 305 310 315 320

Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Asp Ile Thr Leu Thr Trp
 325 330 335

Gln Leu Asn Gly Glu Glu Leu Ile Gln Asp Met Glu Leu Val Glu Thr
 340 345 350

Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ser Val Val Val
 355 360 365

Pro Leu Gly Lys Glu Gln Tyr Tyr Thr Cys His Val Tyr His Gln Gly
 370 375 380

Leu Pro Glu Pro Leu Thr Leu Arg Trp Glu Pro Pro Pro Ser Thr Val
 385 390 395 400

Ser Asn Met Ala Thr Val Ala Val Leu Val Val Leu Gly Ala Ala Ile
405 410 415

Val Thr Gly Ala Val Val Ala Phe Val Met Lys Met Arg Arg Arg Asn
420 425 430

Thr Gly Gly Lys Gly Gly Asp Tyr Ala Leu Ala Pro Gly Ser Gln Thr
435 440 445

Ser Asp Leu Ser Leu Pro Asp Cys Lys Val Met Val His Asp Pro His
450 455 460

Ser Leu Ala
465

<210> 66
<211> 1401
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence derived from mus musculus

<400> 66
atccagaaaa cccctcaaat tcaagtatac tcacgccacc caccggagaa tgggaagccg 60
aacataactga actgctacgt aacacagttc caccgcctc acattgaaat ccaaagtctg 120
aagaacggga aaaaaattcc taaagtagag atgtcagata tgtccttcag caaggactgg 180
tctttctata tcctggctca cactgaattc accccactg agactgatac atacgcctgc 240
agagttaagc atgccagtat ggccgagccc aagaccgtct actgggatcg agacatgggg 300
gggggaggct ccggtggagg ggggtctgga ggggggggggt ctggtggagg cggaagtggc 360
ccacactcgc tgaggtatatt cgtcaccgcc gtgtcccggc ccggcctcgg ggagccccgg 420
tacatggaag tcggctacgt ggacgacacg gagttcgtgc gcttcgacag cgacgcggag 480
aatccgagat atgagccgcg ggcgcggtgg atggagcagg aggggcccga gtattgggag 540
cgggagacac agaaagccaa gggcaatgag cagagtttcc gagtggacct gaggaccctg 600
ctcggctact acaaccagag caagggcggc tctcacacta ttcaggtgat ctctggctgt 660
gaagtgggggt ccgacgggcg actcctccgc gggtaccagc agtacgccta cgacggctgc 720

gattacatcg ccctgaacga agacctgaaa acgtggacgg cggcggacat ggcggcgctg	780
atcaccaaac acaagtggga gcaggctggg gaagcagaga gactcagggc ctacctggag	840
ggcacgtgcg tggagtggct ccgcagatac ctgaagaacg ggaacgcgac gctgctgcgc	900
acagattccc caaaggccca tgtgacctat cacagcagac ctgaagataa agtcaccctg	960
aggtgctggg ccctgggctt ctaccctgct gacatcacc tgacctggca gttgaatggg	1020
gaggagctga tccaggacat ggagcttgtg gagaccaggc ctgcagggga tggaaccttc	1080
cagaagtggg catctgtggg ggtgcctctt gggaaggagc agtattacac atgcatgtg	1140
taccatcagg ggctgcctga gcccctcacc ctgagatggg agcctcctcc atccactgtc	1200
tccaacatgg cgaccgttg tgttctgggt gtccttggag ctgcaatagt cactggagct	1260
gtggtggctt ttgtgatgaa gatgagaagg agaaacacag gtggaaaagg aggggactat	1320
gctctggctc caggctccca gacctctgat ctgtctctcc cagattgtaa agtgatgggt	1380
catgaccctc attctctagc g	1401

<210> 67
 <211> 269
 <212> PRT
 <213> Mus musculus

<400> 67

Val	Asp	Glu	Gln	Leu	Ser	Lys	Ser	Val	Lys	Asp	Lys	Val	Leu	Leu	Pro
1				5					10					15	

Cys	Arg	Tyr	Asn	Ser	Pro	His	Glu	Asp	Glu	Ser	Glu	Asp	Arg	Ile	Tyr
			20					25					30		

Trp	Gln	Lys	His	Asp	Lys	Val	Val	Leu	Ser	Val	Ile	Ala	Gly	Lys	Leu
		35					40					45			

Lys	Val	Trp	Pro	Glu	Tyr	Lys	Asn	Arg	Thr	Leu	Tyr	Asp	Asn	Thr	Thr
	50					55					60				

Tyr	Ser	Leu	Ile	Ile	Leu	Gly	Leu	Val	Leu	Ser	Asp	Arg	Gly	Thr	Tyr
65					70				75						80

Ser	Cys	Val	Val	Gln	Lys	Lys	Glu	Arg	Gly	Thr	Tyr	Glu	Val	Lys	His
				85					90					95	

Leu Ala Leu Val Lys Leu Ser Ile Lys Ala Asp Phe Ser Thr Pro Asn
100 105 110

Ile Thr Glu Ser Gly Asn Pro Ser Ala Asp Thr Lys Arg Ile Thr Cys
115 120 125

Phe Ala Ser Gly Gly Phe Pro Lys Pro Arg Phe Ser Trp Leu Glu Asn
130 135 140

Gly Arg Glu Leu Pro Gly Ile Asn Thr Thr Ile Ser Gln Asp Pro Glu
145 150 155 160

Ser Glu Leu Tyr Thr Ile Ser Ser Gln Leu Asp Phe Asn Thr Thr Arg
165 170 175

Asn His Thr Ile Lys Cys Leu Ile Lys Tyr Gly Asp Ala His Val Ser
180 185 190

Glu Asp Phe Thr Trp Glu Lys Pro Pro Glu Asp Pro Pro Asp Ser Lys
195 200 205

Asn Thr Leu Val Leu Phe Gly Ala Gly Phe Gly Ala Val Ile Thr Val
210 215 220

Val Val Ile Val Val Ile Ile Lys Cys Phe Cys Lys His Arg Ser Cys
225 230 235 240

Phe Arg Arg Asn Glu Ala Ser Arg Glu Thr Asn Asn Ser Leu Thr Phe
245 250 255

Gly Pro Glu Glu Ala Leu Ala Glu Gln Thr Val Phe Leu
260 265

<210> 68

<211> 810

<212> DNA

<213> Mus musculus

<400> 68

gttgatgaac aactgtccaa gtcagtgaag gataaggtat tgctgccttg ccgttacaac

60

tctcctcatg aagatgagtc tgaagaccga atctactggc aaaaacatga caaagtgggtg	120
ctgtctgtca ttgctgggaa actaaaagtg tggcccgagt ataagaaccg gactttatat	180
gacaacacta cctactctct tatcatcctg ggcctgggtcc tttcagaccg gggcacatac	240
agctgtgtcg ttcaaaagaa ggaaagagga acgtatgaag ttaaacactt ggcttttagta	300
aagttgtcca tcaaagctga cttctctacc cccaacataa ctgagtctgg aaacccatct	360
gcagacacta aaaggattac ctgctttgct tccggggggtt tcccaaagcc tcgcttctct	420
tggttggaat atggaagaga attacctggc atcaatacga caatttccca ggatcctgaa	480
tctgaattgt acaccattag tagccaacta gatttcaata cgactcgcaa ccacaccatt	540
aagtgtctca ttaaatatgg agatgctcac gtgtcagagg acttcacctg ggaaaaaccc	600
ccagaagacc ctctgatag caagaacaca cttgtgctct ttggggcagg attcggcgca	660
gtaataacag tcgtcgtcat cgttgtcatc atcaaagct tctgtaagca cagaagctgt	720
ttcagaagaa atgaggcaag cagagaaaca aacaacagcc ttaccttcgg gcctgaagaa	780
gcattagctg aacagaccgt cttcctttag	810

<210> 69

<211> 495

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence derived from mus musculus

<400> 69

Val	Asp	Glu	Gln	Leu	Ser	Lys	Ser	Val	Lys	Asp	Lys	Val	Leu	Leu	Pro
1				5					10				15		

Cys	Arg	Tyr	Asn	Ser	Pro	His	Glu	Asp	Glu	Ser	Glu	Asp	Arg	Ile	Tyr
			20					25					30		

Trp	Gln	Lys	His	Asp	Lys	Val	Val	Leu	Ser	Val	Ile	Ala	Gly	Lys	Leu
		35					40					45			

Lys	Val	Trp	Pro	Glu	Tyr	Lys	Asn	Arg	Thr	Leu	Tyr	Asp	Asn	Thr	Thr
	50					55					60				

Tyr	Ser	Leu	Ile	Ile	Leu	Gly	Leu	Val	Leu	Ser	Asp	Arg	Gly	Thr	Tyr

65

70

75

80

Ser Cys Val Val Gln Lys Lys Glu Arg Gly Thr Tyr Glu Val Lys His
85 90 95

Leu Ala Leu Val Lys Leu Ser Ile Lys Ala Asp Phe Ser Thr Pro Asn
100 105 110

Ile Thr Glu Ser Gly Asn Pro Ser Ala Asp Thr Lys Arg Ile Thr Cys
115 120 125

Phe Ala Ser Gly Gly Phe Pro Lys Pro Arg Phe Ser Trp Leu Glu Asn
130 135 140

Gly Arg Glu Leu Pro Gly Ile Asn Thr Thr Ile Ser Gln Asp Pro Glu
145 150 155 160

Ser Glu Leu Tyr Thr Ile Ser Ser Gln Leu Asp Phe Asn Thr Thr Arg
165 170 175

Asn His Thr Ile Lys Cys Leu Ile Lys Tyr Gly Asp Ala His Val Ser
180 185 190

Glu Asp Phe Thr Trp Glu Lys Pro Pro Glu Asp Pro Pro Asp Ser Lys
195 200 205

Asn Thr Leu Val Leu Phe Gly Ala Gly Phe Gly Ala Val Ile Thr Val
210 215 220

Val Val Ile Val Val Ile Ile Lys Cys Phe Cys Lys His Arg Ser Cys
225 230 235 240

Phe Arg Arg Asn Glu Ala Ser Arg Glu Thr Asn Asn Ser Leu Thr Phe
245 250 255

Gly Pro Glu Glu Ala Leu Ala Glu Gln Thr Val Phe Leu Met Pro Val
260 265 270

Lys Gly Gly Ser Lys Cys Ile Lys Tyr Leu Leu Phe Gly Phe Asn Phe
275 280 285

Ile Phe Trp Leu Ala Gly Ile Ala Val Leu Ala Ile Gly Leu Trp Leu
290 295 300

Arg Phe Asp Ser Gln Thr Lys Ser Ile Phe Glu Gln Glu Asn Asn His
305 310 315 320

Ser Ser Phe Tyr Thr Gly Val Tyr Ile Leu Ile Gly Ala Gly Ala Leu
325 330 335

Met Met Leu Val Gly Phe Leu Gly Cys Cys Gly Ala Val Gln Glu Ser
340 345 350

Gln Cys Met Leu Gly Leu Phe Phe Gly Phe Leu Leu Val Ile Phe Ala
355 360 365

Ile Glu Ile Ala Ala Ala Val Trp Gly Tyr Thr His Lys Asp Glu Val
370 375 380

Ile Lys Glu Leu Gln Glu Phe Tyr Lys Asp Thr Tyr Gln Lys Leu Arg
385 390 395 400

Ser Lys Asp Glu Pro Gln Arg Glu Thr Leu Lys Ala Ile His Met Ala
405 410 415

Leu Asp Cys Cys Gly Ile Ala Gly Pro Leu Glu Gln Phe Ile Ser Asp
420 425 430

Thr Cys Pro Lys Lys Gln Leu Leu Glu Ser Phe Gln Val Lys Pro Cys
435 440 445

Pro Glu Ala Ile Ser Glu Val Phe Asn Asn Lys Phe His Ile Ile Gly
450 455 460

Ala Val Gly Ile Gly Ile Ala Val Val Met Ile Phe Gly Met Ile Phe
465 470 475 480

Ser Met Ile Leu Cys Cys Ala Ile Arg Arg Ser Arg Glu Met Val
485 490 495

<210> 70

<211> 1488
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence derived from mus musculus

<400> 70
gttgatgaac aactgtccaa gtcagtgaag gataaggtat tgctgccttg ccgttacaac 60
tctcctcatg aagatgagtc tgaagaccga atctactggc aaaaacatga caaagtgggtg 120
ctgtctgtca ttgctgggaa actaaaagtg tggcccgagt ataagaaccg gactttatat 180
gacaacacta cctactctct tatcatcctg ggcctgggtcc tttcagaccg gggcacatac 240
agctgtgtcg ttcaaaagaa ggaaagagga acgtatgaag ttaaactt ggcttttagta 300
aagttgtcca tcaaagctga cttctctacc cccaacataa ctgagtctgg aaacccatct 360
gcagacacta aaaggattac ctgctttgct tccgggggtt tcccaaagcc tcgcttctct 420
tggttggaat atggaagaga attacctggc atcaatacga caatttccca ggatcctgaa 480
tctgaattgt acaccattag tagccaacta gatttcaata cgactcgcaa ccacaccatt 540
aagtgtctca ttaaatatgg agatgctcac gtgtcagagg acttcacctg ggaaaaaccc 600
ccagaagacc ctctgatag caagaacaca cttgtgctct ttggggcagg attcggcgca 660
gtaataacag tcgtcgtcat cgttgtcatc atcaaagct tctgtaagca cagaagctgt 720
ttcagaagaa atgaggcaag cagagaaaca aacaacagcc ttaccttcgg gcctgaagaa 780
gcattagctg aacagaccgt cttccttatg ccgggtcaaag gaggtagcaa gtgcatcaaa 840
tacctgctct tcggatttaa cttcatcttc tggctcgctg gcattgcagt gcttgctatt 900
ggactatggc tccgattcga ctctcagacc aagagcatct tcgagcaaga gaataaccat 960
tccagtttct acacaggagt gtacattctg attggagccg gggccctcat gatgctggtt 1020
ggtttcctgg gctgctgtgg agctgtacaa gaggccagct gcatgctggg attgttcttc 1080
gggttcctct tggatgatatt cgccattgag atagccgccg ccgtctgggg ctataccac 1140
aaggatgagg tgattaaaga actccaggag ttttacaagg acacctacca aaagttacgg 1200
agcaaggatg aaccccagcg ggaaacactc aaagccatcc atatggcggt ggactgctgt 1260
ggcatagctg gtcctttgga gcagtttatc tcggacacct gcccagaaga acagcttttg 1320
gaaagtttcc aggttaagcc ctgccctgaa gccatcagtg aggtcttcaa caacaagttc 1380

cacatcattg gagcagtggg tatcggcatc gccgtggtga tgatcttcgg catgatcttc 1440
agcatgatcc tgtgctgcgc catccgcagg agccgagaaa tgggtctag 1488

<210> 71
<211> 233
<212> PRT
<213> Mus musculus

<400> 71

Glu Asp Asp Ile Glu Ala Asp His Val Gly Thr Tyr Gly Ile Ser Val
1 5 10 15

Tyr Gln Ser Pro Gly Asp Ile Gly Gln Tyr Thr Phe Glu Phe Asp Gly
20 25 30

Asp Glu Leu Phe Tyr Val Asp Leu Asp Lys Lys Glu Thr Val Trp Met
35 40 45

Leu Pro Glu Phe Gly Gln Leu Ala Ser Phe Asp Pro Gln Gly Gly Leu
50 55 60

Gln Asn Ile Ala Val Val Lys His Asn Leu Gly Val Leu Thr Lys Arg
65 70 75 80

Ser Asn Ser Thr Pro Ala Thr Asn Glu Ala Pro Gln Ala Thr Val Phe
85 90 95

Pro Lys Ser Pro Val Leu Leu Gly Gln Pro Asn Thr Leu Ile Cys Phe
100 105 110

Val Asp Asn Ile Phe Pro Pro Val Ile Asn Ile Thr Trp Leu Arg Asn
115 120 125

Ser Lys Ser Val Ala Asp Gly Val Tyr Glu Thr Ser Phe Phe Val Asn
130 135 140

Arg Asp Tyr Ser Phe His Lys Leu Ser Tyr Leu Thr Phe Ile Pro Ser
145 150 155 160

Asp Asp Asp Ile Tyr Asp Cys Lys Val Glu His Trp Gly Leu Glu Glu
165 170 175

Pro Val Leu Lys His Trp Glu Pro Glu Ile Pro Ala Pro Met Ser Glu
180 185 190

Leu Thr Glu Thr Val Val Cys Ala Leu Gly Leu Ser Val Gly Leu Val
195 200 205

Gly Ile Val Val Gly Thr Ile Phe Ile Ile Gln Gly Leu Arg Ser Gly
210 215 220

Gly Thr Ser Arg His Pro Gly Pro Leu
225 230

<210> 72
<211> 702
<212> DNA
<213> Mus musculus

<400> 72
gaagacgaca ttgaggccga ccacgtaggc acctatggta taagtgtata tcagtctcct 60
ggagacattg gccagtacac atttgaattt gatggatgatg agttgttcta tgtggacttg 120
gataagaagg agactgtctg gatgcttcct gagtttggcc aattggcaag ctttgacccc 180
caaggtggac tgcaaaacat agctgtagta aaacacaact tgggagtctt gactaagagg 240
tcaaattcca cccagctac caatgaggct cctcaagcga ctgtgttccc caagtcccct 300
gtgctgctgg gtcagcccaa caccctcatc tgctttgtgg acaacatctt ccctcctgtg 360
atcaacatca catggctcag aaatagcaag tcagtcgcag acggtgttta tgagaccagc 420
ttcttcgtca accgtgacta ttccttcac aagctgtctt atctcacctt catcccttct 480
gacgatgaca tttatgactg caaggtggaa cactggggcc tggaggagcc ggttctgaaa 540
cactgggaac ctgagattcc agccccatg tcagagctga cagagactgt ggtctgtgcc 600
ctggggttgt ctgtgggcct tgtgggcatc gtggtgggca ccatcttcat cattcaaggc 660
ctgcgatcag gtggcacctc cagacacca gggcctttat ga 702

<210> 73
<211> 361
<212> PRT
<213> Mus musculus

<400> 73

Leu Ser Thr Ser Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg
1 5 10 15

Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser
20 25 30

Pro Pro Ser Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val
35 40 45

Leu Ala Leu Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala
50 55 60

Asp Pro Glu Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr
65 70 75 80

Arg Val Leu Met Val Asp Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys
85 90 95

Asp Ile Ser His Ser Ile Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg
100 105 110

Glu Ala Val Pro Glu Pro Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu
115 120 125

Gln Arg Leu Lys Ser Ser Val Glu Gln His Val Glu Leu Tyr Gln Lys
130 135 140

Tyr Ser Asn Asn Ser Trp Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro
145 150 155 160

Thr Asp Thr Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg
165 170 175

Gln Trp Leu Asn Gln Gly Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala
180 185 190

His Ser Ser Ser Asp Ser Lys Asp Asn Lys Leu His Val Glu Ile Asn
195 200 205

Gly Ile Ser Pro Lys Arg Arg Gly Asp Leu Gly Thr Ile His Asp Met
210 215 220

Asn Arg Pro Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln
225 230 235 240

His Leu His Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys
245 250 255

Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp
260 265 270

Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr
275 280 285

His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp
290 295 300

Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly
305 310 315 320

Ala Ser Ala Ser Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro
325 330 335

Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn
340 345 350

Met Ile Val Arg Ser Cys Lys Cys Ser
355 360

<210> 74
<211> 1086
<212> DNA
<213> Mus musculus

<400> 74
ctctccacct ctaagaccat cgacatggag ctggtgaaac ggaagcgcac cgaagccatc 60
cgtggccaga tcctgtccaa actaaggctc gccagtcccc caagccaggg ggaggtaccg 120
cccggcccg c tgcccagggc ggtgctcgct ttgtacaaca gcacccgcga ccgggtggca 180
ggcgagagcg ccgacccaga gccggagccc gaagcggact actatgctaa agaggtcacc 240

cgctgtgctaa tgggtggaccg caacaacgcc atctatgaga aaaccaaaga catctcacac 300
 agtatatata tgttcttcaa tacgtcagac attcgggaag cagtggccga acccccattg 360
 ctgtcccgtg cagagctgcg cttgcagaga ttaaaatcaa gtgtggagca acatgtggaa 420
 ctctaccaga aatatagcaa caattcctgg cgttaccttg gtaaccggct gctgaccccc 480
 actgatacgc ctgagtggct gtcttttgac gtcactggag ttgtacggca gtggctgaac 540
 caaggagacg gaatacaggg ctttcgattc agcgctcact cttcttctga cagcaaagat 600
 aacaaactcc acgtggaaat caacgggatc agccccaac gtcggggcga cctgggcacc 660
 atccatgaca tgaaccggcc cttcctgctc ctcatggcca cccccctgga aaggggccag 720
 cacctgcaca gtcacaggca ccggagagcc ctggatacca actattgctt cagctccaca 780
 gagaagaact gctgtgtgcg gcagctgtac attgacttta ggaaggacct gggttggaag 840
 tggatccacg agcccaaggg ctaccatgcc aacttctgtc tgggaccctg cccctatatt 900
 tggagcctgg acacacagta cagcaaggtc cttgccctct acaaccaaca caaccgggc 960
 gcttcggcgt caccgtgctg cgtgccgcag gctttggagc cactgcccac cgtctactac 1020
 gtgggtcgca agcccaaggt ggagcagttg tccaacatga ttgtgcgctc ctgcaagtgc 1080
 agctga 1086

<210> 75
 <211> 807
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> amino acid sequence derived from mus musculus

<400> 75

Leu Ser Thr Ser Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg
 1 5 10 15

Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser
 20 25 30

Pro Pro Ser Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val
 35 40 45

Leu Ala Leu Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala

50

55

60

Asp Pro Glu Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr
 65 70 75 80

Arg Val Leu Met Val Asp Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys
 85 90 95

Asp Ile Ser His Ser Ile Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg
 100 105 110

Glu Ala Val Pro Glu Pro Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu
 115 120 125

Gln Arg Leu Lys Ser Ser Val Glu Gln His Val Glu Leu Tyr Gln Lys
 130 135 140

Tyr Ser Asn Asn Ser Trp Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro
 145 150 155 160

Thr Asp Thr Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg
 165 170 175

Gln Trp Leu Asn Gln Gly Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala
 180 185 190

His Ser Ser Ser Asp Ser Lys Asp Asn Lys Leu His Val Glu Ile Asn
 195 200 205

Gly Ile Ser Pro Lys Arg Arg Gly Asp Leu Gly Thr Ile His Asp Met
 210 215 220

Asn Arg Pro Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln
 225 230 235 240

His Leu His Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys
 245 250 255

Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp
 260 265 270

Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr
275 280 285

His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp
290 295 300

Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly
305 310 315 320

Ala Ser Ala Ser Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro
325 330 335

Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn
340 345 350

Met Ile Val Arg Ser Cys Lys Cys Ser Gly Gly Gly Gly Ser Ala Ser
355 360 365

Gly Asp Phe Cys Asp Ser Ser Leu Cys Leu Asn Gly Gly Thr Cys Leu
370 375 380

Thr Gly Gln Asp Asn Asp Ile Tyr Cys Leu Cys Pro Glu Gly Phe Thr
385 390 395 400

Gly Leu Val Cys Asn Glu Thr Glu Arg Gly Pro Cys Ser Pro Asn Pro
405 410 415

Cys Tyr Asn Asp Ala Lys Cys Leu Val Thr Leu Asp Thr Gln Arg Gly
420 425 430

Glu Ile Phe Thr Glu Tyr Ile Cys Gln Cys Pro Val Gly Tyr Ser Gly
435 440 445

Ile His Cys Glu Thr Glu Thr Asn Tyr Tyr Asn Leu Asp Gly Glu Tyr
450 455 460

Met Phe Thr Thr Ala Val Pro Asn Thr Ala Val Pro Thr Pro Ala Pro
465 470 475 480

Thr Pro Asp Leu Ser Asn Asn Leu Ala Ser Arg Cys Ser Thr Gln Leu

485

490

495

Gly Met Glu Gly Gly Ala Ile Ala Asp Ser Gln Ile Ser Ala Ser Ser
 500 505 510

Val Tyr Met Gly Phe Met Gly Leu Gln Arg Trp Gly Pro Glu Leu Ala
 515 520 525

Arg Leu Tyr Arg Thr Gly Ile Val Asn Ala Trp Thr Ala Ser Asn Tyr
 530 535 540

Asp Ser Lys Pro Trp Ile Gln Val Asn Leu Leu Arg Lys Met Arg Val
 545 550 555 560

Ser Gly Val Met Thr Gln Gly Ala Ser Arg Ala Gly Arg Ala Glu Tyr
 565 570 575

Leu Lys Thr Phe Lys Val Ala Tyr Ser Leu Asp Gly Arg Lys Phe Glu
 580 585 590

Phe Ile Gln Asp Glu Ser Gly Gly Asp Lys Glu Phe Leu Gly Asn Leu
 595 600 605

Asp Asn Asn Ser Leu Lys Val Asn Met Phe Asn Pro Thr Leu Glu Ala
 610 615 620

Gln Tyr Ile Lys Leu Tyr Pro Val Ser Cys His Arg Gly Cys Thr Leu
 625 630 635 640

Arg Phe Glu Leu Leu Gly Cys Glu Leu His Gly Cys Ser Glu Pro Leu
 645 650 655

Gly Leu Lys Asn Asn Thr Ile Pro Asp Ser Gln Met Ser Ala Ser Ser
 660 665 670

Ser Tyr Lys Thr Trp Asn Leu Arg Ala Phe Gly Trp Tyr Pro His Leu
 675 680 685

Gly Arg Leu Asp Asn Gln Gly Lys Ile Asn Ala Trp Thr Ala Gln Ser
 690 695 700

Asn Ser Ala Lys Glu Trp Leu Gln Val Asp Leu Gly Thr Gln Arg Gln
705 710 715 720

Val Thr Gly Ile Ile Thr Gln Gly Ala Arg Asp Phe Gly His Ile Gln
725 730 735

Tyr Val Ala Ser Tyr Lys Val Ala His Ser Asp Asp Gly Val Gln Trp
740 745 750

Thr Val Tyr Glu Glu Gln Gly Ser Ser Lys Val Phe Gln Gly Asn Leu
755 760 765

Asp Asn Asn Ser His Lys Lys Asn Ile Phe Glu Lys Pro Phe Met Ala
770 775 780

Arg Tyr Val Arg Val Leu Pro Val Ser Trp His Asn Arg Ile Thr Leu
785 790 795 800

Arg Leu Glu Leu Leu Gly Cys
805

<210> 76
<211> 2424
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence derived from mus musculus

<400> 76
ctctccacct ctaagaccat cgacatggag ctggtgaaac ggaagcgcac cgaagccatc 60
cgtggccaga tcctgtccaa actaaggctc gccagtcccc caagccaggg ggaggtaccg 120
cccggcccgc tgcccgaggc ggtgctcgct ttgtacaaca gcacccgcga ccgggtggca 180
ggcgagagcg ccgaccaga gccggagccc gaagcggact actatgctaa agaggtcacc 240
cgcgtgctaa tgggtggaccg caacaacgcc atctatgaga aaaccaaaga catctcacac 300
agtatatata tgttcttcaa tacgtcagac attcgggaag cagtgccga accccattg 360
ctgtcccgtg cagagctgcg cttgcagaga ttaaaatcaa gtgtggagca acatgtggaa 420
ctctaccaga aatatagcaa caattcctgg cgttaccttg gtaaccggct gctgaccccc 480

actgatacgc ctgagtggct gtcttttgac gtcactggag ttgtacggca gtggctgaac	540
caaggagacg gaatacaggg ctttcgattc agcgctcact cttcttctga cagcaaagat	600
aacaaactcc acgtggaaat caacgggatc agccccaac gtcggggcga cctgggcacc	660
atccatgaca tgaaccggcc cttcctgctc ctcatggcca cccccctgga aagggccag	720
cacctgcaca gtcacaggca ccggagagcc ctggatacca actattgctt cagctccaca	780
gagaagaact gctgtgtgcg gcagctgtac attgacttta ggaaggacct gggttggaag	840
tggatccacg agcccaaggg ctaccatgcc aacttctgtc tgggaccctg cccctatatt	900
tggagcctgg acacacagta cagcaaggtc cttgccctct acaaccaaca caaccgggc	960
gcttcggcgt caccgtgctg cgtgccgcag gctttggagc cactgcccac cgtctactac	1020
gtgggtcgca agcccaaggt ggagcagttg tccaacatga ttgtgcgctc ctgcaagtgc	1080
agcggaggag gaggaagcgc gtctggtgac ttctgtgact ccagcctgtg cctgaacggt	1140
ggcacctgct tgacgggcca agacaatgac atctactgcc tctgccctga aggcttcaca	1200
ggccttgtgt gcaatgagac tgagagagga ccatgctccc caaaccttg ctacaatgat	1260
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cagtgccctg tgggctactc gggcatccac tgtgaaaccg agaccaacta ctacaacctg	1380
gatggagaat acatgttcac cacagccgtc cccaatactg ccgtccccac cccggcccc	1440
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gccagcaact atgatagcaa gccctggatc caggtgaacc ttctgcggaa gatgcgggta	1680
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cgcttcgagc tcctgggctg tgagttgcac ggatgttctg agcccctggg cctgaagaat	1980
aacacaattc ctgacagcca gatgtcagcc tccagcagct acaagacatg gaacctgcgt	2040
gcttttggct ggtaccccca cttgggaagg ctggataatc agggcaagat caatgcctgg	2100

acggctcaga gcaacagtgc caaggaatgg ctgcaggttg acctgggcac tcagaggcaa 2160
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 tacaaggtag cccacagtga tgatggtgtg cagtggactg tatatgagga gcaaggaagc 2280
 agcaaggtct tccagggcaa cttggacaac aactcccaca agaagaacat cttcgagaaa 2340
 cccttcatgg ctgctacgt gcgtgtcctt ccagtgtcct ggcataaccg catcacctg 2400
 cgcttgagc tgctgggctg ttaa 2424

<210> 77
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthesized amino acid sequence

<400> 77

Thr Ser Gly Gly Ser Gly Gly Thr Gly Gly Ser Gly Gly Thr Gly Gly
 1 5 10 15

Ser

<210> 78
 <211> 51
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> synthesized DNA sequence

<400> 78
 accagcggag gaagcggtag cacaggcggg tctggaggca ccggaggctc a 51

<210> 79
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthesized amino acid sequence

<400> 79

Asn Tyr His Leu Glu Asn Glu Val Ala Arg Leu Lys Lys Leu

1 5 10

<210> 80
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> synthesized DNA sequence

<400> 80
aattaccacc tggagaacga agtggccagg ctgaagaaac tc

42

<210> 81
<211> 274
<212> PRT
<213> Artificial Sequence

<220>
<223> amino acid sequence derived from mus musculus

<400> 81

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
20 25 30

Ala Val Val Thr Gln Glu Ser Ala Leu Thr Ser Ser Pro Gly Glu Thr
35 40 45

Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser Asn
50 55 60

Tyr Ala Ser Trp Val Gln Glu Lys Pro Asp His Leu Phe Thr Gly Leu
65 70 75 80

Ile Gly Gly Thr Asn Asn Arg Ala Pro Gly Val Pro Ala Arg Phe Ser
85 90 95

Gly Ser Leu Ile Gly Asp Lys Ala Ala Leu Thr Ile Thr Gly Ala Gln
100 105 110

Thr Glu Asp Glu Ala Ile Tyr Phe Cys Val Leu Trp Tyr Ser Asp His

115

120

125

Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly
 130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
 145 150 155 160

Ser Asp Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser
 165 170 175

Gln Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Leu Leu Thr Asp
 180 185 190

Tyr Gly Val Asn Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp
 195 200 205

Leu Gly Val Ile Trp Gly Asp Gly Ile Thr Asp Tyr Asn Ser Ala Leu
 210 215 220

Lys Ser Arg Leu Ser Val Thr Lys Asp Asn Ser Lys Ser Gln Val Phe
 225 230 235 240

Leu Lys Met Asn Ser Leu Gln Ser Gly Asp Ser Ala Arg Tyr Tyr Cys
 245 250 255

Val Thr Gly Leu Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val
 260 265 270

Ser Ser

<210> 82

<211> 822

<212> DNA

<213> Artificial Sequence

<220>

<223> DNA sequence derived from mus musculus

<400> 82

atggccttac cagtgaccgc cttgctcctg ccgctggcct tgctgctcca cgccgccagg

60

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ccggagcaga agctgatcag cgaggaggac ctggacgccg ttgtgacca ggaatccgct      120
ctgacctctt ctccaggcga aaccgtgact ctgacttgcc gtagtagcac cggggctgtg      180
accacatcta actatgccag ttgggtccag gaaaaaccgg atcacctgtt tactggcctg      240
attggcggca ccaacaatcg cgcaccgggt gtgcccgtc gtttcagcgg ttccctgatt      300
ggggacaagg cagcactgac tatcaccggc gcccagaccg aagatgaggc gatctatctt      360
tgcgtcctgt ggtacagcga ccattgggtg ttcgggggag gcaccaaact gacagtgtg      420
ggcggaggag gaggttcagg aggaggaggt agcgggggag gcggttcagg gggaggcggt      480
tctgatgtgc agctgcaaga atccgggccca ggactggttg cgccttctca gagtctgtca      540
attacatgta ctgttagtgg ctttctgctg accgactatg gtgtgaactg ggttcgtcag      600
agcccaggca agggctctgga gtggctggga gtgatttggg gggatggaat cacagactac      660
aatagcgcac tgaaatctcg gctgagtgtt accaaagata acagcaagtc ccaggtcttc      720
ctgaagatga acagcctgca aagcggcgac tccgctcgct attactgcgt taccggactg      780
tttgattatt gggggcaggg gacaactctg actgtttcct cc                        822

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<210> 83

<211> 253

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence derived from mus musculus

<400> 83

```

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp Ala Val Val Thr Gln
1           5           10          15

```

```

Glu Ser Ala Leu Thr Ser Ser Pro Gly Glu Thr Val Thr Leu Thr Cys
          20          25          30

```

```

Arg Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Ser Trp Val
          35          40          45

```

```

Gln Glu Lys Pro Asp His Leu Phe Thr Gly Leu Ile Gly Gly Thr Asn
50          55          60

```

```

Asn Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Ile Gly

```

65		70		75		80									
Asp	Lys	Ala	Ala	Leu	Thr	Ile	Thr	Gly	Ala	Gln	Thr	Glu	Asp	Glu	Ala
				85					90					95	
Ile	Tyr	Phe	Cys	Val	Leu	Trp	Tyr	Ser	Asp	His	Trp	Val	Phe	Gly	Gly
			100					105					110		
Gly	Thr	Lys	Leu	Thr	Val	Leu	Gly	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly
		115					120					125			
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Val	Gln	Leu
	130					135					140				
Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Ala	Pro	Ser	Gln	Ser	Leu	Ser	Ile
145					150					155					160
Thr	Cys	Thr	Val	Ser	Gly	Phe	Leu	Leu	Thr	Asp	Tyr	Gly	Val	Asn	Trp
				165					170					175	
Val	Arg	Gln	Ser	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Leu	Gly	Val	Ile	Trp
			180					185					190		
Gly	Asp	Gly	Ile	Thr	Asp	Tyr	Asn	Ser	Ala	Leu	Lys	Ser	Arg	Leu	Ser
	195						200					205			
Val	Thr	Lys	Asp	Asn	Ser	Lys	Ser	Gln	Val	Phe	Leu	Lys	Met	Asn	Ser
	210					215					220				
Leu	Gln	Ser	Gly	Asp	Ser	Ala	Arg	Tyr	Tyr	Cys	Val	Thr	Gly	Leu	Phe
225					230					235					240
Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Thr	Leu	Thr	Val	Ser	Ser			
				245					250						

<210> 84
 <211> 759
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> DNA sequence derived from mus musculus

<400> 84
gagcagaagc tgatcagcga ggaggacctg gacgccgttg tgaccagga atccgctctg 60
acctcttctc caggcgaaac cgtgactctg acttgccgta gtagcaccgg ggctgtgacc 120
acatctaact atgccagttg ggtccaggaa aaaccgcatc acctgtttac tggcctgatt 180
ggcggcacca acaatcgcgc accgggtgtg cccgctcgtt tcagcggttc cctgattggg 240
gacaaggcag cactgactat caccggcgcc cagaccgaag atgaggcgat ctatTTTTgc 300
gtcctgtggg acagcgacca ttgggtgttc gggggaggca ccaaactgac agtgctgggc 360
ggaggaggag gttcaggagg aggaggtagc gggggaggcg gttccggggg aggcggttct 420
gatgtgcagc tgcaagaatc cgggccagga ctggttgcgc cttctcagag tctgtcaatt 480
acatgtactg ttagtggctt tctgctgacc gactatgggtg tgaactgggt tcgtcagagc 540
ccaggcaagg gtctggagtg gctgggagtg atttgggggg atggaatcac agactacaat 600
agcgactga aatctcggct gagtgttacc aaagataaca gcaagtcca ggtcttcctg 660
aagatgaaca gcctgcaaag cggcgactcc gctcgctatt actgcgttac cggactgttt 720
gattattggg ggcaggggac aactctgact gtttcctcc 759

<210> 85
<211> 220
<212> PRT
<213> Mus musculus

<400> 85
Lys Pro Gln Ala Pro Glu Leu Arg Ile Phe Pro Lys Lys Met Asp Ala
1 5 10 15
Glu Leu Gly Gln Lys Val Asp Leu Val Cys Glu Val Leu Gly Ser Val
20 25 30
Ser Gln Gly Cys Ser Trp Leu Phe Gln Asn Ser Ser Ser Lys Leu Pro
35 40 45
Gln Pro Thr Phe Val Val Tyr Met Ala Ser Ser His Asn Lys Ile Thr
50 55 60
Trp Asp Glu Lys Leu Asn Ser Ser Lys Leu Phe Ser Ala Met Arg Asp
65 70 75 80

Thr Asn Asn Lys Tyr Val Leu Thr Leu Asn Lys Phe Ser Lys Glu Asn
85 90 95

Glu Gly Tyr Tyr Phe Cys Ser Val Ile Ser Asn Ser Val Met Tyr Phe
100 105 110

Ser Ser Val Val Pro Val Leu Gln Lys Val Asn Ser Thr Thr Thr Lys
115 120 125

Pro Val Leu Arg Thr Pro Ser Pro Val His Pro Thr Gly Thr Ser Gln
130 135 140

Pro Gln Arg Pro Glu Asp Cys Arg Pro Arg Gly Ser Val Lys Gly Thr
145 150 155 160

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
165 170 175

Ile Cys Val Ala Leu Leu Leu Ser Leu Ile Ile Thr Leu Ile Cys Tyr
180 185 190

His Arg Ser Arg Lys Arg Val Cys Lys Cys Pro Arg Pro Leu Val Arg
195 200 205

Gln Glu Gly Lys Pro Arg Pro Ser Glu Lys Ile Val
210 215 220

<210> 86
<211> 660
<212> DNA
<213> Mus musculus

<400> 86
aagccacagg caccgaact ccgaatcttt ccaaagaaaa tggacgccga acttggtcag 60
aaggtggacc tggatatgtga agtggtgggg tccgtttcgc aaggatgctc ttggctcttc 120
cagaactcca gtcctaaact cccccagccc accttcgttg tctatatggc ttcatccac 180
aacaagataa cgtgggacga gaagctgaat tcgtcgaaac tgttttctgc catgagggac 240
acgaataata agtacgttct caccctgaac aagttcagca aggaaaacga aggctactat 300

ttctgctcag tcatcagcaa ctcggtgatg tactttcagtt ctgtcgtgcc agtccttcag	360
aaagtgaact ctactactac caagccagtg ctgcgaactc cctcacctgt gcaccctacc	420
gggacatctc agccccagag accagaagat tgtcggcccc gtggctcagt gaaggggacc	480
ggattggact tcgcctgtga tatttacatc tgggcaccct tggccggaat ctgcgtggcc	540
cttctgctgt ccttgatcat cactctcatc tgctaccaca ggagccgaaa gcgtgtttgc	600
aaatgtccca ggccgctagt cagacaggaa ggcaagccca gaccttcaga gaaaattgtg	660

<210> 87

<211> 730

<212> PRT

<213> Artificial Sequence

<220>

<223> amion acid sequence derived from mus musculus

<400> 87

Met	Ala	Leu	Pro	Val	Thr	Ala	Leu	Leu	Leu	Pro	Leu	Ala	Leu	Leu	Leu
1				5				10					15		

His	Ala	Ala	Arg	Pro	Glu	Gln	Lys	Leu	Ile	Ser	Glu	Glu	Asp	Leu	Asp
			20					25					30		

Ala	Val	Val	Thr	Gln	Glu	Ser	Ala	Leu	Thr	Ser	Ser	Pro	Gly	Glu	Thr
			35				40					45			

Val	Thr	Leu	Thr	Cys	Arg	Ser	Ser	Thr	Gly	Ala	Val	Thr	Thr	Ser	Asn
		50				55					60				

Tyr	Ala	Ser	Trp	Val	Gln	Glu	Lys	Pro	Asp	His	Leu	Phe	Thr	Gly	Leu
65					70					75					80

Ile	Gly	Gly	Thr	Asn	Asn	Arg	Ala	Pro	Gly	Val	Pro	Ala	Arg	Phe	Ser
				85					90					95	

Gly	Ser	Leu	Ile	Gly	Asp	Lys	Ala	Ala	Leu	Thr	Ile	Thr	Gly	Ala	Gln
			100					105					110		

Thr	Glu	Asp	Glu	Ala	Ile	Tyr	Phe	Cys	Val	Leu	Trp	Tyr	Ser	Asp	His
		115					120					125			

Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145 150 155 160

Ser Asp Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser
165 170 175

Gln Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Leu Leu Thr Asp
180 185 190

Tyr Gly Val Asn Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp
195 200 205

Leu Gly Val Ile Trp Gly Asp Gly Ile Thr Asp Tyr Asn Ser Ala Leu
210 215 220

Lys Ser Arg Leu Ser Val Thr Lys Asp Asn Ser Lys Ser Gln Val Phe
225 230 235 240

Leu Lys Met Asn Ser Leu Gln Ser Gly Asp Ser Ala Arg Tyr Tyr Cys
245 250 255

Val Thr Gly Leu Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val
260 265 270

Ser Ser Lys Pro Gln Ala Pro Glu Leu Arg Ile Phe Pro Lys Lys Met
275 280 285

Asp Ala Glu Leu Gly Gln Lys Val Asp Leu Val Cys Glu Val Leu Gly
290 295 300

Ser Val Ser Gln Gly Cys Ser Trp Leu Phe Gln Asn Ser Ser Ser Lys
305 310 315 320

Leu Pro Gln Pro Thr Phe Val Val Tyr Met Ala Ser Ser His Asn Lys
325 330 335

Ile Thr Trp Asp Glu Lys Leu Asn Ser Ser Lys Leu Phe Ser Ala Met

340

345

350

Arg Asp Thr Asn Asn Lys Tyr Val Leu Thr Leu Asn Lys Phe Ser Lys
 355 360 365

Glu Asn Glu Gly Tyr Tyr Phe Cys Ser Val Ile Ser Asn Ser Val Met
 370 375 380

Tyr Phe Ser Ser Val Val Pro Val Leu Gln Lys Val Asn Ser Thr Thr
 385 390 395 400

Thr Lys Pro Val Leu Arg Thr Pro Ser Pro Val His Pro Thr Gly Thr
 405 410 415

Ser Gln Pro Gln Arg Pro Glu Asp Cys Arg Pro Arg Gly Ser Val Lys
 420 425 430

Gly Thr Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
 435 440 445

Ala Gly Ile Cys Val Ala Leu Leu Leu Ser Leu Ile Ile Thr Leu Ile
 450 455 460

Cys Tyr His Arg Ser Arg Lys Arg Val Cys Lys Cys Pro Arg Pro Leu
 465 470 475 480

Val Arg Gln Glu Gly Lys Pro Arg Pro Ser Glu Lys Ile Val Met Gly
 485 490 495

Val Glu Gly Cys Thr Lys Cys Ile Lys Tyr Leu Leu Phe Val Phe Asn
 500 505 510

Phe Val Phe Trp Leu Ala Gly Gly Val Ile Leu Gly Val Ala Leu Trp
 515 520 525

Leu Arg His Asp Pro Gln Thr Thr Ser Leu Leu Tyr Leu Glu Leu Gly
 530 535 540

Asn Lys Pro Ala Pro Asn Thr Phe Tyr Val Gly Ile Tyr Ile Leu Ile
 545 550 555 560

Ala Val Gly Ala Val Met Met Phe Val Gly Phe Leu Gly Cys Tyr Gly
565 570 575

Ala Ile Gln Glu Ser Gln Cys Leu Leu Gly Thr Phe Phe Thr Cys Leu
580 585 590

Val Ile Leu Phe Ala Cys Glu Val Ala Ala Gly Ile Trp Gly Phe Val
595 600 605

Asn Lys Asp Gln Ile Ala Lys Asp Val Lys Gln Phe Tyr Asp Gln Ala
610 615 620

Leu Gln Gln Ala Val Met Asp Asp Asp Ala Asn Asn Ala Lys Ala Val
625 630 635 640

Val Lys Thr Phe His Glu Thr Leu Asn Cys Cys Gly Ser Asn Ala Leu
645 650 655

Thr Thr Leu Thr Thr Thr Ile Leu Arg Asn Ser Leu Cys Pro Ser Gly
660 665 670

Gly Asn Ile Leu Thr Pro Leu Leu Gln Gln Asp Cys His Gln Lys Ile
675 680 685

Asp Glu Leu Phe Ser Gly Lys Leu Tyr Leu Ile Gly Ile Ala Ala Ile
690 695 700

Val Val Ala Val Ile Met Ile Phe Glu Met Ile Leu Ser Met Val Leu
705 710 715 720

Cys Cys Gly Ile Arg Asn Ser Ser Val Tyr
725 730

<210> 88

<211> 2193

<212> DNA

<213> Artificial Sequence

<220>

<223> DNA sequence derived from mus musculus

<400> 88

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ctgacctctt ctccaggcga aaccgtgact ctgacttgcc gtagtagcac cggggctgtg	180
accacatcta actatgccag ttgggtccag gaaaaaccgg atcacctgtt tactggcctg	240
attggcggca ccaacaatcg cgcaccgggt gtgcccgtc gtttcagcgg ttccctgatt	300
ggggacaagg cagcactgac tatcaccggc gccagaccg aagatgaggc gatctatctt	360
tgcgtcctgt ggtacagcga ccattgggtg ttcgggggag gcaccaaact gacagtgtg	420
ggcggaggag gaggttcagg aggaggaggt agcgggggag gcggttccgg gggaggcgg	480
tctgatgtgc agctgcaaga atccgggcca ggactgggtg cgccttctca gagtctgtca	540
attacatgta ctgttagtgg ctttctgctg accgactatg gtgtgaactg ggttcgtcag	600
agcccaggca agggctctgga gtggctggga gtgatttggg gggatggaat cacagactac	660
aatagcgcac tgaaatctcg gctgagtgtt accaaagata acagcaagtc ccaggtcttc	720
ctgaagatga acagcctgca aagcggcgac tccgctcgct attactgcgt taccggactg	780
tttgattatt gggggcaggg gacaactctg actgtttcct ccaagccaca ggcacccgaa	840
ctccgaatct ttcaaagaa aatggacgcc gaacttggtc agaaggtgga cctggtatgt	900
gaagtgttgg ggtccgtttc gcaaggatgc tcttggtctt tccagaactc cagctccaaa	960
ctccccagc ccaccttctg tgtctatatg gcttcatccc acaacaagat aacgtgggac	1020
gagaagctga attcgtcgaa actgttttct gccatgaggg acacgaataa taagtacgtt	1080
ctcaccctga acaagttcag caaggaaaac gaaggctact atttctgctc agtcatcagc	1140
aactcgggtg tgtacttcag ttctgtcgtg ccagtccttc agaaagtga ctctactact	1200
accaagccag tgctgcgaac tccctcacct gtgcacccta ccgggacatc tcagccccag	1260
agaccagaag attgtcggcc ccgtgggtca gtgaagggga ccggattgga cttcgcctgt	1320
gatatttaca tctgggcacc cttggccgga atctgcgtgg cccttctgct gtccttgatc	1380
atcactctca tctgctacca caggagccga aagcgtgttt gcaaagtgtc caggccgcta	1440
gtcagacagg aaggcaagcc cagaccttca gagaaaattg tgatgggggt ggagggtgc	1500
accaaagtga tcaaatacct gctcttcgtc ttcaatttcg tcttctggct ggctggaggc	1560
gtgatcctag gtgtagctct gtggttgcgt catgatccac agaccaccag cctgctgtac	1620

ctggaactgg gaaacaaacc ggcacccaac accttctacg tgggcatcta cattctcatt	1680
gctgtggggag ctgtgatgat gtttgtaggc ttcctgggggt gctatggggc catccaggag	1740
tcccagtgtc tgctggggac gttcttcacc tgccttgtga tcctgtttgc ctgtgaggtg	1800
gctgcaggca tctggggcctt cgtaaacaaa gaccagatcg ccaaggatgt gaagcagttc	1860
tatgaccagg cccttcagca agctgtgatg gatgatgatg ccaacaatgc caaggctgtg	1920
gtgaagactt tccatgagac gctcaactgt tgtggctcca acgcactgac cacactgact	1980
accaccatac tgaggaacag cctgtgtccc tcaggcggca acatactcac ccccttactg	2040
cagcaagatt gtcatcagaa aatcgatgag ctcttctctg ggaagctgta cctcattgga	2100
attgcagcca ttgtggtagc tgtcattatg atctttgaga tgattctgag catggtgctg	2160
tgctgtggca tccggaacag ctccgtgtac tga	2193

<210> 89
 <211> 709
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> amino acid sequence derived from mus musculus

<400> 89

Glu	Gln	Lys	Leu	Ile	Ser	Glu	Glu	Asp	Leu	Asp	Ala	Val	Val	Thr	Gln
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Glu	Ser	Ala	Leu	Thr	Ser	Ser	Pro	Gly	Glu	Thr	Val	Thr	Leu	Thr	Cys
			20					25					30		

Arg	Ser	Ser	Thr	Gly	Ala	Val	Thr	Thr	Ser	Asn	Tyr	Ala	Ser	Trp	Val
			35				40					45			

Gln	Glu	Lys	Pro	Asp	His	Leu	Phe	Thr	Gly	Leu	Ile	Gly	Gly	Thr	Asn
	50					55					60				

Asn	Arg	Ala	Pro	Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Leu	Ile	Gly
65				70					75					80	

Asp	Lys	Ala	Ala	Leu	Thr	Ile	Thr	Gly	Ala	Gln	Thr	Glu	Asp	Glu	Ala
				85				90						95	

Ile Tyr Phe Cys Val Leu Trp Tyr Ser Asp His Trp Val Phe Gly Gly
100 105 110

Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu
130 135 140

Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Ile
145 150 155 160

Thr Cys Thr Val Ser Gly Phe Leu Leu Thr Asp Tyr Gly Val Asn Trp
165 170 175

Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu Gly Val Ile Trp
180 185 190

Gly Asp Gly Ile Thr Asp Tyr Asn Ser Ala Leu Lys Ser Arg Leu Ser
195 200 205

Val Thr Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser
210 215 220

Leu Gln Ser Gly Asp Ser Ala Arg Tyr Tyr Cys Val Thr Gly Leu Phe
225 230 235 240

Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser Lys Pro Gln
245 250 255

Ala Pro Glu Leu Arg Ile Phe Pro Lys Lys Met Asp Ala Glu Leu Gly
260 265 270

Gln Lys Val Asp Leu Val Cys Glu Val Leu Gly Ser Val Ser Gln Gly
275 280 285

Cys Ser Trp Leu Phe Gln Asn Ser Ser Ser Lys Leu Pro Gln Pro Thr
290 295 300

Phe Val Val Tyr Met Ala Ser Ser His Asn Lys Ile Thr Trp Asp Glu

305		310		315		320									
Lys	Leu	Asn	Ser	Ser	Lys	Leu	Phe	Ser	Ala	Met	Arg	Asp	Thr	Asn	Asn
				325					330					335	
Lys	Tyr	Val	Leu	Thr	Leu	Asn	Lys	Phe	Ser	Lys	Glu	Asn	Glu	Gly	Tyr
			340					345					350		
Tyr	Phe	Cys	Ser	Val	Ile	Ser	Asn	Ser	Val	Met	Tyr	Phe	Ser	Ser	Val
		355					360					365			
Val	Pro	Val	Leu	Gln	Lys	Val	Asn	Ser	Thr	Thr	Thr	Lys	Pro	Val	Leu
	370						375				380				
Arg	Thr	Pro	Ser	Pro	Val	His	Pro	Thr	Gly	Thr	Ser	Gln	Pro	Gln	Arg
385					390					395					400
Pro	Glu	Asp	Cys	Arg	Pro	Arg	Gly	Ser	Val	Lys	Gly	Thr	Gly	Leu	Asp
				405					410					415	
Phe	Ala	Cys	Asp	Ile	Tyr	Ile	Trp	Ala	Pro	Leu	Ala	Gly	Ile	Cys	Val
			420					425					430		
Ala	Leu	Leu	Leu	Ser	Leu	Ile	Ile	Thr	Leu	Ile	Cys	Tyr	His	Arg	Ser
	435						440					445			
Arg	Lys	Arg	Val	Cys	Lys	Cys	Pro	Arg	Pro	Leu	Val	Arg	Gln	Glu	Gly
	450					455					460				
Lys	Pro	Arg	Pro	Ser	Glu	Lys	Ile	Val	Met	Gly	Val	Glu	Gly	Cys	Thr
465					470					475				480	
Lys	Cys	Ile	Lys	Tyr	Leu	Leu	Phe	Val	Phe	Asn	Phe	Val	Phe	Trp	Leu
				485					490					495	
Ala	Gly	Gly	Val	Ile	Leu	Gly	Val	Ala	Leu	Trp	Leu	Arg	His	Asp	Pro
			500					505					510		
Gln	Thr	Thr	Ser	Leu	Leu	Tyr	Leu	Glu	Leu	Gly	Asn	Lys	Pro	Ala	Pro
		515					520					525			

Asn Thr Phe Tyr Val Gly Ile Tyr Ile Leu Ile Ala Val Gly Ala Val
530 535 540

Met Met Phe Val Gly Phe Leu Gly Cys Tyr Gly Ala Ile Gln Glu Ser
545 550 555 560

Gln Cys Leu Leu Gly Thr Phe Phe Thr Cys Leu Val Ile Leu Phe Ala
565 570 575

Cys Glu Val Ala Ala Gly Ile Trp Gly Phe Val Asn Lys Asp Gln Ile
580 585 590

Ala Lys Asp Val Lys Gln Phe Tyr Asp Gln Ala Leu Gln Gln Ala Val
595 600 605

Met Asp Asp Asp Ala Asn Asn Ala Lys Ala Val Val Lys Thr Phe His
610 615 620

Glu Thr Leu Asn Cys Cys Gly Ser Asn Ala Leu Thr Thr Leu Thr Thr
625 630 635 640

Thr Ile Leu Arg Asn Ser Leu Cys Pro Ser Gly Gly Asn Ile Leu Thr
645 650 655

Pro Leu Leu Gln Gln Asp Cys His Gln Lys Ile Asp Glu Leu Phe Ser
660 665 670

Gly Lys Leu Tyr Leu Ile Gly Ile Ala Ala Ile Val Val Ala Val Ile
675 680 685

Met Ile Phe Glu Met Ile Leu Ser Met Val Leu Cys Cys Gly Ile Arg
690 695 700

Asn Ser Ser Val Tyr
705

<210> 90
<211> 2130
<212> DNA
<213> Artificial Sequence

<220>

<223> DNA sequence derived from mus musculus

<400> 90

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acatctaact atgccagttg ggtccaggaa aaaccggatc acctgtttac tggcctgatt	180
ggcggcacca acaatcgcg accgggtgtg cccgctcgtt tcagcggttc cctgattggg	240
gacaaggcag cactgactat caccggcgcc cagaccgaag atgaggcgat ctatTTTTgc	300
gtcctgtggt acagcgacca ttgggtgttc gggggaggca ccaaactgac agtgctgggc	360
ggaggaggag gttcaggagg aggaggtagc gggggaggcg gttccggggg aggcggttct	420
gatgtgcagc tgcaagaatc cgggccagga ctggttgcg cttctcagag tctgtcaatt	480
acatgtactg ttagtggctt tctgctgacc gactatggtg tgaactgggt tcgtcagagc	540
ccaggcaagg gtctggagtg gctgggagtg atttgggggg atggaatcac agactacaat	600
agcgactga aatctcggct gagtgttacc aaagataaca gcaagtcca ggtcttctctg	660
aagatgaaca gcctgcaaag cggcgactcc gctcgctatt actgcgttac cggactgttt	720
gattattggg ggcaggggac aactctgact gtttcctcca agccacaggc acccgaactc	780
cgaatctttc caaagaaaat ggacgccgaa cttggtcaga aggtggacct ggtatgtgaa	840
gtgttggggg ccgtttcgca aggatgctct tggctcttcc agaactccag ctccaaactc	900
ccccagccca cttcgttgt ctatatggct tcatcccaca acaagataac gtgggacgag	960
aagctgaatt cgtcgaaact gttttctgcc atgagggaca cgaataataa gtacgttctc	1020
accctgaaca agttcagcaa ggaaaacgaa ggctactatt tctgctcagt catcagcaac	1080
tcggtgatgt acttcagttc tgtcgtgcca gtccttcaga aagtgaactc tactactacc	1140
aagccagtgc tgcgaactcc ctcacctgtg caccctaccg ggacatctca gccccagaga	1200
ccagaagatt gtcggccccg tggctcagtg aaggggaccg gattggactt cgcctgtgat	1260
atttacatct gggcaccctt ggccggaatc tgcgtggccc ttctgctgtc cttgatcatc	1320
actctcatct gctaccacag gagccgaaag cgtgtttgca aatgtcccag gccgctagtc	1380
agacaggaag gcaagcccag accttcagag aaaattgtga tgggggtgga gggctgcacc	1440
aaatgcatca aatactgct cttcgtcttc aatttcgtct tctggctggc tggaggcgtg	1500

atcctaggtg tagctctgtg gttgcgtcat gatccacaga ccaccagcct gctgtacctg	1560
gaactgggaa acaaaccggc acccaacacc ttctacgtgg gcatctacat tctcattgct	1620
gtgggagctg tgatgatgtt tgtaggcttc ctgggggtgct atggggccat ccaggagtcc	1680
cagtgtctgc tggggacgtt cttcacctgc cttgtgatcc tgtttgccctg tgaggtggct	1740
gcaggcatct ggggcttcgt aaacaaagac cagatcgcca aggatgtgaa gcagttctat	1800
gaccaggccc ttcagcaagc tgtgatggat gatgatgcca acaatgccaa ggctgtgggtg	1860
aagactttcc atgagacgct caactgttgt ggctccaacg cactgaccac actgactacc	1920
accatactga ggaacagcct gtgtccctca ggcggcaaca tactcacccc cttactgcag	1980
caagattgtc atcagaaaat cgatgagctc ttctctggga agctgtacct cattggaatt	2040
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tgtggcatcc ggaacagctc cgtgtactga	2130

<210> 91
 <211> 732
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> sc-Dimer-CD81-IL-12a

<400> 91

Met	Ala	Leu	Gln	Ile	Pro	Ser	Leu	Leu	Leu	Ser	Ala	Ala	Val	Val	Val
1			5					10					15		

Leu	Met	Val	Leu	Ser	Ser	Pro	Gly	Thr	Glu	Gly	Ile	Ser	Gln	Ala	Val
		20						25					30		

His	Ala	Ala	His	Ala	Glu	Ile	Asn	Glu	Ala	Gly	Arg	Gly	Gly	Gly	Gly
	35						40				45				

Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Asp	Ser	Glu	Arg	His	Phe	Val	Tyr
	50					55					60				

Gln	Phe	Met	Gly	Glu	Cys	Tyr	Phe	Thr	Asn	Gly	Thr	Gln	Arg	Ile	Arg
65					70					75				80	

Tyr Val Thr Arg Tyr Ile Tyr Asn Arg Glu Glu Tyr Val Arg Tyr Asp

85

90

95

Ser Asp Val Gly Glu His Arg Ala Val Thr Glu Leu Gly Arg Pro Asp
 100 105 110

Ala Glu Tyr Trp Asn Ser Gln Pro Glu Ile Leu Glu Arg Thr Arg Ala
 115 120 125

Glu Leu Asp Thr Val Cys Arg His Asn Tyr Glu Gly Pro Glu Thr His
 130 135 140

Thr Ser Leu Arg Arg Leu Glu Gln Pro Asn Val Val Ile Ser Leu Ser
 145 150 155 160

Arg Thr Glu Ala Leu Asn His His Asn Thr Leu Val Cys Ser Val Thr
 165 170 175

Asp Phe Tyr Pro Ala Lys Ile Lys Val Arg Trp Phe Arg Asn Gly Gln
 180 185 190

Glu Glu Thr Val Gly Val Ser Ser Thr Gln Leu Ile Arg Asn Gly Asp
 195 200 205

Trp Thr Phe Gln Val Leu Val Met Leu Glu Met Thr Pro Arg Arg Gly
 210 215 220

Glu Val Tyr Thr Cys His Val Glu His Pro Ser Leu Lys Ser Pro Ile
 225 230 235 240

Thr Val Glu Trp Arg Ala Gln Ser Glu Ser Ala Trp Ser Lys Met Leu
 245 250 255

Ser Gly Ile Gly Gly Cys Val Leu Gly Val Ile Phe Leu Gly Leu Gly
 260 265 270

Leu Phe Ile Arg His Arg Ser Gln Lys Gly Pro Arg Gly Pro Pro Pro
 275 280 285

Ala Gly Leu Leu Gln Met Gly Val Glu Gly Cys Thr Lys Cys Ile Lys
 290 295 300

Tyr Leu Leu Phe Val Phe Asn Phe Val Phe Trp Leu Ala Gly Gly Val
305 310 315 320

Ile Leu Gly Val Ala Leu Trp Leu Arg His Asp Pro Gln Thr Thr Ser
325 330 335

Leu Leu Tyr Leu Glu Leu Gly Asn Lys Pro Ala Pro Asn Thr Phe Tyr
340 345 350

Val Gly Ile Tyr Ile Leu Ile Ala Val Gly Ala Val Met Met Phe Val
355 360 365

Gly Phe Leu Gly Cys Tyr Gly Ala Ile Gln Glu Ser Gln Cys Leu Leu
370 375 380

Gly Thr Phe Phe Thr Cys Leu Val Ile Leu Phe Ala Cys Glu Val Ala
385 390 395 400

Ala Gly Ile Trp Gly Phe Val Asn Lys Asp Gln Ile Ala Lys Asp Val
405 410 415

Lys Gln Phe Tyr Asp Gln Ala Leu Gln Gln Ala Val Met Asp Asp Asp
420 425 430

Ala Asn Asn Ala Lys Ala Val Val Lys Thr Phe His Glu Thr Leu Asn
435 440 445

Cys Cys Gly Ser Asn Ala Leu Thr Thr Leu Thr Thr Thr Ile Leu Arg
450 455 460

Asn Ser Leu Cys Pro Ser Gly Gly Gly Gly Ser Arg Val Ile Pro Val
465 470 475 480

Ser Gly Pro Ala Arg Cys Leu Ser Gln Ser Arg Asn Leu Leu Lys Thr
485 490 495

Thr Asp Asp Met Val Lys Thr Ala Arg Glu Lys Leu Lys His Tyr Ser
500 505 510

Cys Thr Ala Glu Asp Ile Asp His Glu Asp Ile Thr Arg Asp Gln Thr

515

520

525

Ser Thr Leu Lys Thr Cys Leu Pro Leu Glu Leu His Lys Asn Glu Ser
 530 535 540

Cys Leu Ala Thr Arg Glu Thr Ser Ser Thr Thr Arg Gly Ser Cys Leu
 545 550 555 560

Pro Pro Gln Lys Thr Ser Leu Met Met Thr Leu Cys Leu Gly Ser Ile
 565 570 575

Tyr Glu Asp Leu Lys Met Tyr Gln Thr Glu Phe Gln Ala Ile Asn Ala
 580 585 590

Ala Leu Gln Asn His Asn His Gln Gln Ile Ile Leu Asp Lys Gly Met
 595 600 605

Leu Val Ala Ile Asp Glu Leu Met Gln Ser Leu Asn His Asn Gly Glu
 610 615 620

Thr Leu Arg Gln Lys Pro Pro Val Gly Glu Ala Asp Pro Tyr Arg Val
 625 630 635 640

Lys Met Lys Leu Cys Ile Leu Leu His Ala Phe Ser Thr Arg Val Val
 645 650 655

Thr Ile Asn Arg Val Met Gly Tyr Leu Ser Ser Ala Gly Gly Gly Gly
 660 665 670

Ser Gly Gly Asn Ile Leu Thr Pro Leu Leu Gln Gln Asp Cys His Gln
 675 680 685

Lys Ile Asp Glu Leu Phe Ser Gly Lys Leu Tyr Leu Ile Gly Ile Ala
 690 695 700

Ala Ile Val Val Ala Val Ile Met Ile Phe Glu Met Ile Leu Ser Met
 705 710 715 720

Val Leu Cys Cys Gly Ile Arg Asn Ser Ser Val Tyr
 725 730

<210> 92
<211> 2238
<212> DNA
<213> Artificial Sequence

<220>
<223> sc-dimer-CD81-IL-12a

<400> 92
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gaagcaggca gaggaggagg aggaagcgga ggaggaggaa gcggaggaga ctccgaaagg 180
catttcgtgt accagttcat gggcgagtgc tacttcacca acgggacgca gcgcatacga 240
tatgtgacca gatacatcta caaccgggag gagtacgtgc gctacgacag cgacgtgggc 300
gagcaccgcg cggtgaccga gctggggcgg ccagacgccg agtactggaa cagccagccg 360
gagatcctgg agcgaacgcg ggccgagctg gacacggtgt gcagacacaa ctacgagggg 420
ccggagaccc acacctccct gcggcggtt gaacagccca atgtcgtcat ctccctgtcc 480
aggacagagg ccctcaacca ccacaacact ctggtctgct cagtgcaga tttctaccca 540
gccaagatca aagtgcgctg gttccggaat ggccaggagg agacggtggg ggtctcatcc 600
acacagctta ttaggaatgg ggactggacc ttccaggtcc tggatcatgct ggagatgacc 660
cctcggcggg gagaggtcta cacctgtcac gtggagcatc ccagcctgaa gagccccatc 720
actgtggagt ggagggcaca gtctgagtct gcctggagca agatgttgag cggcatcggg 780
ggctgcgtgc ttgggggtgat cttcctcggg cttggccttt tcatccgtca caggagtcag 840
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aaatgcatca aatactgct cttcgtcttc aatttcgtct tctggctggc tggaggcgtg 960
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gaactgggaa acaaaccggc acccaacacc ttctacgtgg gcatctacat tctcattgct 1080
gtgggagctg tgatgatgtt tgtaggcttc ctgggggtgct atggggccat ccaggagtcc 1140
cagtgtctgc tggggacgtt cttcacctgc cttgtgatcc tgtttgcctg tgaggtggct 1200
gcaggcatct ggggcttcgt aaacaaagac cagatcgcca aggatgtgaa gcagttctat 1260
gaccaggccc ttcagcaagc tgtgatggat gatgatgcca acaatgcaa ggctgtggtg 1320

aagactttcc atgagacgct caactgttgt ggctccaacg cactgaccac actgactacc	1380
accatactga ggaacagcct gtgtccctca ggaggaggag gaagcagggt cattccagtc	1440
tctggacctg ccaggtgtct tagccagtcc cgaaacctgc tgaagaccac agatgacatg	1500
gtgaagacgg ccagagaaaa actgaaacat tattcctgca ctgctgaaga catcgatcat	1560
gaagacatca cacgggacca aaccagcaca ttgaagacct gtttaccact ggaactacac	1620
aagaacgaga gttgcctggc tactagagag acttcttcca caacaagagg gagctgcctg	1680
ccccacaga agacgtcttt gatgatgacc ctgtgccttg gtagcatcta tgaggacttg	1740
aagatgtacc agacagagtt ccaggccatc aacgcagcac ttcagaatca caaccatcag	1800
cagatcattc tagacaaggg catgctggtg gccatcgatg agctgatgca gtctctgaat	1860
cataatggcg agactctgcg ccagaaacct cctgtgggag aagcagaccc ttacagagtg	1920
aaaatgaagc tctgcatcct gcttcacgcc ttcagcacc gcgtcgtgac catcaacagg	1980
gtgatgggct atctgagctc cgccggagga ggaggaagcg gcggcaacat actcaccccc	2040
ttactgcagc aagattgtca tcagaaaatc gatgagctct tctctgggaa gctgtacctc	2100
attggaattg cagccattgt ggtagctgtc attatgatct ttgagatgat tctgagcatg	2160
gtgctgtgct gtggcatccg gaacagctcc gtgtactgag tgctgtgctg tggcatccgg	2220
aacagctccg tgtactga	2238

<210> 93
 <211> 193
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Il-12a

<400> 93

Arg	Val	Ile	Pro	Val	Ser	Gly	Pro	Ala	Arg	Cys	Leu	Ser	Gln	Ser	Arg
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Asn	Leu	Leu	Lys	Thr	Thr	Asp	Asp	Met	Val	Lys	Thr	Ala	Arg	Glu	Lys
			20					25					30		

Leu	Lys	His	Tyr	Ser	Cys	Thr	Ala	Glu	Asp	Ile	Asp	His	Glu	Asp	Ile
		35					40					45			

Thr Arg Asp Gln Thr Ser Thr Leu Lys Thr Cys Leu Pro Leu Glu Leu
50 55 60

His Lys Asn Glu Ser Cys Leu Ala Thr Arg Glu Thr Ser Ser Thr Thr
65 70 75 80

Arg Gly Ser Cys Leu Pro Pro Gln Lys Thr Ser Leu Met Met Thr Leu
85 90 95

Cys Leu Gly Ser Ile Tyr Glu Asp Leu Lys Met Tyr Gln Thr Glu Phe
100 105 110

Gln Ala Ile Asn Ala Ala Leu Gln Asn His Asn His Gln Gln Ile Ile
115 120 125

Leu Asp Lys Gly Met Leu Val Ala Ile Asp Glu Leu Met Gln Ser Leu
130 135 140

Asn His Asn Gly Glu Thr Leu Arg Gln Lys Pro Pro Val Gly Glu Ala
145 150 155 160

Asp Pro Tyr Arg Val Lys Met Lys Leu Cys Ile Leu Leu His Ala Phe
165 170 175

Ser Thr Arg Val Val Thr Ile Asn Arg Val Met Gly Tyr Leu Ser Ser
180 185 190

Ala

<210> 94
<211> 579
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-12a

<400> 94
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gaagacatcg atcatgaaga catcacacgg gaccaaacca gcacattgaa gacctgttta 180
 ccactggaac tacacaagaa cgagagttgc ctggctacta gagagacttc ttccacaaca 240
 agaggggagct gcctgcccc acagaagacg tctttgatga tgaccctgtg ccttggtagc 300
 atctatgagg acttgaagat gtaccagaca gagttccagg ccatcaacgc agcacttcag 360
 aatcacaacc atcagcagat cattctagac aagggcacgc tgggtggccat cgatgagctg 420
 atgcagtctc tgaatcataa tggcgagact ctgcgccaga aacctcctgt gggagaagca 480
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<210> 95
 <211> 439
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CD81-IL12a

<400> 95

Met Gly Val Glu Gly Cys Thr Lys Cys Ile Lys Tyr Leu Leu Phe Val
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Phe Asn Phe Val Phe Trp Leu Ala Gly Gly Val Ile Leu Gly Val Ala
 20 25 30

Leu Trp Leu Arg His Asp Pro Gln Thr Thr Ser Leu Leu Tyr Leu Glu
 35 40 45

Leu Gly Asn Lys Pro Ala Pro Asn Thr Phe Tyr Val Gly Ile Tyr Ile
 50 55 60

Leu Ile Ala Val Gly Ala Val Met Met Phe Val Gly Phe Leu Gly Cys
 65 70 75 80

Tyr Gly Ala Ile Gln Glu Ser Gln Cys Leu Leu Gly Thr Phe Phe Thr
 85 90 95

Cys Leu Val Ile Leu Phe Ala Cys Glu Val Ala Ala Gly Ile Trp Gly
 100 105 110

Phe Val Asn Lys Asp Gln Ile Ala Lys Asp Val Lys Gln Phe Tyr Asp
115 120 125

Gln Ala Leu Gln Gln Ala Val Met Asp Asp Asp Ala Asn Asn Ala Lys
130 135 140

Ala Val Val Lys Thr Phe His Glu Thr Leu Asn Cys Cys Gly Ser Asn
145 150 155 160

Ala Leu Thr Thr Leu Thr Thr Thr Ile Leu Arg Asn Ser Leu Cys Pro
165 170 175

Ser Gly Gly Gly Gly Ser Arg Val Ile Pro Val Ser Gly Pro Ala Arg
180 185 190

Cys Leu Ser Gln Ser Arg Asn Leu Leu Lys Thr Thr Asp Asp Met Val
195 200 205

Lys Thr Ala Arg Glu Lys Leu Lys His Tyr Ser Cys Thr Ala Glu Asp
210 215 220

Ile Asp His Glu Asp Ile Thr Arg Asp Gln Thr Ser Thr Leu Lys Thr
225 230 235 240

Cys Leu Pro Leu Glu Leu His Lys Asn Glu Ser Cys Leu Ala Thr Arg
245 250 255

Glu Thr Ser Ser Thr Thr Arg Gly Ser Cys Leu Pro Pro Gln Lys Thr
260 265 270

Ser Leu Met Met Thr Leu Cys Leu Gly Ser Ile Tyr Glu Asp Leu Lys
275 280 285

Met Tyr Gln Thr Glu Phe Gln Ala Ile Asn Ala Ala Leu Gln Asn His
290 295 300

Asn His Gln Gln Ile Ile Leu Asp Lys Gly Met Leu Val Ala Ile Asp
305 310 315 320

Glu Leu Met Gln Ser Leu Asn His Asn Gly Glu Thr Leu Arg Gln Lys

325

330

335

Pro Pro Val Gly Glu Ala Asp Pro Tyr Arg Val Lys Met Lys Leu Cys
 340 345 350

Ile Leu Leu His Ala Phe Ser Thr Arg Val Val Thr Ile Asn Arg Val
 355 360 365

Met Gly Tyr Leu Ser Ser Ala Gly Gly Gly Gly Ser Gly Gly Asn Ile
 370 375 380

Leu Thr Pro Leu Leu Gln Gln Asp Cys His Gln Lys Ile Asp Glu Leu
 385 390 395 400

Phe Ser Gly Lys Leu Tyr Leu Ile Gly Ile Ala Ala Ile Val Val Ala
 405 410 415

Val Ile Met Ile Phe Glu Met Ile Leu Ser Met Val Leu Cys Cys Gly
 420 425 430

Ile Arg Asn Ser Ser Val Tyr
 435

<210> 96

<211> 1320

<212> DNA

<213> Artificial Sequence

<220>

<223> CD81-IL12a

<400> 96

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accaccagcc tgctgtacct ggaactggga aacaaaccgg cacccaacac cttctacgtg 180

ggcatctaca ttctcattgc tgtgggagct gtgatgatgt ttgtaggctt cctgggggtgc 240

tatggggcca tccaggagtc ccagtgtctg ctggggacgt tcttcacctg ctttgtgatc 300

ctgtttgcct gtgagggtggc tgcaggcatc tggggcttcg taaacaaaga ccagatcgcc 360

aaggatgtga agcagttcta tgaccaggcc cttcagcaag ctgtgatgga tgatgatgcc 420

aacaatgccaggctgtggtgaagactttccatgagacgc tcaactgttg tggctccaac 480
gcactgacca cactgactac caccatactg aggaacagcc tgtgtccctc aggaggagga 540
ggaagcaggg tcattccagt ctctggacct gccagggtgtc ttagccagtc ccgaaacctg 600
ctgaagacca cagatgacat ggtgaagacg gccagagaaa aactgaaaca ttattcctgc 660
actgctgaag acatcgatca tgaagacatc acacgggacc aaaccagcac attgaagacc 720
tgtttaccac tggaactaca caagaacgag agttgcctgg ctactagaga gacttcttcc 780
acaacaagag ggagctgcct gccccacag aagacgtctt tgatgatgac cctgtgcctt 840
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cttcagaatc acaaccatca gcagatcatt ctagacaagg gcatgctggt ggccatcgat 960
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cgcgctcgtga ccatcaacag ggtgatgggc tatctgagct ccgccggagg aggaggaagc 1140
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ttctctggga agctgtacct cattggaatt gcagccattg tggtagctgt cattatgatc 1260
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<210> 97
<211> 335
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-12b

<400> 97

Met Cys Pro Gln Lys Leu Thr Ile Ser Trp Phe Ala Ile Val Leu Leu
1 5 10 15

Val Ser Pro Leu Met Ala Met Trp Glu Leu Glu Lys Asp Val Tyr Val
20 25 30

Val Glu Val Asp Trp Thr Pro Asp Ala Pro Gly Glu Thr Val Asn Leu
35 40 45

Thr Cys Asp Thr Pro Glu Glu Asp Asp Ile Thr Trp Thr Ser Asp Gln

50

55

60

Arg His Gly Val Ile Gly Ser Gly Lys Thr Leu Thr Ile Thr Val Lys
65 70 75 80

Glu Phe Leu Asp Ala Gly Gln Tyr Thr Cys His Lys Gly Gly Glu Thr
85 90 95

Leu Ser His Ser His Leu Leu Leu His Lys Lys Glu Asn Gly Ile Trp
100 105 110

Ser Thr Glu Ile Leu Lys Asn Phe Lys Asn Lys Thr Phe Leu Lys Cys
115 120 125

Glu Ala Pro Asn Tyr Ser Gly Arg Phe Thr Cys Ser Trp Leu Val Gln
130 135 140

Arg Asn Met Asp Leu Lys Phe Asn Ile Lys Ser Ser Ser Ser Pro
145 150 155 160

Asp Ser Arg Ala Val Thr Cys Gly Met Ala Ser Leu Ser Ala Glu Lys
165 170 175

Val Thr Leu Asp Gln Arg Asp Tyr Glu Lys Tyr Ser Val Ser Cys Gln
180 185 190

Glu Asp Val Thr Cys Pro Thr Ala Glu Glu Thr Leu Pro Ile Glu Leu
195 200 205

Ala Leu Glu Ala Arg Gln Gln Asn Lys Tyr Glu Asn Tyr Ser Thr Ser
210 215 220

Phe Phe Ile Arg Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn Leu Gln
225 230 235 240

Met Lys Pro Leu Lys Asn Ser Gln Val Glu Val Ser Trp Glu Tyr Pro
245 250 255

Asp Ser Trp Ser Thr Pro His Ser Tyr Phe Ser Leu Lys Phe Phe Val
260 265 270

Arg Ile Gln Arg Lys Lys Glu Lys Met Lys Glu Thr Glu Glu Gly Cys
275 280 285

Asn Gln Lys Gly Ala Phe Leu Val Glu Lys Thr Ser Thr Glu Val Gln
290 295 300

Cys Lys Gly Gly Asn Val Cys Val Gln Ala Gln Asp Arg Tyr Tyr Asn
305 310 315 320

Ser Ser Cys Ser Lys Trp Ala Cys Val Pro Cys Arg Val Arg Ser
325 330 335

<210> 98
<211> 1008
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-12b

<400> 98
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gcccctggag aaacagtga cctcacctgt gacacgcctg aagaagatga catcacctgg 180
acctcagacc agagacatgg agtcataggc tctggaaaga ccctgacct cactgtcaaa 240
gagtttctag atgctggcca gtacacctgc caaaaggag gcgagactct gagccactca 300
catctgctgc tccacaagaa ggaaaatgga atttggtcca ctgaaatttt aaaaaatttc 360
aaaaacaaga ctttcctgaa gtgtgaagca ccaaattact ccggacggtt cacgtgtc 420
tggctggtgc aaagaaacat ggacttgaag ttcaacatca agagcagtag cagttcccct 480
gactctcggg cagtgcacatg tggaatggcg tctctgtctg cagagaaggt cacttgga 540
caaagggact atgagaagta ttcagtgtcc tgccaggagg atgtcacctg cccaactgcc 600
gaggagaccc tgcccattga actggcggtg gaagcacggc agcagaataa atatgagaac 660
tacagcacca gtttcttcat caggacatc atcaaaccag acccgcccaa gaacttgcag 720
atgaagcctt tgaagaactc acaggtggag gtcagctggg agtaccctga ctctggagc 780
actccccatt cctacttctc cctcaagttc ttgttcgaa tccagcgcaa gaaagaaaag 840

atgaaggaga cagaggaggg gtgtaaccag aaaggtgcgt tcctcgtaga gaagacatct 900
accgaagtcc aatgcaaagg cgggaatgtc tgcgtgcaag ctcaggatcg ctattacaat 960
tcctcatgca gcaagtgggc atgtgttccc tgcagggtcc gatacctag 1008

<210> 99
<211> 187
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-6

<400> 99

Phe Pro Thr Ser Gln Val Arg Arg Gly Asp Phe Thr Glu Asp Thr Thr
1 5 10 15

Pro Asn Arg Pro Val Tyr Thr Thr Ser Gln Val Gly Gly Leu Ile Thr
20 25 30

His Val Leu Trp Glu Ile Val Glu Met Arg Lys Glu Leu Cys Asn Gly
35 40 45

Asn Ser Asp Cys Met Asn Asn Asp Asp Ala Leu Ala Glu Asn Asn Leu
50 55 60

Lys Leu Pro Glu Ile Gln Arg Asn Asp Gly Cys Tyr Gln Thr Gly Tyr
65 70 75 80

Asn Gln Glu Ile Cys Leu Leu Lys Ile Ser Ser Gly Leu Leu Glu Tyr
85 90 95

His Ser Tyr Leu Glu Tyr Met Lys Asn Asn Leu Lys Asp Asn Lys Lys
100 105 110

Asp Lys Ala Arg Val Leu Gln Arg Asp Thr Glu Thr Leu Ile His Ile
115 120 125

Phe Asn Gln Glu Val Lys Asp Leu His Lys Ile Val Leu Pro Thr Pro
130 135 140

Ile Ser Asn Ala Leu Leu Thr Asp Lys Leu Glu Ser Gln Lys Glu Trp

145		150		155		160									
Leu	Arg	Thr	Lys	Thr	Ile	Gln	Phe	Ile	Leu	Lys	Ser	Leu	Glu	Glu	Phe
				165					170				175		

Leu	Lys	Val	Thr	Leu	Arg	Ser	Thr	Arg	Gln	Thr
			180					185		

<210> 100
 <211> 561
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> IL-6

<400> 100
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 atgagaaaag agttgtgcaa tggcaattct gattgtatga acaacgatga tgcacttgca 180
 gaaaacaatc tgaaacttcc agagatacaa agaaatgatg gatgctacca aactggatat 240
 aatcaggaaa tttgcctatt gaaaatttcc tctggtcttc tggagtagca tagctacctg 300
 gagtacatga agaacaactt aaaagataac aagaaagaca aagccagagt ccttcagaga 360
 gatacagaaa ctctaattca tatcttcaac caagaggtaa aagatttaca taaaatagtc 420
 cttcctaccc caatttcaa tgctctccta acagataagc tggagtcaca gaaggagtgg 480
 ctaaggacca agaccatcca attcatcttg aaatcacttg aagaatttct aaaagtcact 540
 ttgagatcta ctcggcaaac c 561

<210> 101
 <211> 433
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CD81-IL6

<400> 101

Met	Gly	Val	Glu	Gly	Cys	Thr	Lys	Cys	Ile	Lys	Tyr	Leu	Leu	Phe	Val
1				5					10					15	

Phe Asn Phe Val Phe Trp Leu Ala Gly Gly Val Ile Leu Gly Val Ala
20 25 30

Leu Trp Leu Arg His Asp Pro Gln Thr Thr Ser Leu Leu Tyr Leu Glu
35 40 45

Leu Gly Asn Lys Pro Ala Pro Asn Thr Phe Tyr Val Gly Ile Tyr Ile
50 55 60

Leu Ile Ala Val Gly Ala Val Met Met Phe Val Gly Phe Leu Gly Cys
65 70 75 80

Tyr Gly Ala Ile Gln Glu Ser Gln Cys Leu Leu Gly Thr Phe Phe Thr
85 90 95

Cys Leu Val Ile Leu Phe Ala Cys Glu Val Ala Ala Gly Ile Trp Gly
100 105 110

Phe Val Asn Lys Asp Gln Ile Ala Lys Asp Val Lys Gln Phe Tyr Asp
115 120 125

Gln Ala Leu Gln Gln Ala Val Met Asp Asp Asp Ala Asn Asn Ala Lys
130 135 140

Ala Val Val Lys Thr Phe His Glu Thr Leu Asn Cys Cys Gly Ser Asn
145 150 155 160

Ala Leu Thr Thr Leu Thr Thr Thr Ile Leu Arg Asn Ser Leu Cys Pro
165 170 175

Ser Gly Gly Gly Gly Ser Phe Pro Thr Ser Gln Val Arg Arg Gly Asp
180 185 190

Phe Thr Glu Asp Thr Thr Pro Asn Arg Pro Val Tyr Thr Thr Ser Gln
195 200 205

Val Gly Gly Leu Ile Thr His Val Leu Trp Glu Ile Val Glu Met Arg
210 215 220

Lys Glu Leu Cys Asn Gly Asn Ser Asp Cys Met Asn Asn Asp Asp Ala

[illegible]

<210> 102
<211> 1302
<212> DNA
<213> Artificial Sequence

<220>
<223> CD81-IL6

<400> 102
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ttctggctgg ctggaggcgt gatcctaggt gtagctctgt gggtgcgtca tgatccacag 120
accaccagcc tgctgtacct ggaactggga aacaaaccgg cacccaacac cttctacgtg 180
ggcatctaca ttctcattgc tgtgggagct gtgatgatgt ttgtaggctt cctgggggtgc 240
tatggggcca tccaggagtc ccagtgtctg ctggggacgt tcttcacctg ctttgtgatc 300
ctgtttgcct gtgagggtggc tgcaggcatc tggggcttcg taaacaaaga ccagatcgcc 360
aaggatgtga agcagttcta tgaccaggcc cttcagcaag ctgtgatgga tgatgatgcc 420
aacaatgcca aggctgtggg gaagactttc catgagacgc tcaactgttg tggctccaac 480
gcactgacca cactgactac caccatactg aggaacagcc tgtgtccctc aggaggagga 540
ggaagcttcc ctacttcaca agtccggaga ggagacttca cagaggatac cactcccaac 600
agacctgtct ataccacttc acaagtcgga ggcttaatta cacatgttct ctgggaaatc 660
gtggaaatga gaaaagagtt gtgcaatggc aattctgatt gtatgaacaa cgatgatgca 720
cttgcaaaa acaatctgaa acttccagag atacaaagaa atgatggatg ctaccaaact 780
ggatataatc aggaaatttg cctattgaaa atttcctctg gtcttctgga gtaccatagc 840
tacctggagt acatgaagaa caacttaaaa gataacaaga aagacaaagc cagagtcctt 900
cagagagata cagaaactct aattcatatc ttcaaccaag aggtaaaaga tttacataaa 960
atagtccttc ctaccccaat ttccaatgct ctcctaacag ataagctgga gtcacagaag 1020
gagtggctaa ggaccaagac catccaattc atcttgaaat cacttgaaga atttctaaaa 1080
gtcactttga gatctactcg gcaaaccgga ggaggaggaa gcggcggcaa catactcacc 1140
cccttactgc agcaagattg tcatcagaaa atcgatgagc tcttctctgg gaagctgtac 1200
ctcattggaa ttgcagccat tgtggtagct gtcattatga tctttgagat gattctgagc 1260
atggtgctgt gctgtggcat ccggaacagc tccgtgtact ga 1302

<210> 103
<211> 288
<212> PRT
<213> Artificial Sequence

<220>
<223> hCD80

<400> 103

Met Gly His Thr Arg Arg Gln Gly Thr Ser Pro Ser Lys Cys Pro Tyr
1 5 10 15

Leu Asn Phe Phe Gln Leu Leu Val Leu Ala Gly Leu Ser His Phe Cys
20 25 30

Ser Gly Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu
35 40 45

Ser Cys Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile
50 55 60

Tyr Trp Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp
65 70 75 80

Met Asn Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr
85 90 95

Asn Asn Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly
100 105 110

Thr Tyr Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg
115 120 125

Glu His Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr
130 135 140

Pro Ser Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile
145 150 155 160

Ile Cys Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu
165 170 175

Glu Asn Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp
180 185 190

Pro Glu Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met
195 200 205

Thr Thr Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg
210 215 220

Val Asn Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro
225 230 235 240

Asp Asn Leu Leu Pro Ser Trp Ala Ile Thr Leu Ile Ser Val Asn Gly
245 250 255

Ile Phe Val Ile Cys Cys Leu Thr Tyr Cys Phe Ala Pro Arg Cys Arg
260 265 270

Glu Arg Arg Arg Asn Glu Arg Leu Arg Arg Glu Ser Val Arg Pro Val
275 280 285

<210> 104
<211> 864
<212> DNA
<213> Artificial Sequence

<220>
<223> hCD81

<400> 104
atgggccaca cacggaggca gggaacatca ccatccaagt gtccatacct caatttcttt 60
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gaagtgaaag aagtggcaac gctgtcctgt ggtcacaatg tttctgttga agagctggca 180
caaaactgca tctactggca aaaggagaag aaaatggtgc tgactatgat gtctggggac 240
atgaatatat ggcccagta caagaaccgg accatctttg atatcactaa taacctctcc 300
attgtgatcc tggctctgcg cccatctgac gagggcacat acgagtgtgt tgttctgaag 360
tatgaaaaag acgctttcaa gcgggaacac ctggctgaag tgacgttatc agtcaaagct 420
gacttccta cacctagtat atctgacttt gaaattccaa cttctaatat tagaaggata 480

atttgc tcaa cctctggagg ttttccagag cctcacctct cctggttgga aaatggagaa 540
 gaattaaatg ccatcaacac aacagtttcc caagatcctg aaactgagct ctatgctgtt 600
 agcagcaaac tggatttcaa tatgacaacc aaccacagct tcatgtgtct catcaagtat 660
 ggacatttaa gagtgaatca gaccttcaac tggaatacaa ccaagcaaga gcattttcct 720
 gataacctgc tcccatcctg ggccattacc ttaatctcag taaatggaat ttttgtgata 780
 tgctgcctga cctactgctt tgccccaaga tgcagagaga gaaggaggaa tgagagattg 840
 agaagggaaa gtgtacgccc tgta 864

<210> 105
 <211> 228
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> hCD9

<400> 105

Met Pro Val Lys Gly Gly Thr Lys Cys Ile Lys Tyr Leu Leu Phe Gly
1 5 10 15

Phe Asn Phe Ile Phe Trp Leu Ala Gly Ile Ala Val Leu Ala Ile Gly
20 25 30

Leu Trp Leu Arg Phe Asp Ser Gln Thr Lys Ser Ile Phe Glu Gln Glu
35 40 45

Thr Asn Asn Asn Asn Ser Ser Phe Tyr Thr Gly Val Tyr Ile Leu Ile
50 55 60

Gly Ala Gly Ala Leu Met Met Leu Val Gly Phe Leu Gly Cys Cys Gly
65 70 75 80

Ala Val Gln Glu Ser Gln Cys Met Leu Gly Leu Phe Phe Gly Phe Leu
85 90 95

Leu Val Ile Phe Ala Ile Glu Ile Ala Ala Ala Ile Trp Gly Tyr Ser
100 105 110

His Lys Asp Glu Val Ile Lys Glu Val Gln Glu Phe Tyr Lys Asp Thr

115

120

125

Tyr Asn Lys Leu Lys Thr Lys Asp Glu Pro Gln Arg Glu Thr Leu Lys
 130 135 140

Ala Ile His Tyr Ala Leu Asn Cys Cys Gly Leu Ala Gly Gly Val Glu
 145 150 155 160

Gln Phe Ile Ser Asp Ile Cys Pro Lys Lys Asp Val Leu Glu Thr Phe
 165 170 175

Thr Val Lys Ser Cys Pro Asp Ala Ile Lys Glu Val Phe Asp Asn Lys
 180 185 190

Phe His Ile Ile Gly Ala Val Gly Ile Gly Ile Ala Val Val Met Ile
 195 200 205

Phe Gly Met Ile Phe Ser Met Ile Leu Cys Cys Ala Ile Arg Arg Asn
 210 215 220

Arg Glu Met Val
 225

<210> 106
 <211> 687
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> hCD9

<400> 106
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 accaagagca tcttcgagca agaaactaat aataataatt ccagcttcta cacaggagtc 180
 tatattctga tcggagccgg cgccctcatg atgctggtgg gcttcctggg ctgctgcggg 240
 gctgtgcagg agtcccagtg catgctggga ctgttcttcg gcttcctctt ggtgatattc 300
 gccattgaaa tagctgcggc catctgggga tattcccaca aggatgaggt gattaaggaa 360
 gtccaggagt ttacaagga cacctacaac aagctgaaaa ccaaggatga gccccagcgg 420

gaaacgctga aagccatcca ctatgcgttg aactgctgtg gtttggctgg gggcgtggaa 480
 cagtttatct cagacatctg cccaagaag gacgtactcg aaaccttcac cgtgaagtcc 540
 tgtcctgatg ccatcaaaga ggtcttcgac aataaattcc acatcatcgg cgcagtgggc 600
 atcggcattg ccgtgggtcat gatatttggc atgatcttca gtatgatctt gtgctgtgct 660
 atccgcagga accgcgagat ggtctag 687

<210> 107
 <211> 392
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> hCD80-hCD9

<400> 107

Met Gly His Thr Arg Arg Gln Gly Thr Ser Pro Ser Lys Cys Pro Tyr
 1 5 10 15

Leu Asn Phe Phe Gln Leu Leu Val Leu Ala Gly Leu Ser His Phe Cys
 20 25 30

Ser Gly Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu
 35 40 45

Ser Cys Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile
 50 55 60

Tyr Trp Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp
 65 70 75 80

Met Asn Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr
 85 90 95

Asn Asn Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly
 100 105 110

Thr Tyr Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg
 115 120 125

Glu His Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr

130

135

140

Pro Ser Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile
 145 150 155 160

Ile Cys Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu
 165 170 175

Glu Asn Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp
 180 185 190

Pro Glu Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met
 195 200 205

Thr Thr Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg
 210 215 220

Val Asn Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro
 225 230 235 240

Asp Asn Leu Leu Pro Ser Trp Ala Ile Thr Leu Ile Ser Val Asn Gly
 245 250 255

Ile Phe Val Ile Cys Cys Leu Thr Tyr Cys Phe Ala Pro Arg Cys Arg
 260 265 270

Glu Arg Arg Arg Asn Glu Arg Leu Arg Arg Glu Ser Val Arg Pro Val
 275 280 285

Met Pro Val Lys Gly Gly Thr Lys Cys Ile Lys Tyr Leu Leu Phe Gly
 290 295 300

Phe Asn Phe Ile Phe Trp Leu Ala Gly Ile Ala Val Leu Ala Ile Gly
 305 310 315 320

Leu Trp Leu Arg Phe Asp Ser Gln Thr Lys Ser Ile Phe Glu Gln Glu
 325 330 335

Thr Asn Asn Asn Asn Ser Ser Phe Tyr Thr Gly Val Tyr Ile Leu Ile
 340 345 350

Gly Ala Gly Ala Leu Met Met Leu Val Gly Phe Leu Gly Cys Cys Gly
355 360 365

Ala Val Gln Glu Ser Gln Cys Met Leu Gly Leu Phe Phe Gly Phe Leu
370 375 380

Leu Val Ile Phe Ala Ile Glu Ile
385 390

<210> 108
<211> 1551
<212> DNA
<213> Artificial Sequence

<220>
<223> hCD80-hCD9

<400> 108
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gaagtgaaag aagtggcaac gctgtcctgt ggtcacaatg tttctgttga agagctggca 180
caaaactcgca tctactggca aaaggagaag aaaatgggtgc tgactatgat gtctggggac 240
atgaatatat ggcccagta caagaaccgg accatctttg atatcactaa taacctctcc 300
attgtgatcc tggctctgcg cccatctgac gagggcacat acgagtgtgt tgttctgaag 360
tatgaaaaag acgctttcaa gcgggaacac ctggctgaag tgacgttatc agtcaaagct 420
gacttcccta cacctagtat atctgacttt gaaattccaa cttctaatat tagaaggata 480
atttgctcaa cctctggagg ttttccagag cctcacctct cctggttgga aaatggagaa 540
gaattaaatg ccatcaacac aacagtttcc caagatcctg aaactgagct ctatgctgtt 600
agcagcaaac tggatttcaa tatgacaacc aaccacagct tcatgtgtct catcaagtat 660
ggacatttaa gagtgaatca gaccttcaac tggaatacaa ccaagcaaga gcattttcct 720
gataacctgc tcccacctg ggccattacc ttaatctcag taaatggaat ttttgtgata 780
tgctgcctga cctactgctt tgccccaaga tgcagagaga gaaggaggaa tgagagattg 840
agaagggaaa gtgtacgcc tgtaatgccg gtcaaaggag gcaccaagtg catcaaatac 900
ctgctgttcg gatttaactt catcttctgg cttgccggga ttgctgtcct tgccattgga 960

ctatggctcc gattcgactc tcagaccaag agcatcttcg agcaagaaac taataataat 1020
 aattccagct tctacacagg agtctatatt ctgatcggag cgggcgcctt catgatgctg 1080
 gtgggcttcc tgggctgctg cggggctgtg caggagtccc agtgcattgct gggactgttc 1140
 ttcggcttcc tcttgggtgat attcgccatt gaaatagctg cggccatctg gggatattcc 1200
 cacaaggatg aggtgattaa ggaagtccag gagttttaca aggacaccta caacaagctg 1260
 aaaaccaagg atgagcccca gcgggaaacg ctgaaagcca tccactatgc gttgaactgc 1320
 tgtggtttgg ctgggggctg ggaacagttt atctcagaca tctgccccaa gaaggacgta 1380
 ctcgaaacct tcaccgtgaa gtcctgtcct gatgccatca aagaggtctt cgacaataaa 1440
 ttccacatca tcggcgcagt gggcatcggc attgccgtgg tcatgatatt tggcatgatc 1500
 ttcagtatga tcttgtgctg tgctatccgc aggaaccgag agatggtcta g 1551

<210> 109
 <211> 133
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> hIL-2

<400> 109

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
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Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
 20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
 35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
 50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
 65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
 85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 110
<211> 399
<212> DNA
<213> Artificial Sequence

<220>
<223> hIL-2

<400> 110
gcacctactt caagttctac aaagaaaaca cagctacaac tggagcattt actgctggat 60
ttacagatga ttttgaatgg aattaataat tacaagaatc ccaaactcac caggatgctc 120
acatttaagt ttacatgcc caagaaggcc acagaactga aacatcttca gtgtctagaa 180
gaagaactca aacctctgga ggaagtgcta aatttagctc aaagcaaaaa ctttcactta 240
agaccaggg acttaatcag caatatcaac gtaatagttc tggaactaaa gggatctgaa 300
acaacattca tgtgtgaata tgctgatgag acagcaacca ttgtagaatt tctgaacaga 360
tggattacct tttgtcaaag catcatctca acactgact 399

<210> 111
<211> 170
<212> PRT
<213> Artificial Sequence

<220>
<223> hCD63 1-170

<400> 111

Met Ala Val Glu Gly Gly Met Lys Cys Val Lys Phe Leu Leu Tyr Val
1 5 10 15

Leu Leu Leu Ala Phe Cys Ala Cys Ala Val Gly Leu Ile Ala Val Gly
20 25 30

Val Gly Ala Gln Leu Val Leu Ser Gln Thr Ile Ile Gln Gly Ala Thr
35 40 45

Pro Gly Ser Leu Leu Pro Val Val Ile Ile Ala Val Gly Val Phe Leu
50 55 60

Phe Leu Val Ala Phe Val Gly Cys Cys Gly Ala Cys Lys Glu Asn Tyr
65 70 75 80

Cys Leu Met Ile Thr Phe Ala Ile Phe Leu Ser Leu Ile Met Leu Val
85 90 95

Glu Val Ala Ala Ala Ile Ala Gly Tyr Val Phe Arg Asp Lys Val Met
100 105 110

Ser Glu Phe Asn Asn Asn Phe Arg Gln Gln Met Glu Asn Tyr Pro Lys
115 120 125

Asn Asn His Thr Ala Ser Ile Leu Asp Arg Met Gln Ala Asp Phe Lys
130 135 140

Cys Cys Gly Ala Ala Asn Tyr Thr Asp Trp Glu Lys Ile Pro Ser Met
145 150 155 160

Ser Lys Asn Arg Val Pro Asp Ser Cys Cys
165 170

<210> 112
<211> 510
<212> DNA
<213> Artificial Sequence

<220>
<223> hCD63 1-170

<400> 112
atggcggtgg aaggaggaat gaaatgtgtg aagttcttgc tctacgtcct cctgctggcc 60
ttttgcgctt gtgcagtggg actgattgcc gtgggtgtcg gggcacagct tgtcctgagt 120
cagaccataa tccagggggc taccctggc tctctgttgc cagtggtcac catcgcagtg 180
gggtgtcttcc tcttctgggt ggcttttgtg ggctgtgtcg gggcctgcaa ggagaactat 240

tgtcttatga tcacgtttgc catctttctg tctcttatca tgttggtgga ggtggccgca	300
gccattgctg gctatgtggt tagagataag gtgatgtcag agtttaataa caacttccgg	360
cagcagatgg agaattaccc gaaaaacaac cacactgctt cgatcctgga caggatgcag	420
gcagatttta agtgctgtgg ggctgctaac tacacagatt gggagaaaaat cccttccatg	480
tcgaagaacc gagtccccga ctcctgctgc	510

<210> 113
 <211> 68
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> hCD63 171-238

<400> 113

Ile	Asn	Val	Thr	Val	Gly	Cys	Gly	Ile	Asn	Phe	Asn	Glu	Lys	Ala	Ile
1				5				10						15	

His	Lys	Glu	Gly	Cys	Val	Glu	Lys	Ile	Gly	Gly	Trp	Leu	Arg	Lys	Asn
		20						25					30		

Val	Leu	Val	Val	Ala	Ala	Ala	Ala	Leu	Gly	Ile	Ala	Phe	Val	Glu	Val
		35					40					45			

Leu	Gly	Ile	Val	Phe	Ala	Cys	Cys	Leu	Val	Lys	Ser	Ile	Arg	Ser	Gly
	50					55					60				

Tyr	Glu	Val	Met
65			

<210> 114
 <211> 207
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> hCD63 171-238

<400> 114

attaatgtta ctgtgggctg tgggattaat ttcaacgaga aggcgatcca taaggagggc	60

tgtgtggaga agattggggg ctggctgagg aaaaatgtgc tggtggtagc tgcagcagcc	120

cttgggaattg cttttgtcga ggttttggga attgtctttg cctgctgcct cgtgaagagt 180
atcagaagtg gctacgaggt gatgtag 207

<210> 115
<211> 381
<212> PRT
<213> Artificial Sequence

<220>
<223> hCD63-IL2

<400> 115

Met Ala Val Glu Gly Gly Met Lys Cys Val Lys Phe Leu Leu Tyr Val
1 5 10 15

Leu Leu Leu Ala Phe Cys Ala Cys Ala Val Gly Leu Ile Ala Val Gly
20 25 30

Val Gly Ala Gln Leu Val Leu Ser Gln Thr Ile Ile Gln Gly Ala Thr
35 40 45

Pro Gly Ser Leu Leu Pro Val Val Ile Ile Ala Val Gly Val Phe Leu
50 55 60

Phe Leu Val Ala Phe Val Gly Cys Cys Gly Ala Cys Lys Glu Asn Tyr
65 70 75 80

Cys Leu Met Ile Thr Phe Ala Ile Phe Leu Ser Leu Ile Met Leu Val
85 90 95

Glu Val Ala Ala Ala Ile Ala Gly Tyr Val Phe Arg Asp Lys Val Met
100 105 110

Ser Glu Phe Asn Asn Asn Phe Arg Gln Gln Met Glu Asn Tyr Pro Lys
115 120 125

Asn Asn His Thr Ala Ser Ile Leu Asp Arg Met Gln Ala Asp Phe Lys
130 135 140

Cys Cys Gly Ala Ala Asn Tyr Thr Asp Trp Glu Lys Ile Pro Ser Met
145 150 155 160

Ser Lys Asn Arg Val Pro Asp Ser Cys Cys Gly Gly Gly Gly Ser Ala
165 170 175

Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His Leu
180 185 190

Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn
195 200 205

Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys
210 215 220

Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro
225 230 235 240

Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg
245 250 255

Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu Lys
260 265 270

Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr
275 280 285

Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile
290 295 300

Ser Thr Leu Thr Gly Gly Gly Gly Ser Ile Asn Val Thr Val Gly Cys
305 310 315 320

Gly Ile Asn Phe Asn Glu Lys Ala Ile His Lys Glu Gly Cys Val Glu
325 330 335

Lys Ile Gly Gly Trp Leu Arg Lys Asn Val Leu Val Val Ala Ala Ala
340 345 350

Ala Leu Gly Ile Ala Phe Val Glu Val Leu Gly Ile Val Phe Ala Cys
355 360 365

Cys Leu Val Lys Ser Ile Arg Ser Gly Tyr Glu Val Met

370

375

380

<210> 116
 <211> 1146
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> hCD63-IL2

<400> 116
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 ttttgcgcct gtgcagtggg actgattgcc gtgggtgtcg gggcacagct tgtcctgagt 120
 cagaccataa tccagggggc tacccttggc tctctgttgc cagtgggtcat catcgcagtg 180
 ggtgtcttcc tcttcctggg ggcttttgtg ggctgctgcg gggcctgcaa ggagaactat 240
 tgtcttatga tcacgtttgc catctttctg tctcttatca tgttggtgga ggtggccgca 300
 gccattgctg gctatgtgtt tagagataag gtgatgtcag agtttaataa caacttccgg 360
 cagcagatgg agaattaccc gaaaaacaac cacactgctt cgatcctgga caggatgcag 420
 gcagatttta agtgctgtgg ggctgctaac tacacagatt gggagaaaat cccttccatg 480
 tcgaagaacc gagtccccga ctctgctgc ggaggaggag gaagcgcacc tacttcaagt 540
 tctacaaaga aaacacagct acaactggag catttactgc tggatttaca gatgattttg 600
 aatggaatta ataattacaa gaatcccaa ctcaccagga tgctcacatt taagttttac 660
 atgccaaga aggccacaga actgaaacat cttcagtgtc tagaagaaga actcaaacct 720
 ctggaggaag tgctaaattt agctcaaagc aaaaactttc acttaagacc cagggactta 780
 atcagcaata tcaacgtaat agttctggaa ctaaagggat ctgaaacaac attcatgtgt 840
 gaatatgctg atgagacagc aaccattgta gaatttctga acagatggat taccttttgt 900
 caaagcatca tctcaacact gactggagga ggaggaagca ttaatgttac tgtgggctgt 960
 gggattaatt tcaacgagaa ggcgatccat aaggagggtc gtgtggagaa gattgggggc 1020
 tggctgagga aaaatgtgct ggtggtagct gcagcagccc ttggaattgc ttttgtcgag 1080
 gttttgggaa ttgtctttgc ctgctgcctc gtgaagagta tcagaagtgg ctacgaggtg 1140
 atgtag 1146

<210> 117

<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> hb2mg signal

<400> 117

Met Ser Arg Ser Val Ala Leu Ala Val Leu Ala Leu Leu Ser Leu Ser
1 5 10 15

Gly Leu Glu Ala
20

<210> 118
<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<223> hb2mg signal

<400> 118
atgtctcgct ccgtggcctt agctgtgctc gcgctactct ctctttctgg cctggaggct 60

<210> 119
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> WT1

<400> 119

Cys Tyr Thr Trp Asn Gln Met Asn Leu
1 5

<210> 120
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> WT1

<400> 120
tgctacacct ggaaccagat gaacctg 27

<210> 121
<211> 99
<212> PRT
<213> Artificial Sequence

<220>
<223> hb2mg

<400> 121

Ile Gln Arg Thr Pro Lys Ile Gln Val Tyr Ser Arg His Pro Ala Glu
1 5 10 15

Asn Gly Lys Ser Asn Phe Leu Asn Cys Tyr Val Ser Gly Phe His Pro
20 25 30

Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys
35 40 45

Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp Ser Phe Tyr Leu
50 55 60

Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp Glu Tyr Ala Cys
65 70 75 80

Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile Val Lys Trp Asp
85 90 95

Arg Asp Met

<210> 122
<211> 297
<212> DNA
<213> Artificial Sequence

<220>
<223> hb2mg

<400> 122

atccagcgta ctccaaagat tcaggtttac tcacgtcatc cagcagagaa tggaaagtca 60
aatttcctga attgctatgt gtctgggttt catccatccg acattgaagt tgacttactg 120
aagaatggag agagaattga aaaagtggag cattcagact tgtctttcag caaggactgg 180

tctttctatc tcttgacta cactgaattc acccccactg aaaaagatga gtatgcctgc 240

cgtgtgaacc atgtgacttt gtcacagccc aagatagtta agtgggatcg agacatg 297

<210> 123

<211> 341

<212> PRT

<213> Artificial Sequence

<220>

<223> hMHCIa

<400> 123

Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Glu Glu Thr
50 55 60

Gly Lys Val Lys Ala His Ser Gln Thr Asp Arg Glu Asn Leu Arg Ile
65 70 75 80

Ala Leu Arg Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
85 90 95

Met Met Phe Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
100 105 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
115 120 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
130 135 140

Arg Lys Trp Glu Ala Ala His Val Ala Glu Gln Gln Arg Ala Tyr Leu
145 150 155 160

Glu Gly Thr Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
165 170 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
180 185 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
195 200 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Pro Ser Ser Gln Pro Thr Val Pro Ile Val Gly Ile Ile
275 280 285

Ala Gly Leu Val Leu Leu Gly Ala Val Ile Thr Gly Ala Val Val Ala
290 295 300

Ala Val Met Trp Arg Arg Asn Ser Ser Asp Arg Lys Gly Gly Ser Tyr
305 310 315 320

Ser Gln Ala Ala Ser Ser Asp Ser Ala Gln Gly Ser Asp Val Ser Leu
325 330 335

Thr Ala Cys Lys Val
340

<210> 124
<211> 1023
<212> DNA
<213> Artificial Sequence

<220>

<223> hMHCIa

<400> 124

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ggctcccact ccatgaggta tttctccaca tccgtgtccc ggcccggccg cggggagccc      60
cgcttcatcg ccgtgggcta cgtggacgac acgcagttcg tgcggttcga cagcgacgcc      120
gcgagccaga ggatggagcc gcgggcgccg tggatagagc aggagggggcc ggagtattgg      180
gacgaggaga cagggaaagt gaaggcccac tcacagactg accgagagaa cctgcggatc      240
gcgctccgct actacaacca gagcgaggcc ggttctcaca ccctccagat gatgtttggc      300
tgcgacgtgg ggtcggacgg gcgcttcctc cgcggggtacc accagtacgc ctacgacggc      360
aaggattaca tcgccctgaa agaggacctg cgctcttgga ccgcggcgga catggcggct      420
cagatcacca agcgcaagtg ggaggcggcc catgtggcgg agcagcagag agcctacctg      480
gagggcacgt gcgtggacgg gctccgcaga tacctggaga acgggaagga gacgctgcag      540
cgcacggacc cccccaagac acatatgacc caccaccca tctctgacca tgaggccact      600
ctgagatgct gggccctggg cttctaccct gcggagatca cactgacctg gcagcgggat      660
ggggaggacc agaccagga cacggagctt gtggagacca ggcctgcagg ggatggaacc      720
ttccagaagt gggcagctgt ggtggtacct tctggagagg agcagagata cacctgccat      780
gtgcagcatg agggctctgc caagcccctc accctgagat gggagccatc ttcccagccc      840
accgtcccca tcgtgggcat cattgctggc ctggttctcc ttggagctgt gatcactgga      900
gctgtggtcg ctgctgtgat gtggaggagg aacagctcag atagaaaagg agggagctac      960
tctcaggctg caagcagtga cagtgccag ggctctgatg tgtctctcac agcttgtaaa     1020
gtg                                                                    1023
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<210> 125

<211> 460

<212> PRT

<213> Artificial Sequence

<220>

<223> hsMHCI

<400> 125

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Ile Gln Arg Thr Pro Lys Ile Gln Val Tyr Ser Arg His Pro Ala Glu
1           5           10          15
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Asn Gly Lys Ser Asn Phe Leu Asn Cys Tyr Val Ser Gly Phe His Pro
20 25 30

Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys
35 40 45

Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp Ser Phe Tyr Leu
50 55 60

Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp Glu Tyr Ala Cys
65 70 75 80

Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile Val Lys Trp Asp
85 90 95

Arg Asp Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
100 105 110

Gly Ser Gly Gly Gly Gly Ser Gly Ser His Ser Met Arg Tyr Phe Ser
115 120 125

Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala Val
130 135 140

Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala Ala
145 150 155 160

Ser Gln Arg Met Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly Pro
165 170 175

Glu Tyr Trp Asp Glu Glu Thr Gly Lys Val Lys Ala His Ser Gln Thr
180 185 190

Asp Arg Glu Asn Leu Arg Ile Ala Leu Arg Tyr Tyr Asn Gln Ser Glu
195 200 205

Ala Gly Ser His Thr Leu Gln Met Met Phe Gly Cys Asp Val Gly Ser
210 215 220

Asp Gly Arg Phe Leu Arg Gly Tyr His Gln Tyr Ala Tyr Asp Gly Lys

225		230		235		240									
Asp	Tyr	Ile	Ala	Leu	Lys	Glu	Asp	Leu	Arg	Ser	Trp	Thr	Ala	Ala	Asp
				245					250						255
Met	Ala	Ala	Gln	Ile	Thr	Lys	Arg	Lys	Trp	Glu	Ala	Ala	His	Val	Ala
			260					265					270		
Glu	Gln	Gln	Arg	Ala	Tyr	Leu	Glu	Gly	Thr	Cys	Val	Asp	Gly	Leu	Arg
		275					280					285			
Arg	Tyr	Leu	Glu	Asn	Gly	Lys	Glu	Thr	Leu	Gln	Arg	Thr	Asp	Pro	Pro
	290					295					300				
Lys	Thr	His	Met	Thr	His	His	Pro	Ile	Ser	Asp	His	Glu	Ala	Thr	Leu
305					310					315					320
Arg	Cys	Trp	Ala	Leu	Gly	Phe	Tyr	Pro	Ala	Glu	Ile	Thr	Leu	Thr	Trp
				325					330					335	
Gln	Arg	Asp	Gly	Glu	Asp	Gln	Thr	Gln	Asp	Thr	Glu	Leu	Val	Glu	Thr
			340					345					350		
Arg	Pro	Ala	Gly	Asp	Gly	Thr	Phe	Gln	Lys	Trp	Ala	Ala	Val	Val	Val
		355					360					365			
Pro	Ser	Gly	Glu	Glu	Gln	Arg	Tyr	Thr	Cys	His	Val	Gln	His	Glu	Gly
	370					375					380				
Leu	Pro	Lys	Pro	Leu	Thr	Leu	Arg	Trp	Glu	Pro	Ser	Ser	Gln	Pro	Thr
385					390					395					400
Val	Pro	Ile	Val	Gly	Ile	Ile	Ala	Gly	Leu	Val	Leu	Leu	Gly	Ala	Val
				405					410					415	
Ile	Thr	Gly	Ala	Val	Val	Ala	Ala	Val	Met	Trp	Arg	Arg	Asn	Ser	Ser
			420					425					430		
Asp	Arg	Lys	Gly	Gly	Ser	Tyr	Ser	Gln	Ala	Ala	Ser	Ser	Asp	Ser	Ala
		435					440					445			

Gln Gly Ser Asp Val Ser Leu Thr Ala Cys Lys Val
 450 455 460

<210> 126
 <211> 1380
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> hsMHCI

<400> 126
 atccagcgta ctccaaagat tcaggtttac tcacgtcatc cagcagagaa tggaaagtca 60
 aatttcctga attgctatgt gtctggggtt catccatccg acattgaagt tgacttactg 120
 aagaatggag agagaattga aaaagtggag cattcagact tgtctttcag caaggactgg 180
 tctttctatc tcttgtaact cactgaattc acccccactg aaaaagatga gtatgcctgc 240
 cgtgtgaacc atgtgacttt gtcacagccc aagatagtta agtgggatcg agacatgggg 300
 gggggaggct ccggtggagg ggggtctgga ggggggggggt ctggtggagg cggaagtggc 360
 tcccactcca tgaggatatt ctccacatcc gtgtcccggc ccggccgcgg ggagccccgc 420
 ttcatcgccg tgggctacgt ggacgacacg cagttcgtgc ggttcgacag cgacgccgcg 480
 agccagagga tggagccgcg ggcgccgtgg atagagcagg aggggcccga gtattgggac 540
 gaggagacag ggaaagtga ggcccactca cagactgacc gagagaacct gcggatcgcg 600
 ctccgctact acaaccagag cgaggccggt tctcacaccc tccagatgat gtttggctgc 660
 gacgtgggggt cggacgggcg cttcctccgc ggggtaccacc agtacgccta cgacggcaag 720
 gattacatcg ccctgaaaga ggacctgcgc tcttggaccg cggcggacat ggcggctcag 780
 atcaccaagc gcaagtggga ggcggcccat gtggcggagc agcagagagc ctacctggag 840
 ggcacgtgcg tggacgggct ccgcagatac ctggagaacg ggaaggagac gctgcagcgc 900
 acggaccccc ccaagacaca tatgaccac caccatct ctgaccatga ggccactctg 960
 agatgctggg ccctgggctt ctaccctgcg gagatcacac tgacctggca gcgggatggg 1020
 gaggaccaga cccaggacac ggagcttggt gagaccaggc ctgcagggga tggaaccttc 1080
 cagaagtggg cagctgtggt ggtaccttct ggagaggagc agagatacac ctgccatgtg 1140
 cagcatgagg gtctgcccac gccctcacc ctgagatggg agccatcttc ccagcccacc 1200

gtcccatcg tgggcatcat tgctggcctg gttctccttg gagctgtgat cactggagct 1260
 gtggtcgctg ctgtgatgtg gaggaggaac agctcagata gaaaaggagg gagctactct 1320
 caggctgcaa gcagtgcacag tgcccagggc tctgatgtgt ctctcacagc ttgtaaagtg 1380

<210> 127
 <211> 504
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> hsc-Trimer

<400> 127

Met Ser Arg Ser Val Ala Leu Ala Val Leu Ala Leu Leu Ser Leu Ser
 1 5 10 15

Gly Leu Glu Ala Cys Tyr Thr Trp Asn Gln Met Asn Leu Gly Gly Gly
 20 25 30

Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Gln Arg Thr
 35 40 45

Pro Lys Ile Gln Val Tyr Ser Arg His Pro Ala Glu Asn Gly Lys Ser
 50 55 60

Asn Phe Leu Asn Cys Tyr Val Ser Gly Phe His Pro Ser Asp Ile Glu
 65 70 75 80

Val Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu His Ser
 85 90 95

Asp Leu Ser Phe Ser Lys Asp Trp Ser Phe Tyr Leu Leu Tyr Tyr Thr
 100 105 110

Glu Phe Thr Pro Thr Glu Lys Asp Glu Tyr Ala Cys Arg Val Asn His
 115 120 125

Val Thr Leu Ser Gln Pro Lys Ile Val Lys Trp Asp Arg Asp Met Gly
 130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly

145		150		155		160									
Gly	Gly	Ser	Gly	Ser	His	Ser	Met	Arg	Tyr	Phe	Ser	Thr	Ser	Val	Ser
				165					170					175	
Arg	Pro	Gly	Arg	Gly	Glu	Pro	Arg	Phe	Ile	Ala	Val	Gly	Tyr	Val	Asp
			180					185					190		
Asp	Thr	Gln	Phe	Val	Arg	Phe	Asp	Ser	Asp	Ala	Ala	Ser	Gln	Arg	Met
		195					200					205			
Glu	Pro	Arg	Ala	Pro	Trp	Ile	Glu	Gln	Glu	Gly	Pro	Glu	Tyr	Trp	Asp
	210					215					220				
Glu	Glu	Thr	Gly	Lys	Val	Lys	Ala	His	Ser	Gln	Thr	Asp	Arg	Glu	Asn
225					230					235					240
Leu	Arg	Ile	Ala	Leu	Arg	Tyr	Tyr	Asn	Gln	Ser	Glu	Ala	Gly	Ser	His
				245					250					255	
Thr	Leu	Gln	Met	Met	Phe	Gly	Cys	Asp	Val	Gly	Ser	Asp	Gly	Arg	Phe
			260					265					270		
Leu	Arg	Gly	Tyr	His	Gln	Tyr	Ala	Tyr	Asp	Gly	Lys	Asp	Tyr	Ile	Ala
		275					280					285			
Leu	Lys	Glu	Asp	Leu	Arg	Ser	Trp	Thr	Ala	Ala	Asp	Met	Ala	Ala	Gln
	290					295					300				
Ile	Thr	Lys	Arg	Lys	Trp	Glu	Ala	Ala	His	Val	Ala	Glu	Gln	Gln	Arg
305					310					315					320
Ala	Tyr	Leu	Glu	Gly	Thr	Cys	Val	Asp	Gly	Leu	Arg	Arg	Tyr	Leu	Glu
				325					330					335	
Asn	Gly	Lys	Glu	Thr	Leu	Gln	Arg	Thr	Asp	Pro	Pro	Lys	Thr	His	Met
			340					345					350		
Thr	His	His	Pro	Ile	Ser	Asp	His	Glu	Ala	Thr	Leu	Arg	Cys	Trp	Ala
		355					360					365			

Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly
370 375 380

Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly
385 390 395 400

Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu
405 410 415

Glu Gln Arg Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro
420 425 430

Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Pro Thr Val Pro Ile Val
435 440 445

Gly Ile Ile Ala Gly Leu Val Leu Leu Gly Ala Val Ile Thr Gly Ala
450 455 460

Val Val Ala Ala Val Met Trp Arg Arg Asn Ser Ser Asp Arg Lys Gly
465 470 475 480

Gly Ser Tyr Ser Gln Ala Ala Ser Ser Asp Ser Ala Gln Gly Ser Asp
485 490 495

Val Ser Leu Thr Ala Cys Lys Val
500

<210> 128
<211> 1512
<212> DNA
<213> Artificial Sequence

<220>
<223> hsc-Trimer

<400> 128
atgtctcgct ccgtggcctt agctgtgctc gcgctactct ctctttctgg cctggaggct 60
tgctacacct ggaaccagat gaacctgggc ggaggtgcct ctggcggtgg gggcagcggt 120
ggaggggggca gtatccagcg tactccaaag attcaggttt actcacgtca tccagcagag 180
aatggaaagt caaatttcct gaattgctat gtgtctgggt ttcattccatc cgacattgaa 240

gttgacttac tgaagaatgg agagagaatt gaaaaagtgg agcattcaga cttgtctttc	300
agcaaggact ggtcttttcta tctcttgtac tacactgaat tcacccccac tgaaaaagat	360
gagtatgcct gccgtgtgaa ccatgtgact ttgtcacagc ccaagatagt taagtgggat	420
cgagacatgg gggggggagg ctccggtgga ggggggtctg gagggggggg gtctggtgga	480
ggcgggaagtg gctcccactc catgaggtat ttctccacat ccgtgtcccg gcccgccgc	540
ggggagcccc gcttcatcgc cgtgggctac gtggacgaca cgagttcgt gcggttcgac	600
agcgacgccg cgagccagag gatggagccg cgggcgccgt ggatagagca ggaggggccg	660
gagtattggg acgaggagac agggaaagtg aaggcccact cacagactga ccgagagaac	720
ctgcggatcg cgctccgcta ctacaaccag agcgaggccg gttctcacac cctccagatg	780
atgtttggct gcgacgtggg gtcggacggg cgcttcctcc gcgggtacca ccagtacgcc	840
tacgacggca aggattacat cgccctgaaa gaggacctgc gctcttgga cgcggcggac	900
atggcggctc agatcaccaa gcgcaagtgg gaggcggccc atgtggcgga gcagcagaga	960
gcctacctgg agggcacgtg cgtggacggg ctccgcagat acctggagaa cgggaaggag	1020
acgctgcagc gcacggaccc cccaagaca catatgaccc accaccccat ctctgacat	1080
gaggccactc tgagatgctg ggccctgggc ttctaccctg cgagatcac actgacctgg	1140
cagcgggatg gggaggacca gaccaggac acggagcttg tggagaccag gcctgcaggg	1200
gatggaacct tccagaagtg ggcagctgtg gtggtacctt ctggagagga gcagagatac	1260
acctgccatg tgcagcatga gggctctgcc aagcccctca ccctgagatg ggagccatct	1320
tcccagccca ccgtcccat cgtgggcatc attgctggcc tggttctcct tggagctgtg	1380
atcactggag ctgtggtcgc tgctgtgatg tggaggagga acagctcaga tagaaaagga	1440
gggagctact ctcaggctgc aagcagtgc agtgcccagg gctctgatgt gtctctcaca	1500
gcttgtaaag tg	1512

<210> 129
 <211> 236
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> hCD81

<400> 129

Met Gly Val Glu Gly Cys Thr Lys Cys Ile Lys Tyr Leu Leu Phe Val
1 5 10 15

Phe Asn Phe Val Phe Trp Leu Ala Gly Gly Val Ile Leu Gly Val Ala
20 25 30

Leu Trp Leu Arg His Asp Pro Gln Thr Thr Asn Leu Leu Tyr Leu Glu
35 40 45

Leu Gly Asp Lys Pro Ala Pro Asn Thr Phe Tyr Val Gly Ile Tyr Ile
50 55 60

Leu Ile Ala Val Gly Ala Val Met Met Phe Val Gly Phe Leu Gly Cys
65 70 75 80

Tyr Gly Ala Ile Gln Glu Ser Gln Cys Leu Leu Gly Thr Phe Phe Thr
85 90 95

Cys Leu Val Ile Leu Phe Ala Cys Glu Val Ala Ala Gly Ile Trp Gly
100 105 110

Phe Val Asn Lys Asp Gln Ile Ala Lys Asp Val Lys Gln Phe Tyr Asp
115 120 125

Gln Ala Leu Gln Gln Ala Val Val Asp Asp Asp Ala Asn Asn Ala Lys
130 135 140

Ala Val Val Lys Thr Phe His Glu Thr Leu Asp Cys Cys Gly Ser Ser
145 150 155 160

Thr Leu Thr Ala Leu Thr Thr Ser Val Leu Lys Asn Asn Leu Cys Pro
165 170 175

Ser Gly Ser Asn Ile Ile Ser Asn Leu Phe Lys Glu Asp Cys His Gln
180 185 190

Lys Ile Asp Asp Leu Phe Ser Gly Lys Leu Tyr Leu Ile Gly Ile Ala
195 200 205

Ala Ile Val Val Ala Val Ile Met Ile Phe Glu Met Ile Leu Ser Met

210

215

220

Val Leu Cys Cys Gly Ile Arg Asn Ser Ser Val Tyr
 225 230 235

<210> 130
 <211> 711
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> hCD81

<400> 130
 atgggagtgg agggctgcac caagtgcac aagtacctgc tcttcgtctt caatttcgtc 60
 ttctggctgg ctggaggcgt gacacctgggt gtggccctgt ggctccgcca tgaccgcgac 120
 accaccaacc tcctgtatct ggagctggga gacaagcccg cgcccaacac cttctatgta 180
 ggcatctaca tcctcatcgc tgtgggcgct gtcacgatgt tcgttggtt cctgggctgc 240
 tacggggcca tccaggaatc ccagtgcctg ctggggacgt tcttcacctg cctggatcac 300
 ctgtttgcct gtgaggtggc cgccggcatc tggggctttg tcaacaagga ccagatcgcc 360
 aaggatgtga agcagttcta tgaccaggcc ctacagcagg ccgtggtgga tgatgacgcc 420
 aacaacgcca aggctgtggt gaagaccttc cacgagacgc ttgactgctg tggctccagc 480
 aactgactg ctttgaccac ctcatgtctc aagaacaatt tgtgtccctc gggcagcaac 540
 atcatcagca acctcttcaa ggaggactgc caccagaaga tcgatgacct cttctccggg 600
 aagctgtacc tcatcggcat tgctgccatc gtggctgctg tgatcatgat cttcgagatg 660
 atcctgagca tgggtgctgtg ctgtggcatc cggaacagct ccgtgtactg a 711

<210> 131
 <211> 740
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> hsc-Trimer-CD81

<400> 131

Met Ser Arg Ser Val Ala Leu Ala Val Leu Ala Leu Leu Ser Leu Ser
 1 5 10 15

Gly Leu Glu Ala Cys Tyr Thr Trp Asn Gln Met Asn Leu Gly Gly Gly
20 25 30

Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Gln Arg Thr
35 40 45

Pro Lys Ile Gln Val Tyr Ser Arg His Pro Ala Glu Asn Gly Lys Ser
50 55 60

Asn Phe Leu Asn Cys Tyr Val Ser Gly Phe His Pro Ser Asp Ile Glu
65 70 75 80

Val Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu His Ser
85 90 95

Asp Leu Ser Phe Ser Lys Asp Trp Ser Phe Tyr Leu Leu Tyr Tyr Thr
100 105 110

Glu Phe Thr Pro Thr Glu Lys Asp Glu Tyr Ala Cys Arg Val Asn His
115 120 125

Val Thr Leu Ser Gln Pro Lys Ile Val Lys Trp Asp Arg Asp Met Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser
165 170 175

Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp
180 185 190

Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met
195 200 205

Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp
210 215 220

Glu Glu Thr Gly Lys Val Lys Ala His Ser Gln Thr Asp Arg Glu Asn

225		230		235		240
Leu Arg Ile Ala	Leu Arg Tyr Tyr	Asn Gln Ser Glu Ala Gly	Ser His			
	245		250		255	
Thr Leu Gln Met Met Phe Gly Cys Asp Val Gly Ser Asp Gly Arg Phe						
	260		265		270	
Leu Arg Gly Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala						
	275		280		285	
Leu Lys Glu Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln						
	290		295		300	
Ile Thr Lys Arg Lys Trp Glu Ala Ala His Val Ala Glu Gln Gln Arg						
305		310		315		320
Ala Tyr Leu Glu Gly Thr Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu						
	325		330		335	
Asn Gly Lys Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met						
	340		345		350	
Thr His His Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala						
	355		360		365	
Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly						
	370		375		380	
Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly						
385		390		395		400
Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu						
	405		410		415	
Glu Gln Arg Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro						
	420		425		430	
Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Pro Thr Val Pro Ile Val						
	435		440		445	

Gly Ile Ile Ala Gly Leu Val Leu Leu Gly Ala Val Ile Thr Gly Ala
450 455 460

Val Val Ala Ala Val Met Trp Arg Arg Asn Ser Ser Asp Arg Lys Gly
465 470 475 480

Gly Ser Tyr Ser Gln Ala Ala Ser Ser Asp Ser Ala Gln Gly Ser Asp
485 490 495

Val Ser Leu Thr Ala Cys Lys Val Met Gly Val Glu Gly Cys Thr Lys
500 505 510

Cys Ile Lys Tyr Leu Leu Phe Val Phe Asn Phe Val Phe Trp Leu Ala
515 520 525

Gly Gly Val Ile Leu Gly Val Ala Leu Trp Leu Arg His Asp Pro Gln
530 535 540

Thr Thr Asn Leu Leu Tyr Leu Glu Leu Gly Asp Lys Pro Ala Pro Asn
545 550 555 560

Thr Phe Tyr Val Gly Ile Tyr Ile Leu Ile Ala Val Gly Ala Val Met
565 570 575

Met Phe Val Gly Phe Leu Gly Cys Tyr Gly Ala Ile Gln Glu Ser Gln
580 585 590

Cys Leu Leu Gly Thr Phe Phe Thr Cys Leu Val Ile Leu Phe Ala Cys
595 600 605

Glu Val Ala Ala Gly Ile Trp Gly Phe Val Asn Lys Asp Gln Ile Ala
610 615 620

Lys Asp Val Lys Gln Phe Tyr Asp Gln Ala Leu Gln Gln Ala Val Val
625 630 635 640

Asp Asp Asp Ala Asn Asn Ala Lys Ala Val Val Lys Thr Phe His Glu
645 650 655

Thr Leu Asp Cys Cys Gly Ser Ser Thr Leu Thr Ala Leu Thr Thr Ser

660

665

670

Val Leu Lys Asn Asn Leu Cys Pro Ser Gly Ser Asn Ile Ile Ser Asn
675 680 685

Leu Phe Lys Glu Asp Cys His Gln Lys Ile Asp Asp Leu Phe Ser Gly
690 695 700

Lys Leu Tyr Leu Ile Gly Ile Ala Ala Ile Val Val Ala Val Ile Met
705 710 715 720

Ile Phe Glu Met Ile Leu Ser Met Val Leu Cys Cys Gly Ile Arg Asn
725 730 735

Ser Ser Val Tyr
740

<210> 132
<211> 2223
<212> DNA
<213> Artificial Sequence

<220>
<223> hsc-Trimer-CD81

<400> 132
atgtctcgct ccgtggcctt agctgtgctc gcgctactct ctctttctgg cctggaggct 60
tgctacacct ggaaccagat gaacctgggc ggaggtgcct ctggcgggtg gggcagcggc 120
ggaggggggca gtatccagcg tactccaaag attcaggttt actcacgtca tccagcagag 180
aatggaaagt caaatttcct gaattgctat gtgtctgggt ttcattccatc cgacattgaa 240
gttgacttac tgaagaatgg agagagaatt gaaaaagtgg agcattcaga cttgtctttc 300
agcaaggact ggtctttcta tctcttgtag tacactgaat tcacccccac tgaaaaagat 360
gagtatgcct gccgtgtgaa ccatgtgact ttgtcacagc ccaagatagt taagtgggat 420
cgagacatgg gggggggagg ctccgggtgga ggggggtctg gagggggggg gtctggtgga 480
ggcggaagtg gctcccactc catgaggtat ttctccacat ccgtgtcccg gcccggccgc 540
ggggagcccc gcttcatcgc cgtgggctac gtggacgaca cgagttcgt gcggttcgac 600
agcgacgccg cgagccagag gatggagccg cgggcgccgt ggatagagca ggagggggccg 660

gagtattggg acgaggagac agggaaagtg aaggcccact cacagactga ccgagagaac	720
ctgcggatcg cgctccgcta ctacaaccag agcgaggccg gttctcacac cctccagatg	780
atgtttggct gcgacgtggg gtcggacggg cgcttcctcc gcgggtacca ccagtacgcc	840
tacgacggca aggattacat cgccctgaaa gaggacctgc gctcttgac cgcggcggac	900
atggcggctc agatcaccaa gcgcaagtgg gaggcggccc atgtggcgga gcagcagaga	960
gcctacctgg agggcacgtg cgtggacggg ctccgcagat acctggagaa cgggaaggag	1020
acgctgcagc gcacggaccc cccaagaca catatgacct accaccccat ctctgacct	1080
gaggccactc tgagatgctg ggccctgggc ttctaccctg cggagatcac actgacctgg	1140
cagcgggatg gggaggacca gaccaggac acggagcttg tggagaccag gcctgcaggg	1200
gatggaacct tccagaagtg ggcagctgtg gtggtacctt ctggagagga gcagagatac	1260
acctgccatg tgcagcatga gggctgccc aagcccctca ccctgagatg ggagccatct	1320
tcccagccca ccgtcccat cgtgggcatc attgctggcc tggttctcct tggagctgtg	1380
atcactggag ctgtggtcgc tgctgtgatg tggaggagga acagctcaga tagaaaagga	1440
gggagctact ctcaggctgc aagcagtgc agtgcccagg gctctgatgt gtctctcaca	1500
gcttgtaaag tgatgggagt ggagggtgc accaagtgc tcaagtacct gctcttcgtc	1560
ttcaatttcg tcttctggct ggctggaggc gtgacacctg gtgtggccct gtggctccgc	1620
catgacccgc agaccaccaa cctcctgtat ctggagctgg gagacaagcc cgcgcccaac	1680
accttctatg taggcatcta catcctcatc gctgtgggcg ctgtcatgat gttcgttggc	1740
ttcctgggct gctacggggc catccaggaa tcccagtgcc tgctggggac gttcttcacc	1800
tgcttggtca tcctgtttgc ctgtgaggtg gccgccggca tctggggctt tgtcaacaag	1860
gaccagatcg ccaaggatgt gaagcagttc tatgaccagg ccctacagca ggccgtggtg	1920
gatgatgacg ccaacaacgc caaggctgtg gtgaagacct tccacgagac gcttgactgc	1980
tgtggctcca gcacactgac tgctttgacc acctcagtgc tcaagaacaa tttgtgtccc	2040
tcgggcagca acatcatcag caacctcttc aaggaggact gccaccagaa gatcgatgac	2100
ctcttctccg ggaagctgta cctcatcggc attgctgcc a tctgtggtcgc tgtgatcatg	2160
atcttcgaga tgatcctgag catggtgctg tgctgtggca tccggaacag ctccgtgtac	2220
tga	2223

<210> 133
<211> 395
<212> PRT
<213> Artificial Sequence

<220>
<223> CD81-IL-2

<400> 133

Met Gly Val Glu Gly Cys Thr Lys Cys Ile Lys Tyr Leu Leu Phe Val
1 5 10 15

Phe Asn Phe Val Phe Trp Leu Ala Gly Gly Val Ile Leu Gly Val Ala
20 25 30

Leu Trp Leu Arg His Asp Pro Gln Thr Thr Ser Leu Leu Tyr Leu Glu
35 40 45

Leu Gly Asn Lys Pro Ala Pro Asn Thr Phe Tyr Val Gly Ile Tyr Ile
50 55 60

Leu Ile Ala Val Gly Ala Val Met Met Phe Val Gly Phe Leu Gly Cys
65 70 75 80

Tyr Gly Ala Ile Gln Glu Ser Gln Cys Leu Leu Gly Thr Phe Phe Thr
85 90 95

Cys Leu Val Ile Leu Phe Ala Cys Glu Val Ala Ala Gly Ile Trp Gly
100 105 110

Phe Val Asn Lys Asp Gln Ile Ala Lys Asp Val Lys Gln Phe Tyr Asp
115 120 125

Gln Ala Leu Gln Gln Ala Val Met Asp Asp Asp Ala Asn Asn Ala Lys
130 135 140

Ala Val Val Lys Thr Phe His Glu Thr Leu Asn Cys Cys Gly Ser Asn
145 150 155 160

Ala Leu Thr Thr Leu Thr Thr Thr Ile Leu Arg Asn Ser Leu Cys Pro
165 170 175

Ser Gly Gly Gly Gly Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser
180 185 190

Thr Ala Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln
195 200 205

His Leu Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met
210 215 220

Glu Asn Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe
225 230 235 240

Tyr Leu Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu
245 250 255

Asp Glu Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys
260 265 270

Ser Phe Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val
275 280 285

Thr Val Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe
290 295 300

Asp Asp Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala
305 310 315 320

Phe Cys Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser
325 330 335

Gly Gly Asn Ile Leu Thr Pro Leu Leu Gln Gln Asp Cys His Gln Lys
340 345 350

Ile Asp Glu Leu Phe Ser Gly Lys Leu Tyr Leu Ile Gly Ile Ala Ala
355 360 365

Ile Val Val Ala Val Ile Met Ile Phe Glu Met Ile Leu Ser Met Val
370 375 380

Leu Cys Cys Gly Ile Arg Asn Ser Ser Val Tyr

385

390

395

<210> 134
<211> 1188
<212> DNA
<213> Artificial Sequence

<220>
<223> CD81-IL2

<400> 134
atgggggtgg agggctgcac caaatgcatc aaatacctgc tcttcgtctt caatttcgtc 60
ttctggctgg ctggaggcgt gatcctaggt gtagctctgt ggttgctca tgatccacag 120
accaccagcc tgctgtacct ggaactggga aacaaaccgg caccacaacac cttctacgtg 180
ggcatctaca ttctcattgc tgtgggagct gtgatgatgt ttgtaggctt cctgggggtgc 240
tatggggcca tccaggagtc ccagtgtctg ctggggacgt tcttcacctg ctttgtgatc 300
ctgtttgcct gtgagggtggc tgcaggcatc tggggcttcg taaacaaaga ccagatcgcc 360
aaggatgtga agcagttcta tgaccaggcc cttcagcaag ctgtgatgga tgatgatgcc 420
aacaatgcca aggctgtggt gaagactttc catgagacgc tcaactgttg tggctccaac 480
gcactgacca cactgactac caccatactg aggaacagcc tgtgtccctc aggaggagga 540
ggaagcgcac ccacttcaag ctccacttca agctctacag cggaagcaca gcagcagcag 600
cagcagcagc agcagcagca gcagcacctg gagcagctgt tgatggacct acaggagctc 660
ctgagcagga tggagaatta caggaacctg aaactcccca ggatgctcac cttcaaattt 720
tacttgccca agcaggccac agaattgaaa gatcttcagt gcctagaaga tgaacttgga 780
cctctgcggc atgttctgga ttgactcaa agcaaaagct ttcaattgga agatgctgag 840
aatttcatca gcaatatcag agtaactgtt gtaaaactaa agggctctga caacacattt 900
gagtgccaat tcgatgatga gtcagcaact gtggtggact ttctgaggag atggatagcc 960
ttctgtcaaa gcatcatctc aacaagccct caaggaggag gaggaagcgg cggcaacata 1020
ctcaccctt tactgcagca agattgtcat cagaaaatcg atgagctctt ctctgggaag 1080
ctgtacctca ttggaattgc agccattgtg gtagctgtca ttatgatctt tgagatgatt 1140
ctgagcatgg tgctgtgctg tggcatccgg aacagctccg tgtactga 1188

<210> 135

<211> 905
<212> PRT
<213> Artificial Sequence

<220>
<223> sc-Trimer-CD81-IL-2

<400> 135

Met Ala Arg Ser Val Thr Leu Val Phe Leu Val Leu Val Ser Leu Thr
1 5 10 15

Gly Leu Tyr Ala Ser Ile Ile Asn Phe Glu Lys Leu Gly Gly Gly Ala
20 25 30

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Gln Lys Thr Pro
35 40 45

Gln Ile Gln Val Tyr Ser Arg His Pro Pro Glu Asn Gly Lys Pro Asn
50 55 60

Ile Leu Asn Cys Tyr Val Thr Gln Phe His Pro Pro His Ile Glu Ile
65 70 75 80

Gln Met Leu Lys Asn Gly Lys Lys Ile Pro Lys Val Glu Met Ser Asp
85 90 95

Met Ser Phe Ser Lys Asp Trp Ser Phe Tyr Ile Leu Ala His Thr Glu
100 105 110

Phe Thr Pro Thr Glu Thr Asp Thr Tyr Ala Cys Arg Val Lys His Ala
115 120 125

Ser Met Ala Glu Pro Lys Thr Val Tyr Trp Asp Arg Asp Met Gly Gly
130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Pro His Ser Leu Arg Tyr Phe Val Thr Ala Val Ser Arg
165 170 175

Pro Gly Leu Gly Glu Pro Arg Tyr Met Glu Val Gly Tyr Val Asp Asp

180

185

190

Thr Glu Phe Val Arg Phe Asp Ser Asp Ala Glu Asn Pro Arg Tyr Glu
 195 200 205

Pro Arg Ala Arg Trp Met Glu Gln Glu Gly Pro Glu Tyr Trp Glu Arg
 210 215 220

Glu Thr Gln Lys Ala Lys Gly Asn Glu Gln Ser Phe Arg Val Asp Leu
 225 230 235 240

Arg Thr Leu Leu Gly Tyr Tyr Asn Gln Ser Lys Gly Gly Ser His Thr
 245 250 255

Ile Gln Val Ile Ser Gly Cys Glu Val Gly Ser Asp Gly Arg Leu Leu
 260 265 270

Arg Gly Tyr Gln Gln Tyr Ala Tyr Asp Gly Cys Asp Tyr Ile Ala Leu
 275 280 285

Asn Glu Asp Leu Lys Thr Trp Thr Ala Ala Asp Met Ala Ala Leu Ile
 290 295 300

Thr Lys His Lys Trp Glu Gln Ala Gly Glu Ala Glu Arg Leu Arg Ala
 305 310 315 320

Tyr Leu Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Lys Asn
 325 330 335

Gly Asn Ala Thr Leu Leu Arg Thr Asp Ser Pro Lys Ala His Val Thr
 340 345 350

His His Ser Arg Pro Glu Asp Lys Val Thr Leu Arg Cys Trp Ala Leu
 355 360 365

Gly Phe Tyr Pro Ala Asp Ile Thr Leu Thr Trp Gln Leu Asn Gly Glu
 370 375 380

Glu Leu Ile Gln Asp Met Glu Leu Val Glu Thr Arg Pro Ala Gly Asp
 385 390 395 400

Gly Thr Phe Gln Lys Trp Ala Ser Val Val Val Pro Leu Gly Lys Glu
405 410 415

Gln Tyr Tyr Thr Cys His Val Tyr His Gln Gly Leu Pro Glu Pro Leu
420 425 430

Thr Leu Arg Trp Glu Pro Pro Pro Ser Thr Val Ser Asn Met Ala Thr
435 440 445

Val Ala Val Leu Val Val Leu Gly Ala Ala Ile Val Thr Gly Ala Val
450 455 460

Val Ala Phe Val Met Lys Met Arg Arg Arg Asn Thr Gly Gly Lys Gly
465 470 475 480

Gly Asp Tyr Ala Leu Ala Pro Gly Ser Gln Thr Ser Asp Leu Ser Leu
485 490 495

Pro Asp Cys Lys Val Met Val His Asp Pro His Ser Leu Ala Met Gly
500 505 510

Val Glu Gly Cys Thr Lys Cys Ile Lys Tyr Leu Leu Phe Val Phe Asn
515 520 525

Phe Val Phe Trp Leu Ala Gly Gly Val Ile Leu Gly Val Ala Leu Trp
530 535 540

Leu Arg His Asp Pro Gln Thr Thr Ser Leu Leu Tyr Leu Glu Leu Gly
545 550 555 560

Asn Lys Pro Ala Pro Asn Thr Phe Tyr Val Gly Ile Tyr Ile Leu Ile
565 570 575

Ala Val Gly Ala Val Met Met Phe Val Gly Phe Leu Gly Cys Tyr Gly
580 585 590

Ala Ile Gln Glu Ser Gln Cys Leu Leu Gly Thr Phe Phe Thr Cys Leu
595 600 605

Val Ile Leu Phe Ala Cys Glu Val Ala Ala Gly Ile Trp Gly Phe Val

610

615

620

Asn Lys Asp Gln Ile Ala Lys Asp Val Lys Gln Phe Tyr Asp Gln Ala
 625 630 635 640

Leu Gln Gln Ala Val Met Asp Asp Asp Ala Asn Asn Ala Lys Ala Val
 645 650 655

Val Lys Thr Phe His Glu Thr Leu Asn Cys Cys Gly Ser Asn Ala Leu
 660 665 670

Thr Thr Leu Thr Thr Thr Ile Leu Arg Asn Ser Leu Cys Pro Ser Gly
 675 680 685

Gly Gly Gly Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala
 690 695 700

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu
 705 710 715 720

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn
 725 730 735

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu
 740 745 750

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu
 755 760 765

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe
 770 775 780

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val
 785 790 795 800

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp
 805 810 815

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys
 820 825 830

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser Gly Gly
835 840 845

Asn Ile Leu Thr Pro Leu Leu Gln Gln Asp Cys His Gln Lys Ile Asp
850 855 860

Glu Leu Phe Ser Gly Lys Leu Tyr Leu Ile Gly Ile Ala Ala Ile Val
865 870 875 880

Val Ala Val Ile Met Ile Phe Glu Met Ile Leu Ser Met Val Leu Cys
885 890 895

Cys Gly Ile Arg Asn Ser Ser Val Tyr
900 905

<210> 136
<211> 2718
<212> DNA
<213> Artificial Sequence

<220>
<223> sc-Trimer-CD81-IL-2

<400> 136
atggctcgct cggtgaccct ggtctttctg gtgcttgtct cactgaccgg cctgtatgct 60
tccattataa attttgaaaa gttgggcgga ggtgcctctg gcggtggggg cagcgggtgga 120
gggggcagta tccagaaaac ccctcaaatt caagtatact cacgccaccc accggagaat 180
gggaagccga acatactgaa ctgctacgta acacagttcc accgcctca cattgaaatc 240
caaatgctga agaacgggaa aaaaattcct aaagtagaga tgtcagatat gtccttcagc 300
aaggactggg ctttctatat cctggctcac actgaattca cccccactga gactgataca 360
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gagccccggt acatggaagt cggctacgtg gacgacacgg agttcgtgcg cttcgacagc 600
gacgcggaga atccgagata tgagccgcgg gcgcgggtgga tggagcagga ggggcccagag 660
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tacctggagg gcacgtgcgt ggagtggctc cgcagatacc tgaagaacgg gaacgcgacg	1020
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gtcacctga ggtgctgggc cctgggcttc taccctgctg acatcacct gacctggcag	1140
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catgagacgc tcaactgttg tggctccaac gcactgacca cactgactac caccatactg	2040
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agctctacag cggaagcaca gcagcagcag cagcagcagc agcagcagca gcagcacctg	2160
gagcagctgt tgatggacct acaggagctc ctgagcagga tggagaatta caggaacctg	2220
aaactcccca ggatgctcac cttcaaattt tacttgccca agcaggccac agaattgaaa	2280
gatcttcagt gcctagaaga tgaacttgga cctctgcggc atgttctgga tttgactcaa	2340

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 cagaaaatcg atgagctctt ctctgggaag ctgtacctca ttggaattgc agccattgtg 2640
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<210> 137
 <211> 550
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Aka-Luc

<400> 137

Met Glu Asp Ala Lys Asn Ile Lys Lys Gly Pro Ala Pro Phe Tyr Pro
 1 5 10 15

Leu Glu Asp Gly Thr Ala Gly Glu Gln Leu His Lys Ala Met Lys Arg
 20 25 30

Tyr Ala Leu Val Pro Gly Ala Ile Ala Phe Thr Asp Ala His Ile Gln
 35 40 45

Val Asp Val Thr Tyr Ala Glu Tyr Phe Glu Met Ser Val Arg Leu Ala
 50 55 60

Glu Ala Met Arg Arg Tyr Gly Leu Asn Thr Asn His Arg Ile Val Val
 65 70 75 80

Cys Ser Glu Asn Ser Ser Gln Phe Phe Met Pro Val Leu Gly Ala Leu
 85 90 95

Phe Ile Gly Val Ala Val Ala Pro Ala Asn Asp Ile Tyr Asn Glu Arg
 100 105 110

Glu Leu Leu Asn Ser Met Gly Ile Ser Gln Pro Thr Val Val Phe Val

115

120

125

Ser Lys Lys Gly Leu Arg Lys Val Leu Asn Val Gln Lys Lys Leu Pro
 130 135 140

Ile Ile Arg Lys Ile Ile Ile Met Asp Ser Lys Thr Asp Tyr Gln Gly
 145 150 155 160

Phe Gln Ser Met Tyr Thr Phe Val Thr Ser His Leu Pro Pro Ser Phe
 165 170 175

Asn Glu Tyr Asp Phe Val Pro Glu Ser Phe Asp Arg Asp Lys Thr Ile
 180 185 190

Ala Leu Ile Met Asn Ser Ser Gly Ser Thr Gly Leu Pro Lys Gly Val
 195 200 205

Ala Leu Pro His Arg Thr Ala Cys Val Arg Phe Ser His Ala Arg Asp
 210 215 220

Pro Ile Phe Gly Tyr Gln Asn Ile Pro Asp Thr Ala Ile Leu Ser Val
 225 230 235 240

Val Pro Phe His His Gly Phe Gly Met Phe Thr Thr Leu Gly Tyr Leu
 245 250 255

Ile Cys Gly Phe Arg Val Val Leu Met Tyr Arg Phe Glu Glu Glu Leu
 260 265 270

Phe Leu Arg Ser Leu Gln Asp Tyr Lys Ile Gln Ser Ala Leu Leu Val
 275 280 285

Pro Thr Leu Phe Ser Cys Leu Ala Lys Ser Thr Leu Ile Asp Lys Tyr
 290 295 300

Asp Leu Ser Ser Leu Arg Glu Ile Ala Ser Gly Gly Ala Pro Leu Ser
 305 310 315 320

Lys Glu Val Gly Glu Ala Val Ala Lys Arg Phe Arg Leu Pro Gly Ile
 325 330 335

Arg Gln Gly Tyr Gly Leu Thr Glu Thr Thr Asn Ala Val Met Ile Thr
340 345 350

Pro Glu Gly Asp Arg Lys Pro Gly Ser Val Gly Lys Val Val Pro Phe
355 360 365

Phe Glu Ala Lys Val Val Asp Leu Val Thr Gly Lys Thr Leu Gly Val
370 375 380

Asn Gln Arg Gly Glu Leu Cys Val Arg Gly Pro Met Ile Met Ser Gly
385 390 395 400

Tyr Val Asn Asn Pro Glu Ala Thr Asn Ala Leu Ile Asp Lys Asp Gly
405 410 415

Trp Leu His Ser Gly Asp Ile Ala Tyr Trp Asp Glu Asp Glu His Phe
420 425 430

Phe Ile Val Asp Arg Leu Lys Ser Leu Ile Lys Tyr Lys Gly Tyr Gln
435 440 445

Val Ala Pro Ala Glu Leu Glu Gly Ile Leu Leu Gln His Pro Tyr Ile
450 455 460

Phe Asp Ala Gly Val Ala Gly Leu Pro Asp Asp Asp Ala Gly Glu Leu
465 470 475 480

Pro Ala Ala Val Val Val Leu Glu His Gly Lys Thr Met Thr Glu Lys
485 490 495

Glu Ile Val Asp Tyr Val Ala Ser Gln Val Thr Thr Ala Lys Lys Leu
500 505 510

Arg Gly Gly Val Val Phe Val Asp Glu Val Pro Arg Gly Ser Thr Gly
515 520 525

Lys Leu Asp Ala Arg Lys Ile Arg Glu Ile Leu Thr Lys Ala Lys Lys
530 535 540

Asp Gly Lys Ile Ala Val

545

550

<210> 138
 <211> 1650
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Aka-Luc

<400> 138
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 gcctttaccg acgcacatat tcaggtggac gttacctacg ccgagtactt cgagatgagc 180
 gttcggctgg cagaagctat gaggcgctat gggctgaata caaacatcg gatcgtggtg 240
 tgcagcgaga atagctcgca gttcttcatg cccgtgttgg gtgccctgtt catcgggtgtg 300
 gctgtggccc cagctaacga catctacaac gagcgcgagc tgctgaacag catgggcatc 360
 agccagccca ccgtcgtatt cgtgagcaag aaagggtgc gaaaggtcct caacgtgcaa 420
 aagaagctac cgatcatacg aaagatcatc atcatggata gcaagaccga ctaccagggc 480
 ttccaaagca tgtacacctt cgtgacttcc catttgccac ccagcttcaa cgagtacgac 540
 ttcgtgcccc agagcttcga ccgggacaaa accatcgccc tgatcatgaa cagtagtggt 600
 agtacaggat tacccaaggg cgtagcccta ccgcaccgca ccgcttgtgt ccgattcagt 660
 catgcccgcg accccatctt cggctaccag aacatccccg acaccgctat cctcagcgtg 720
 gtgccatttc accacggctt cggcatgttc accacgctgg gctacttgat ctgcggcttt 780
 cgggtcgtgc tcatgtaccg cttcgaggag gagctattct tgcgcagctt gcaagactat 840
 aagattcaat ctgccctgct ggtgcccaca ctatttagct gcctcgctaa gagcactctc 900
 atcgacaagt acgacctaag cagcttgccg gagatcgcca gcggcggggc gccgctcagc 960
 aaggaggtag gtgaggccgt ggccaaacgc ttccgcctac caggcatccg ccagggtat 1020
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 tcagtaggca aggtggtgcc cttcttcgag gctaaggtgg tagacttggt caccggtgaa 1140
 aactgggtg tgaaccagcg cggtagctg tgcgtccgtg gcccatgat catgagcggc 1200
 tacgttaaca accccgaggc tacgaacgct ctcatcgaca aggacggctg gctgcacagc 1260

ggcgacatcg cctactggga cgaggacgag cacttcttca tcgtggaccg gctgaagagc 1320
 ctgatcaaata acaagggcta ccaggtagcc ccagccgaac tggagggcat cctgctgcaa 1380
 caccctaca tcttcgacgc cggagtcgcc ggcctgccc acgacgatgc cggcgagctg 1440
 cccgccgcag tcgtcgtgtt ggaacacggt aaaaccatga ccgagaaaga gatcgtggac 1500
 tatgtggcca gccaggttac aaccgccaag aagctgcgcg gtggtgttgt gtttgtggat 1560
 gaagtcccta gaggatcgac cggcaagtta gacgcccgca agatccgcga gattctcact 1620
 aaggccaaga aggacggcaa gatcgccgtg 1650

<210> 139
 <211> 798
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CD63-Aka-Luc

<400> 139

Met Ala Val Glu Gly Gly Met Lys Cys Val Lys Phe Leu Leu Tyr Val
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Leu Leu Leu Ala Phe Cys Ala Cys Ala Val Gly Leu Ile Ala Ile Gly
 20 25 30

Val Ala Val Gln Val Val Leu Lys Gln Ala Ile Thr His Glu Thr Thr
 35 40 45

Ala Gly Ser Leu Leu Pro Val Val Ile Ile Ala Val Gly Ala Phe Leu
 50 55 60

Phe Leu Val Ala Phe Val Gly Cys Cys Gly Ala Cys Lys Glu Asn Tyr
 65 70 75 80

Cys Leu Met Ile Thr Phe Ala Ile Phe Leu Ser Leu Ile Met Leu Val
 85 90 95

Glu Val Ala Val Ala Ile Ala Gly Tyr Val Phe Arg Asp Gln Val Lys
 100 105 110

Ser Glu Phe Asn Lys Ser Phe Gln Gln Gln Met Gln Asn Tyr Leu Lys

115

120

125

Asp Asn Lys Thr Ala Thr Ile Leu Asp Lys Leu Gln Lys Glu Asn Asn
 130 135 140

Cys Cys Gly Ala Ser Asn Tyr Thr Asp Trp Glu Asn Ile Pro Gly Met
 145 150 155 160

Ala Lys Asp Arg Val Pro Asp Ser Cys Cys Gly Gly Gly Gly Ser Met
 165 170 175

Glu Asp Ala Lys Asn Ile Lys Lys Gly Pro Ala Pro Phe Tyr Pro Leu
 180 185 190

Glu Asp Gly Thr Ala Gly Glu Gln Leu His Lys Ala Met Lys Arg Tyr
 195 200 205

Ala Leu Val Pro Gly Ala Ile Ala Phe Thr Asp Ala His Ile Gln Val
 210 215 220

Asp Val Thr Tyr Ala Glu Tyr Phe Glu Met Ser Val Arg Leu Ala Glu
 225 230 235 240

Ala Met Arg Arg Tyr Gly Leu Asn Thr Asn His Arg Ile Val Val Cys
 245 250 255

Ser Glu Asn Ser Ser Gln Phe Phe Met Pro Val Leu Gly Ala Leu Phe
 260 265 270

Ile Gly Val Ala Val Ala Pro Ala Asn Asp Ile Tyr Asn Glu Arg Glu
 275 280 285

Leu Leu Asn Ser Met Gly Ile Ser Gln Pro Thr Val Val Phe Val Ser
 290 295 300

Lys Lys Gly Leu Arg Lys Val Leu Asn Val Gln Lys Lys Leu Pro Ile
 305 310 315 320

Ile Arg Lys Ile Ile Ile Met Asp Ser Lys Thr Asp Tyr Gln Gly Phe
 325 330 335

Gln Ser Met Tyr Thr Phe Val Thr Ser His Leu Pro Pro Ser Phe Asn
340 345 350

Glu Tyr Asp Phe Val Pro Glu Ser Phe Asp Arg Asp Lys Thr Ile Ala
355 360 365

Leu Ile Met Asn Ser Ser Gly Ser Thr Gly Leu Pro Lys Gly Val Ala
370 375 380

Leu Pro His Arg Thr Ala Cys Val Arg Phe Ser His Ala Arg Asp Pro
385 390 395 400

Ile Phe Gly Tyr Gln Asn Ile Pro Asp Thr Ala Ile Leu Ser Val Val
405 410 415

Pro Phe His His Gly Phe Gly Met Phe Thr Thr Leu Gly Tyr Leu Ile
420 425 430

Cys Gly Phe Arg Val Val Leu Met Tyr Arg Phe Glu Glu Glu Leu Phe
435 440 445

Leu Arg Ser Leu Gln Asp Tyr Lys Ile Gln Ser Ala Leu Leu Val Pro
450 455 460

Thr Leu Phe Ser Cys Leu Ala Lys Ser Thr Leu Ile Asp Lys Tyr Asp
465 470 475 480

Leu Ser Ser Leu Arg Glu Ile Ala Ser Gly Gly Ala Pro Leu Ser Lys
485 490 495

Glu Val Gly Glu Ala Val Ala Lys Arg Phe Arg Leu Pro Gly Ile Arg
500 505 510

Gln Gly Tyr Gly Leu Thr Glu Thr Thr Asn Ala Val Met Ile Thr Pro
515 520 525

Glu Gly Asp Arg Lys Pro Gly Ser Val Gly Lys Val Val Pro Phe Phe
530 535 540

Glu Ala Lys Val Val Asp Leu Val Thr Gly Lys Thr Leu Gly Val Asn

545		550		555		560									
Gln	Arg	Gly	Glu	Leu	Cys	Val	Arg	Gly	Pro	Met	Ile	Met	Ser	Gly	Tyr
			565						570					575	
Val	Asn	Asn	Pro	Glu	Ala	Thr	Asn	Ala	Leu	Ile	Asp	Lys	Asp	Gly	Trp
			580					585					590		
Leu	His	Ser	Gly	Asp	Ile	Ala	Tyr	Trp	Asp	Glu	Asp	Glu	His	Phe	Phe
		595					600					605			
Ile	Val	Asp	Arg	Leu	Lys	Ser	Leu	Ile	Lys	Tyr	Lys	Gly	Tyr	Gln	Val
	610					615					620				
Ala	Pro	Ala	Glu	Leu	Glu	Gly	Ile	Leu	Leu	Gln	His	Pro	Tyr	Ile	Phe
625					630					635					640
Asp	Ala	Gly	Val	Ala	Gly	Leu	Pro	Asp	Asp	Asp	Ala	Gly	Glu	Leu	Pro
				645					650					655	
Ala	Ala	Val	Val	Val	Leu	Glu	His	Gly	Lys	Thr	Met	Thr	Glu	Lys	Glu
			660					665					670		
Ile	Val	Asp	Tyr	Val	Ala	Ser	Gln	Val	Thr	Thr	Ala	Lys	Lys	Leu	Arg
		675					680					685			
Gly	Gly	Val	Val	Phe	Val	Asp	Glu	Val	Pro	Arg	Gly	Ser	Thr	Gly	Lys
	690					695					700				
Leu	Asp	Ala	Arg	Lys	Ile	Arg	Glu	Ile	Leu	Thr	Lys	Ala	Lys	Lys	Asp
705					710					715					720
Gly	Lys	Ile	Ala	Val	Gly	Gly	Gly	Gly	Ser	Ile	Asn	Ile	Thr	Val	Gly
			725						730					735	
Cys	Gly	Asn	Asp	Phe	Lys	Glu	Ser	Thr	Ile	His	Thr	Gln	Gly	Cys	Val
			740					745					750		
Glu	Thr	Ile	Ala	Ile	Trp	Leu	Arg	Lys	Asn	Ile	Leu	Leu	Val	Ala	Ala
		755					760					765			

Ala Ala Leu Gly Ile Ala Phe Val Glu Val Leu Gly Ile Ile Phe Ser
770 775 780

Cys Cys Leu Val Lys Ser Ile Arg Ser Gly Tyr Glu Val Met
785 790 795

<210> 140
<211> 2397
<212> DNA
<213> Artificial Sequence

<220>
<223> CD63-Aka-Luc

<400> 140
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ttctgcgccct gtgcagtggg attgatcgcc attggtgtag cggttcaggt tgtcttgaag 120
caggccatta cccatgagac tactgctggc tcgctgttgc ctgtgggtcat cattgcagtg 180
ggcgccttcc tcttcctggg ggcctttgtg ggctgctgtg gggcctgcaa ggagaactac 240
tgtctcatga ttacatttgc catcttcctg tctcttatca tgcttgtgga ggtggctgtg 300
gccattgctg gctatgtgtt tagagaccag gtgaagtcag agtttaataa aagcttcag 360
cagcagatgc agaattacct taaagacaac aaaacagcca ctattttgga caaattgcag 420
aaagaaaata actgctgtgg agcttctaac tacacagact gggaaaacat ccccgcatg 480
gccaaggaca gagtccccga ttcttgctgc ggtgggtggg gttctatgga agatgccaaa 540
aacattaaga agggcccagc gccgttctac ccactcgaag acgggaccgc cggcgagcag 600
ctgcacaaag ccatgaagcg ctacgccctg gtgcccggcg ccatcgctt taccgacgca 660
catattcagg tggacgttac ctacgccgag tacttcgaga tgagcgttcg gctggcagaa 720
gctatgaggc gctatgggct gaatacaaac catcggatcg tggtgtgcag cgagaatagc 780
tcgcagttct tcatgcccgt gttgggtgcc ctgttcatcg gtgtggctgt ggccccagct 840
aacgacatct acaacgagcg cgagctgctg aacagcatgg gcatcagcca gccaccgtc 900
gtattcgtga gcaagaaagg gctgcgaaag gtcctcaacg tgcaaaaagaa gctaccgatc 960
atacgaaaga tcatcatcat ggatagcaag accgactacc agggcttcca aagcatgtac 1020
accttcgtga cttcccatth gccaccagc ttcaacgagt acgacttcgt gcccgagagc 1080

ttcgaccggg acaaaacat cgccctgac atgaacagta gtggtagtag aggattaccc	1140
aagggcgtag ccctaccgca ccgcaccgct tgtgtccgat tcagtcatgc ccgcgacccc	1200
atcttcggct accagaacat ccccgacacc gctatcctca gcgtggtgcc atttcaccac	1260
ggcttcggca tggtcaccac gctgggctac ttgatctgcg gctttcgggt cgtgctcatg	1320
taccgcttcg aggaggagct attcttgctc agcttgcaag actataagat tcaatctgcc	1380
ctgctggtgc ccacactatt tagctgcctc gctaagagca ctctcatcga caagtacgac	1440
ctaagcagct tgcgcgagat cgccagcggc ggggcgcgc tcagcaagga ggtaggtgag	1500
gccgtggcca aacgcttcg cctaccaggc atccgccagg gctatggcct gacagaaaca	1560
accaacgccg tcatgatcac ccccgagggg gaccgtaagc ctggctcagt aggcaaggtg	1620
gtgcccttct tcgaggctaa ggtggtagac ttggtcaccg gtaagacact ggggtgtgaac	1680
cagcgcgggtg agctgtgctg ccgtggcccc atgatcatga gcggctacgt taacaacccc	1740
gaggctacga acgctctcat cgacaaggac ggctggctgc acagcggcga catcgcctac	1800
tgggacgagg acgagcactt cttcatcgtg gaccggctga agagcctgat caaatacaag	1860
ggctaccagg tagccccagc cgaactggag ggcatcctgc tgcaacaccc ctacatcttc	1920
gacgccggag tcgccggcct gcccagcagc gatgccggcg agctgcccgc cgcagtcgtc	1980
gtgttgaac acggtaaaac catgaccgag aaagagatcg tggactatgt ggccagccag	2040
gttacaaccg ccaagaagct gcgcgggtgg gttgtgtttg tggatgaagt ccctagagga	2100
tcgaccggca agttagacgc ccgcaagatc cgcgagattc tcactaaggc caagaaggac	2160
ggcaagatcg ccgtgggtgg tgggtggttct atcaacataa ctgtgggctg tgggaatgat	2220
ttcaaggaat ccactatcca taccagggc tgcgtggaga ctatagcaat atggctaagg	2280
aagaacatac tgctggtggc tgcagcggcc ctgggcattg cttttgtgga ggtcttggga	2340
attatcttct cctgctgtct ggtgaagagt attcgaagt gctatgaagt aatgtag	2397

<210> 141
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> SAR-CoV2 peptide

<400> 141

Lys Leu Trp Ala Gln Cys Val Gln Leu
1 5

<210> 142
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> SARS-CoV2 DNA

<400> 142
aaactgtggg cccagtgtgt gcagctg

27

<210> 143
<211> 341
<212> PRT
<213> Artificial Sequence

<220>
<223> HLA-A0201

<400> 143

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
50 55 60

Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
85 90 95

Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
100 105 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
115 120 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
130 135 140

His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145 150 155 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
165 170 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
180 185 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
195 200 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Pro Ser Ser Gln Pro Thr Ile Pro Ile Val Gly Ile Ile
275 280 285

Ala Gly Leu Val Leu Phe Gly Ala Val Ile Thr Gly Ala Val Val Ala
290 295 300

Ala Val Met Trp Arg Arg Lys Ser Ser Asp Arg Lys Gly Gly Ser Tyr
305 310 315 320

Ser Gln Ala Ala Ser Ser Asp Ser Ala Gln Gly Ser Asp Val Ser Leu

Thr Ala Cys Lys Val
340

<210> 144
<211> 1023
<212> DNA
<213> Artificial Sequence

<220>
<223> HLA-A0201

<400> 144
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cgcttcatcg cagtgggcta cgtggacgac acgcagttcg tgcggttcga cagcgacgcc 120
gcgagccaga ggatggagcc gcgggcgccg tggatagagc aggaggggtcc ggagtattgg 180
gacggggaga cacggaaagt gaaggccac tcacagactc accgagtgga cctggggacc 240
ctgcgaggct actacaacca gagcgaggcc ggttctcaca ccgtccagag gatgtatggc 300
tgcgacgtgg ggtcggactg gcgcttcctc cgcggggtacc accagtacgc ctacgacggc 360
aaggattaca tcgccctgaa agaggacctg cgctcttgga ccgcggcgga catggcagct 420
cagaccacca agcacaagtg ggaggcggcc catgtggcgg agcagttgag agcctacctg 480
gagggcacgt gcgtggagtg gctccgcaga tacctggaga acgggaagga gacgctgcag 540
cgcacggacg cccccaaaac gcatatgact caccacgctg tctctgacca tgaagccacc 600
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ttccagaagt gggcggtgtg ggtggtgcct tctggacagg agcagagata cacctgccat 780
gtgcagcatg agggtttgcc caagcccctc accctgagat gggagccgtc ttcccagccc 840
accatcccca tcgtgggcat cattgctggc ctggttctct ttggagctgt gatcactgga 900
gctgtggtcg ctgctgtgat gtggaggagg aagagctcag atagaaaagg agggagctac 960
tctcaggctg caagcagtga cagtgccag ggctctgatg tgtctctcac agcttgtaaa 1020
gtg 1023

<210> 145

<211> 460
<212> PRT
<213> Artificial Sequence

<220>
<223> hsMHC-I

<400> 145

Ile Gln Arg Thr Pro Lys Ile Gln Val Tyr Ser Arg His Pro Ala Glu
1 5 10 15

Asn Gly Lys Ser Asn Phe Leu Asn Cys Tyr Val Ser Gly Phe His Pro
20 25 30

Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys
35 40 45

Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp Ser Phe Tyr Leu
50 55 60

Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp Glu Tyr Ala Cys
65 70 75 80

Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile Val Lys Trp Asp
85 90 95

Arg Asp Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
100 105 110

Gly Ser Gly Gly Gly Gly Ser Gly Ser His Ser Met Arg Tyr Phe Phe
115 120 125

Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala Val
130 135 140

Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala Ala
145 150 155 160

Ser Gln Arg Met Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly Pro
165 170 175

Glu Tyr Trp Asp Gly Glu Thr Arg Lys Val Lys Ala His Ser Gln Thr

180

185

190

His Arg Val Asp Leu Gly Thr Leu Arg Gly Tyr Tyr Asn Gln Ser Glu
 195 200 205

Ala Gly Ser His Thr Val Gln Arg Met Tyr Gly Cys Asp Val Gly Ser
 210 215 220

Asp Trp Arg Phe Leu Arg Gly Tyr His Gln Tyr Ala Tyr Asp Gly Lys
 225 230 235 240

Asp Tyr Ile Ala Leu Lys Glu Asp Leu Arg Ser Trp Thr Ala Ala Asp
 245 250 255

Met Ala Ala Gln Thr Thr Lys His Lys Trp Glu Ala Ala His Val Ala
 260 265 270

Glu Gln Leu Arg Ala Tyr Leu Glu Gly Thr Cys Val Glu Trp Leu Arg
 275 280 285

Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Thr Asp Ala Pro
 290 295 300

Lys Thr His Met Thr His His Ala Val Ser Asp His Glu Ala Thr Leu
 305 310 315 320

Arg Cys Trp Ala Leu Ser Phe Tyr Pro Ala Glu Ile Thr Leu Thr Trp
 325 330 335

Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu Thr
 340 345 350

Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val Val
 355 360 365

Pro Ser Gly Gln Glu Gln Arg Tyr Thr Cys His Val Gln His Glu Gly
 370 375 380

Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Pro Thr
 385 390 395 400

Ile Pro Ile Val Gly Ile Ile Ala Gly Leu Val Leu Phe Gly Ala Val
405 410 415

Ile Thr Gly Ala Val Val Ala Ala Val Met Trp Arg Arg Lys Ser Ser
420 425 430

Asp Arg Lys Gly Gly Ser Tyr Ser Gln Ala Ala Ser Ser Asp Ser Ala
435 440 445

Gln Gly Ser Asp Val Ser Leu Thr Ala Cys Lys Val
450 455 460

<210> 146
<211> 1380
<212> DNA
<213> Artificial Sequence

<220>
<223> hsMHC-I

<400> 146
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aatctcctga attgctatgt gtctgggttt catccatccg acattgaagt tgacttactg 120
aagaatggag agagaattga aaaagtggag cattcagact tgtctttcag caaggactgg 180
tctttctatc tcttgtacta cactgaattc acccccactg aaaaagatga gtatgcctgc 240
cgtgtgaacc atgtgacttt gtcacagccc aagatagtta agtgggatcg agacatggga 300
ggcggcgggt ctggcggcgg cggcagtggt ggtggcggta gcggcggagg tggatctggc 360
tctcactcca tgaggtatct cttcacatcc gtgtcccggc ccggccgcgg ggagccccgc 420
ttcatcgcag tgggctacgt ggacgacacg cagttcgtgc ggttcgacag cgacgccgcg 480
agccagagga tggagccgcg ggcgccgtgg atagagcagg aggggtccgga gtattgggac 540
ggggagacac ggaaagtga ggcccactca cagactcacc gagtggacct ggggaccctg 600
cgcggtact acaaccagag cgaggccggt tctcacaccg tccagaggat gtatggctgc 660
gacgtgggggt cggactggcg cttcctccgc gggtaccacc agtacgccta cgacggcaag 720
gattacatcg ccctgaaaga ggacctgcgc tcttgaccg cggcggacat ggcagctcag 780
accaccaagc acaagtggga ggcggcccat gtggcggagc agttgagagc ctacctggag 840

ggacgtgcg tggagtggct ccgcagatac ctggagaacg ggaaggagac gctgcagcgc 900
 acggacgccc ccaaaacgca tatgactcac cacgctgtct ctgacctga agccaccctg 960
 aggtgctggg ccctgagctt ctaccctgcg gagatcacac tgacctggca gcgggatggg 1020
 gaggaccaga cccaggacac ggagctcgtg gagaccaggc ctgcagggga tggaaccttc 1080
 cagaagtggg cggctgtggt ggtgccttct ggacaggagc agagatacac ctgccatgtg 1140
 cagcatgagg gtttgcccaa gcccctcacc ctgagatggg agccgtcttc ccagcccacc 1200
 atccccatcg tgggcatcat tgctggcctg gttctctttg gagctgtgat cactggagct 1260
 gtggtcgtg ctgtgatgtg gaggaggaag agctcagata gaaaaggagg gagctactct 1320
 caggctgcaa gcagtgcag tgcccagggc tctgatgtgt ctctcacagc ttgtaaagtg 1380

<210> 147
 <211> 504
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> SARS-CoV2sc-Trimer

<400> 147

Met Ser Arg Ser Val Ala Leu Ala Val Leu Ala Leu Leu Ser Leu Ser
 1 5 10 15

Gly Leu Glu Ala Lys Leu Trp Ala Gln Cys Val Gln Leu Gly Gly Gly
 20 25 30

Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Gln Arg Thr
 35 40 45

Pro Lys Ile Gln Val Tyr Ser Arg His Pro Ala Glu Asn Gly Lys Ser
 50 55 60

Asn Phe Leu Asn Cys Tyr Val Ser Gly Phe His Pro Ser Asp Ile Glu
 65 70 75 80

Val Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu His Ser
 85 90 95

Asp Leu Ser Phe Ser Lys Asp Trp Ser Phe Tyr Leu Leu Tyr Tyr Thr

100

105

110

Glu Phe Thr Pro Thr Glu Lys Asp Glu Tyr Ala Cys Arg Val Asn His
 115 120 125

Val Thr Leu Ser Gln Pro Lys Ile Val Lys Trp Asp Arg Asp Met Gly
 130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 145 150 155 160

Gly Gly Ser Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser
 165 170 175

Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp
 180 185 190

Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met
 195 200 205

Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp
 210 215 220

Gly Glu Thr Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp
 225 230 235 240

Leu Gly Thr Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His
 245 250 255

Thr Val Gln Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe
 260 265 270

Leu Arg Gly Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala
 275 280 285

Leu Lys Glu Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln
 290 295 300

Thr Thr Lys His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg
 305 310 315 320

Ala Tyr Leu Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu
325 330 335

Asn Gly Lys Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met
340 345 350

Thr His His Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala
355 360 365

Leu Ser Phe Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly
370 375 380

Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly
385 390 395 400

Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln
405 410 415

Glu Gln Arg Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro
420 425 430

Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Pro Thr Ile Pro Ile Val
435 440 445

Gly Ile Ile Ala Gly Leu Val Leu Phe Gly Ala Val Ile Thr Gly Ala
450 455 460

Val Val Ala Ala Val Met Trp Arg Arg Lys Ser Ser Asp Arg Lys Gly
465 470 475 480

Gly Ser Tyr Ser Gln Ala Ala Ser Ser Asp Ser Ala Gln Gly Ser Asp
485 490 495

Val Ser Leu Thr Ala Cys Lys Val
500

<210> 148
<211> 1512
<212> DNA
<213> Artificial Sequence

<220>

<223> SARS-CoV2sc-Trimer

<400> 148

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ggaggtggga gtatccagcg tactccaaag attcaggttt actcacgtca tccagcagag	180
aatggaaagt caaatttcct gaattgctat gtgtctgggt ttcattccatc cgacattgaa	240
gttgacttac tgaagaatgg agagagaatt gaaaaagtgg agcattcaga cttgtctttc	300
agcaaggact ggtctttcta tctcttgtag tacactgaat tcacccccac tgaaaaagat	360
gagtatgcct gccgtgtgaa ccatgtgact ttgtcacagc ccaagatagt taagtgggat	420
cgagacatgg gaggcggcgg gtctggcggc ggcggcagtg gcggtggcgg tagcggcgga	480
ggtggatctg gctctcactc catgaggtat ttcttcacat ccgtgtcccg gcccgccgc	540
ggggagcccc gcttcacgc agtgggctac gtggacgaca cgagttcgt gcggttcgac	600
agcgacgccg cgagccagag gatggagccg cgggcgccgt ggatagagca ggagggtccg	660
gagtattggg acggggagac acggaaagtg aaggcccact cacagactca ccgagtggac	720
ctggggaccc tgcgcggcta ctacaaccag agcgaggccg gttctcacac cgtccagagg	780
atgtatggct gcgacgtggg gtcggactgg cgcttcctcc gcgggtacca ccagtacgcc	840
tacgacggca aggattacat cgccctgaaa gaggacctgc gctcttggac cgcggcggac	900
atggcagctc agaccaccaa gcacaagtgg gaggcggccc atgtggcgga gcagttgaga	960
gcctacctgg agggcacgtg cgtggagtgg ctccgcagat acctggagaa cgggaaggag	1020
acgctgcagc gcacggacgc ccccaaacg catatgactc accacgctgt ctctgaccat	1080
gaagccaccc tgaggtgctg ggccctgagc ttctaccctg cggagatcac actgacctgg	1140
cagcgggatg gggaggacca gaccaggac acggagctcg tggagaccag gcctgcaggg	1200
gatggaacct tccagaagtg ggcggctgtg gtggtgcctt ctggacagga gcagagatac	1260
acctgccatg tgcagcatga gggtttgccc aagcccctca ccctgagatg ggagccgtct	1320
tcccagccca ccatcccat cgtgggcatc attgctggcc tggttctctt tggagctgtg	1380
atcactggag ctgtggtcgc tgctgtgatg tggaggagga agagctcaga tagaaaagga	1440
gggagctact ctcaggctgc aagcagtgc agtgcccagg gctctgatgt gtctctcaca	1500

gcttgtaaag tg

1512

<210> 149
<211> 740
<212> PRT
<213> Artificial Sequence

<220>
<223> SARS-CoV2sc-Trimer-CD81

<400> 149

Met Ser Arg Ser Val Ala Leu Ala Val Leu Ala Leu Leu Ser Leu Ser
1 5 10 15

Gly Leu Glu Ala Lys Leu Trp Ala Gln Cys Val Gln Leu Gly Gly Gly
20 25 30

Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Gln Arg Thr
35 40 45

Pro Lys Ile Gln Val Tyr Ser Arg His Pro Ala Glu Asn Gly Lys Ser
50 55 60

Asn Phe Leu Asn Cys Tyr Val Ser Gly Phe His Pro Ser Asp Ile Glu
65 70 75 80

Val Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu His Ser
85 90 95

Asp Leu Ser Phe Ser Lys Asp Trp Ser Phe Tyr Leu Leu Tyr Tyr Thr
100 105 110

Glu Phe Thr Pro Thr Glu Lys Asp Glu Tyr Ala Cys Arg Val Asn His
115 120 125

Val Thr Leu Ser Gln Pro Lys Ile Val Lys Trp Asp Arg Asp Met Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser

165

170

175

Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp
 180 185 190

Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met
 195 200 205

Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp
 210 215 220

Gly Glu Thr Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp
 225 230 235 240

Leu Gly Thr Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His
 245 250 255

Thr Val Gln Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe
 260 265 270

Leu Arg Gly Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala
 275 280 285

Leu Lys Glu Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln
 290 295 300

Thr Thr Lys His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg
 305 310 315 320

Ala Tyr Leu Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu
 325 330 335

Asn Gly Lys Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met
 340 345 350

Thr His His Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala
 355 360 365

Leu Ser Phe Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly
 370 375 380

Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly
385 390 395 400

Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln
405 410 415

Glu Gln Arg Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro
420 425 430

Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Pro Thr Ile Pro Ile Val
435 440 445

Gly Ile Ile Ala Gly Leu Val Leu Phe Gly Ala Val Ile Thr Gly Ala
450 455 460

Val Val Ala Ala Val Met Trp Arg Arg Lys Ser Ser Asp Arg Lys Gly
465 470 475 480

Gly Ser Tyr Ser Gln Ala Ala Ser Ser Asp Ser Ala Gln Gly Ser Asp
485 490 495

Val Ser Leu Thr Ala Cys Lys Val Met Gly Val Glu Gly Cys Thr Lys
500 505 510

Cys Ile Lys Tyr Leu Leu Phe Val Phe Asn Phe Val Phe Trp Leu Ala
515 520 525

Gly Gly Val Ile Leu Gly Val Ala Leu Trp Leu Arg His Asp Pro Gln
530 535 540

Thr Thr Asn Leu Leu Tyr Leu Glu Leu Gly Asp Lys Pro Ala Pro Asn
545 550 555 560

Thr Phe Tyr Val Gly Ile Tyr Ile Leu Ile Ala Val Gly Ala Val Met
565 570 575

Met Phe Val Gly Phe Leu Gly Cys Tyr Gly Ala Ile Gln Glu Ser Gln
580 585 590

Cys Leu Leu Gly Thr Phe Phe Thr Cys Leu Val Ile Leu Phe Ala Cys

595

600

605

Glu Val Ala Ala Gly Ile Trp Gly Phe Val Asn Lys Asp Gln Ile Ala
 610 615 620

Lys Asp Val Lys Gln Phe Tyr Asp Gln Ala Leu Gln Gln Ala Val Val
 625 630 635 640

Asp Asp Asp Ala Asn Asn Ala Lys Ala Val Val Lys Thr Phe His Glu
 645 650 655

Thr Leu Asp Cys Cys Gly Ser Ser Thr Leu Thr Ala Leu Thr Thr Ser
 660 665 670

Val Leu Lys Asn Asn Leu Cys Pro Ser Gly Ser Asn Ile Ile Ser Asn
 675 680 685

Leu Phe Lys Glu Asp Cys His Gln Lys Ile Asp Asp Leu Phe Ser Gly
 690 695 700

Lys Leu Tyr Leu Ile Gly Ile Ala Ala Ile Val Val Ala Val Ile Met
 705 710 715 720

Ile Phe Glu Met Ile Leu Ser Met Val Leu Cys Cys Gly Ile Arg Asn
 725 730 735

Ser Ser Val Tyr
 740

<210> 150
 <211> 2223
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> SARS-CoV2sc-Trimer-CD81

<400> 150
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 ggaggtggga gtatccagcg tactccaaag attcaggttt actcacgtca tccagcagag 180

aatggaaagt caaatttcct gaattgctat gtgtctgggt ttcattccatc cgacattgaa	240
gttgacttac tgaagaatgg agagagaatt gaaaaagtgg agcattcaga cttgtctttc	300
agcaaggact ggtcttttcta tctcttgtag tacactgaat tcacccccac tgaaaaagat	360
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cgagacatgg gaggcggcgg gtctggcggc ggccggcagtg gcggtggcgg tagcggcggg	480
ggtggatctg gctctcactc catgaggtat ttcttcacat ccgtgtcccg gcccgccgc	540
ggggagcccc gcttcatcgc agtgggctac gtggacgaca cgagttcgt gcggttcgac	600
agcgacgccg cgagccagag gatggagccg cgggcgccgt ggatagagca ggagggtccg	660
gagtattggg acggggagac acggaaagtg aaggcccact cacagactca ccgagtggac	720
ctggggaccc tgcgcggcta ctacaaccag agcgaggccg gttctcacac cgtccagagg	780
atgtatggct gcgacgtggg gtcggactgg cgcttctcc gcgggtacca ccagtacgcc	840
tacgacggca aggattacat cgccctgaaa gaggacctgc gctcttgac cgcgccggac	900
atggcagctc agaccaccaa gcacaagtgg gaggcggccc atgtggcgga gcagttgaga	960
gcctacctgg agggcacgtg cgtggagtgg ctccgcagat acctggagaa cgggaaggag	1020
acgctgcagc gcacggacgc ccccaaacg catatgactc accacgctgt ctctgaccat	1080
gaagccaccc tgaggtgctg ggccctgagc ttctaccctg cggagatcac actgacctgg	1140
cagcgggatg gggaggacca gaccaggac acggagctcg tggagaccag gcctgcaggg	1200
gatggaacct tccagaagtg ggcggctgtg gtggtgcctt ctggacagga gcagagatac	1260
acctgccatg tgcagcatga gggtttgccc aagcccctca ccctgagatg ggagccgtct	1320
tcccagccca ccatcccat cgtgggcac cttgtctggc ttgttctctt tggagctgtg	1380
atcactggag ctgtggtcgc tgctgtgatg tggaggagga agagctcaga tagaaaagga	1440
gggagctact ctgaggtgc aagcagtgc agtgcccagg gctctgatgt gtctctcaca	1500
gcttgtaaag tgatgggagt ggagggtgc accaagtgc tcaagtacct gctcttcgtc	1560
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catgacccgc agaccaccaa cctcctgtat ctggagctgg gagacaagcc cgcgcccaac	1680
accttctatg taggcatcta catcctcatc gctgtgggcg ctgtcatgat gttcgttggc	1740
ttcctgggct gctacggggc catccaggaa tcccagtgc tgctggggac gttcttcacc	1800

tgcttggtca tcctgtttgc ctgtgaggtg gccgccggca tctggggctt tgtcaacaag	1860
gaccagatcg ccaaggatgt gaagcagttc tatgaccagg ccctacagca ggccgtggtg	1920
gatgatgacg ccaacaacgc caaggctgtg gtgaagacct tccacgagac gcttgactgc	1980
tgtggctcca gcacactgac tgctttgacc acctcagtcg tcaagaacaa tttgtgtccc	2040
tcgggcagca acatcatcag caacctcttc aaggaggact gccaccagaa gatcgatgac	2100
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tga	2223