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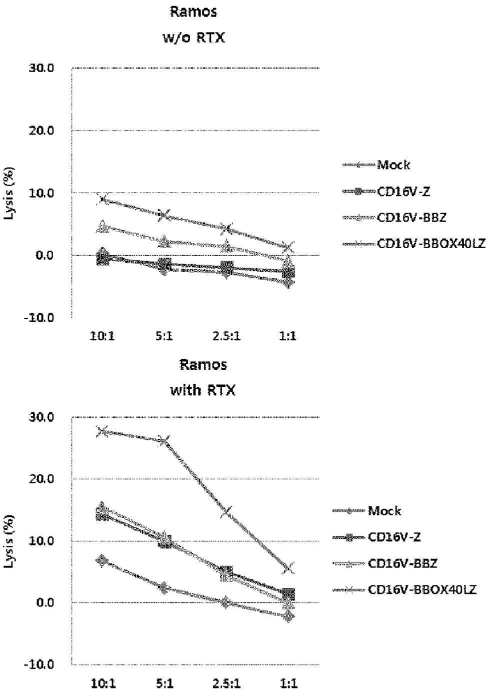
(54) Title: CHIMERIC ANTIGEN RECEPTOR AND NATURAL KILLER CELLS EXPRESSING SAME

(54) 발명의 명칭: 키메라 항원 수용체 및 이를 발현하는 자연 살해 세포



(57) Abstract: The present invention relates to a chimeric antigen receptor and natural killer cells expressing the same and, more particularly, to a chimeric antigen receptor (CAR) comprising an intracellular signaling domain including all or a part of an OX40 ligand (CD252), thereby having an excellent anticancer activity enhancing effect on immune cells, and immune cells expressing the same.

(57) 요약서: 본 발명은 키메라 항원 수용체 및 이를 발현하는 자연 살해 세포에 관한 것으로서, OX40 리간드 (CD252) 의 전체 또는 일부를 포함하는 세포내 신호전달 도메인 (intracellular signaling domain) 을 포함함으로써 면역세포의 항암 활성 증대 효과가 우수한 키메라 항원 수용체 (chimeric antigen receptor, CAR) 및 이를 발현하는 면역세포에 관한 것이다.

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[다음 쪽 계속]

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【DESCRIPTION】

【Invention Title】

CHIMERIC ANTIGEN RECEPTOR AND NATURAL KILLER CELLS EXPRESSING SAME

【Technical Field】

[1] The present invention relates to a chimeric antigen receptor and natural killer cells expressing the same.

【Background Art】

[2] Human natural killer cells (NK cells) play an important role in innate immune defense against malignant lymphoma cells, and thus may be suitable for adoptive immune therapy (i.e., adoptive cellular immunotherapy). However, due to difficulties in *ex vivo* cell expansion and differences in activities of NK cells in individual patients, it is difficult to use the NK cells.

[3] In a field of immune cell therapy using T cells, that is, T cell therapy field, a chimeric antigen receptor for treatment of autoimmune cells has been developed. The chimeric antigen receptor has been known to help activation of T cells by reprogramming T cells in order to improve treatment effects to specific cancers or overcome resistance against T cell treatment.

[4] OX40 ligand (CD252) is a protein belonging to a TNFR superfamily, and is known to be expressed in antigen-presenting cells (APCs), some of NK cells and some of B cells, as well as known to be expressed in several hours to a few days after activation of these cells.

[5] As a receptor of OX40 ligand (CD252), OX40 (CD134) is known to be expressed in T cells, and also known to be expressed in 24 hours after activation of T cells by antigen and CD28. It is known that expression of CD134 may further enhance a response of T cells by CD28 activation, so as to increase proliferation of T cells, and cytokine secretion and survival.

[6] However, a role of OX40 ligand in enhancement of anticancer activity of NK cells is not well known, and an attempt to use the OX40 ligand for the chimeric antigen receptor is still not yet reported.

[7] In order to research functional roles of CD252 in antitumor response of NK cells, the present inventors have constructed two different kinds of NK receptors containing CAR. First, a variety of stimulatory cofactors known to increase cytotoxicity of NK cells in a signaling domain were genetically engineered to produce lentivirus encoding high affinity recombination FCRG3A V158 variants (CD16V). CD16V receptors including different intercellular signaling molecules were transduced in NK cells, followed by detecting expression thereof. Further, antitumor responses of the transduced NK cells were investigated using lymphoma cell lines *in vitro* in the presence of rituximab specific to CD20 molecules.

[8] As a second approach, functional roles of CD252 in NKG2D-mediated antitumor activity was tested. NKG2D as a key receptor in NK cell activation can recognize MHC class 1 chain-related A (MICA), MICB and other diverse UL 16-binding proteins (ULBP), which are preferentially expressed after genotoxic stress, infection and/or cytotoxicity.

[9] A variety of NKG2D chimeric antigen receptors containing different signaling molecules were genetically engineered, transduced, and expressed in NK92MI cells. Thereafter, the transduced cells were subjected to evaluation of antitumor effects *in vitro*.

[10] The present inventors have found that, as one approach to overcome limitations of current immune cell therapy like NK cells, a chimeric antigen receptor containing OX40 ligand has significantly improved in anticancer activities of NK cells, as compared to the other signaling domains known, thereby completing the present invention.

【Disclosure】

【Technical Problem】

[11] Accordingly, it is an object of the present invention to provide a chimeric antigen receptor capable of increasing anticancer immune cell treatment efficiency using natural killer (NK) cells.

【Technical Solution】

[12] 1. A chimeric antigen receptor, including: an intracellular signaling domain which includes the whole or a portion of OX40 ligand (CD252).

[13] 2. The chimeric antigen receptor according to the above 1, further including: a transmembrane domain linked to the intracellular signaling domain; a spacer domain linked to the transmembrane domain; and an extracellular domain linked to the spacer domain.

[14] 3. The chimeric antigen receptor according to the above 2, further comprising a signal sequence linked to the extracellular domain.

[15] 4. The chimeric antigen receptor according to the above 3, wherein the signal sequence includes the whole or a portion of CD16, or the whole or a portion of CD8α.

[16] 5. The chimeric antigen receptor according to the above 2, wherein the extracellular domain includes the whole or a portion of any one selected from the group consisting of an antigen-binding fragment of an antibody, an Fc receptor, a natural cytotoxicity receptor, NKG2D, 2B4 and DNAM-1.

[17] 6. The chimeric antigen receptor according to the above 5, wherein the antigen-binding fragment is Fab fragment, F(ab') fragment, F(ab')2 fragment or Fv fragment.

[18] 7. The chimeric antigen receptor according to the above 6, wherein the Fv fragment is a single-chain variable fragment (ScFv).

[19] 8. The chimeric antigen receptor according to the above 5, wherein the Fc receptor is selected from the group consisting of CD16, CD32, CD64, CD23, CD89 and variants thereof.

[20] 9. The chimeric antigen receptor according to the above 8, wherein the Fc receptor is CD16 or variants thereof.

[21] 10. The chimeric antigen receptor according to the above 5, wherein the natural cytotoxicity receptor is selected from the group consisting of NKp46, NKp30, NKp44, NKp80 and NKp65 receptors.

[22] 11. The chimeric antigen receptor according to the above 2, wherein the spacer domain includes the whole or a portion of any one selected from the group consisting of CD8α and CD28.

[23] 12. The chimeric antigen receptor according to the above 2, wherein the transmembrane domain includes the whole or a portion of any one selected from the group consisting of CD8α and CD28.

[24] 13. The chimeric antigen receptor according to the above 1, wherein the intracellular signaling domain further includes the whole or a portion of CD3-zeta.

[25] 14. The chimeric antigen receptor according to the above 13, wherein the whole or the portion of CD3-zeta and the whole or the portion of OX40 ligand are arranged in order from a cell membrane toward an inside of the cell.

[26] 15. The chimeric antigen receptor according to the above 2, further comprising an AAA linker between the extracellular domain and the spacer domain.

[27] 16. A chimeric antigen receptor, comprising intracellular signaling domains which include: a first intracellular signaling domain including the whole or a portion of any one selected from the group consisting of CD28 and 4-1BB; a second intracellular signaling domain including the whole or a portion of any one selected from the group consisting of OX40 ligand, OX40 and 4-1BB; and a third intracellular signaling domain including the whole or a portion of CD3-zeta, wherein the first, second and third intracellular signaling domains are arranged in order from a cell membrane toward an inside of the cell.

[28] 17. The chimeric antigen receptor according to the above 16, further including: a transmembrane domain linked to the intracellular signaling domain; a spacer domain linked to the transmembrane domain; and an extracellular domain linked to the spacer domain.

[29] 18. The chimeric antigen receptor according to the above 17, further comprising a signal sequence linked to the extracellular domain.

[30] 19. The chimeric antigen receptor according to the above 18, wherein the signal sequence includes the whole or a portion of CD16, or the whole or a portion of CD8α.

[31] 20. The chimeric antigen receptor according to the above 17, wherein the extracellular domain includes the whole or a portion of any one selected from the group consisting of an antigen-binding fragment of an antibody, an Fc receptor, a natural cytotoxicity receptor, NKG2D, 2B4 and DNAM-1.

[32] 21. The chimeric antigen receptor according to the above 17, wherein the spacer domain includes the whole or a portion of any one selected from the group consisting of

CD8α and CD28.

[33] 22. The chimeric antigen receptor according to the above 17, wherein the transmembrane domain includes the whole or a portion of any one selected from the group consisting of CD8α and CD28.

[34] 23. The chimeric antigen receptor according to the above 16, wherein the first intracellular signaling domain includes the whole or a portion of CD28; the second intracellular signaling domain includes the whole or a portion of the OX40 ligand; and the third intracellular signaling domain includes the whole or a portion of CD3-zeta.

[35] 24. The chimeric antigen receptor according to the above 17, further comprising an AAA linker between the extracellular domain and the spacer domain.

[36] 25. An immune cell expressing the chimeric antigen receptor according to any one of the above 1 to 24.

[37] 26. The immune cell according to the above 25, wherein the immune cell is a natural killer cell (NK cell).

[38] 27. A pharmaceutical composition for treatment of tumor, comprising the immune cell according to the above 25 as an active ingredient.

[39] 28. The pharmaceutical composition according to the above 27, further comprising an antibody as an active ingredient when the extracellular domain is an Fc receptor.

[40] 29. A nucleic acid sequence encoding the chimeric antigen receptor according to any one of the above 1 to 24.

[41] 30. The nucleic acid sequence according to the above 29, wherein the nucleic acid sequence encodes one or more amino acid sequences selected from the group consisting of SEQ ID NOs: 33, 41, 43, 45, 47, 49, 51, 53, 55, 69, 71, 77, 81, 83, 85, 87, 89, 91 and 93, or variants thereof having a sequence identity of 80% or more.

[42] 31. The nucleic acid sequence according to the above 30, wherein the nucleic acid sequence includes one or more nucleic acid sequence selected from the group consisting of SEQ ID NOs: 32, 40, 42, 44, 46, 48, 50, 52, 54, 68, 70, 76, 80, 82, 84, 86, 88, 90 and 92, or variants thereof having a sequence identity of 80% or more.

[43] 32. A method for treatment of tumor, comprising administering the immune cell according to the above 25 to a subject.

【Advantageous effects】

[44] The chimeric antigen receptor according to the present invention is excellent in NK cell activation efficiency.

[45] The chimeric antigen receptor according to the present invention may be used along with various cancer-target antibodies depending on cancer types to be targeted.

[46] The chimeric antigen receptor according to the present invention is applicable to diverse cancer types by applying different antigen recognition sites.

[47] The NK cells expressing the chimeric antigen receptor according to the present invention are excellent in cytotoxicity on cancer cells.

[48] The NK cells expressing the chimeric antigen receptor according to the present invention may be usefully used in immune cell treatment.

【Description of Drawings】

[49] FIG. 1 shows CAR expression levels of NK92MI cells transduced with CD16V-Z CAR (1st generation), CD16V-28Z CAR (2nd generation), CD16V-BBZ CAR (2nd generation), CD16V-OX40Z CAR (2nd generation) or CD16V-28OX40LZ CAR (3rd generation), respectively, according to an embodiment of the present invention.

[50] FIG. 1B shows intrinsic cell killing ability (i.e., ‘cytotoxicity’) of NK92MI cells transduced with CD16V-Z CAR (1st generation), CD16V-28Z CAR (2nd generation), CD16V-BBZ CAR (2nd generation), CD16V-OX40Z CAR (2nd generation) or CD16V-28OX40LZ CAR (3rd generation), respectively, which is obtained through assessment of cytotoxicity on K562 cells.

[51] FIG. 1C shows assessment of NK cell-mediated cytotoxicity of NK92MI cells transduced with CD16V-Z CAR (1st generation), CD16V-28Z CAR (2nd generation), CD16V-BBZ CAR (2nd generation), CD16V-OX40Z CAR (2nd generation) or CD16V-28OX40LZ CAR (3rd generation), respectively, according to an embodiment of the present invention, when combined with an antibody to Ramos cells.

[52] FIG. 1D shows CAR expression levels of NK92MI cells transduced with CD16V–Z CAR (1st generation) and CD16V-OX40LZ CAR (2nd generation), respectively, according to an embodiment of the present invention.

[53] FIG. 1E shows assessment of NK cell-mediated cytotoxicity of NK92MI cells transduced with CD16V-Z CAR (1st generation) and CD16V-OX40LZ CAR (2nd generation), respectively, according to an embodiment of the present invention, when combined with an antibody to Ramos cells.

[54] FIG. 1F shows CAR expression levels of NK92MI cells transduced with CD16V-Z CAR (1st generation) and CD16V-ZOX40L CAR (2nd generation), respectively, according to an embodiment of the present invention.

[55] FIG. 1G shows assessment of NK cell-mediated cytotoxicity of NK92MI cells transduced with CD16V-Z CAR (1st generation) or CD16V-ZOX40L CAR (2nd generation), respectively, according to an embodiment of the present invention, when combined with an antibody to Ramos cells.

[56] FIG. 2A shows CAR expression levels of NK92MI cells transduced with

CD16V-Z CAR (1st generation), CD16V-BBZ CAR (2nd generation) or CD16V-BBOX40LZ CAR (3rd generation), respectively, according to an embodiment of the present invention.

[57] FIG. 2B shows assessment of NK cell-mediated cytotoxicity of NK92MI cells expressing CD16V-Z CAR (1st generation), CD16V-BBZ CAR (2nd generation) or CD16V-BBOX40LZ CAR (3rd generation), respectively, according to an embodiment of the present invention, when combined with an antibody to Ramos cells.

[58] FIG. 3A shows CAR expression levels of NK92MI cells transduced with CD16V-28OX40LZ CAR, CD16V-28OX40Z CAR or CD16V-28BBZ CAR, respectively, all of which are 3rd generation CARs, according to an embodiment of the present invention.

[59] FIG. 3B shows assessment of NK cell-mediated cytotoxicity of NK92MI cells expressing CD16V-28OX40LZ CAR, CD16V-28OX40Z CAR or CD16V-28BBZ CAR, respectively, all of which are 3rd generation CARs, according to an embodiment of the present, when combined with an antibody to Ramos cells.

[60] FIG. 4A shows CAR expression levels of NK92MI cells transduced with CD16V-28(H)BBZ CAR, CD16V-28(H)OX40Z CAR, or CD16V-28(H)OX40LZ CAR, respectively, all of which are 3rd generation CARs each containing CD28 at a hinge, according to an embodiment of the present invention.

[61] FIG. 4B shows assessment of NK cell-mediated cytotoxicity of NK91MI cells expressing CD16V-28(H)BBZ CAR, CD16V-28(H)OX40Z CAR or CD16V-28(H)OX40LZ CAR, respectively, all of which are 3rd generation CARs each having CD28 at a hinge, according to an embodiment of the present invention, when combined with an antibody to Ramos cells.

[62] FIG. 5A shows CAR expression levels of NK92MI cells transduced with

NKG2D-Z CAR (1st generation), NKG2D-28Z CAR (2nd generation), NKG2D-BBZ CAR (2nd generation) or NKG2D-OX40Z CAR (2nd generation), respectively, according to an embodiment of the present invention.

[63] FIG. 5B shows assessment of NK cell-mediated cytotoxicity of NK92MI cells transduced with NKG2D-Z CAR (1st generation), NKG2D-28Z CAR (2nd generation), NKG2D-BBZ CAR (2nd generation) or NKG2D-OX40Z CAR (2nd generation), respectively, against human breast cancer cell lines MCF-7, according to an embodiment of the present invention.

[64] FIG. 6A shows CAR expression levels of NK92MI cells transduced with NKG2D-Z CAR (1st generation), NKG2D-28BBZ CAR (3rd generation) including CD28 signaling domain or NKG2D-28OX40Z CAR (3rd generation), respectively, according to the present invention.

[65] FIG. 6B shows assessment of NK cell-mediated cytotoxicity of NK92MI cells transduced with NKG2D-Z CAR (1st generation), NKG2D-28BBZ CAR including CD28 signaling domain (3rd generation) or NKG2D-28OX40Z CAR (3rd generation), respectively, against human breast cancer cell lines MCF-7, according to an embodiment of the present invention.

[66] FIG 7A shows CAR expression levels of NK92MI cells transduced with NKG2D-Z CAR (1st generation), NKG2D-28Z CAR (2nd generation), NKG2D-28(H)OX40LZ CAR (3rd generation) or NKG2D-AAA-28(H)OX40LZ CAR (3rd generation) including AAA sequence between NKG2D extracellular domain and CD28 hinge, respectively, according to an embodiment of the present invention.

[67] FIG. 7B shows assessment of NK cell-mediated cytotoxicity of NK92MI cells transduced with NKG2D-Z CAR (1st generation), NKG2D-28Z CAR (2nd generation), NKG2D-28(H)OX40LZ CAR (3rd generation) or NKG2D-AAA-

28(H)OX40LZ CAR (3rd generation) including AAA sequence between NKG2D extracellular domain and CD28 hinge, respectively, against human breast cell lines MCF-7, according to an embodiment of the present invention.

[68] FIG. 8A shows CAR expression levels of NK92MI cells transduced with NKG2D-Z CAR (1st generation) or NKG2D-AAA-28(H)OX40LZ CAR (3rd generation) including AAA sequence between NKG2D extracellular domain and CD28 hinge, respectively, according to an embodiment of the present invention.

[69] FIG. 8B shows expression levels of different NKG2D ligands in human lung cancer cell lines H1299 and H1944 according to an embodiment of the present invention.

[70] FIG. 8C shows assessment of NK-mediated cytotoxicity of NK92MI cells transduced with NKG2D-Z CAR (1st generation) or NKG2D-AAA-28(H)OX40LZ (3rd generation) including AAA sequence between NKG2D extracellular domain and CD28 hinge, respectively, against human lung cancer cell lines H1299 and H1944, according to an embodiment of the present invention.

【Best mode】

[71] The present invention discloses a chimeric antigen receptor and NK cells expressing the same, and more particularly, a chimeric antigen receptor (CAR) with excellent effects of increasing anticancer activity of immune cells, by including an intracellular signaling domain which contains the whole or a portion of OX40 ligand (CD252), as well as immune cells expressing the same.

[72] Hereinafter, the present invention will be described in detail.

[73] The chimeric antigen receptor of the present invention may include an intracellular signaling domain which contains the whole or a portion of OX40 ligand (CD252).

[74] According to one embodiment of the present invention, the chimeric antigen receptor may be one further including a transmembrane domain linked to the intracellular signaling domain; a spacer domain linked to the transmembrane domain; and an extracellular domain linked to the spacer domain. In addition, according to one embodiment of the present invention, the chimeric antigen receptor may be one further including a signal sequence linked to a terminal of the extracellular domain that is not linked with the spacer domain. According to one embodiment of the present invention, the above-described domains may be directly linked to one another or may be linked by a linker.

[75] According to one embodiment of the present invention, the signal sequence may allow the extracellular domain to be positioned outside a cell membrane of immune cells (e.g., NK cells) when the chimeric antigen receptor is expressed. For example, the signal sequence may include the whole or a portion of CD16.

[76] According to one embodiment of the present invention, the extracellular domain is a domain to be specifically linked to an antibody or to specifically recognize an antigen, and may include, for example, an Fc receptor, an antigen-binding fragment such as a single-chain variable fragment (ScFv) in an antibody, a natural cytotoxicity receptor, NKG2D, 2B4 or DNAM-1. Accordingly, in the present disclosure, the term “extracellular domain” is used with the same meanings as “antigenic recognition site,” “antigen-binding fragment” and/or “antibody binding site.”

[77] The chimeric antigen receptor according to one embodiment of the present invention may include an Fc receptor as the extracellular domain and thus be used associated with different antibodies depending on cell types of cancer to be treated. According to one embodiment, the Fc receptor may be any one selected from the group consisting of CD16, CD32, CD64, CD23 and CD89. According to a more specific embodiment, the Fc receptor may be one including the whole or a portion of the CD16 V158 variant (CD16V).

[78] According to another embodiment, the chimeric antigen receptor of the present invention may further include an antigen-binding fragment of an antibody, as an extracellular domain, which can directly recognize the antigen without co-administration along with the antibody. According to one embodiment, the antigen-binding fragment may be an Fab fragment, F(ab') fragment, F(ab')2 fragment or Fv fragment. According to one embodiment of the present invention, the antibody may be any one of various types of antibodies capable of binding antigen-specifically, briefly, having antigen-specific binding ability. For example, the antibody may be one in which one light chain and one heavy chain are bonded with each other, or one in which two light chains and two heavy chains are bonded with each other. For example, when two light chains and two heavy chains are bonded with each other, the antibody may be one in which a first unit including a first light chain and a first heavy chain bonded with each other and a second unit including a second light chain and a second heavy chain bonded with each other are combined with each other. Herein, the bond may be a disulfide bond, but it is not limited thereto. According to embodiments of the present invention, the above two units may be the same as or different from each other. For example, the first unit including the first light chain and the first heavy chain and the second unit including the second light chain and the second heavy chain may be the same as or different from each other. As such, an antibody prepared to recognize two different antigens by the first unit and the second unit, respectively, is typically referred to as a ‘bispecific antibody.’ In addition, for example, the antibody may be one in which three or more of the above-described units are combined with one another. The antigen-binding fragment of the present invention may be derived from various types of antibodies as described above, but it is not limited thereto.

[79] According to another embodiment of the present invention, the extracellular domain used herein may be a natural killer receptor (also referred to as a 'natural cytotoxicity receptor'). According to a specific embodiment, the NK receptor may include NKp46, NKp30, NKp44, NKp80 and NKp65 receptors, but it is not limited thereto.

[80] According to one embodiment of the present invention, the transmembrane domain penetrates through the cell membrane, and may be any one without limitation as long as the domain can penetrate through the cell membrane without interfering with functions of the extracellular domain and the intracellular signaling domain. For example, the transmembrane domain may include the whole or a portion of any one selected from the group consisting of CD8α and CD28.

[81] According to one embodiment of the present invention, the extracellular domain and the transmembrane domain may be linked to each other by a spacer domain. For example, the spacer domain may be a hinge domain. According to a specific embodiment, the spacer domain may include the whole or a portion of any one selected from the group consisting of CD8α and CD28.

[82] According to one embodiment of the present invention, the intracellular signaling domain is a portion located on an inner side of the cell membrane of NK cell, that is, on the cytoplasm thereof, and may include a sequence that can transmit a signal to activate NK cells when an antibody linked to the extracellular domain is combined with a target antigen.

[83] According to one embodiment of the present invention, the chimeric antigen receptor may include one or more intracellular signaling domain(s). When including two or more intracellular signaling domains, the intracellular signaling domains may be linked in series with each other. For example, when including three intracellular signaling domains, a terminal of a first intracellular signaling domain may be linked to a terminal of the transmembrane domain that is not linked with the spacer domain, a terminal of a second intracellular signaling domain may be linked to a terminal of the first intracellular signaling domain that is not linked with the transmembrane domain, and a terminal of a third intracellular signaling domain may be linked to a terminal of the second intracellular signaling domain that is not linked with the first intracellular signaling domain. That is, the first, second and third intracellular signaling domains may be arranged in order from a cell membrane toward an inside of the cell. Further, even when including two, four or more intracellular signaling domains, these domains may be linked to one another in the same manner as described above. According to one embodiment of the present invention, such the respective domains may be directly linked to one another or may be linked by a linker.

[84] According to one embodiment of the present invention, the chimeric antigen receptor may include two intracellular signaling domains. For example, the chimeric antigen receptor may include a first intracellular signaling domain linked to the transmembrane domain and a second intracellular signaling domain linked to a terminal of the first intracellular signaling domain that is not linked with the transmembrane domain. According to a more specific embodiment, the first intracellular signaling domain may include the whole or a portion of any one selected from the group consisting of OX40 (CD134), OX40 ligand (OX40L, CD252), 4-1BB (CD137), CD28, DAP10, CD3-zeta (CD3ζ) and DAP12, and the second intracellular signaling domain may include the whole or a portion of any one selected from the group consisting of OX40 ligand, CD3-zeta and DAP12. In this case, at least one of the first intracellular signaling domain and the second intracellular signaling domain includes the whole or a portion of

OX40 ligand. For example, the chimeric antigen receptor may include a first intracellular signaling domain containing the whole or a portion of OX40 ligand and a second intracellular signaling domain containing the whole or a portion of any one selected from CD3-zeta and DAP12. Further, for example, the chimeric antigen receptor may include a first intracellular signaling domain containing the whole or a portion of any one selected from the group consisting of CD3-zeta and DAP12 and a second intracellular signaling domain containing the whole or a portion of OX40 ligand.

[85] According to another embodiment of the present invention, the chimeric antigen receptor may include three intracellular signaling domains. For example, the chimeric antigen receptor may include: a first intracellular signaling domain linked to the transmembrane domain; a second intracellular signaling domain linked to a terminal of the first intracellular signaling domain that is not linked with the transmembrane domain; and a third intracellular signaling domain linked to a terminal of the second intracellular signaling domain that is not linked with the first intracellular signaling domain. According to a more specific embodiment, the first intracellular signaling domain may include the whole or a portion of any one selected from the group consisting of 4-1BB, OX40, OX40 ligand, CD28 and DAP10, the second intracellular signaling domain may include the whole or a portion of any one selected from the group consisting of OX40 ligand, OX40 and 4-1BB, and the third intracellular signaling domain may include the whole or a portion of any one selected from the group consisting of OX40 ligand, CD3-zeta and DAP12. In such a case, at least one of the first intracellular signaling domain, the second intracellular signaling domain and the third intracellular signaling domain may include the whole or a portion of OX40 ligand.

[86]

[87] In another aspect, the present invention may provide a chimeric antigen receptor, which includes: a first intracellular signaling domain containing the whole or a portion of any one selected from the group consisting of CD28 and 4-1BB; a second intracellular signaling domain containing the whole or a portion of any one selected from the group consisting of OX40 ligand, OX40 and 4-1BB; and a third intracellular signaling domain containing the whole or a portion of CD3-zeta, wherein the first, second and third intracellular signaling domains are arranged in order from the cell membrane toward the inside of the cell. According to one embodiment of the present invention, the above respective domains may be directly linked to one another or may be linked by a linker.

[88] According to one embodiment of the present invention, the chimeric antigen receptor may further include: a transmembrane domain linked to the first intracellular signaling domain; a spacer domain linked to the transmembrane domain; and an extracellular domain linked to the spacer domain. In addition, the chimeric antigen receptor may further include a signal sequence linked to the extracellular domain. According to one embodiment of the present invention, the above respective domains may be directly linked to one another or may be linked by a linker.

[89] According to one embodiment of the present invention, the extracellular domain is a domain for specifically binding with an antibody or specifically recognizing an antigen, for example, an Fc receptor, an antigen-binding fragment of an antibody such as a single-chain variable fragment (ScFv), NK receptor (natural cytotoxicity receptor), NKG2D, 2B4 or DNAM-1, etc. Thus, in the present disclosure, the term “extracellular domain” is used with the same meanings as the “antigenic recognition site”, “antigen-binding fragment” and/or “antibody binding site.”

[90] The chimeric antigen receptor according to an embodiment of the present invention may include an Fc receptor as the extracellular domain, and therefore, can be used along with a variety of antibodies depending on cell types of cancer to be treated. According to one embodiment, the Fc receptor may include any one selected from the group consisting of CD16, CD32, CD64, CD23 and CD89, and variants thereof. According to a more specific embodiment, the Fc receptor may include CD16 or variants thereof, and most specifically, may include the whole or a portion of CD16 V158 variant (CD16V).

[91] According to another embodiment, the chimeric antigen receptor of the present invention may include, as the extracellular domain, an antigen-binding fragment of an antibody which directly recognizes the antigen without co-administration along with the antibody. According to one embodiment, the antigen-binding fragment may be an Fab fragment, F(ab') fragment, F(ab')2 fragment or Fv fragment. According to one embodiment of the present invention, the antibody may be any one of various types of antibodies capable of binding antigen-specifically. For example, the antibody may be one in which one light chain and one heavy chain are bonded with each other, or one in which two light chains and two heavy chains are bonded with each other. For example, when two light chains and two heavy chains are bonded with each other, the antibody may be one in which the first unit including the first light chain and the first heavy chain bonded with each other and the second unit including the second light chain and the second heavy chain bonded with each other are combined with each other. The bond may be a disulfide bond, but it is not limited thereto. According to an embodiment of the present invention, the above two units may be the same as or different from each other. For example, the first unit including the first light chain and the first heavy chain and the second unit including the second light chain and the second heavy chain may be the same as or different from each other. As such, an antibody prepared to recognize two different antigens by the first unit and the second unit, respectively, is commonly referred to as a 'bispecific antibody' in the related art. In addition, for example, the antibody may be one in which the above three or more units are combined with one another. The antigen-binding fragment of the present invention may be derived from various types of antibodies as described above, but it is not limited thereto.

[92] According to another embodiment of the present invention, the extracellular domain used herein may be a NK receptor (natural cytotoxicity receptor). According to a specific embodiment, the NK receptor may include NKp46, NKp30, NKp44, NKp80 and NKp65 receptors, but it is not limited thereto.

[93] According to one embodiment, the signal sequence may include the whole or a portion of CD16. According to another embodiment, the extracellular domain may include the whole or a portion of CD16 V158 variant (CD16V). According to another embodiment, the spacer domain may include the whole or a portion of any one selected from the group consisting of CD8α (CD8-alpha) and CD28. According to another embodiment, the transmembrane domain may include the whole or a portion of any one selected from the group consisting of CD8α and CD28.

[94] According to a specific embodiment, the chimeric antigen receptor may include one or more amino acid sequence selected from the group consisting of SEQ ID NOs: 33, 41, 43, 45, 47, 49, 51, 53, 55, 69, 71, 77, 81, 83, 85, 87, 89, 91 and 93 or variants thereof having a sequence identity of 80% or more.

[95] According to another aspect, the present invention provides immune cells (e.g., NK cells) to express the above-described chimeric antigen receptor according to the present invention.

[96] The immune cells of the present invention may exhibit toxicity to tumor cells. It is determined that the chimeric antigen receptor according to the invention exhibits specific toxicity to what types of tumor cells depending on what types of antibodies are combined with the extracellular domains. Therefore, the types of tumor cells, to which the immune cells expressing the chimeric antigen receptor according to the present invention may exhibit specific toxicity, are not particularly limited. According to one embodiment, when the immune cells (e.g., NK cells) of the present invention are used along with rituximab, the cells may exhibit toxicity to malignant lymphoma cells. For example, the malignant lymphoma cells may express CD20. Further, for example, the malignant lymphoma may be B-cell lymphoma.

[97]

[98] According to another aspect, the invention further provides a pharmaceutical composition for prevention or treatment of tumor or tumor metastasis, which includes the immune cells (e.g., NK cells) expressing the above-described chimeric antigen receptor according to the present invention, in the number of 2 to 7.5 times the number of tumor cells (e.g., malignant lymphoma cells) in a subject to be treated (‘treatment target’).

[99] According to one embodiment of the present invention, the number of immune cells (e.g., NK cells) included in the pharmaceutical composition of the present invention in a single dose may range from 0.75 to 10 times the number of tumor cells (e.g., malignant lymphoma cells) in the treatment target. For example, the number of the immune cells (e.g., NK cells) in a single dose may range from 2 to 7.5 times the number of tumor cells (e.g., malignant lymphoma cells) in the treatment target.

[100]

[101] According to another aspect, the present invention further provides a nucleic acid sequence encoding the above-described chimeric antigen receptor according to the present invention.

[102] According to one embodiment of the present invention, the nucleic acid sequence may include one or more nucleotide sequences selected from the group consisting of SEQ ID NOs: 32, 40, 42, 44, 46, 48, 50, 52, 54, 68, 70, 76, 80, 82, 84, 86, 88, 90 and 92 or variants thereof having a sequence identity of 80% or more.

[103] According to another aspect, the present invention further provides a vector including the above-described nucleic acid sequence according to the present invention.

[104]

[105] According to another aspect, the present invention further provides a method of treating tumor which includes administering the above-described immune cells to a subject.

[106] According to another aspect, the present invention further provides a method of preventing tumor metastases which includes administering the above-described immune cells to a subject.

[107] The subject may be a mammal having a tumor, specifically, a human, but it is not limited thereto.

[108] Administration may be performed in such a way that the number of immune cells (e.g., NK cells) expressing the chimeric antigen receptor according to the present invention may be in a range of 2 to 7.5 times the number of tumor cells (e.g., malignant lymphoma cells) in the treatment target.

[109] An administration method is not particularly limited and, for example, may include administration through an oral or parenteral route.

[110] Tumor is not particularly limited but may include, for example, malignant lymphoma, leukemia, breast cancer, lung cancer, etc., and more specifically, B-cell lymphoma.

[111]

[112] Hereinafter, the present invention will be described in more detail by way of the following examples. These examples are proposed only for describing the present invention in detail and the scope of the present invention is not limited to the contents illustrated in the examples.

[113] **Example 1: Methods and Reagents**

[114] **Cell Lines**

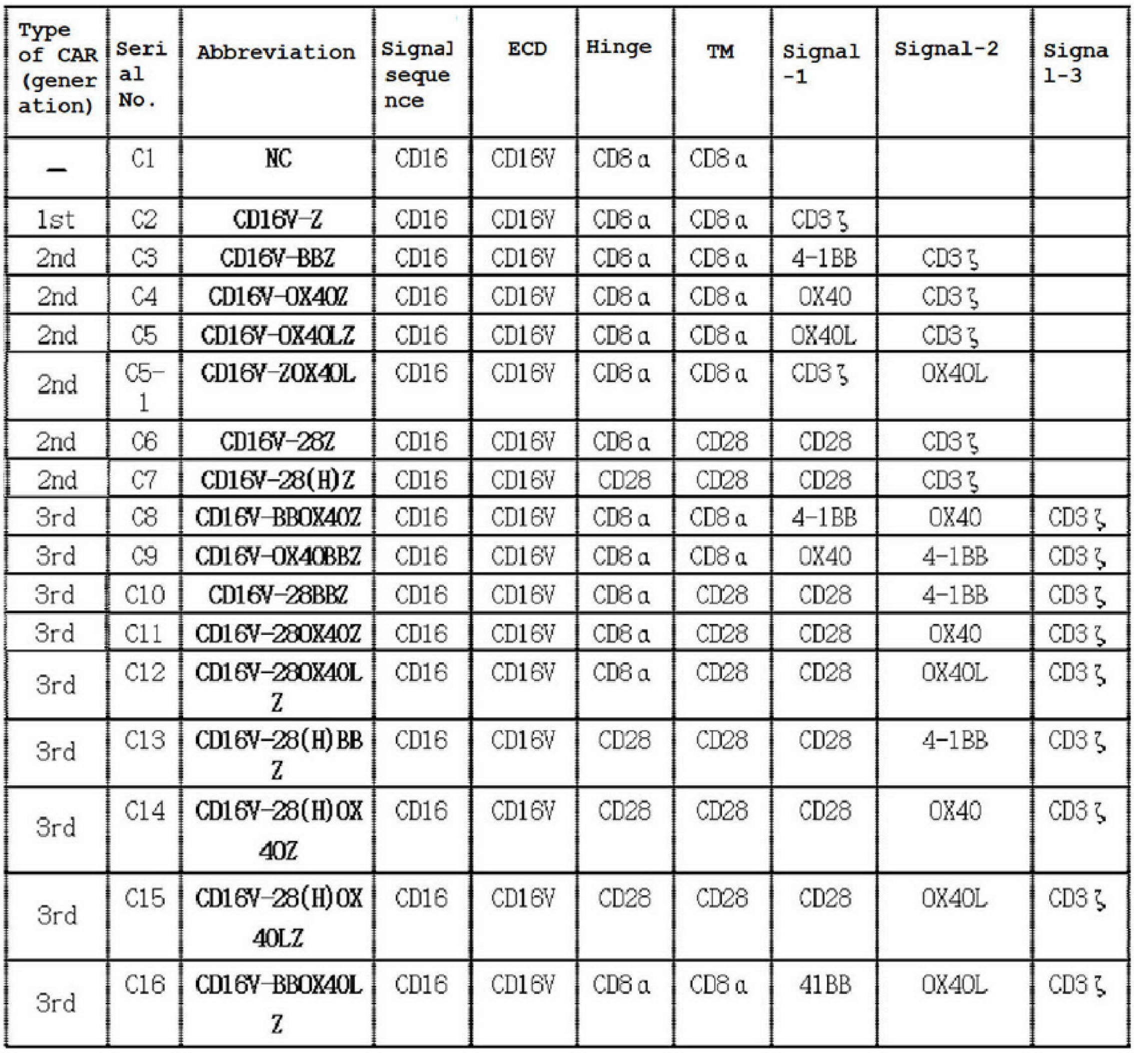
[115] The human B-series cell line Ramos, human erythroleukemic cell line K562, human breast cancer cell line MCF-7, H1299 and H1944 of human lung cancer cell lines, as well as NK-92MI are supplied from American Type Culture Collection (ATCC, Manassas, VA, USA). K562 was maintained in RPMI-1640 containing 10% FBS (Gibco, Grand Island, NY, USA). Ramos was maintained in RPMI-1640 (ATCC) (Manassas, VA) containing 10% FBS (fetal bovine serum; Gibco, Grand Island, NY, USA). MCF-7 was maintained in EMEM (ATCC) + 10% FBS (Gibco) medium, while H1299 and H1944 cell lines were maintained in RPMI-1640 (ATCC) + 10% FBS (Gibco). In addition, NK-92MI and transduced NK-92MI cells were maintained in CellGro® serum-free medium containing 1% human plasma. The human embryonic kidney fibroblast, that is, 293T cell line was supplied from the ATCC. This cell line was maintained in DMEM (Gibco, Grand Island, NY, USA) containing 10% FBS (Gibco, Grand Island, NY, USA).

[116] **Plasmid**

[117] The signal sequence and the extracellular domain of the FCRG3A V158 mutant (CD16V); the extracellular domain of NKG2D; the signal sequence of CD8α, the hinge and transmembrane domains of CD8α; the hinge and transmembrane domains of CD28; and the intracellular signaling domains of 4-1BB, OX40, OX40 ligand (OX40L) and CD3ζ, respectively, were synthesized artificially. The above listed materials were assembled in various combinations through splicing by overlapping extension by PCR ('SOE-PCR'). The PCR products were confirmed by direct sequencing. Each PCR product was cut into Nhe1 and EcoRI, and then inserted into (i.e., ligated to) Nhe1 and EcoRI sites of a 3rd generation self-inactivating lentiviral expression vector such as MSCV-EF1α-GFP vector or EF1a-MCS vector.

[118] Chimeric antigen receptors (CAR) according to embodiments of the present invention have been summarized in Table 1 below. The domains of all CARs according to the embodiments of the present invention have been linked in series (in tandem) to one another and also linked in frame.

[119] [TABLE 1]



Type of CAR (generation)	Serial No.	Abbreviation	Signal sequence	ECD	Hinge	TM	Signal-1	Signal-2	Signal-3
–	C1	NC	CD16	CD16V	CD8α	CD8α			
1st	C2	CD16V-Z	CD16	CD16V	CD8α	CD8α	CD3ζ		
2nd	C3	CD16V-BBZ	CD16	CD16V	CD8α	CD8α	4-1BB	CD3ζ	
2nd	C4	CD16V-OX40Z	CD16	CD16V	CD8α	CD8α	OX40	CD3ζ	
2nd	C5	CD16V-OX40LZ	CD16	CD16V	CD8α	CD8α	OX40L	CD3ζ	
2nd	C5-1	CD16V-ZOX40L	CD16	CD16V	CD8α	CD8α	CD3ζ	OX40L	
2nd	C6	CD16V-28Z	CD16	CD16V	CD8α	CD28	CD28	CD3ζ	
2nd	C7	CD16V-28(H)Z	CD16	CD16V	CD28	CD28	CD28	CD3ζ	
3rd	C8	CD16V-BBOX40Z	CD16	CD16V	CD8α	CD8α	4-1BB	OX40	CD3ζ
3rd	C9	CD16V-OX40BBZ	CD16	CD16V	CD8α	CD8α	OX40	4-1BB	CD3ζ
3rd	C10	CD16V-28BBZ	CD16	CD16V	CD8α	CD28	CD28	4-1BB	CD3ζ
3rd	C11	CD16V-28OX40Z	CD16	CD16V	CD8α	CD28	CD28	OX40	CD3ζ
3rd	C12	CD16V-28OX40LZ	CD16	CD16V	CD8α	CD28	CD28	OX40L	CD3ζ
3rd	C13	CD16V-28(H)BBZ	CD16	CD16V	CD28	CD28	CD28	4-1BB	CD3ζ
3rd	C14	CD16V-28(H)OX40Z	CD16	CD16V	CD28	CD28	CD28	OX40	CD3ζ
3rd	C15	CD16V-28(H)OX40LZ	CD16	CD16V	CD28	CD28	CD28	OX40L	CD3ζ
3rd	C16	CD16V-BBOX40LZ	CD16	CD16V	CD8α	CD8α	41BB	OX40L	CD3ζ

[120]

[121] CD16V-Z CAR (1st generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[122] CD16V-BBZ CAR (2nd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[123] CD16V-OX40Z CAR (2nd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD134-derived intracellular signaling domain (nucleotides 733-840, GenBank AB590584.1); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[124] CD16V-OX40LZ CAR (2nd generation) is provided by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD252-derived intracellular signaling domain (nucleotides 141-206, GenBank NM 003326.4); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[125] CD16V-ZOX40L CAR (2nd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); CD252-derived intracellular signaling domain (nucleotides 141-206, GenBank NM 003326.4); and stop codon TGA. CD16V-28Z CAR (2nd generation) is produced by connecting: the signal sequence domain of CD16 (34-84 nucleotides, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); human CD8α-derived hinge domain (nucleotides 1292-1435, GenBank NM 001768.6); CD28-derived transmembrane and intracellular signaling domains (nucleotides 679-882, GenBank NM 006139.3); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[126] CD16V-28(H)Z CAR (2nd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); CD28-derived hinge, transmembrane and intracellular signaling domains (nucleotides 562-882, GenBank NM 006139.3); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[127] CD16V-BBOX40Z CAR (3rd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD134-derived intracellular signaling domain (nucleotides 733-840, GenBank AB590584.1); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[128] CD16V-OX40BBZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD134-derived intracellular signaling domain (nucleotides 733-840, GenBank AB590584.1); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[129] CD16V-28BBZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); CD8α-derived hinge domain (nucleotides 1292-1435, GenBank NM 001768.6); CD28-derived transmembrane and intracellular signaling domains (nucleotides 679-882, GenBank NM 006139.3); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[130] CD16V-28OX40Z CAR (3rd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); CD8α-derived hinge domain (nucleotides 1292-1435, GenBank NM 001768.6); CD28-derived transmembrane and intracellular signaling domains (nucleotides 679-882, GenBank NM 006139.3); CD134-derived intracellular signaling domain (nucleotides 733-840, GenBank AB590584.1); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[131] CD16V-28OX40LZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); CD8α-derived hinge domain (nucleotides 1292-1435, GenBank NM 001768.6); CD28-derived transmembrane and intracellular signaling domains (nucleotides 679-882, GenBank NM 006139.3); CD252-derived intracellular signaling domain (nucleotides 141-206, GenBank NM 003326.4); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[132] CD16V-28(H)BBZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No.

X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); CD28-derived hinge, transmembrane and intracellular signaling domains (nucleotides 562-882, GenBank NM 006139.3); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[133] CD16V-28(H)OX40Z CAR (3rd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); CD28-derived hinge, transmembrane and intracellular signaling domains (nucleotides 562-882, GenBank NM 006139.3); CD134-derived intracellular signaling domain (nucleotides 733-840, GenBank AB590584.1); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[134] CD16V-28(H)OX40LZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); CD28-derived hinge, transmembrane and intracellular signaling domains (nucleotides 562-882, GenBank NM 006139.3); CD252-derived intracellular signaling domain (nucleotides 141-206, GenBank NM 003326.4); and CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3) and stop codon TGA.

[135] CD16V-BBOX40LZ (3rd generation) is produced by connecting: the signal sequence domain of CD16 (nucleotides 34-84, GenBank Accession No. X52645); the extracellular domain of CD16V (FCRG3A V158) (nucleotides 85-651, G mutation of nucleotide No. 559 in GenBank Accession No. X52645); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD252-derived intracellular signaling domain (nucleotides 141-206, GenBank NM 003326.4); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[136] The sequence listings of the domains used for the chimeric antigen receptors (CARs) and a preparation method thereof according to the embodiments of the present invention are summarized in Table 2 below.

[137] [TABLE 2]

Sequence No.	Name of sequence	Details of sequence
1	CD16 nucleotide	Signal sequence and extracellular domain of CD16 (34-651 nucleotides, GenBank Accession No. X52645)
2	CD16 amino acid	Amino acid sequence corresponding to SEQ ID NO. 1
3	CD16V nucleotide	G mutation of nucleotide No. 559 among signal sequence and extracellular domain of CD16V (34-651 nucleotides, GenBank Accession No. X52645)
4	CD16V nucleotide codon optimization	Codon optimized sequence of SEQ ID NO. 3
5	CD16V amino acid	Amino acid sequence corresponding to SEQ ID NOs. 3 and 4
6	CD8α nucleotide	Human CD8α-derived hinge and transmembrane domains (1292-1507 nucleotides, GenBank NM 001768.6)
7	CD8α nucleotide codon optimization	Codon optimized sequence of SEQ ID NO. 6
8	CD8α amino acid	Amino acid sequence corresponding to SEQ ID NOs. 6 and 7
9	CD28 nucleotide	CD28-derived hinge, transmembrane and intracellular signaling domains (562-882 nucleotides, GenBank MM 006139.3)
10	CD28 nucleotide codon optimization	Codon optimized sequence of SEQ ID NO. 9
11	CD28 amino acid	Amino acid sequence corresponding to SEQ ID NOs. 9 and 10
12	CD3ζ nucleotide	CD3ζ-derived intracellular signaling domain (299-634 nucleotides, GenBank NM 000734.3)
13	CD3ζ nucleotide codon optimization	Codon optimized sequence of SEQ ID NO. 12
14	CD3ζ amino acid	Amino acid sequence corresponding to SEQ ID NOs. 12 and 13
15	OX40L (CD252) nucleotide	OX40L (CD252)-derived intracellular signaling domain (141-206 nucleotides, GenBank NM 003326.4)
16	OX40L (CD252) nucleotide	Codon optimized sequence of SEQ ID NO. 15

	codon optimization	
17	OX40L (CD252) amino acid	Amino acid sequence corresponding to SEQ ID NOs. 15 and 16
18	OX40 (CD134) nucleotide	OX40 (CD134)-derived intracellular signaling domain (733-840 nucleotides, GenBank AB 590584.1)
19	OX40 (CD134) nucleotide codon optimization	Codon optimized sequence of SEQ ID NO. 18
20	OX40 (CD134) amino acid	Amino acid sequence corresponding to SEQ ID NOs. 18 and 19
21	4-1BB (CD137) nucleotide	4-1BB (CD137)-derived intracellular signaling domain (901-1026 nucleotides, GenBank NM 001561.5)
22	4-1BB (CD137) nucleotide codon optimization	Codon optimized sequence of SEQ ID NO. 21
23	4-1BB (CD137) amino acid	Amino acid sequence corresponding to SEQ ID NOs. 21 and 22
24	CD16V-Z nucleotide	Codon optimized nucleotide sequence of CD16V-Z CAR
25	CD16V-Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 24
26	CD16V-BBZ nucleotide	Codon optimized nucleotide sequence of CD16V-BBZ CAR
27	CD16V-BBZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 26
28	CD16V-OX40Z nucleotide	Codon optimized nucleotide sequence Of CD16V-OX40Z CAR
29	CD16V-OX40Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 28
30	CD16V-OX40LZ nucleotide	Codon optimized nucleotide sequence of CD16V-OX30LZ CAR
31	CD16V-OX40LZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 30
32	CD16V-28Z nucleotide	Codon optimized nucleotide sequence of CD16V-28Z CAR
33	CD16V-28Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 32
34	CD16V-28(H)Z nucleotide	Codon optimized nucleotide sequence of CD16V-28(H)Z CAR
35	CD16V-28(H)Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 34
36	CD16V-BBOX40Z nucleotide	Codon optimized nucleotide sequence of CD16V-BBOX40Z CAR
37	CD16V-BBOX40Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 36
38	CD16V-OX40BBZ nucleotide	Codon optimized nucleotide sequence of CD16V-OX40BBZ CAR
39	CD16V-OX40BBZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 38
40	CD16V-28BBZ nucleotide	Codon optimized nucleotide sequence of CD16V-28BBZ CAR
41	CD16V-28BBZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 40
42	CD16V-28OX40Z nucleotide	Codon optimized nucleotide sequence of CD16V-28OX40Z CAR
43	CD16V-28OX40Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 42
44	CD16V-28OX40LZ nucleotide	Codon optimized nucleotide sequence of CD16V-28OX40LZ CAR
45	CD16V-28OX40LZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 44
46	CD16V-28(H)BBZ nucleotide	Codon optimized nucleotide sequence of CD16V-28(H)BBZ CAR
47	CD16V-28(H)BBZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 46
48	CD16V-28(H)OX40Z nucleotide	Codon optimized nucleotide sequence of CD16V-28(H)OX40Z CAR
49	CD16V-28(H)OX40Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 48
50	CD16V-28(H)OX40LZ nucleotide	Codon optimized nucleotide sequence of CD16V-28(H)OX40LZ CAR
51	CD16V-28(H)OX40LZ amino	Amino acid sequence corresponding to SEQ ID NO. 50

	acid	
52	CD16V-BBOX40LZ nucleotide	Codon optimized nucleotide sequence of CD16V-BBOX40LZ CAR
53	CD16V-BBOX40LZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 52
54	CD16V-ZOX40L nucleotide	Codon optimized nucleotide sequence of CD16V-ZOX40L CAR
55	CD16V-ZOX40L amino acid	Amino acid sequence corresponding to SEQ ID NO. 54

[138]

[139] In addition, the chimeric antigen receptors (CARs) according to the embodiments of the present invention are summarized in Table 3 below. Domains of each of all CARs according to the embodiments of the present invention are linked in series (in tandem) to one other and also linked in the frame.

[140]

[141] [TABLE 3]

Type of CAR (generation)	Serial No.	Abbreviation	Signal sequence	ECD	Hinge	TM	Signal-1	Signal-2	Signal-3
-	C17	**NC**	CD8α	NKG2D	CD8α	CD8α			
1st	C18	**NKG2D-Z**	CD8α	NKG2D	CD8α	CD8α	CD3ζ		
2nd	C19	**NKG2D-BBZ**	CD8α	NKG2D	CD8α	CD8α	4-1BB	CD3ζ	
2nd	C20	**NKG2D-OX40Z**	CD8α	NKG2D	CD8α	CD8α	OX40	CD3ζ	
2nd	C21	**NKG2D-ZOX40L**	CD8α	NKG2D	CD8α	CD8α	CD3ζ	OX40L	
2nd	C22	**NKG2D-28Z**	CD8α	NKG2D	CD8α	CD28	CD28	CD3ζ	
2nd	C23	**NKG2D-28(H)Z**	CD8α	NKG2D	CD28	CD28	CD28	CD3ζ	
3rd	C24	**NKG2D-BBOX40Z**	CD8α	NKG2D	CD8α	CD8α	4-1BB	OX40	CD3ζ
3rd	C25	**NKG2D-BBOX40LZ**	CD8α	NKG2D	CD8α	CD8α	4-1BB	OX40L	CD3ζ
3rd	C26	**NKG2D-OX40BBZ**	CD8α	NKG2D	CD8α	CD8α	OX40	4-1BB	CD3ζ
3rd	C27	**NKG2D-28BBZ**	CD8α	NKG2D	CD8α	CD28	CD28	4-1BB	CD3ζ
3rd	C28	**NKG2D-28OX40Z**	CD8α	NKG2D	CD8α	CD28	CD28	OX40	CD3ζ
3rd	C29	**NKG2D-28OX40LZ**	CD8α	NKG2D	CD8α	CD28	CD28	OX40L	CD3ζ
3rd	C30	**NKG2D-28(H)BBZ**	CD8α	NKG2D	CD28	CD28	CD28	4-1BB	CD3ζ
3rd	C31	**NKG2D-28(H)OX40Z**	CD8α	NKG2D	CD28	CD28	CD28	OX40	CD3ζ
3rd	C32	**NKG2D-28(H)OX40LZ**	CD8α	NKG2D	CD28	CD28	CD28	OX40L	CD3ζ
3rd	C33	**NKG2D-AAA-28(H)OX40LZ**	CD8α	NKG2D-AAA	CD28	CD28	CD28	OX40L	CD3ζ

[142]

[143] NKG2D-Z CAR (1st generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[144] NKG2D-BBZ CAR (2nd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[145] NKG2D-OX40Z CAR (2nd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD134-derived intracellular signaling domain (nucleotides 733-840, GenBank AB590584.1); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[146] NKG2D-ZOX40L CAR (2nd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); CD252-derived intracellular signaling domain (nucleotides 141-206, GenBank NM 003326.4); and CD3ζ stop codon TGA.

[147] NKG2D-28Z CAR (2nd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); human CD8α-derived hinge domain (nucleotides 1292-1435, GenBank NM 001768.6); CD28-derived transmembrane and intracellular signaling domains (nucleotides 679-882, GenBank NM 006139.3); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[148] NKG2D-28(H)Z CAR (2nd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); CD28-derived hinge, transmembrane and intracellular signaling domains (nucleotides 562-882, GenBank NM 006139.3); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[149] NKG2D-BBOX40Z CAR (3rd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD134-derived intracellular signaling domain (nucleotides 733-840, GenBank AB590584.1); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[150] NKG2D-BBOX40LZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD252-derived intracellular signaling domain (nucleotides 141-206, GenBank NM 003326.4); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[151] NKG2D-OX40BBZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); human CD8α-derived hinge and transmembrane domains (nucleotides 1292-1507, GenBank NM 001768.6); CD134-derived intracellular signaling domain (nucleotides 733-840, GenBank AB590584.1); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[152] NKG2D-28BBZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); CD8α-derived hinge domain (nucleotides 1292-1435, GenBank NM 001768.6); CD28-derived transmembrane and intracellular signaling domains (nucleotides 679-882, GenBank NM 006139.3); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[153] NKG2D-28OX40Z CAR (3rd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); CD8α-derived hinge domain (nucleotides 1292-1435, GenBank NM 001768.6); CD28-derived transmembrane and intracellular signaling domains (nucleotides 679-882, GenBank NM 006139.3); CD134-derived intracellular signaling domain (nucleotides 733-840, GenBank AB590584.1); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[154] NKG2D-28OX40LZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID:

AF461811.1); CD8α-derived hinge domain (nucleotides 1292-1435, GenBank NM 001768.6); CD28-derived transmembrane and intracellular signaling domains (nucleotides 679-882, GenBank NM 006139.3); CD252-derived intracellular signaling domain (nucleotides 141-206, GenBank NM 003326.4); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[155] NKG2D-28(H)BBZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); CD28-derived hinge, transmembrane and intracellular signaling domains (nucleotides 562-882, GenBank NM 006139.3); CD137-derived intracellular signaling domain (nucleotides 901-1026, GenBank NM 001561.5); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[156] NKG2D-28(H)OX40Z CAR (3rd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); CD28-derived hinge, transmembrane and intracellular signaling domains (nucleotides 562-882, GenBank NM 006139.3); CD134-derived intracellular signaling domain (nucleotides 733-840, GenBank AB590584.1); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[157] NKG2D-28(H)OX40LZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); CD28-derived hinge, transmembrane and intracellular signaling domains (nucleotides 562-882, GenBank NM 006139.3); CD252-derived intracellular signaling domain (nucleotides 141-206, GenBank NM 003326.4); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[158] NKG2D-AAA-28(H)OX40LZ CAR (3rd generation) is produced by connecting: the signal sequence domain of CD8α (nucleotides 890-952, GenBank NM 001768.6); the extracellular domain of NKG2D (nucleotides 788-1192, GenBank ID: AF461811.1); AAA (Triple alanine); CD28-derived hinge, transmembrane and intracellular signaling domains (nucleotides 562-882, GenBank NM 006139.3); CD252-derived intracellular signaling domain (nucleotides 141-206, GenBank NM 003326.4); CD3ζ-derived intracellular signaling domain (nucleotides 299-634, GenBank NM 000734.3); and stop codon TGA.

[159] The sequence listings of the domains used for the chimeric antigen receptors (CARs) and a method for preparation thereof according to the embodiments of the present invention are summarized in Table 4 below.

[160] [TABLE 4]

Sequence No.	Name of sequence	Details of sequence
56	CD8α nucleotide	Signal sequence domain of CD8α (890-952 nucleotides, GenBank NM 001768.6)
57	CD8α nucleotide codon optimization	Codon optimized sequence of SEQ ID NO. 56
58	CD8α amino acid	Amino acid sequence corresponding to SEQ ID NOs. 56 and 57
59	NKG2D nucleotide	Extracellular domain of NKG2D (788-1192 nucleotides, GenBank ID: AF 461811.1)
60	NKG2D nucleotide codon optimization	Codon optimized sequence of SEQ ID NO. 59
61	NKG2D amino acid	Amino acid sequence corresponding to SEQ ID NOs. 59 and 60
62	NKG2D-Z nucleotide	Codon optimized nucleotide sequence of NKG2D-Z CAR
63	NKG2D-Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 62
64	NKG2D-BBZ nucleotide	Codon optimized nucleotide sequence of NKG2D-BBZ CAR
65	NKG2D-BBZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 64
66	NKG2D-OX40Z nucleotide	Codon optimized nucleotide sequence of NKG2D-OX40Z CAR
67	NKG2D-OX40Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 66
68	NKG2D-ZOX40L nucleotide	Codon optimized nucleotide sequence of NKG2D-ZOX40L CAR
69	NKG2D-ZOX40L amino acid	Amino acid sequence corresponding to SEQ ID NO. 68
70	NKG2D-28Z nucleotide	Codon optimized nucleotide sequence of NKG2D-28Z CAR

71	NKG2D-28Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 70
72	NKG2D-28(H)Z nucleotide	Codon optimized nucleotide sequence of NKG2D-28(H)Z CAR
73	NKG2D-28(H)Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 72
74	NKG2D-BBOX40Z nucleotide	Codon optimized nucleotide sequence of NKG2D-BBOX40Z CAR
75	NKG2D-BBOX40Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 74
76	NKG2D-BBOX40LZ nucleotide	Codon optimized nucleotide sequence of NKG2D-BBOX40LZ CAR
77	NKG2D-BBOX40LZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 76
78	NKG2D-OX40BBZ nucleotide	Codon optimized nucleotide sequence of NKG2D-OX40BBZ CAR
79	NKG2D-OX40BBZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 78
80	NKG2D-28BBZ nucleotide	Codon optimized nucleotide sequence of NKG2D-28BBZ CAR
81	NKG2D-28BBZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 80
82	NKG2D-28OX40Z nucleotide	Codon optimized nucleotide sequence of NKG2D-28OX40Z CAR
83	NKG2D-28OX40Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 82
84	NKG2D-28OX40LZ nucleotide	Codon optimized nucleotide sequence of NKG2D-28OX40LZ CAR
85	NKG2D-28OX40LZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 84
86	NKG2D-28(H)BBZ nucleotide	Codon optimized nucleotide sequence of NKG2D-28(H)BBZ CAR
87	NKG2D-28(H)BBZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 86
88	NKG2D-28(H)OX40Z nucleotide	Codon optimized nucleotide sequence of NKG2D-28(H)OX40Z CAR
89	NKG2D-28(H)OX40Z amino acid	Amino acid sequence corresponding to SEQ ID NO. 88
90	NKG2D-28(H)OX40LZ nucleotide	Codon optimized nucleotide sequence of NKG2D-28(H)OX40LZ CAR
91	NKG2D-28(H)OX40LZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 90
92	NKG2D-AAA-28(H)OX40LZ Nucleotide	Codon optimized nucleotide sequence of NKG2D-AAA-28(H)OX40LZ CAR
93	NKG2D-AAA-28(H)OX40LZ amino acid	Amino acid sequence corresponding to SEQ ID NO. 92

[161]

[162] Virus production and gene transfer

[163] In order to prepare VSVG-pseudotyped lentivirus, 293T cells cultured in a DMEM medium were co-transfected with various types of vectors such as PCDH1-MSCV-CD16-construct-EF1-copGFP vector, EF1a-NKG2D-construct vector, PCDH1-MSCV-EF1-copGFP control vector, or EF1a-GFP control vector (for production of Mock infection virus using empty vector) together with HIV-based pPACKH1 lentivirus

Package Kit (System Biosciences). For this purpose, Lipofectamine 2000 reagent (Invitrogen, Carlsbad, CA) was used. Various types of CD16V constructs are as follows; CD16V-Z CAR, CD16V-BBZ CAR, CD16V-OX40Z CAR, CD16V-OX40LZ CAR, CD16V-ZOX40L, CD16V-28Z CAR, CD16V-28(H)Z CAR, CD16V-BBOX40Z CAR, CD16V-BBOX40LZ CAR, CD16V-OX40BBZ CAR, CD16V-28BBZ CAR, CD16V-28OX40Z CAR, CD16V-28OX40LZ CAR, CD16V-28(H)BBZ CAR, CD16V-28(H)OX40Z CAR, CD16V-28(H)OX40LZ CAR. Further, various types of NKG2D constructs are as follows; NKG2D-Z CAR, NKG2D-BBZ CAR, NKG2D-OX40Z CAR, NKG2D-ZOX40L CAR, NKG2D-28Z CAR, NKG2D-28(H)Z CAR, NKG2D-BBOX40Z CAR, NKG2D-BBOX40LZ CAR, NKG2D-OX40BBZ CAR, NKG2D-28BBZ CAR, NKG2D-28OX40Z CAR, NKG2D-28OX40LZ CAR, NKG2D-28(H)BBZ CAR, NKG2D-28(H)OX40Z CAR, NKG2D-28(H)OX40LZ CAR, NKG2D-AAA-28(H)OX40LZ. Each lentivirus was prepared by transfection of 80% dense HEK293T cells in a flask with: various types of CD16V construct expression vectors, various types of NKG2D construct expression vectors or a control plasmid together with pPACKH1 lentivirus packaging plasmids. After 6 hours, the medium was replaced by a DMEM medium containing 10% FBS. The conditioned medium containing lentivirus was collected after 48 hours of transfection, followed by filtering with a 0.45 µm filter unit (Milliopore, Billerica, MA, USA) in order to remove cell debris. A viral supernatant containing the virus was concentrated about 50 times by centrifugation at 3000 rpm and 4°C for 20 minutes using Amicon Filter (Millipore). The concentrated virus was stored at -80°C.

[164] For the lentiviral infection, NK92MI cells in an exponential growth phase was adjusted to a concentration of 1 x 10^{6} cells/ml using Cellgro (Cellgenix) including 1% human plasma, and then a lentiviral supernatant in 50 to 100 MOI was added in the presence of 8 μg/ml polybrene, followed by centrifugation at 1800 g for 90 minutes. After centrifugation, the cells were left in a humidified incubator at 37°C and 5% CO_2 conditions for 48 hours. Thereafter, the cells were washed twice with RPMI-1640, and then left in RPMI-1640 including 10% FBS for future use. Control cells were transduced with a vector only.

[165]

[166] **Detection of expression of receptor including CD16V or NKG2D**

[167] CD16V CAR-transduced NK92MI cells, NKG2D CAR- transduced NK92MI cells, the control vector-transduced NK92MI (NK92MI-Mock) or NK-92MI parent cells were washed twice with FACS buffer, and the washed cells were stained using 7-AAD (Beckman coulter), anti-CD3, anti-CD56 and anti-CD16 (BD Biosciences) mAbs. An expression ratio and a mean fluorescence intensity (MFI) of the stained cells were measured using a BD LSRFortessa.

[168] The transduction efficiency using the NKG2D construct was determined by flow cytometric analysis of cells expressing NKG2D among CD3-CD56+ cells. First, NK92MI cells were gated in regard to singlet, and then gated in regard to 7AAD- and CD3-CD56+. The transformation efficiency using the CD16 constructs was determined by flow cytometric analysis of cells expressing GFP and CD16 among CD3-CD56+ cells.

[169]

[170] **Calcein releasing cytotoxicity assay**

[171] Target cells were labeled at 37°C for 1 hour with 30 μM calcein-acetoxymethyl ester (Calcein-AM; Molecular probes). After washing, the labeled target cells were dispensed to 1 x 10^4 cells per well in 96-well plates. NK92MI cells were harvested, washed, and then were added at different E/T (effector-to-target) ratios under conditions with or without rituximab at various concentrations. As a control group

independent of the rituximab, an anti-human antibody (Sigma aldrich) was used. After 2 hours, the plates were centrifuged at 2000 rpm for 3 minutes, and a supernatant of 100 μL was collected and subjected to measurement of calcein release using a fluorescence microplate reader (Victor3, PerkinElmer) at an excitation wavelength of 485 nm and an emission wavelength of 535 nm. Specific calcein release amount was calculated by the following equation: percent specific lysis = (test release - spontaneous release) x 100/(maximal release - spontaneous release). For maximal lysis, a 1% Triton X-100 was used.

[172]

[173] **Example 2: Assessment of cytotoxicity of NK92MI cells expressing OX40 ligand (CD252)-containing chimeric antigen receptor (CAR) against CD20-positive lymphoma cells**

[174]

[175] **Transduction and expression of chimeric antigen receptor containing CD16V associated with the co-stimulating motif**

[176] V158 variant (polymorphism) of FCRG3A (CD16) is a high affinity immunoglobulin Fc receptor and is considered to exhibit good effects in antibody treatment. The present inventors have prepared the V158 variant of FCRG3A (CD16) and combined the prepared variant with: the hinge and transmembrane domains of CD8α; a T cell stimulatory molecule, that is, CD3ζ; and intracellular domains of different costimulatory molecules such as CD28, 4-1BB, OX-40 and OX-40 ligand in various combinations thereof (Table 1). The prepared CD16V-containing chimeric antigen receptors (e.g., CD16V-Z CAR (1st generation), CD16V-28Z CAR (2nd generation), CD16V-BBZ CAR (2nd generation), CD16V-OX40Z CAR (2nd generation) or CD16V-28OX40LZ CAR (3rd generation)) were expressed in NK92MI cells by a lentiviral vector

including a MSCV promoter. We confirmed surface expression of each CAR on NK92MI cells by detection of the human CD16, using a monoclonal mouse anti-human antibody. By repetitive experiments involving flow cytometric analysis, it was demonstrated that CARs were transduced with efficiency more than 90% in NK92MI cells (FIG. 1A). An amount of lentivirus used herein is equal to the multiple of infection (MOI) of 50 or more.

[177]

[178] **Increase of tumor killing effect of NK92MI cells expressing CD16V receptor combined with CD252 (OX40 ligand) against CD20-positive lymphoma**

[179] In order to determine whether genetic modification according to the invention induces an increase in cancer cell death, cytotoxicity of NK92MI cells transduced with an empty vector and NK92MI cells expressing a CD16-containing receptor on CD20-positive lymphoma cells (Ramos cells) was evaluated by calcein-AM release assay.

[180] Before test for lymphoma cells, K562, a human erythroleukemic cell line, was used as a standard control to assess intrinsic cell killing ability (i.e., cytotoxicity) of the transduced NK92MI cells. By transduction using lentivirus having multiple of infection (MOI) of 50 or more, each of CARs according to the present invention (CD16V-Z CAR (1st generation), CD16V-28Z CAR (2nd generation), CD16V-BBZ CAR (2nd generation), CD16V-OX40Z CAR (2nd generation) or CD16V-28OX40LZ CAR (3rd generation)) was expressed at a high level in 90% or more NK92MI cells (FIG. 1A).

[181] It was demonstrated that cytotoxicity of NK92MI cells expressing CARs according to the invention on K562 was similar to cytotoxicity of a control group (Mock) transduced with an empty vector. This means that the intrinsic cytotoxicity of NK92MI cells on a target was not increased by side effects due to the genetic modification itself (FIG. 1B). In FIG. 1B, a ratio of the number of NK92MI cells as effector cells to the number of K562 cells as target cells is indicated by 5:1, 2.5:1, 1:1 and 0.5:1.

[182] In order to assess how diverse co-stimulatory molecules affect *in vitro* on antigen-specific antitumor activity of NK92MI cells expressing CD16V-containing receptor, transduced NK92MI cells and cancer cells (B-cell lymphoma cell line, that is, Ramos) were subjected to co-incubation, followed by assessment of lysis of the cancer cells according to calcein-AM release assay (FIG. 1C). In Figure 1C, ratios of the number of NK92MI cells (effector cells) to the number of Ramos cells (target cells) are indicated by 5:1, 2.5:1, 1:1 and 0.5:1. It has been shown that rituximab does not increase NK-92MI mediated cytotoxicity significantly because NK92MI does not express CD16.

[183] As shown in FIG. 1C, we found that expression of various CARs according to the present invention without rituximab did not increase significantly NK-92MI mediated cytotoxicity over that cytotoxicity induced by the control (Mock), NK-92MI cells transduced with the vector containing only GFP.

[184] CD16V-Z CAR (first generation), which was previously shown to enhance cytotoxicity in various CAR applications, served as positive control. In order to increase cytotoxicity of the CD16V-containing receptor, the present inventors have introduced CD28, CD134 (OX40), CD137 (4-1BB) or CD252 (OX40 ligand) into CD16V-Z-CAR. In 2 hour *in vitro* cytotoxicity assays, NK-92MI cells expressing CD16V-Z CAR (1st generation), CD16V-28Z CAR (2nd generation), CD16V-BBZ CAR (2nd generation), CD16V-OX40Z CAR (2nd generation) or CD16V-28OX40LZ CAR (3rd generation) exhibited high cytotoxicity in the presence of rituximab at effector cells to target cells ratio of 5:1 and 2.5:1. Among them, in particular, 3rd generation CAR including OX40 ligand, that is, CD16V-28OX40LZ CAR exhibited the highest cytotoxicity, compared to the other CARs (FIG. 1C).

[185] In order to investigate whether 2nd generation CAR containing OX40 ligand can enhance anticancer activity of NK92MI cells, CD16V-OX40LZ CAR was prepared and subjected to evaluation of cytotoxicity. When NK92MI cells were transduced with CD16-OX40LZ using a lentiviral vector, CD16V-OX40LZ CAR was not expressed (FIG. 1D). Even in the presence of rituximab, cytotoxicity on Ramos cells mediated by CD16V-OX40LZ CAR was not exhibited (FIG. 1E). Accordingly, the present inventors noticed a fact that OX40 ligand is type II protein and CD3ζ linked to the OX40 ligand is type I protein, and has prepared CD16V-ZOX40L CAR having CD3ζ at N-terminal and OX40 ligand at C-terminal by changing the order of the above two domains. When NK92MI cells were transduced with CD16V-ZOX40L using a lentiviral vector having an MSCV promoter, NK92MI cells effectively expressed CD16V-OX40LZ CAR compared with CD16V-OX40LZ (FIG. 1F). Further, as a result of assessing anticancer activity of 2nd generation CAR having CD16V-ZOX40L introduced therein, high cytotoxicity on Ramos cells was demonstrated at ratios of effector cells to target cells of 10:1, 5:1 and 2.5:1 in the presence of rituximab (FIG. 1G). It was determined that, in addition to CD16V-28OX40LZ CAR (3rd generation) containing OX40 ligand, CD16V-ZOX40L CAR (2nd generation) also has anticancer activity superior to CD16V-Z CAR used as a positive control.

[186]

[187] **Assessment of efficacy of CD16V-BBOX40LZ CAR**

[188] By introducing OX40 ligand into CD137 (41BB) signaling domain-based CAR, NK92MI cells were subjected to assessment of expression and cytotoxicity. Both of CD16V-BBZ CAR (2nd generation) and CD16V-BBOX40LZ CAR (3rd generation) were expressed at high levels in NK92MI cells (FIG. 2A). When rituximab is not present in an *in vitro* test for cytotoxicity, all of CD16V-Z, CD16V-BBZ and CD16V-BBOX40LZ exhibited low cytotoxicity to Ramos cells. On the other hand, in the

presence of rituximab, CD16V-BBOX40LZ in combination with OX40 ligand exhibited highest cytotoxicity at even any ratio of effector cells to target cells (FIG. 2B).

[189]

[190] **Comparison of efficacies between CD16V-28OX40LZ CAR and other CARs**

[191] Next, the present inventors have compared the cytotoxicity of NK92MI cells expressing CD16V-28OX40LZ CAR and the cytotoxicity of NK92MI cells expressing 3rd generation CAR that has other intracellular signaling domains. The 3rd generation CARs used in the present experiment (CD16V-28OX40LZ CAR, CD16V-28OX40Z CAR and CD16V-28BBZ CAR) were all proven to be expressed at high levels in NK92MI cells (FIG. 3A).

[192] After comparing NK cell activating efficacies of various 3rd generation CARs (that is, 3rd generation chimeric antigen receptors) according to the present invention, results thereof are summarized in FIG. 3B. As shown in FIG. 3B, all of these CARs show low cytotoxicity to Ramos cells when rituximab is not present, and an extent of the cytotoxicity is all similar. On the other hand, in the presence of rituximab, all of CD16V-28OX40LZ CAR, CD16V-28OX40Z CAR and CAR CD16V-28BBZ showed high cytotoxicity to Ramos cells. Among them, in particular, CD16V-28OX40LZ CAR containing OX40 ligand exhibited the most excellent cytotoxicity (FIG. 3B).

[193]

[194] **Assessment of efficacy of 3rd generation CAR including OX40 ligand having CD28 at hinge**

[195] In order for the CAR expressing NK cells to recognize a cancer cell antigen in an optimized condition, not only cancer cell antigen-recognizing receptor itself, but also hinge sequence and composition between an antigen-specific receptor and a cell

membrane are also important. The hinge sequence and composition may need to be designed differently depending on target molecules.

[196] The CARs used in the experiments described above use the fragment of CD8α as spacer domains (‘hinge’). As compared to this, variation of cytotoxicity of CARs when the fragment of CD28 is used at the hinge, was assessed and results thereof are summarized in FIG. 4. The present inventors have produced a lentiviral vector including an extracellular domain (ectodomain) of CD16V and the hinge of CD28. In 3rd generation CARs containing CD28 fragment as spacer, CD28-derived hinge, transmembrane and intracellular signaling domains were linked to a signaling module of CD134 (OX40), CD137 (4-1BB) or OX40 ligand (CD252). Such produced 3rd generation CARs were expressed on NK92MI cells using the lentiviral vector. It was demonstrated that the transduced NK92MI cells could express the above 3rd generation CARs, that is, CD16V-28(H)BBZ CAR, CD16V-28(H)OX40Z CAR or CD16V-28(H)OX40LZ CAR) at high levels, respectively (FIG. 4A).

[197] As shown in FIG. 4B, when rituximab is not present, all of CD16V-28(H)BBZ CAR, CD16V-28(H)OX40Z CAR and CD16V-28(H)OX40LZ CAR do not exhibit cytotoxicity. On the other hand, in the presence of rituximab, all of CD16V-28(H)BBZ CAR, CD16V-28(H)OX40Z CAR and CD16V-28(H)OX40LZ CAR exhibit high cytotoxicity. Among them, in particular, CD16V-28(H)OX40LZ CAR including OX40 ligand has the highest cytotoxicity.

[198] The experimental results described above demonstrate that, when a novel CAR particularly including OX40 ligand as an intracellular signaling domain discovered by the present inventors is expressed in natural killer cells, excellent antitumor effects may be attained.

[199]

[200] **Example 3: Assessment of cytotoxicity of NK92MI cells expressing OX40 ligand (CD252)-containing NKG2D chimeric antigen receptor (NKG2D-CAR) on human breast cancer cells and lung cancer cells**

[201] **Transduction and expression of a chimeric antigen receptor including NKG2D associated with co-stimulatory motif**

[202] The present inventors synthesized a human NKG2D gene and combined the same with diverse combinations of: hinge and transmembrane domains of CD8α; and intracellular domains of T-cell stimulatory molecules CD3ζ and cofactors including CD28, 4-1BB, OX-40 and OX-40 ligand to significantly enhance activity of T or NK cells (Table 3). Such NKG2D CAR constructs were expressed in NK92MI cells using a lentiviral vector. The present inventors have identified surface expression of each NKG2D CAR in NK92MI cells by means of detection of human NKG2D using a monoclonal mouse anti-human antibody. By repetitive experiments involving flow cytometric analysis, it was demonstrated that CARs were transduced with 70% or more efficiency in NK92MI cells.

[203]

[204] **Increase of tumor killing effect of NK92MI cells expressing NKG2D receptor, which contains various co-stimulatory signaling domains, against MCF7 breast cancer cell line**

[205] In order to investigate variation in killing activity due to genetic modification, cytotoxicity of NK-92MI cells, which express NKG2D CAR, on MCF7 breast cancer cells was compared by calcein-AM release assay.

[206] In order to assess *in vitro* effects of various co-stimulatory signaling domains on antigen-specific antitumor functions of NK-92MI cells expressing NKG2D CAR, transduced NK-92MI cells and cancer cells were co-cultured, followed by measuring

lysis of tumor cells through calcein-AM release. According to previous studies, it was known that adding the co-stimulatory signaling domains to the chimeric receptor exhibits increased cytotoxicity of T and NK lymphocytes. In order to increase the cytotoxicity of NKG2D CAR, the present inventors have introduced signaling domains of the most well-known three cofactors, that is, CD28, CD134 (OX-40) and CD137 (4-1BB) into the NKG2D CAR. The NK92MI cells containing the introduced NKG2D-Z CAR (1st generation), NKG2D-28Z CAR, NKG2D-BBZ CAR, NKG2D-OX40Z CAR (2nd generation) showed efficient expression of NKG2D (FIG. 5A). *In vitro* cytotoxicity analysis for two hours, it was demonstrated that NK-92MI cells expressing NKG2D-Z CAR (1st generation), NKG2D-28Z CAR, NKG2D-BBZ CAR and NKG2D-OX40Z CAR (2nd generation) exhibited cytotoxicity to MCF7 breast cancer cells. However, addition of CD134 (OX-40) or CD137 (4-1BB) signaling domain to a backbone of NKG2D-Z 1st generation CAR did not exhibit higher cytotoxicity than the cytotoxicity of NKG2D-Z CAR (1st generation). Cancer cell killing by NK-92MI cells including NKG2D-28Z CAR (2nd generation) was superior to the positive control, NK-92MI cells expressing NKG2D-Z CAR (1st generation) (FIG. 5B).

[207]

[208] **Increase of tumor killing effect of NK92MI cells expressing NKG2D receptor, which contains CD28 intracellular domain, against MCF7 breast cancer cell line**

[209] 3rd generation CAR is known to increase antitumor activity. In physiological T cell response, the optimal lymphocyte activation needs one or more cofactor receptors combined with a co-stimulatory molecule such as CD28. Among the cofactor receptors, the most important receptors are CD137 (4-1BB) and OX40 (CD134) which are members of tumor necrosis factor (TNFR).

[210] In order to investigate effects of different cofactors in NK-92MI cells expressing NKG2D CAR (3rd generation), the present inventors have produced NKG2D-28OX40Z CAR (3rd generation) and NKG2D-28BBZ CAR (3rd generation). The NKG2D CAR (3rd generation) constructs were expressed in NK92MI cells using a lentiviral vector. The transduced NK92MI cells efficiently expressed various NKG2D receptors containing 3rd generation CAR (FIG. 6A). As compared to NK92MI cells transduced with a control vector, NK92MI cells expressing various NKG2D CARs (3rd generation) have efficiently killed MCF7 cells *in vitro*. However, 3rd generation NKG2D-28OX40Z CAR and NKG2D-28BBZ CAR, each of which includes CD134 or CD137 co-stimulatory signaling domain in a backbone of NKG2D-28Z CAR (2nd generation), did not exhibit higher cytotoxicity than NKG2D-Z CAR (1st generation) (FIG. 6B).

[211]

[212] **Comparison of NKG2D-AAA-28(H)OX40LZ CAR (3rd generation) and other receptors**

[213] In order to assess CD252 (OX40 ligand) co-stimulatory signaling domain effects, the signaling domain of the OX40 ligand was fused to the backbone of NKG2D-28Z CAR (2nd generation), so as to build NKG2D-28(H)OX40LZ CAR (3rd generation). In the tumor killing assay, tumor specific cytotoxicity to MCF7 cells, which was induced by NKG2D-28(H)OX40LZ CAR (3rd generation), is greatly enhanced compared to NKG2D-Z CAR (1st generation), however, is substantially similar to NKG2D-28Z CAR (2nd generation) (FIG. 7B).

[214] For optimal CAR T-cell recognition, it was determined that, not only tumor antigen recognition receptor itself, but also hinge and linker sequences between the antigen-specific receptor and the cell membrane are also important. In the present experiment, additional effects of the spacer to the function of NKG2D-28(H)OX40LZ CAR (3rd generation) were analyzed. The present inventors have introduced an AAA (triple alanine) linker between the NKG2D extracellular domain and CD28 hinge. NKG2D-AAA-28(H)OX40LZ CAR (3rd generation) containing AAA linker introduced therein was expressed in NK92MI cells using a lentiviral vector (FIG. 7A). In the present experiment, MCF7 cell killing by NK-92MI cells expressing NKG2D-AAA-28(H)OX40LZ CAR (3rd generation) was compared with MCF7 cell killing by NK-92MI cells expressing NKG2D-Z CAR (1st generation), NKG2D-28Z CAR (2nd generation) or NKG2D-28(H)OX40LZ CAR (3rd generation). In particular, introduction of the AAA linker between NKG2D extracellular domain and CD28 hinge of NKG2D-28(H)OX40LZ CAR (3rd generation) has resulted in better target cell killing than parental NKG2D-28(H)OX40LZ CAR (3rd generation) without AAA, NKG2D-Z CAR (1st generation) and/or NKG2D-28Z CAR (2nd generation) (FIG. 7B).

[215]

[216] **Increase of tumor killing effect of NK92MI cells expressing NKG2D-AAA-28(H)OX40LZ CAR (3rd generation) against the lung cancer cell line**

[217] In order to assess whether NK92MI cells transduced with NKG2D-AAA-28(H)OX40LZ CAR (3rd generation) can recognize NKG2D ligand in the lung cancer cells, NKG2D ligand-positive tumor cells (H1299 and H1944) were used as a target of NK92MI cells including NKG2D-AAA-28(H)OX40L CAR (3rd generation). The transduced NK92MI cells efficiently expressed NKG2D-Z CAR (1st generation) or NKG2D-AAA-28(H)OX40L CAR (3rd generation) (FIG. 8A). Next, the NKG2D ligand expression in H1299 and H1944 cells was assessed. The present inventors have identified that the NKG2D ligand expression was detected in H1299 and H1944 cells by a flow cytometric analysis (FIG. 8B). As shown in FIG. 8C, NK92MI cells including

NKG2D-AAA-28(H)OX40L CAR (3rd generation) could more efficiently killed the target cells expressing NKG2D ligand *in vitro* than the NK92MI cells as a control group and NK92MI cells expressing NKG2D-Z CAR (1st generation). Furthermore, specificity of target cell killing was obviously confirmed because H1299 and H1944 cells are not killed by NKG2D non-expressing NK92MI cells transduced by a control empty vector.

The claims defining the invention are as follows:

1. A chimeric antigen receptor, comprising an intracellular signaling domain which comprises a OX40 ligand (CD252) or a functional portion thereof.

2. The chimeric antigen receptor according to claim 1 , further comprising:
   a transmembrane domain linked to the intracellular signaling domain;
   a spacer domain linked to the transmembrane domain; and
   an extracellular domain linked to the spacer domain.

3. The chimeric antigen receptor according to claim 2, wherein:
   the chimeric antigen receptor further comprises a signal sequence linked to the extracellular domain;
   the spacer domain comprises CD8α or CD28 or a functional portion thereof;
   the transmembrane domain comprises CD8α or CD28 or a functional portion thereof;
   the extracellular domain comprises an antigen-binding fragment of an antibody, a Fc receptor, a natural cytotoxicity receptor, NKG2D, 2B4 or DNAM-1; and/or
   the chimeric antigen receptor further comprises an AAA linker between the extracellular domain and the spacer domain.

4. The chimeric antigen receptor according to claim 3, wherein:
   the signal sequence comprises CD16 or a functional portion thereof or CD8α or a functional portion thereof;
   the antigen-binding fragment is Fab fragment, F(ab') fragment, F(ab')2 fragment or Fv fragment;
   the Fc receptor is selected from the group consisting of CD16, CD32, CD64, CD23, CD89 and variants thereof; and/or
   the natural cytotoxicity receptor is selected from the group consisting of NKp46, NKp30, NKp44, NKp80 and NKp65 receptors.

5. The chimeric antigen receptor according to claim 4, wherein:
   the Fv fragment is a single-chain variable fragment (ScFv); and/or
   the Fc receptor is CD16 or a variant thereof.

6. The chimeric antigen receptor according to claim 1 or any one of claims 2 to 5 , wherein the intracellular signaling domain further comprises CD3-zeta or a functional portion thereof.

7. The chimeric antigen receptor according to claim 6, wherein the CD3-zeta or functional portion thereof and the OX40 ligand or functional portion thereof are arranged in order from a cell membrane toward an inside of the cell.

8. An immune cell expressing the chimeric antigen receptor according to any one of claims 1 to 7.

9. The immune cell according to claim 8, wherein the immune cell is a natural killer cell (NK cell).

10. A pharmaceutical composition comprising the immune cell according to claim 8 or 9 as an active ingredient.

11. The pharmaceutical composition according to claim 10, further comprising an antibody as an active ingredient when the extracellular domain is a Fc receptor.

12. A nucleic acid molecule comprising a nucleotide sequence encoding the chimeric antigen receptor according to any one of claims 1 to 7.

13. The nucleic acid molecule according to claim 12, wherein the nucleotide sequence encodes one or more amino acid sequences selected from the group consisting of SEQ ID NOs: 45, 51, 53, 55, 69, 77, 85, 91 and 93, or variants thereof having a sequence identity of 80% or more relative thereto.

14. The nucleic acid molecule according to claim 13, wherein the nucleotide sequence includes one or more sequences selected from the group consisting of SEQ ID NOs: 44, 50, 52, 54, 68, 76, 84, 90 and 92, or variants thereof having a sequence identity of 80% or more relative thereto.

15. An expression vector comprising a nucleic acid molecule according to any one of claims 12 to 14 operably-linked to a promoter.

16. A method for treating cancer in a subject suffering therefrom, comprising administering the immune cell according to claim 8 or 9 or a pharmaceutical composition according to claim 10 or 11 to the subject, wherein the cancer is malignant lymphoma, leukemia, breast cancer or lung cancer.

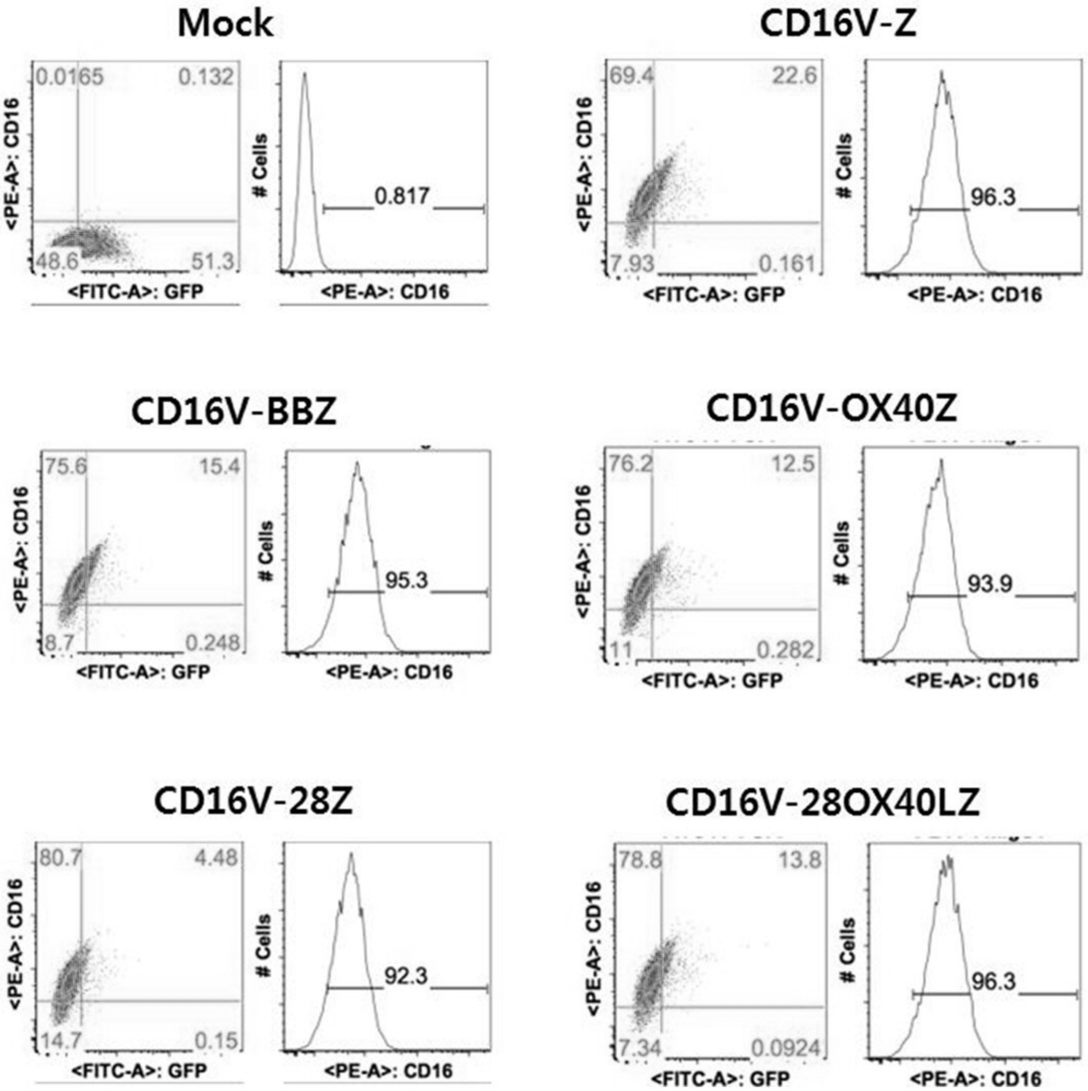
17. A method for preventing tumor metastases in a subject suffering from cancer, comprising administering the immune cell according to claim 8 or 9 or a pharmaceutical composition according to claim 10 or 11 to the subject.

18. Use of the chimeric antigen receptor of any of one of claims 1 to 7 or the immune cell of claim 8 or 9 of the pharmaceutical composition of claim 10 or 11 or the nucleic acid molecule according to any one of claims 12 to 14 or the expression vector of claim 15 in the preparation of a medicament for treating cancer in a subject suffering therefrom, wherein the cancer is malignant lymphoma, leukemia, breast cancer or lung cancer.

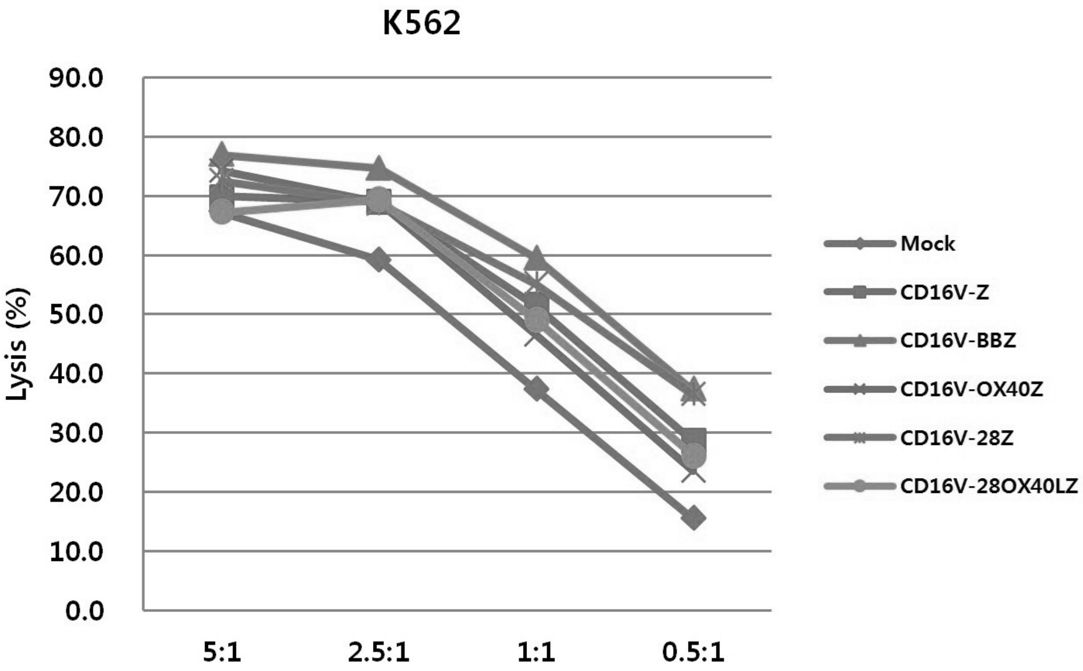
19. Use of the chimeric antigen receptor of any of one of claims 1 to 7 or the immune cell of claim 8 or 9 of the pharmaceutical composition of claim 10 or 11 or the nucleic acid molecule according to any one of claims 12 to 14 or the expression vector of claim 15 in the preparation of a medicament for preventing tumor metastases in a subject suffering from cancer.

20. The method of claim 17 or the use of claim 19, wherein the cancer is malignant lymphoma, leukemia, breast cancer or lung cancer.

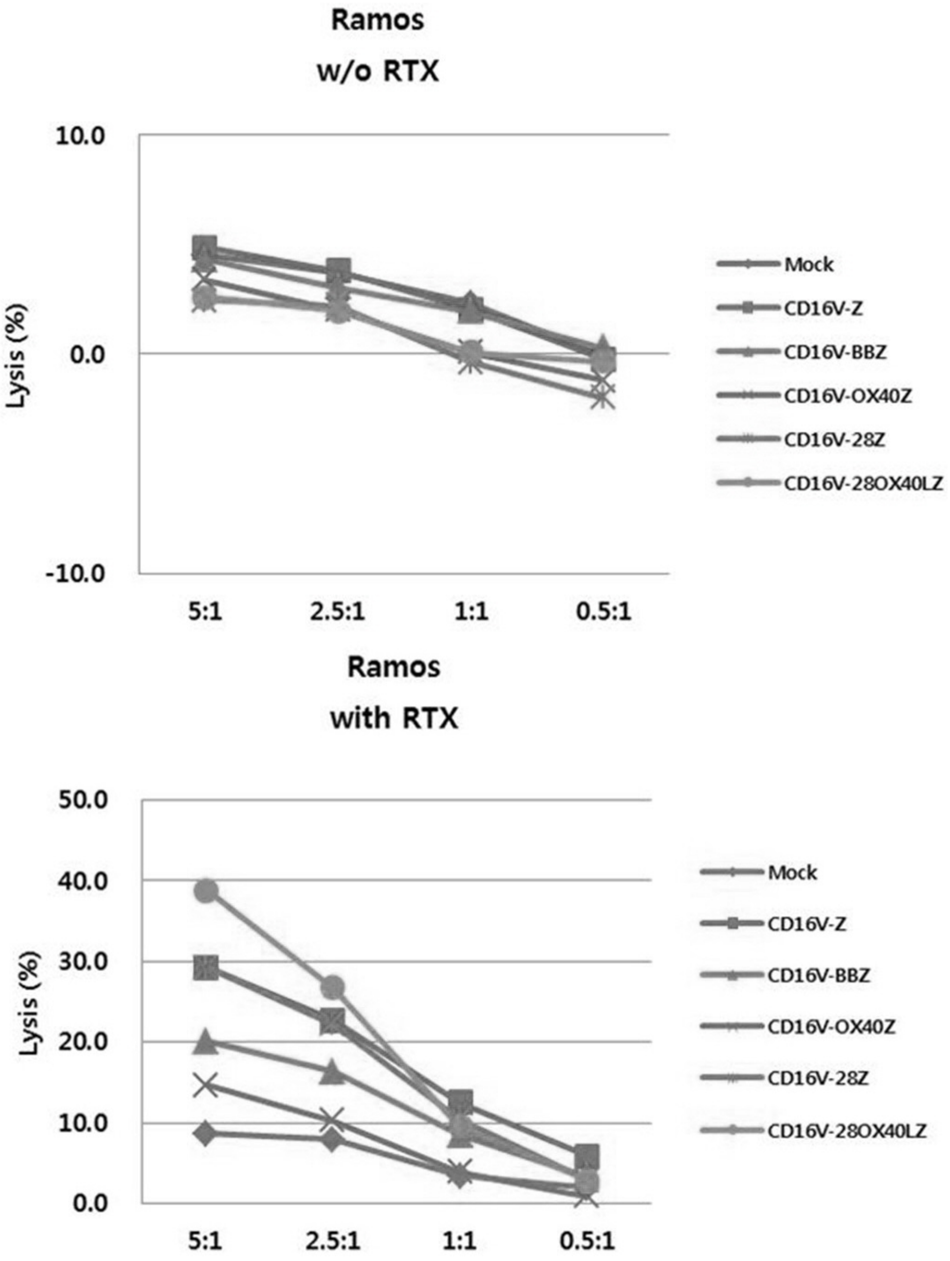
【FIG. 1a】


Mock
0.0165
0.132
48.6
51.3
<PE-A>: CD16
<FITC-A>: GFP
Cells
0.817
<PE-A>: CD16
CD16V-Z
69.4
22.6
7.93
0.161
<PE-A>: CD16
<FITC-A>: GFP
Cells
96.3
<PE-A>: CD16
CD16V-BBZ
75.6
15.4
8.7
0.248
<PE-A>: CD16
<FITC-A>: GFP
Cells
95.3
<PE-A>: CD16
CD16V-OX40Z
76.2
12.5
11
0.282
<PE-A>: CD16
<FITC-A>: GFP
Cells
93.9
<PE-A>: CD16
CD16V-28Z
80.7
4.48
14.7
0.15
<PE-A>: CD16
<FITC-A>: GFP
Cells
92.3
<PE-A>: CD16
CD16V-28OX40LZ
78.8
13.8
7.34
0.0924
<PE-A>: CD16
<FITC-A>: GFP
Cells
96.3
<PE-A>: CD16

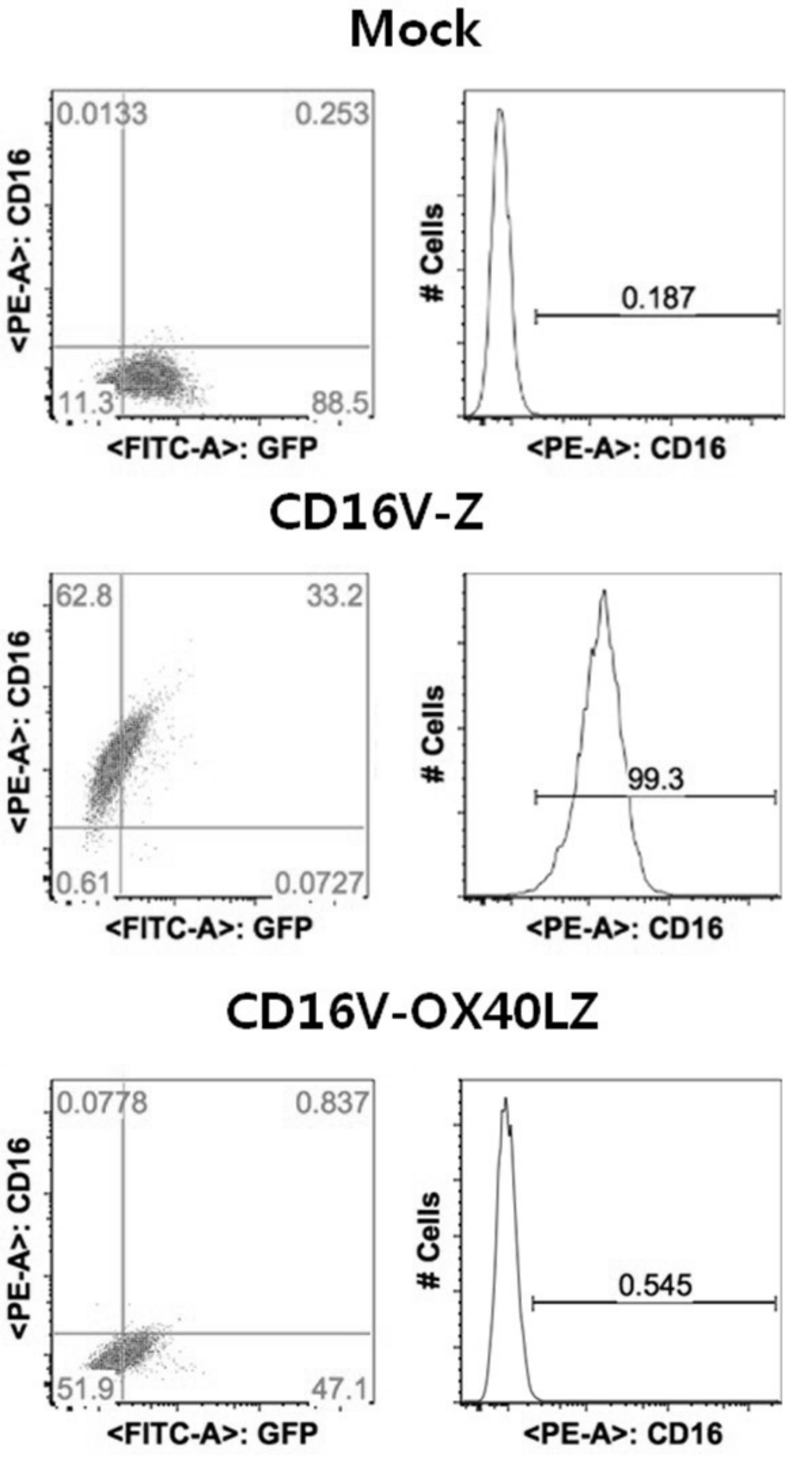
【FIG. 1b】


K562
Lysis (%)
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
5:1
2.5:1
1:1
0.5:1
Mock
CD16V-Z
CD16V-BBZ
CD16V-OX40Z
CD16V-28Z
CD16V-28OX40LZ

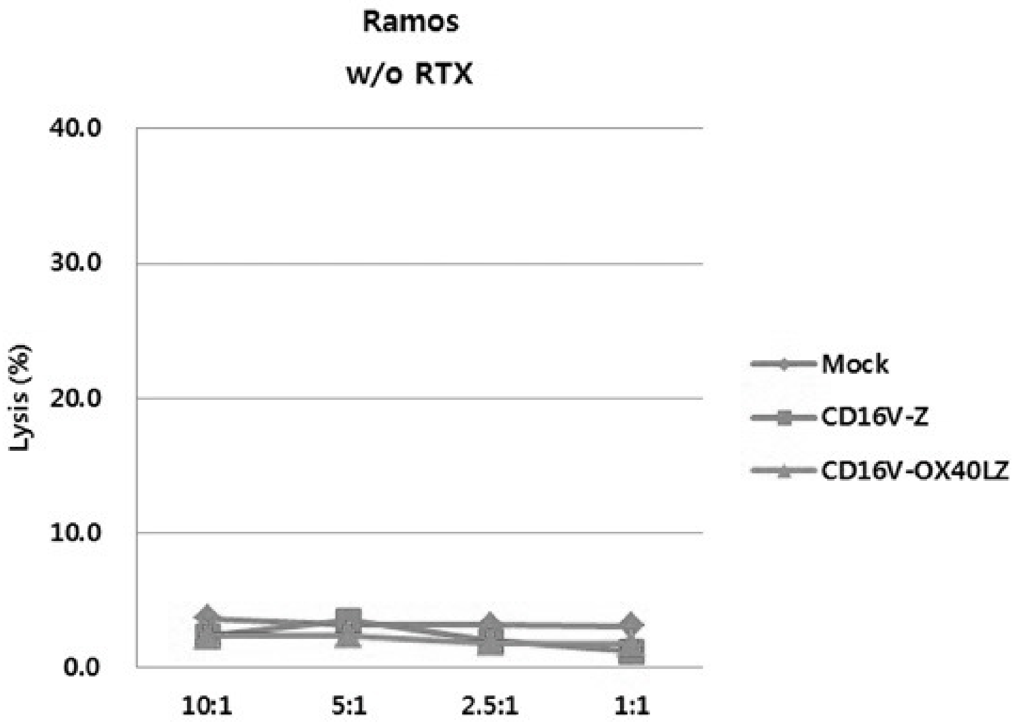
【FIG. 1c】

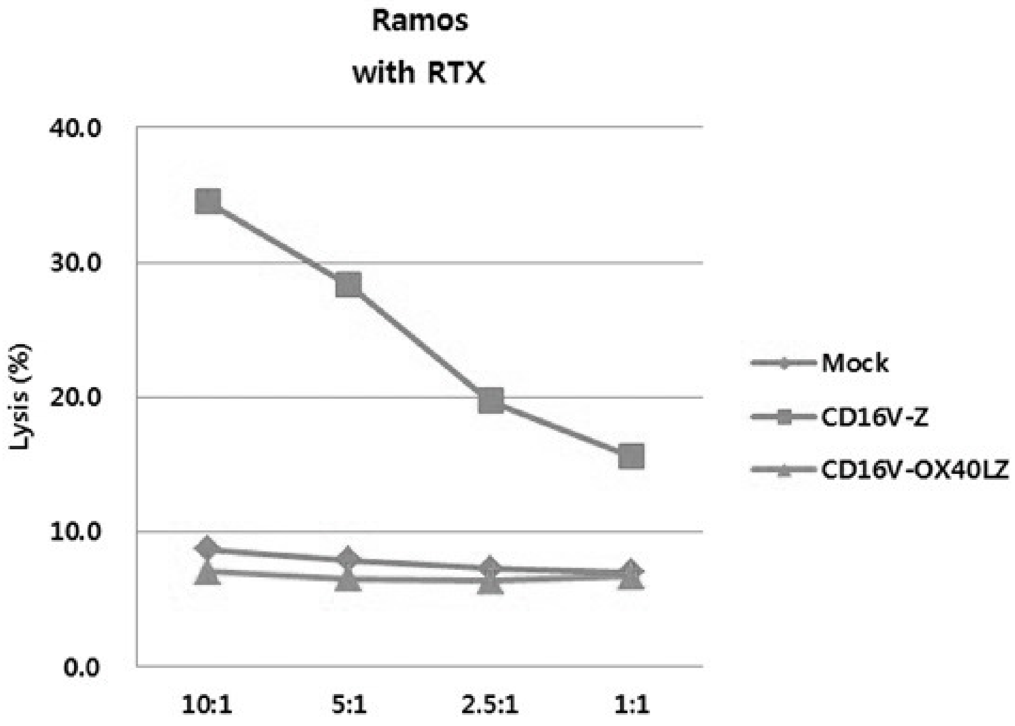

Ramos
w/o RTX
10.0
0.0
-10.0
Lysis (%)
5:1
2.5:1
1:1
0.5:1
Mock
CD16V-Z
CD16V-BBZ
CD16V-OX40Z
CD16V-28Z
CD16V-28OX40LZ
Ramos
with RTX
50.0
40.0
30.0
20.0
10.0
0.0
Lysis (%)
5:1
2.5:1
1:1
0.5:1
Mock
CD16V-Z
CD16V-BBZ
CD16V-OX40Z
CD16V-28Z
CD16V-28OX40LZ

【FIG. 1d】

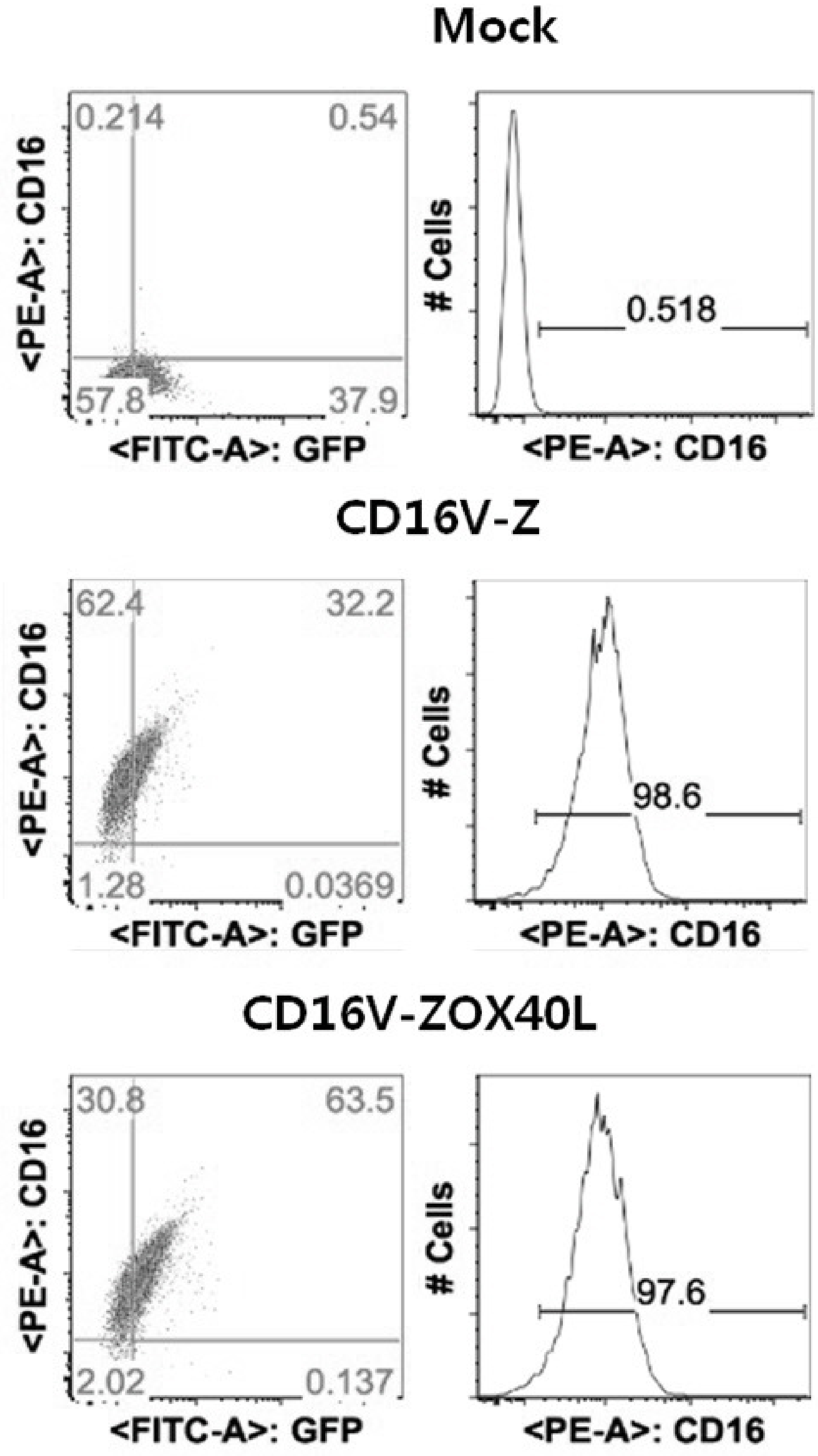

Mock
0.0133
0.253
11.3
88.5
<PE-A>: CD16
<FITC-A>: GFP
Cells
0.187
<PE-A>: CD16
CD16V-Z
62.8
33.2
0.61
0.0727
<PE-A>: CD16
<FITC-A>: GFP
Cells
99.3
<PE-A>: CD16
CD16V-OX40LZ
0.0778
0.837
51.9
47.1
<PE-A>: CD16
<FITC-A>: GFP
Cells
0.545
<PE-A>: CD16

【FIG. 1e】

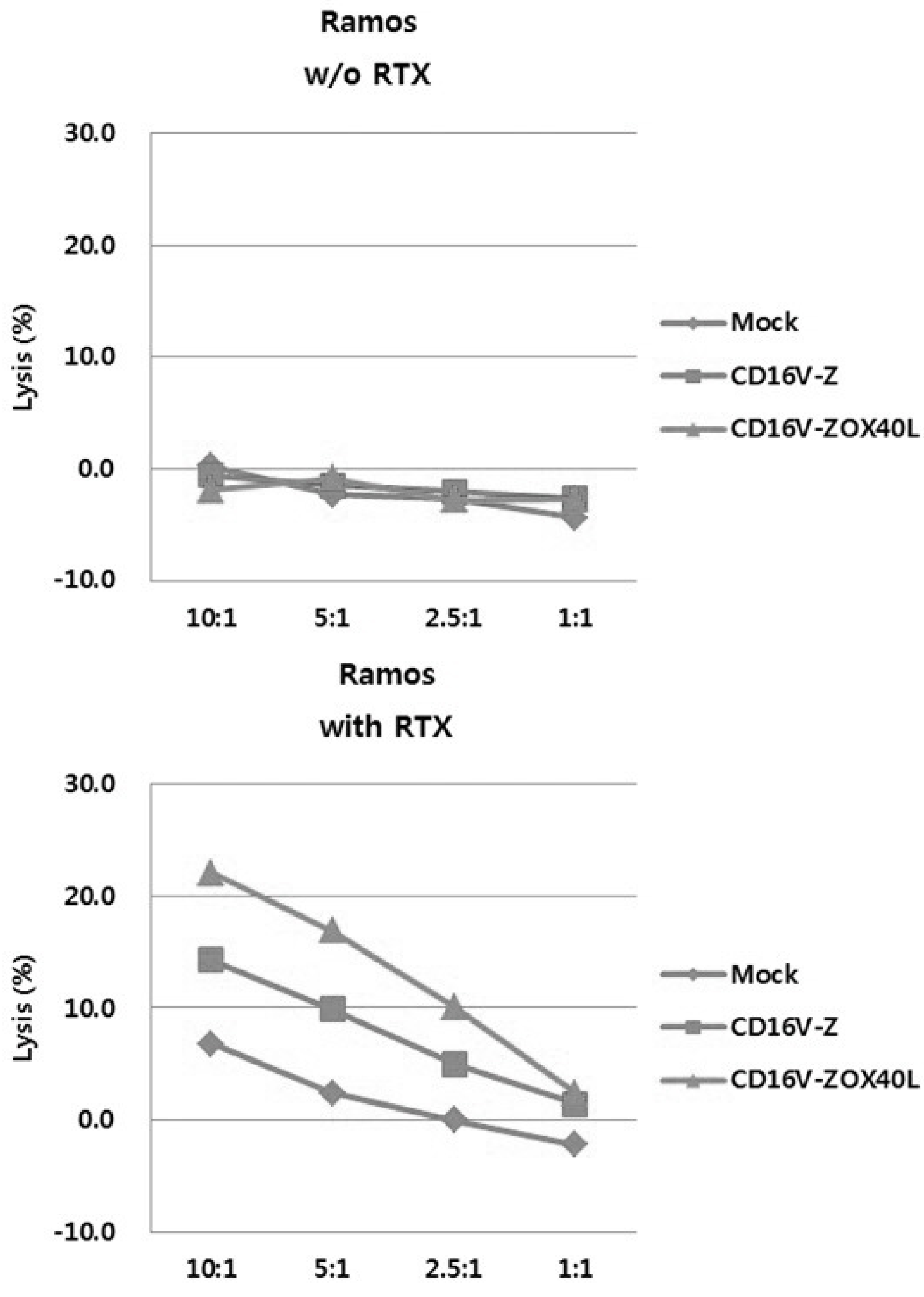

Ramos
w/o RTX
40.0
30.0
20.0
10.0
0.0
Lysis (%)
10:1
5:1
2.5:1
1:1
Mock
CD16V-Z
CD16V-OX40LZ


Ramos
with RTX
40.0
30.0
20.0
10.0
0.0
Lysis (%)
10:1
5:1
2.5:1
1:1
Mock
CD16V-Z
CD16V-OX40LZ

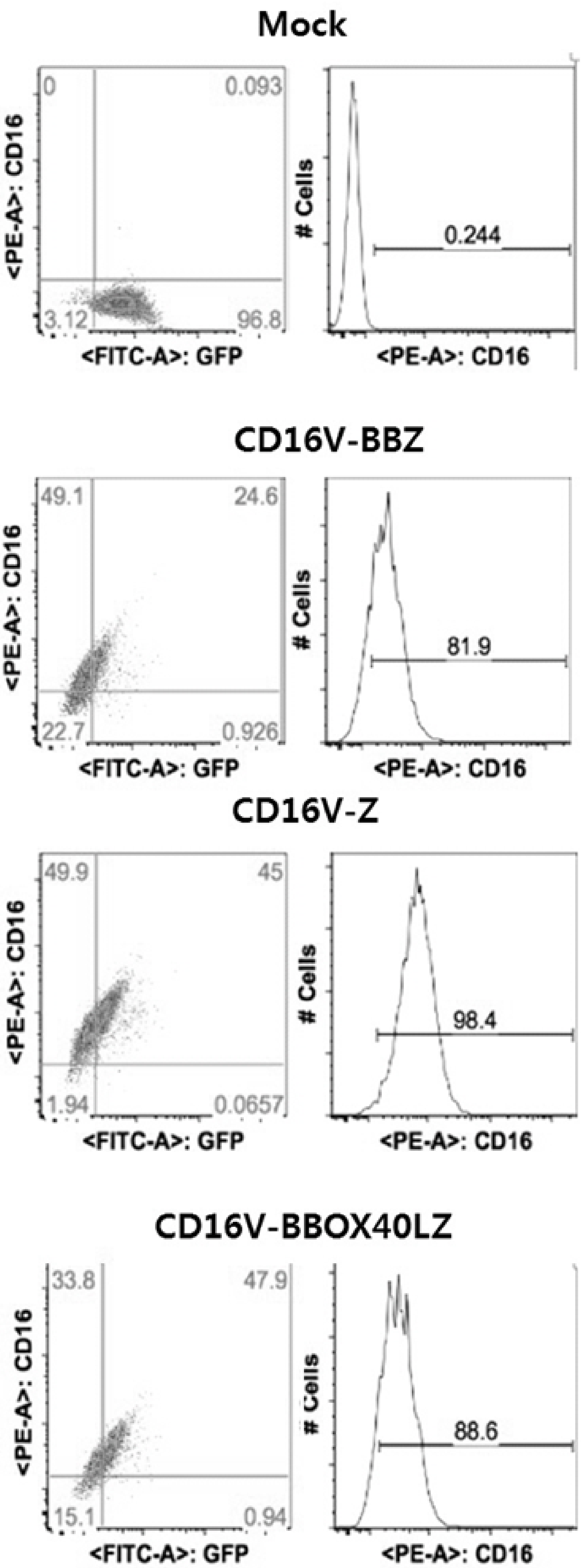
【FIG. 1f】


Mock
0.214
0.54
57.8
37.9
<PE-A>: CD16
<FITC-A>: GFP
Cells
0.518
<PE-A>: CD16
CD16V-Z
62.4
32.2
1.28
0.0369
<PE-A>: CD16
<FITC-A>: GFP
Cells
98.6
<PE-A>: CD16
CD16V-ZOX40L
30.8
63.5
2.02
0.137
<PE-A>: CD16
<FITC-A>: GFP
Cells
97.6
<PE-A>: CD16

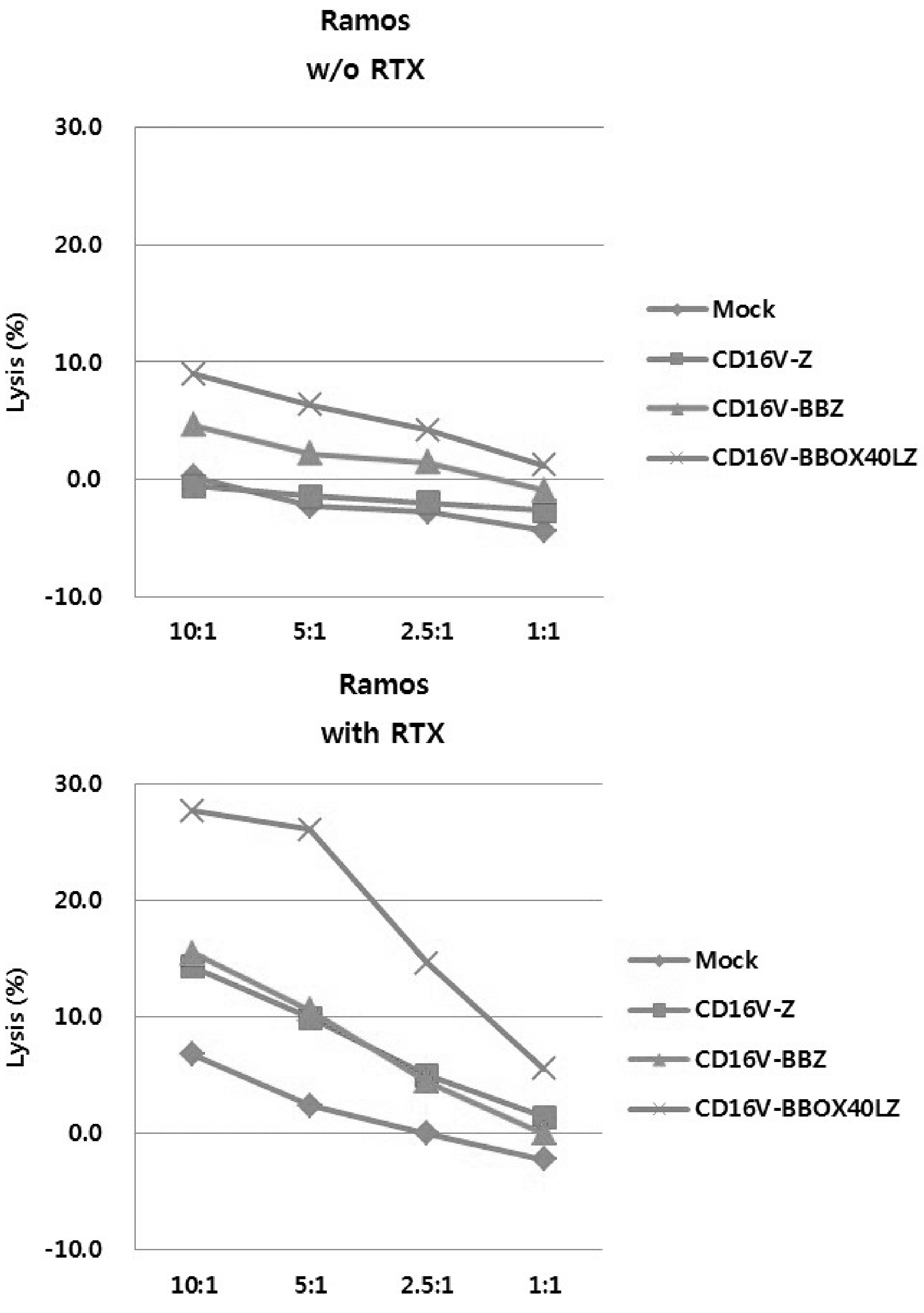
【FIG. 1g】


Ramos
w/o RTX
30.0
20.0
10.0
0.0
-10.0
Lysis (%)
10:1
5:1
2.5:1
1:1
Mock
CD16V-Z
CD16V-ZOX40L
Ramos
with RTX
30.0
20.0
10.0
0.0
-10.0
Lysis (%)
10:1
5:1
2.5:1
1:1
Mock
CD16V-Z
CD16V-ZOX40L

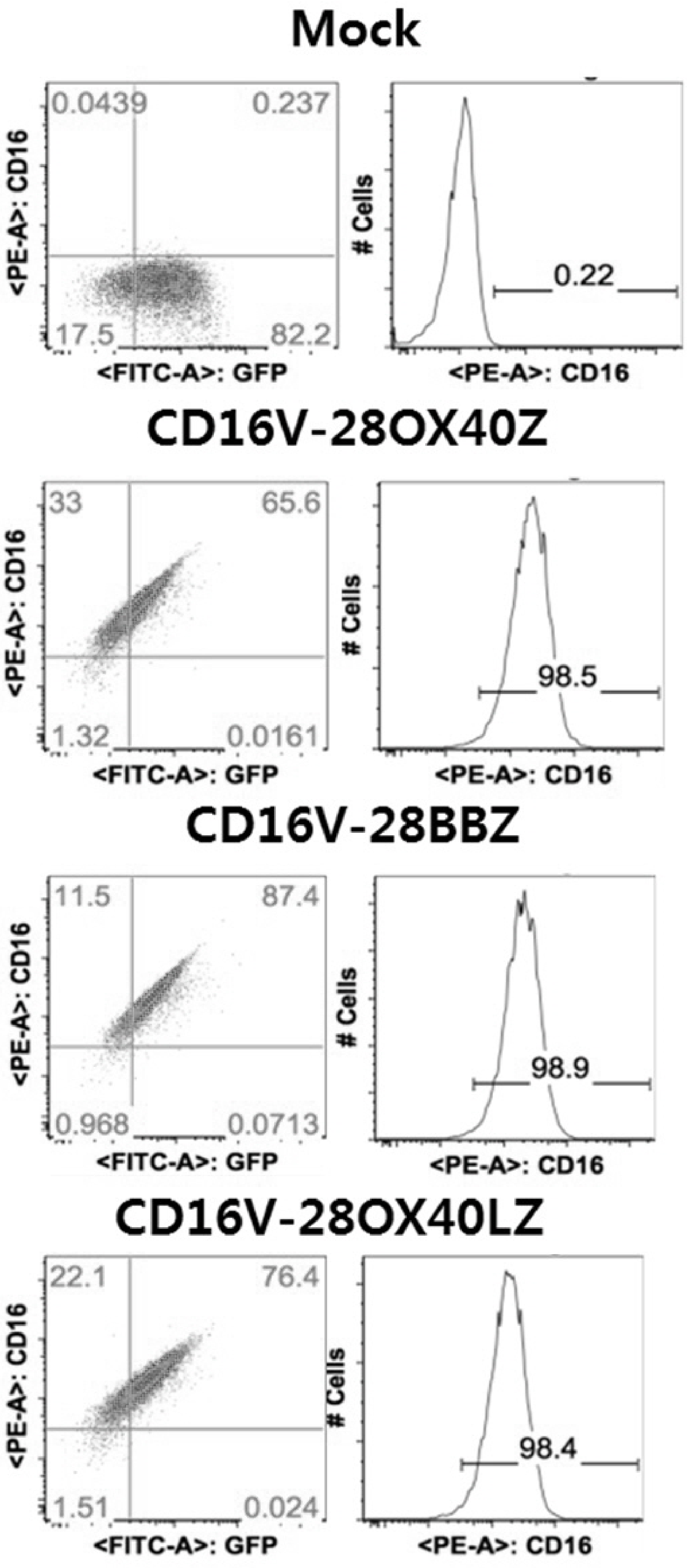
【FIG. 2a】


Mock
0
0.093
3.12
96.8
<PE-A>: CD16
<FITC-A>: GFP
Cells
0.244
<PE-A>: CD16
CD16V-BBZ
49.1
24.6
22.7
0.926
<PE-A>: CD16
<FITC-A>: GFP
Cells
81.9
<PE-A>: CD16
CD16V-Z
49.9
45
1.94
0.0657
<PE-A>: CD16
<FITC-A>: GFP
Cells
98.4
<PE-A>: CD16
CD16V-BBOX40LZ
33.8
47.9
15.1
0.94
<PE-A>: CD16
<FITC-A>: GFP
Cells
88.6
<PE-A>: CD16

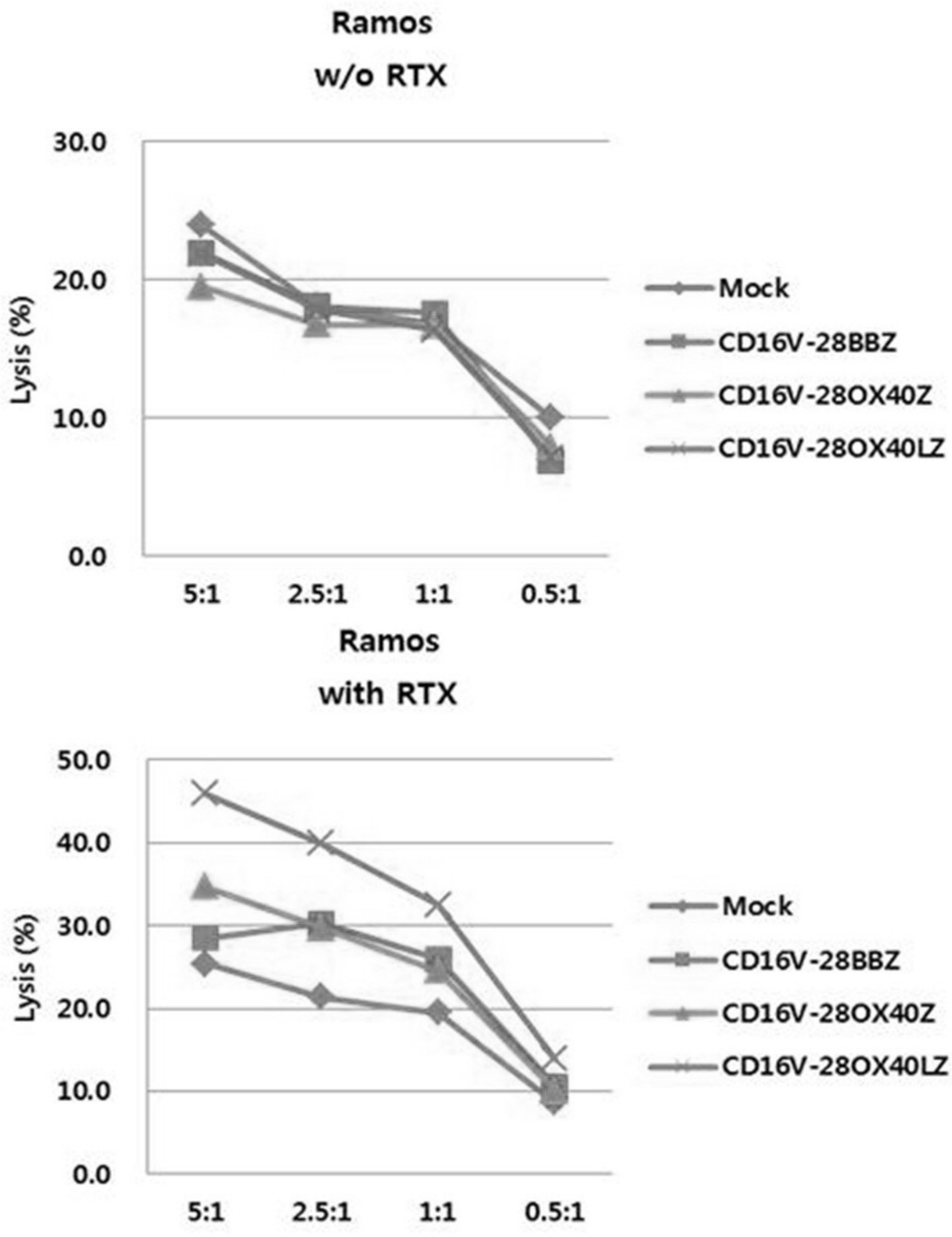
【FIG. 2b】


Ramos
w/o RTX
Lysis (%)
30.0
20.0
10.0
0.0
-10.0
10:1
5:1
2.5:1
1:1
Mock
CD16V-Z
CD16V-BBZ
CD16V-BBOX40LZ
Ramos
with RTX
Lysis (%)
30.0
20.0
10.0
0.0
-10.0
10:1
5:1
2.5:1
1:1
Mock
CD16V-Z
CD16V-BBZ
CD16V-BBOX40LZ

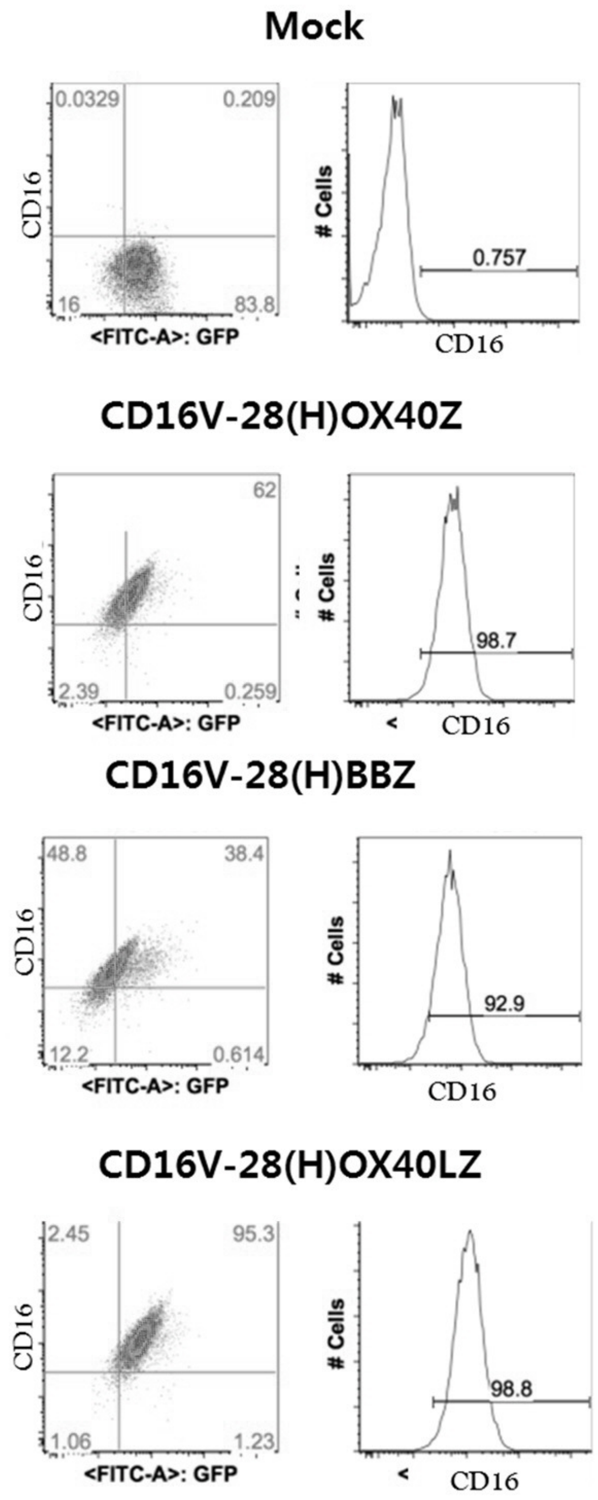
【FIG. 3a】


Mock
0.0439
0.237
17.5
82.2
<PE-A>: CD16
<FITC-A>: GFP
Cells
0.22
<PE-A>: CD16
CD16V-28OX40Z
33
65.6
1.32
0.0161
<PE-A>: CD16
<FITC-A>: GFP
Cells
98.5
<PE-A>: CD16
CD16V-28BBZ
11.5
87.4
0.968
0.0713
<PE-A>: CD16
<FITC-A>: GFP
Cells
98.9
<PE-A>: CD16
CD16V-28OX40LZ
22.1
76.4
1.51
0.024
<PE-A>: CD16
<FITC-A>: GFP
Cells
98.4
<PE-A>: CD16

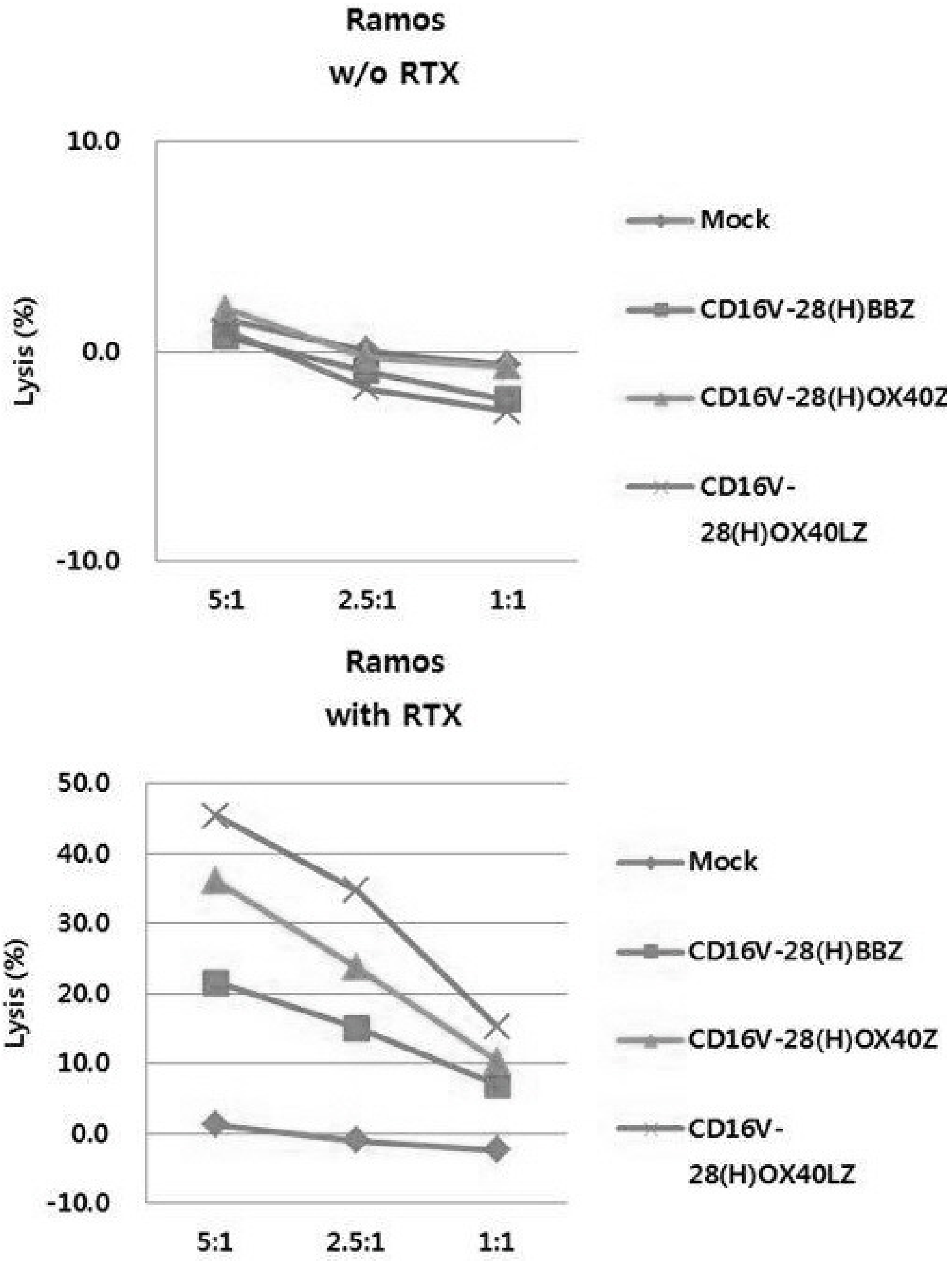
【FIG. 3b】


Ramos
w/o RTX
Lysis (%)
30.0
20.0
10.0
0.0
5:1
2.5:1
1:1
0.5:1
Mock
CD16V-28BBZ
CD16V-28OX40Z
CD16V-28OX40LZ
Ramos
with RTX
Lysis (%)
50.0
40.0
30.0
20.0
10.0
0.0
5:1
2.5:1
1:1
0.5:1
Mock
CD16V-28BBZ
CD16V-28OX40Z
CD16V-28OX40LZ

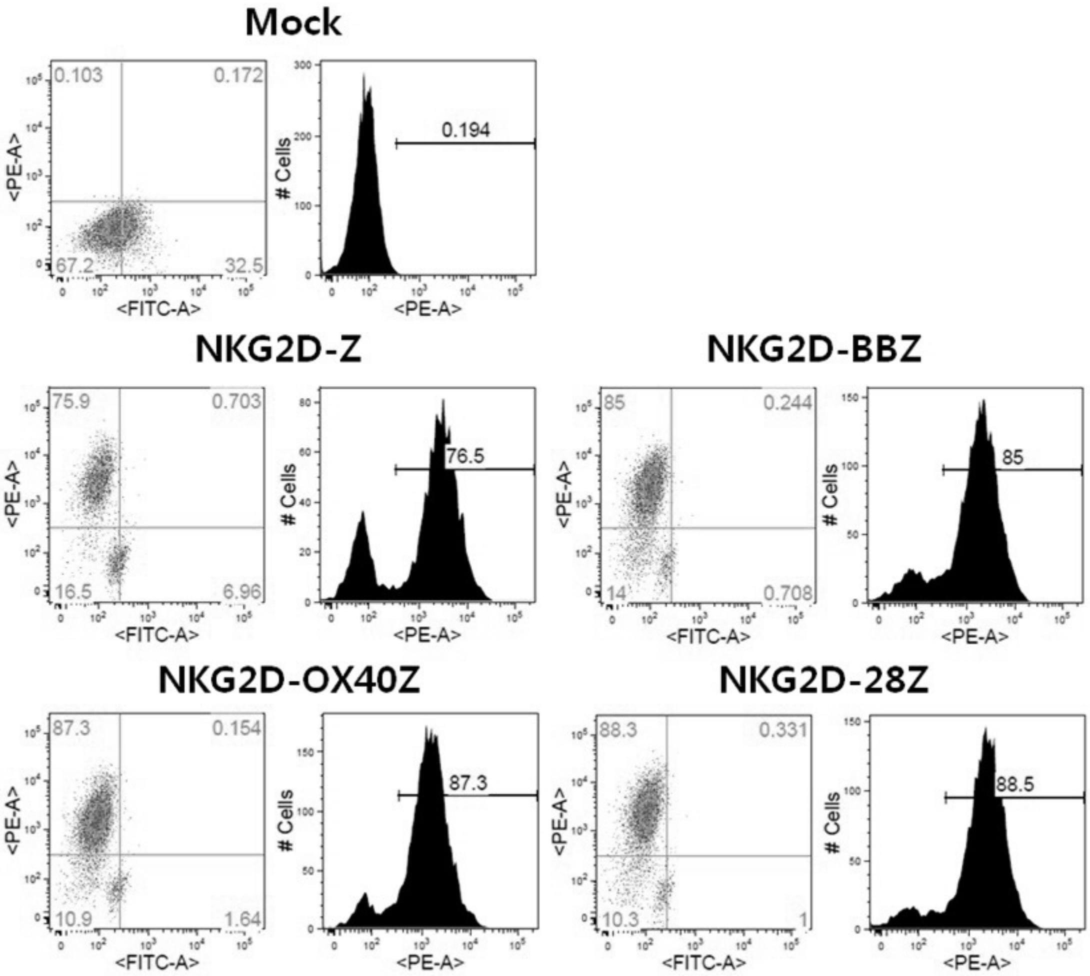
【FIG. 4a】


Mock
0.0329
0.209
16
83.8
CD16
<FITC-A>: GFP
Cells
0.757
CD16
CD16V-28(H)OX40Z
62
2.39
0.259
CD16
<FITC-A>: GFP
Cells
98.7
CD16
CD16V-28(H)BBZ
48.8
38.4
12.2
0.614
CD16
<FITC-A>: GFP
Cells
92.9
CD16
CD16V-28(H)OX40LZ
2.45
95.3
1.06
1.23
CD16
<FITC-A>: GFP
Cells
98.8
CD16

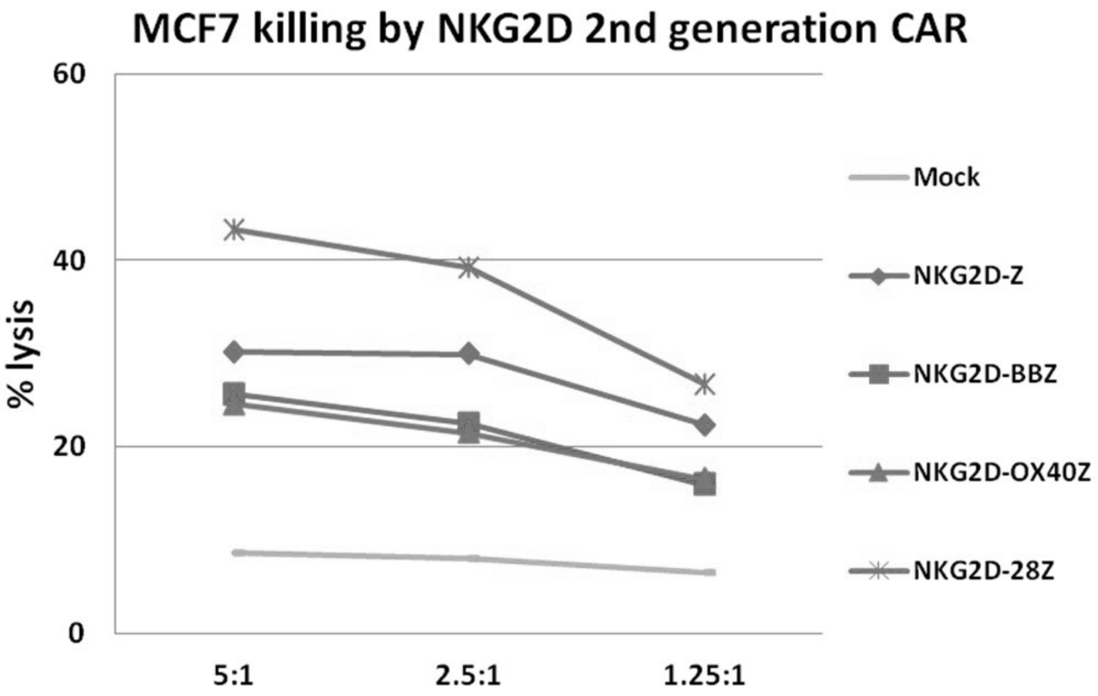
【FIG. 4b】


Ramos
w/o RTX
10.0
0.0
-10.0
Lysis (%)
5:1
2.5:1
1:1
Mock
CD16V-28(H)BBZ
CD16V-28(H)OX40Z
CD16V-28(H)OX40LZ
Ramos
with RTX
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
Lysis (%)
5:1
2.5:1
1:1
Mock
CD16V-28(H)BBZ
CD16V-28(H)OX40Z
CD16V-28(H)OX40LZ

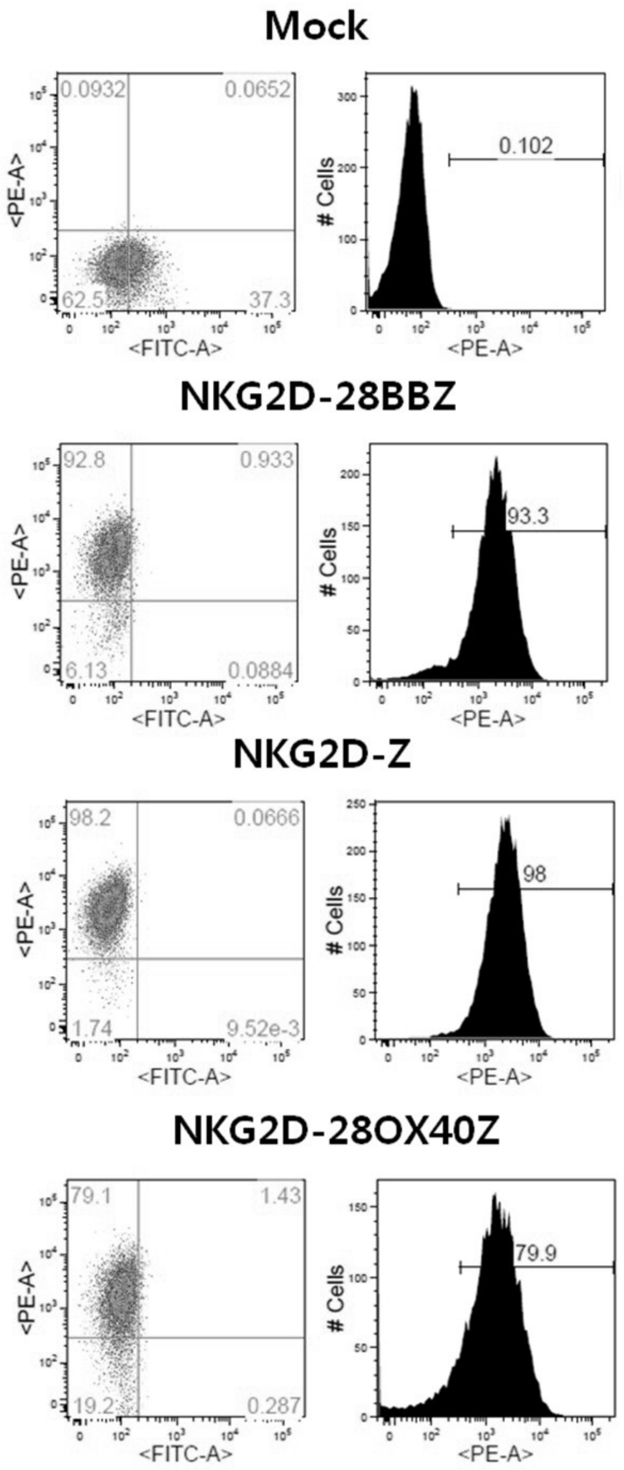
【FIG. 5a】


Mock
0.103
0.172
67.2
32.5
<PE-A>
<FITC-A>
Cells
0.194
<PE-A>
NKG2D-Z
75.9
0.703
16.5
6.96
76.5
NKG2D-BBZ
85
0.244
14
0.708
85
NKG2D-OX40Z
87.3
0.154
10.9
1.64
87.3
NKG2D-28Z
88.3
0.331
10.3
1
88.5

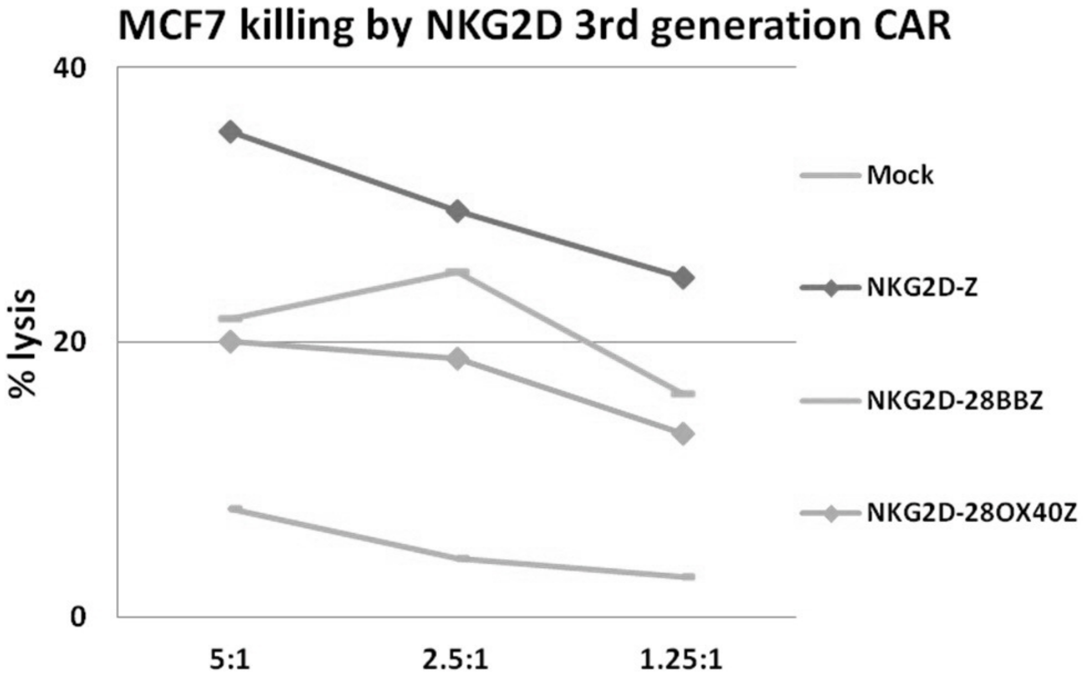
【FIG. 5b】


MCF7 killing by NKG2D 2nd generation CAR
% lysis
0
20
40
60
5:1
2.5:1
1.25:1
Mock
NKG2D-Z
NKG2D-BBZ
NKG2D-OX40Z
NKG2D-28Z

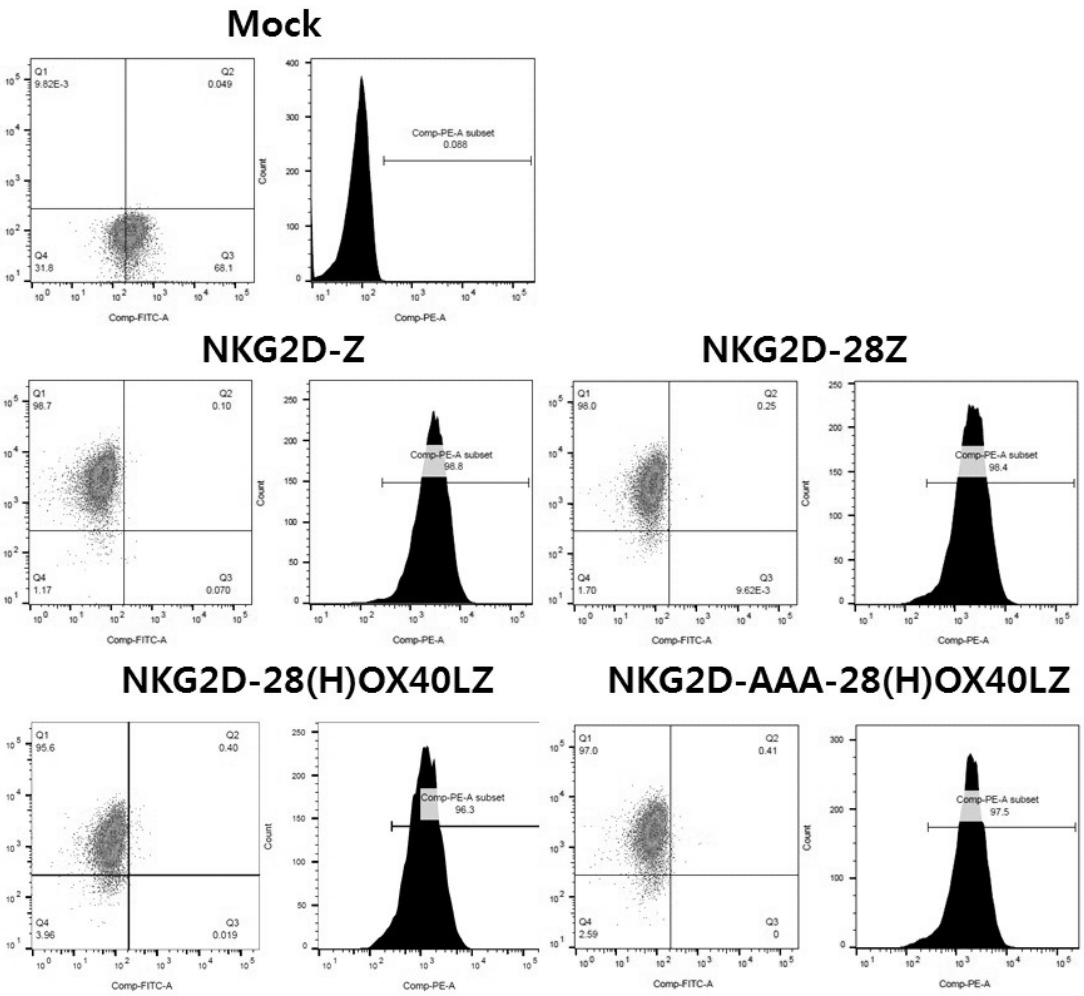
【FIG. 6a】


Mock
0.0932
0.0652
62.5
37.3
<PE-A>
<FITC-A>
0.102
Cells
<PE-A>
NKG2D-28BBZ
92.8
0.933
6.13
0.0884
<PE-A>
<FITC-A>
93.3
Cells
<PE-A>
NKG2D-Z
98.2
0.0666
1.74
9.52e-3
<PE-A>
<FITC-A>
98
Cells
<PE-A>
NKG2D-28OX40Z
79.1
1.43
19.2
0.287
<PE-A>
<FITC-A>
79.9
Cells
<PE-A>

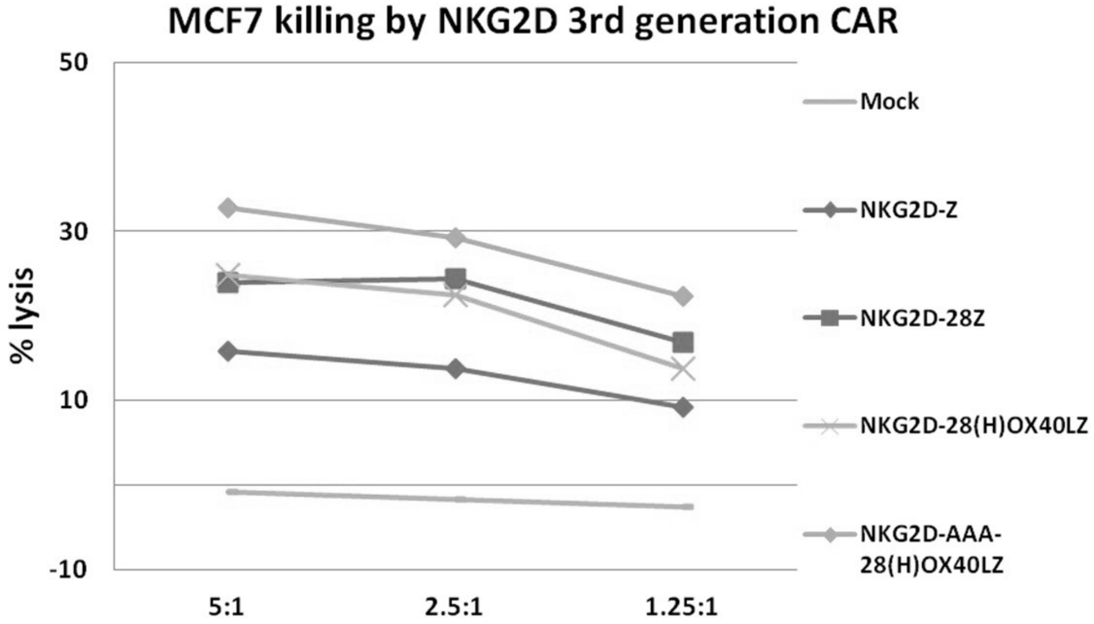
【FIG. 6b】


MCF7 killing by NKG2D 3rd generation CAR
% lysis
40
20
0
5:1
2.5:1
1.25:1
Mock
NKG2D-Z
NKG2D-28BBZ
NKG2D-28OX40Z

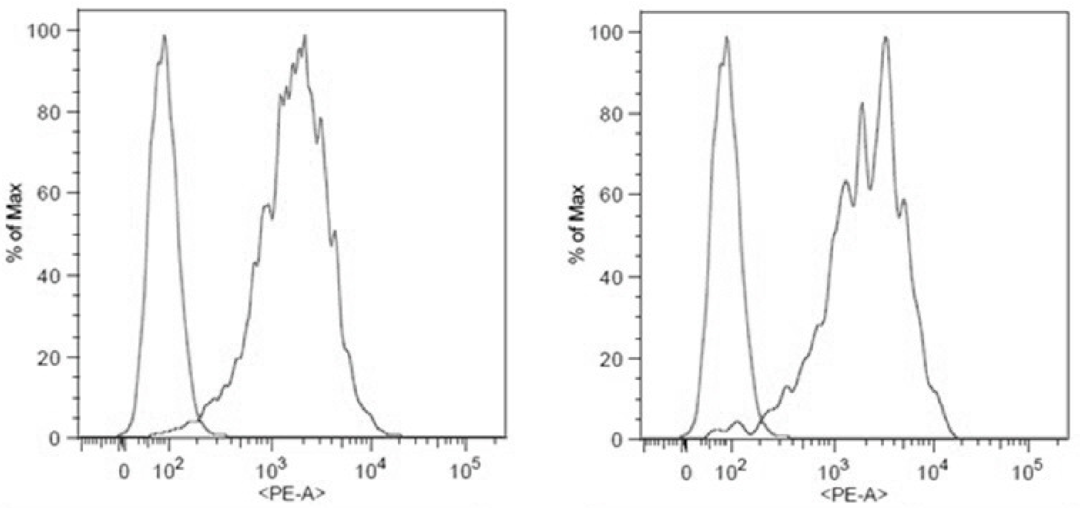
【FIG. 7a】


Mock
Q1 9.82E-3
Q2 0.049
Q4 31.8
Q3 68.1
Comp-PE-A subset 0.088
NKG2D-Z
Q1 98.7
Q2 0.10
Q4 1.17
Q3 0.070
Comp-PE-A subset 98.8
NKG2D-28Z
Q1 98.0
Q2 0.25
Q4 1.70
Q3 9.62E-3
Comp-PE-A subset 98.4
NKG2D-28(H)OX40LZ
Q1 95.6
Q2 0.40
Q4 3.96
Q3 0.019
Comp-PE-A subset 96.3
NKG2D-AAA-28(H)OX40LZ
Q1 97.0
Q2 0.41
Q4 2.59
Q3 0
Comp-PE-A subset 97.5
Comp-FITC-A
Comp-PE-A
Count

【FIG. 7b】



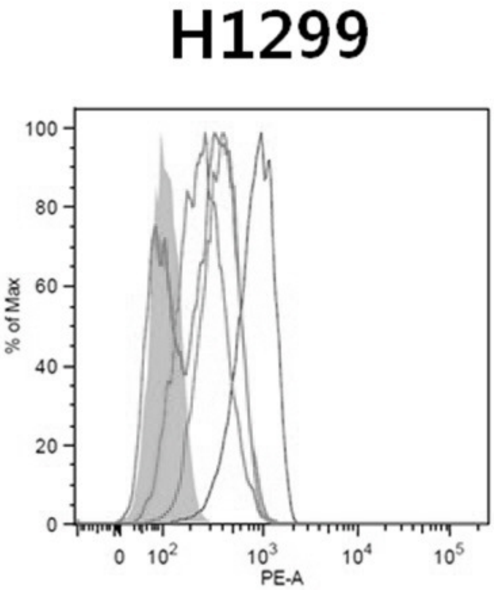
【FIG. 8a】



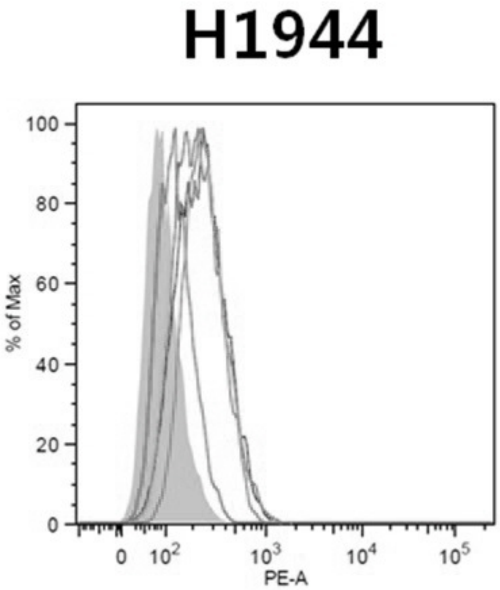
Mock MFI	89.1
NKG2D-Z MFI	2188

Mock MFI	89.1
NKG2D-AAA-28(H)OX40LZ MFI	2871

【FIG. 8b】

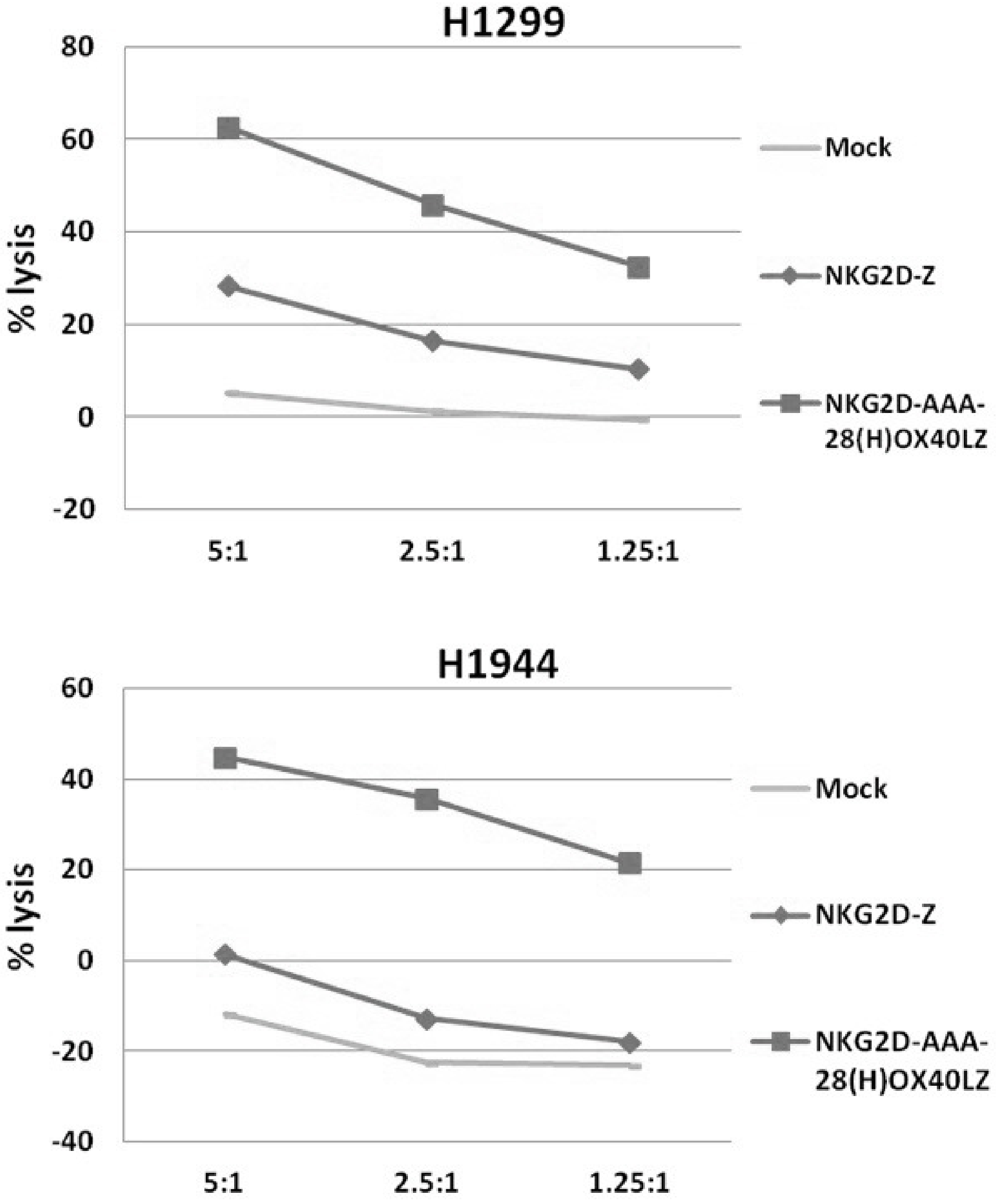


IgG1a	112
MIC-A/B	894
ULBP-1	290
ULBP-2/5/6	280
ULBP-3	401



IgG1a	100
MIC-A/B	263
ULBP-1	253
ULBP-2/5/6	136
ULBP-3	267

【FIG. 8c】


H1299
80
60
40
20
0
-20
% lysis
5:1
2.5:1
1.25:1
Mock
NKG2D-Z
NKG2D-AAA-28(H)OX40LZ
H1944
60
40
20
0
-20
-40
% lysis
5:1
2.5:1
1.25:1
Mock
NKG2D-Z
NKG2D-AAA-28(H)OX40LZ

<110>   Green Cross Labcell

<120>   Chimeric antigen receptor and natural killer cell expressing the
         same

<130>   16P10085

<150>   KR 10-2016-0181119
<151>   2016-12-28

<160>   93

<170>   KoPatentIn 3.0

<210>   1
<211>   618
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   CD16 nucleotide

<400>   1
atgtggcagc tgctcctccc aactgctctg ctacttctag tttcagctgg catgcggact
60

gaagatctcc caaaggctgt ggtgttcctg gagcctcaat ggtacagggt gctcgagaag
120

gacagtgtga ctctgaagtg ccagggagcc tactcccctg aggacaattc cacacagtgg
180

tttcacaatg agagcctcat ctcaagccag gcctcgagct acttcattga cgctgccaca
240

gtcgacgaca gtggagagta caggtgccag acaaacctct ccaccctcag tgacccggtg
300

cagctagaag tccatatcgg ctggctgttg ctccaggccc ctcggtgggt gttcaaggag
360

gaagacccta ttcacctgag gtgtcacagc tggaagaaca ctgctctgca taaggtcaca
420

tatttacaga atggcaaagg caggaagtat tttcatcata attctgactt ctacattcca
480

aaagccacac tcaaagacag cggctcctac ttctgcaggg ggctttttgg gagtaaaaat
540

gtgtcttcag agactgtgaa catcaccatc actcaaggtt tggcagtgtc aaccatctca
600

tcattctttc cacctggg
618

<210> 2
<211> 206
<212> PRT
<213> Artificial Sequence

<220>
<223> CD16 amino acid

<400> 2
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1 5 10 15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
20 25 30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
50 55 60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65 70 75 80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
85 90 95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
100 105 110

```
Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
        195                 200                 205



<210>    3
<211>    618
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    CD16V nucleotide


<400>    3
atgtggcagc  tgctcctccc  aactgctctg  ctacttctag  tttcagctgg  catgcggact
60

gaagatctcc  caaaggctgt  ggtgttcctg  gagcctcaat  ggtacagggt  gctcgagaag
120

gacagtgtga  ctctgaagtg  ccagggagcc  tactcccctg  aggacaattc  cacacagtgg
180

tttcacaatg  agagcctcat  ctcaagccag  gcctcgagct  acttcattga  cgctgccaca
240

gtcgacgaca  gtggagagta  caggtgccag  acaaacctct  ccaccctcag  tgacccggtg
300
```

cagctagaag tccatatcgg ctggctgttg ctccaggccc ctcggtgggt gttcaaggag
360

gaagacccta ttcacctgag gtgtcacagc tggaagaaca ctgctctgca taaggtcaca
420

tatttacaga atggcaaagg caggaagtat tttcatcata attctgactt ctacattcca
480

aaagccacac tcaaagacag cggctcctac ttctgcaggg ggcttgttgg gagtaaaaat
540

gtgtcttcag agactgtgaa catcaccatc actcaaggtt tggcagtgtc aaccatctca
600

tcattctttc cacctggg
618

<210> 4
<211> 618
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V nucleotide codon optimization

<400> 4
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggg
618

<210> 5
<211> 206
<212> PRT
<213> Artificial Sequence

<220>
<223> CD16V amino acid

<400> 5
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1   5   10   15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20   25   30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35   40   45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50   55   60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65   70   75   80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu

85 90 95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
100 105 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
115 120 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
130 135 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145 150 155 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
165 170 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
180 185 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
195 200 205

<210> 6
<211> 216
<212> DNA
<213> Artificial Sequence

<220>
<223> CD8a nucleotide

<400> 6
gcgaagccca ccacgacgcc agcgccgcga ccaccaacac cggcgcccac catcgcgtcg
60

cagcccctgt ccctgcgccc agaggcgtgc cggccagcgg cggggggcgc agtgcacacg
120

agggggctgg acttcgcctg tgatatctac atctgggcgc ccttggccgg gacttgtggg
180

gtccttctcc tgtcactggt tatcaccctt tactgc
216

<210> 7
<211> 216
<212> DNA
<213> Artificial Sequence

<220>
<223> CD8a nucleotide codon optimization

<400> 7
gccaaaccta ccacaactcc tgctccaaga ccacccacac ccgctcctac tattgcatct
60

cagccactga gtctgcgacc agaggcctgc cggcccgccg ccggcggggc cgtgcatacc
120

aggggcctgg acttcgcctg tgatatctac atttgggctc cactggctgg gacttgcggc
180

gtgctgctgc tgtctctggt catcactctg tattgt
216

<210> 8
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8a amino acid

<400> 8
Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
1 5 10 15

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
20 25 30

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
35 40 45

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
50 55 60

Ser Leu Val Ile Thr Leu Tyr Cys
65 70

<210> 9
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> CD28 nucleotide

<400> 9
attgaagtta tgtatcctcc tccttaccta gacaatgaga agagcaatgg aaccattatc
60

catgtgaaag ggaaacacct ttgtccaagt cccctatttc ccggaccttc taagcccttt
120

tgggtgctgg tggtggttgg tggagtcctg gcttgctata gcttgctagt aacagtggcc
180

tttattattt tctgggtgag gagtaagagg agcaggctcc tgcacagtga ctacatgaac
240

atgactcccc gccgccccgg gcccacccgc aagcattacc agccctatgc cccaccacgc
300

gacttcgcag cctatcgctc c
321

<210> 10
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> CD28 nucleotide codon optimization

```
<400>   10
atcgaggtca tgtacccccc tccatatctg gacaacgaaa agtccaatgg aactatcatt
60

cacgtgaagg gcaaacatct gtgcccatct cccctgttcc ctgggccaag taaacctttt
120

tgggtcctgg tggtcgtggg aggggtgctg gcatgttact cactgctggt caccgtggcc
180

ttcatcatct tctgggtgcg gagcaagagg tcccgcctgc tgcacagcga ctatatgaac
240

atgaccccac ggagacccgg ccctacacgg aaacattacc agccctatgc tccaccccgg
300

gacttcgcag cttacagaag t
321


<210>   11
<211>   107
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   CD28 amino acid


<400>   11
Ile Glu Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser Asn
  1               5                  10                  15

Gly Thr Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser Pro Leu
             20                  25                  30

Phe Pro Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly
         35                  40                  45

Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe
     50                  55                  60

Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn
 65                  70                  75                  80
```

Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr
85 90 95

Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
100 105

<210> 12
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<223> CD3z nucleotide

<400> 12
agagtgaagt tcagcaggag cgcagacgcc cccgcgtacc agcagggcca gaaccagctc
60

tataacgagc tcaatctagg acgaagagag gagtacgatg ttttggacaa gagacgtggc
120

cgggaccctg agatgggggg aaagccgaga aggaagaacc ctcaggaagg cctgtacaat
180

gaactgcaga aagataagat ggcggaggcc tacagtgaga ttgggatgaa aggcgagcgc
240

cggaggggca aggggcacga tggcctttac cagggtctca gtacagccac caaggacacc
300

tacgacgccc ttcacatgca ggccctgccc cctcgc
336

<210> 13
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<223> CD3z nucleotide codon optimization

<400> 13
cgagtgaagt tcagcaggtc cgccgacgct cctgcatacc agcagggaca gaaccagctg
60

tataacgagc tgaatctggg ccggagagag gaatacgacg tgctggacaa aaggcggggc
120

cgggaccccg aaatgggagg gaagccacga cggaaaaacc cccaggaggg cctgtacaat
180

gagctgcaaa aggacaaaat ggccgaggct tattctgaaa tcgggatgaa gggagagaga
240

aggcgcggaa aaggccacga tggcctgtac caggggctga gcaccgctac aaaggacacc
300

tatgatgcac tgcacatgca ggccctgccc cctcgg
336

<210> 14
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> CD3z amino acid

<400> 14
Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
1 5 10 15

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
20 25 30

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
35 40 45

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
50 55 60

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65 70 75 80

```
Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
                 85                  90                  95

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            100                 105                 110




<210>    15
<211>    66
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    OX40L (CD252) nucleotide


<400>    15
gaaagggtcc  aacccctgga  agagaatgtg  ggaaatgcag  ccaggccaag  attcgagagg
60

a             a             c             a             a             g
66


<210>    16
<211>    66
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    OX40L (CD252) nucleotide codon optimization


<400>    16
gaaagagtgc  agcccctgga  agagaatgtc  gggaatgccg  ctcgcccaag  atttgaaagg
60

a             a             c             a             a             a
66


<210>    17
```

<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> OX40L (CD252) amino acid

<400> 17

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Glu Arg Val Gln Pro Leu Glu Glu Asn Val Gly Asn Ala Ala Arg Pro
  1               5                  10                  15

Arg Phe Glu Arg Asn Lys
             20
```

<210> 18
<211> 108
<212> DNA
<213> Artificial Sequence

<220>
<223> OX40 (CD134) nucleotide

<400> 18

```
agggaccaga ggctgccccc cgatgcccac aagcccccctg ggggaggcag tttccggacc
60

cccatccaag aggagcaggc cgacgcccac tccaccctgg ccaagatc
108
```

<210> 19
<211> 108
<212> DNA
<213> Artificial Sequence

<220>
<223> OX40 (CD134) nucleotide codon optimization

<400> 19

```
cgggaccaga gactgccacc tgatgcacac aagccaccag gaggaggcag cttcaggacc
60
```

cccatccagg aggaacaggc cgacgctcat tccacactgg ccaaaatt
108

<210> 20
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> OX40 (CD134) amino acid

<400> 20
Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro Pro Gly Gly Gly
1 5 10 15

Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp Ala His Ser Thr
20 25 30

Leu Ala Lys Ile
35

<210> 21
<211> 126
<212> DNA
<213> Artificial Sequence

<220>
<223> 4-1BB (CD137) nucleotide

<400> 21
aaacggggca gaaagaaact cctgtatata ttcaaacaac catttatgag accagtacaa
60

actactcaag aggaagatgg ctgtagctgc cgatttccag aagaagaaga aggaggatgt
120

g a a c t g
126

<210> 22
<211> 126
<212> DNA
<213> Artificial Sequence

<220>
<223> 4-1BB (CD137) nucleotide codon optimization

<400> 22
aagcggggaa gaaagaaact gctgtacatc ttcaaacagc cctttatgag gcctgtgcag
60

accacacagg aggaagacgg ctgctcctgc cggttccccg aggaagagga aggcgggtgc
120

g a g c t g
126

<210> 23
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> 4-1BB (CD137) amino acid

<400> 23
Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
35 40

<210> 24
<211> 1173
<212> DNA
<213> Artificial Sequence

<220>
<223>   CD16V-Z nucleotide

<400>   24
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc
660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc
720

ggcggggccg tgcataccag gggcctggac ttcgcctgtg atatctacat ttgggctcca
780

ctggctggga cttgcggcgt gctgctgctg tctctggtca ttactctgta ttgtcgagtg
840

aagttcagca ggtccgccga cgctcctgca taccagcagg gacagaacca gctgtataac
900

gagctgaatc tgggccggag agaggaatac gacgtgctgg acaaaaggcg gggccgggac
960

cccgaaatgg gagggaagcc acgacggaaa aacccccagg agggcctgta caatgagctg
1020

caaaaggaca aaatggccga ggcttattct gaaatcggga tgaagggaga gagaaggcgc
1080

ggaaaaggcc acgatggcct gtaccagggg ctgagcaccg ctacaaagga cacctatgat
1140

gcactgcaca tgcaggccct gccccctcgg tga
1173

<210> 25
<211> 390
<212> PRT
<213> Artificial Sequence

<220>
<223> CD16V-Z amino acid

<400> 25
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1 5 10 15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
20 25 30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
50 55 60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65 70 75 80

```
Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
        195                 200                 205

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
    210                 215                 220

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
                245                 250                 255

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
            260                 265                 270

Val Ile Thr Leu Tyr Cys Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
        275                 280                 285

Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
    290                 295                 300

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
305                 310                 315                 320
```

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
325 330 335

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
340 345 350

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
355 360 365

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
370 375 380

Gln Ala Leu Pro Pro Arg
385 390

<210> 26
<211> 1299
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-BBZ nucleotide

<400> 26
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc
660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc
720

ggcggggccg tgcataccag gggcctggac ttcgcctgtg atatctacat ttgggctcca
780

ctggctggga cttgcggcgt gctgctgctg tctctggtca ttactctgta ttgtaagcgg
840

ggaagaaaga aactgctgta catcttcaaa cagcccttta tgaggcctgt gcagaccaca
900

caggaggaag acggctgctc ctgccggttc cccgaggaag aggaaggcgg gtgcgagctg
960

cgagtgaagt tcagcaggtc cgccgacgct cctgcatacc agcagggaca gaaccagctg
1020

tataacgagc tgaatctggg ccggagagag gaatacgacg tgctggacaa aaggcggggc
1080

cgggaccccg aaatgggagg gaagccacga cggaaaaacc cccaggaggg cctgtacaat
1140

gagctgcaaa aggacaaaat ggccgaggct tattctgaaa tcgggatgaa gggagagaga
1200

aggcgcggaa aaggccacga tggcctgtac caggggctga gcaccgctac aaaggacacc
1260

tatgatgcac tgcacatgca ggccctgccc cctcggtga
1299

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<210>    27
<211>    432
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    CD16V-BBZ amino acid


<400>    27
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
  1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
             20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
         35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
     50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175
```

```
Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
        195                 200                 205

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
    210                 215                 220

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
                245                 250                 255

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
            260                 265                 270

Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile
        275                 280                 285

Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp
    290                 295                 300

Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
305                 310                 315                 320

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
                325                 330                 335

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            340                 345                 350

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        355                 360                 365

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    370                 375                 380

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
385                 390                 395                 400

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
                405                 410                 415
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Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
420 425 430

<210> 28
<211> 1281
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-OX40Z nucleotide

<400> 28
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc 60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag 120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg 180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca 240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg 300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag 360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca 420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc 480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac 540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc 600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc
660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc
720

ggcggggccg tgcataccag gggcctggac ttcgcctgtg atatctacat ttgggctcca
780

ctggctggga cttgcggcgt gctgctgctg tccctggtca tcactctgta ttgtcgggac
840

cagagactgc cacctgatgc acacaagcca ccaggaggag gcagcttcag gacccccatc
900

caggaggaac aggccgacgc tcattccaca ctggccaaaa ttcgagtgaa gttcagcagg
960

tccgccgacg ctcctgcata ccagcaggga cagaaccagc tgtataacga gctgaatctg
1020

ggccggagag aggaatacga cgtgctggac aaaaggcggg gccgggaccc cgaaatggga
1080

gggaagccac gacggaaaaa cccccaggag ggcctgtaca atgagctgca aaaggacaaa
1140

atggccgagg cttattctga aatcgggatg aagggagaga gaaggcgcgg aaaaggccac
1200

gatggcctgt accaggggct gagcaccgct acaaaggaca cctatgatgc actgcacatg
1260

caggccctgc cccctcggtg a
1281

<210> 29
<211> 426
<212> PRT
<213> Artificial Sequence

<220>
<223> CD16V-OX40Z amino acid

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<400>    29
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
  1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
             20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
         35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
     50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
        195                 200                 205

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
    210                 215                 220
```

```
Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
                245                 250                 255

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
            260                 265                 270

Val Ile Thr Leu Tyr Cys Arg Asp Gln Arg Leu Pro Pro Asp Ala His
        275                 280                 285

Lys Pro Pro Gly Gly Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln
    290                 295                 300

Ala Asp Ala His Ser Thr Leu Ala Lys Ile Arg Val Lys Phe Ser Arg
305                 310                 315                 320

Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn
                325                 330                 335

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
            340                 345                 350

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
        355                 360                 365

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
    370                 375                 380

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
385                 390                 395                 400

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
                405                 410                 415

Ala Leu His Met Gln Ala Leu Pro Pro Arg
            420                 425


<210>    30
<211>    1239
<212>    DNA
<213>    Artificial Sequence
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<220>
<223>   CD16V-OX40LZ nucleotide

<400>   30
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc
660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc
720

ggcggggccg tgcataccag gggcctggac ttcgcctgtg atatctacat ttgggctcca
780

ctggctggga cttgcggcgt gctgctgctg tctctggtca ttactctgta ttgtgaaaga
840

gtgcagcccc tggaagagaa tgtcgggaat gccgctcgcc caagatttga aaggaacaaa
900

cgagtgaagt tcagcaggtc cgccgacgct cctgcatacc agcagggaca gaaccagctg
960

tataacgagc tgaatctggg ccggagagag gaatacgacg tgctggacaa aaggcggggc
1020

cgggaccccg aaatgggagg gaagccacga cggaaaaacc cccaggaggg cctgtacaat
1080

gagctgcaaa aggacaaaat ggccgaggct tattctgaaa tcgggatgaa gggagagaga
1140

aggcgcggaa aaggccacga tggcctgtac caggggctga gcaccgctac aaaggacacc
1200

tatgatgcac tgcacatgca ggccctgccc cctcggtga
1239

<210> 31
<211> 412
<212> PRT
<213> Artificial Sequence

<220>
<223> CD16V-OX40LZ amino acid

<400> 31
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1 5 10 15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
20 25 30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
50 55 60

```
Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
        195                 200                 205

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
    210                 215                 220

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
                245                 250                 255

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
            260                 265                 270

Val Ile Thr Leu Tyr Cys Glu Arg Val Gln Pro Leu Glu Glu Asn Val
        275                 280                 285

Gly Asn Ala Ala Arg Pro Arg Phe Glu Arg Asn Lys Arg Val Lys Phe
    290                 295                 300
```

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
305 310 315 320

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
325 330 335

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
340 345 350

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
355 360 365

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
370 375 380

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
385 390 395 400

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
405 410

<210> 32
<211> 1305
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-28Z nucleotide

<400> 32
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat tttgtcgggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc
660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc
720

ggcggggccg tgcataccag gggcctggac ttcgcctgtg atttttgggt cctggtggtc
780

gtgggagggg tgctggcatg ttactcactg ctggtcaccg tggccttcat catcttctgg
840

gtgcggagca agaggtcccg cctgctgcac agcgactata tgaacatgac cccacggaga
900

cccggcccta cacggaaaca ttaccagccc tatgctccac cccgggactt cgcagcttac
960

agaagtcgag tgaagttcag caggtccgcc gacgctcctg cataccagca gggacagaac
1020

cagctgtata acgagctgaa tctgggccgg agagaggaat acgacgtgct ggacaaaagg
1080

cggggccggg accccgaaat gggagggaag ccacgacgga aaaacccccca ggagggcctg
1140

tacaatgagc tgcaaaagga caaaatggcc gaggcttatt ctgaaatcgg gatgaaggga
1200

gagagaaggc gcggaaaagg ccacgatggc ctgtaccagg ggctgagcac cgctacaaag
1260

gacacctatg atgcactgca catgcaggcc ctgccccctc ggtga
1305

<210> 33
<211> 434
<212> PRT
<213> Artificial Sequence

<220>
<223> CD16V-28Z amino acid

<400> 33
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1 5 10 15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
20 25 30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
50 55 60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65 70 75 80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
85 90 95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
100 105 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
115 120 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
130 135 140

```
Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
        195                 200                 205

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
    210                 215                 220

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp
                245                 250                 255

Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val
            260                 265                 270

Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu
        275                 280                 285

Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr
    290                 295                 300

Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr
305                 310                 315                 320

Arg Ser Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln
                325                 330                 335

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
            340                 345                 350

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
        355                 360                 365

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
    370                 375                 380
```

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
385   390   395   400

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
                405   410   415

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
            420   425   430

Pro Arg

<210> 34
<211> 1278
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-28(H)Z nucleotide

<400> 34
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac 540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc 600

tctttctttc cccctgggat cgaggtcatg taccccctc catatctgga caacgaaaag 660

tccaatggaa ctatcattca cgtgaagggc aaacatctgt gcccatctcc cctgttccct 720

gggccaagta aaccttttg ggtcctggtg gtcgtgggag gggtgctggc atgttactca 780

ctgctggtca ccgtggcctt catcatcttc tgggtgcgga gcaagaggtc ccgcctgctg 840

cacagcgact atatgaacat gacccccacgg agacccggcc ctacacggaa acattaccag 900

ccctatgctc caccccggga cttcgcagct tacagaagtc gagtgaagtt cagcaggtcc 960

gccgacgctc ctgcatacca gcagggacag aaccagctgt ataacgagct gaatctgggc 1020

cggagagagg aatacgacgt gctggacaaa aggcggggcc gggaccccga aatgggaggg 1080

aagccacgac ggaaaaaccc ccaggagggc ctgtacaatg agctgcaaaa ggacaaaatg 1140

gccgaggctt attctgaaat cgggatgaag ggagagagaa ggcgcggaaa aggccacgat 1200

ggcctgtacc aggggctgag caccgctaca aaggacacct atgatgcact gcacatgcag 1260

gccctgcccc ctcggtga 1278

<210> 35

```
<211>    425
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    CD16V-28(H)Z amino acid


<400>    35
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
  1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
             20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
         35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
     50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190
```

```
Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ile Glu
        195                 200                 205

Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser Asn Gly Thr
    210                 215                 220

Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser Pro Leu Phe Pro
225                 230                 235                 240

Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly Val Leu
                245                 250                 255

Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val
            260                 265                 270

Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr
        275                 280                 285

Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
    290                 295                 300

Pro Arg Asp Phe Ala Ala Tyr Arg Ser Arg Val Lys Phe Ser Arg Ser
305                 310                 315                 320

Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu
                325                 330                 335

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
            340                 345                 350

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
        355                 360                 365

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
    370                 375                 380

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
385                 390                 395                 400

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
                405                 410                 415

Leu His Met Gln Ala Leu Pro Pro Arg
            420                 425
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<210> 36
<211> 1407
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-BBOX40Z nucleotide

<400> 36
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc
660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc
720

ggcggggccg tgcataccag gggcctggac ttcgcctgtg atatctacat ttgggctcca
780

ctggctggga cttgcggcgt gctgctgctg tctctggtca ttactctgta ttgtaagcgg
840

ggaagaaaga aactgctgta catcttcaaa cagcccttta tgaggcctgt gcagaccaca
900

caggaggaag acggctgctc ctgccggttc cccgaggaag aggaaggcgg gtgcgagctg
960

cgggaccaga gactgccacc tgatgcacac aagccaccag gaggaggcag cttcaggacc
1020

cccatccagg aggaacaggc cgacgctcat tccacactgg ccaaaattcg agtgaagttc
1080

agcaggtccg ccgacgctcc tgcataccag cagggacaga accagctgta taacgagctg
1140

aatctgggcc ggagagagga atacgacgtg ctggacaaaa ggcggggccg ggaccccgaa
1200

atgggaggga agccacgacg gaaaaacccc caggagggcc tgtacaatga gctgcaaaag
1260

gacaaaatgg ccgaggctta ttctgaaatc gggatgaagg gagagagaag gcgcggaaaa
1320

ggccacgatg gcctgtacca ggggctgagc accgctacaa aggacaccta tgatgcactg
1380

cacatgcagg ccctgccccc tcggtga
1407

<210> 37
<211> 468
<212> PRT
<213> Artificial Sequence

<220>
<223> CD16V-BBOX40Z amino acid

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<400>    37
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
  1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
             20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
         35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
     50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
             100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
         115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
     130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
             180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
         195                 200                 205

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
     210                 215                 220
```

```
Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
                245                 250                 255

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
            260                 265                 270

Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile
        275                 280                 285

Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp
    290                 295                 300

Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
305                 310                 315                 320

Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro Pro Gly Gly Gly
                325                 330                 335

Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp Ala His Ser Thr
            340                 345                 350

Leu Ala Lys Ile Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
        355                 360                 365

Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
    370                 375                 380

Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
385                 390                 395                 400

Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
                405                 410                 415

Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
            420                 425                 430

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
        435                 440                 445

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
    450                 455                 460
```

Leu Pro Pro Arg
465

<210> 38
<211> 1407
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-OX40BBZ nucleotide

<400> 38
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat tttgtcgggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc
660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc
720

ggcggggccg tgcataccag gggcctggac ttcgcctgtg atatctacat ttgggctcca
780

ctggctggga cttgcggcgt gctgctgctg tccctggtca tcactctgta ttgtcgggac
840

cagagactgc cacctgatgc acacaagcca ccaggaggag gcagcttcag gacccccatc
900

caggaggaac aggccgacgc tcattccaca ctggccaaaa ttaagcgggg aagaaagaaa
960

ctgctgtaca tcttcaaaca gccctttatg aggcctgtgc agaccacaca ggaggaagac
1020

ggctgctcct gccggttccc cgaggaagag gaaggcgggt gcgagctgcg agtgaagttc
1080

agcaggtccg ccgacgctcc tgcataccag cagggacaga accagctgta taacgagctg
1140

aatctgggcc ggagagagga atacgacgtg ctggacaaaa ggcggggccg ggaccccgaa
1200

atgggaggga agccacgacg gaaaaacccc caggagggcc tgtacaatga gctgcaaaag
1260

gacaaaatgg ccgaggctta ttctgaaatc gggatgaagg gagagagaag gcgcggaaaa
1320

ggccacgatg gcctgtacca ggggctgagc accgctacaa aggacaccta tgatgcactg
1380

cacatgcagg ccctgccccc tcggtga
1407

<210> 39
<211> 468
<212> PRT
<213> Artificial Sequence

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<220>
<223>    CD16V-OX40BBZ amino acid


<400>    39
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
  1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
             20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
         35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
     50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
        195                 200                 205
```

```
Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
    210                 215                 220

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
                245                 250                 255

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
            260                 265                 270

Val Ile Thr Leu Tyr Cys Arg Asp Gln Arg Leu Pro Pro Asp Ala His
        275                 280                 285

Lys Pro Pro Gly Gly Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln
    290                 295                 300

Ala Asp Ala His Ser Thr Leu Ala Lys Ile Lys Arg Gly Arg Lys Lys
305                 310                 315                 320

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
                325                 330                 335

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
            340                 345                 350

Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
        355                 360                 365

Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
    370                 375                 380

Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
385                 390                 395                 400

Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
                405                 410                 415

Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
            420                 425                 430

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
        435                 440                 445
```

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
    450   455   460

Leu Pro Pro Arg
465

<210> 40
<211> 1431
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-28BBZ nucleotide

<400> 40
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat tttgtcgggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc 660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc 720

ggcggggccg tgcataccag gggcctggac tttgcctgcg atttttgggt cctggtggtc 780

gtgggagggg tgctggcatg ttactcactg ctggtcaccg tggccttcat catcttctgg 840

gtgcggagca agaggtcccg cctgctgcac agcgactata tgaacatgac cccacggaga 900

cccggcccta cacggaaaca ttaccagccc tatgctccac cccgggactt cgcagcttac 960

agaagtaagc ggggaagaaa gaaactgctg tacatcttca aacagccctt tatgaggcct 1020

gtgcagacca cacaggagga agacggctgc tcctgccggt tccccgagga agaggaaggc 1080

gggtgcgagc tgcgagtgaa gttcagcagg tccgccgacg ctcctgcata ccagcaggga 1140

cagaaccagc tgtataacga gctgaatctg ggccggagag aggaatacga cgtgctggac 1200

aaaaggcggg gccgggaccc cgaaatggga gggaagccac gacggaaaaa cccccaggag 1260

ggcctgtaca atgagctgca aaaggacaaa atggccgagg cttattctga aatcgggatg 1320

aagggagaga gaaggcgcgg aaaaggccac gatggcctgt accaggggct gagcaccgct 1380

acaaaggaca cctatgatgc actgcacatg caggccctgc cccctcggtg a 1431

<210> 41

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<211>    476
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    CD16V-28BBZ amino acid


<400>    41
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
  1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
             20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
         35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
     50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190
```

```
Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
        195                 200                 205

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
    210                 215                 220

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp
                245                 250                 255

Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val
            260                 265                 270

Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu
        275                 280                 285

Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr
    290                 295                 300

Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr
305                 310                 315                 320

Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
                325                 330                 335

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
            340                 345                 350

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
        355                 360                 365

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
    370                 375                 380

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
385                 390                 395                 400

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
                405                 410                 415

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
            420                 425                 430
```

```
Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
        435                 440                 445

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
    450                 455                 460

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
465                 470                 475


<210>    42
<211>    1413
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    CD16V-28OX40Z nucleotide


<400>    42
atgtggcagc  tgctgctgcc  taccgctctg  ctgctgctgg  tctccgctgg  gatgcgaacc
60

gaggatctgc  ctaaagccgt  ggtcttcctg  gagcctcagt  ggtacagagt  gctggagaag
120

gactctgtga  cactgaaatg  ccagggcgct  tattcaccag  aggataacag  cactcagtgg
180

ttccacaatg  aatccctgat  cagctcccag  gcatctagtt  actttattga  cgccgctaca
240

gtggacgatt  ctggagagta  tcgatgccag  actaacctga  gcaccctgtc  cgatcccgtg
300

cagctggaag  tccacatcgg  atggctgctg  ctccaggcac  caagatgggt  cttcaaggag
360

gaagacccca  ttcacctgcg  ctgtcatagc  tggaagaata  ccgctctgca  taaagtgaca
420

tacctccaga  acggaaaggg  ccgaaaatac  ttccaccata  attccgactt  ttatatcccc
480

aaggcaaccc  tgaaagatag  tgggtcatat  ttttgtcggg  ggctggtggg  aagtaaaaac
540
```

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc
660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc
720

ggcggggccg tgcataccag gggcctggac tttgcctgcg atttttgggt cctggtggtc
780

gtgggagggg tgctggcatg ttactcactg ctggtcaccg tggccttcat catcttctgg
840

gtgcggagca agaggtcccg cctgctgcac agcgactata tgaacatgac cccacggaga
900

cccggcccta cacggaaaca ttaccagccc tatgctccac cccgggactt cgcagcttac
960

agaagtcggg accagagact gccacctgat gcacacaagc caccaggagg aggcagcttc
1020

aggaccccca tccaggagga acaggccgac gctcattcca cactggccaa aattcgagtg
1080

aagttcagca ggtccgccga cgctcctgca taccagcagg gacagaacca gctgtataac
1140

gagctgaatc tgggccggag agaggaatac gacgtgctgg acaaaaggcg gggccgggac
1200

cccgaaatgg gagggaagcc acgacggaaa aacccccagg agggcctgta caatgagctg
1260

caaaaggaca aaatggccga ggcttattct gaaatcggga tgaagggaga gagaaggcgc
1320

ggaaaaggcc acgatggcct gtaccagggg ctgagcaccg ctacaaagga cacctatgat
1380

gcactgcaca tgcaggccct gccccctcgg tga
1413

```
<210>    43
<211>    470
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    CD16V-28OX40Z amino acid


<400>    43
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
  1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
             20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
         35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
     50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175
```

```
Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
        195                 200                 205

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
    210                 215                 220

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp
                245                 250                 255

Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val
            260                 265                 270

Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu
        275                 280                 285

Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr
    290                 295                 300

Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr
305                 310                 315                 320

Arg Ser Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro Pro Gly
                325                 330                 335

Gly Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp Ala His
            340                 345                 350

Ser Thr Leu Ala Lys Ile Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
        355                 360                 365

Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
    370                 375                 380

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
385                 390                 395                 400

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
                405                 410                 415
```

```
Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
            420                 425                 430

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
        435                 440                 445

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
    450                 455                 460

Gln Ala Leu Pro Pro Arg
465                 470


<210>    44
<211>    1371
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    CD16V-28OX40LZ nucleotide


<400>    44
atgtggcagc  tgctgctgcc  taccgctctg  ctgctgctgg  tctccgctgg  gatgcgaacc
60

gaggatctgc  ctaaagccgt  ggtcttcctg  gagcctcagt  ggtacagagt  gctggagaag
120

gactctgtga  cactgaaatg  ccagggcgct  tattcaccag  aggataacag  cactcagtgg
180

ttccacaatg  aatccctgat  cagctcccag  gcatctagtt  actttattga  cgccgctaca
240

gtggacgatt  ctggagagta  tcgatgccag  actaacctga  gcaccctgtc  cgatcccgtg
300

cagctggaag  tccacatcgg  atggctgctg  ctccaggcac  caagatgggt  cttcaaggag
360

gaagacccca  ttcacctgcg  ctgtcatagc  tggaagaata  ccgctctgca  taaagtgaca
420

tacctccaga  acggaaaggg  ccgaaaatac  ttccaccata  attccgactt  ttatatcccc
480
```

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc
660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc
720

ggcggggccg tgcataccag gggcctggac ttcgcctgtg atttttgggt cctggtggtc
780

gtgggagggg tgctggcatg ttactcactg ctggtcaccg tggccttcat catcttctgg
840

gtgcggagca agaggtcccg cctgctgcac agcgactata tgaacatgac cccacggaga
900

cccggcccta cacggaaaca ttaccagccc tatgctccac cccgggactt cgcagcttac
960

agaagtgaaa gagtgcagcc cctggaagag aatgtcggga atgccgctcg cccaagattt
1020

gaaaggaaca aacgagtgaa gttcagcagg tccgccgacg ctcctgcata ccagcaggga
1080

cagaaccagc tgtataacga gctgaatctg ggccggagag aggaatacga cgtgctggac
1140

aaaaggcggg gccgggaccc cgaaatggga gggaagccac gacggaaaaa cccccaggag
1200

ggcctgtaca atgagctgca aaaggacaaa atggccgagg cttattctga aatcgggatg
1260

aagggagaga gaaggcgcgg aaaaggccac gatggcctgt accaggggct gagcaccgct
1320

acaaaggaca cctatgatgc actgcacatg caggccctgc cccctcggtg a
1371

```
<210>    45
<211>    456
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    CD16V-28OX40LZ amino acid


<400>    45
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
  1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
             20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
         35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
     50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175
```

```
Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
        195                 200                 205

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
    210                 215                 220

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp
                245                 250                 255

Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val
            260                 265                 270

Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu
        275                 280                 285

Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr
    290                 295                 300

Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr
305                 310                 315                 320

Arg Ser Glu Arg Val Gln Pro Leu Glu Glu Asn Val Gly Asn Ala Ala
                325                 330                 335

Arg Pro Arg Phe Glu Arg Asn Lys Arg Val Lys Phe Ser Arg Ser Ala
            340                 345                 350

Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
        355                 360                 365

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
    370                 375                 380

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
385                 390                 395                 400

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
                405                 410                 415
```

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
            420   425   430

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
        435   440   445

His Met Gln Ala Leu Pro Pro Arg
    450   455

<210> 46
<211> 1404
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-28(H)BBZ nucleotide

<400> 46
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc 60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag 120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg 180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca 240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg 300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag 360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca 420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc 480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac 540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctgggat cgaggtcatg taccccccctc catatctgga caacgaaaag
660

tccaatggaa ctatcattca cgtgaagggc aaacatctgt gcccatctcc cctgttccct
720

gggccaagta aacctttttg ggtcctggtg gtcgtgggag gggtgctggc atgttactca
780

ctgctggtca ccgtggcctt catcatcttc tgggtgcgga gcaagaggtc ccgcctgctg
840

cacagcgact atatgaacat gaccccacgg agacccggcc ctacacggaa acattaccag
900

ccctatgctc caccccggga cttcgcagct tacagaagta agcggggaag aaagaaactg
960

ctgtacatct tcaaacagcc ctttatgagg cctgtgcaga ccacacagga ggaagacggc
1020

tgctcctgcc ggttccccga ggaagaggaa ggcgggtgcg agctgcgagt gaagttcagc
1080

aggtccgccg acgctcctgc ataccagcag ggacagaacc agctgtataa cgagctgaat
1140

ctgggccgga gagaggaata cgacgtgctg gacaaaaggc ggggccggga ccccgaaatg
1200

ggagggaagc cacgacggaa aaacccccag gagggcctgt acaatgagct gcaaaaggac
1260

aaaatggccg aggcttattc tgaaatcggg atgaagggag agagaaggcg cggaaaaggc
1320

cacgatggcc tgtaccaggg gctgagcacc gctacaaagg acacctatga tgcactgcac
1380

atgcaggccc tgccccctcg gtga
1404

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<210>    47
<211>    467
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    CD16V-28(H)BBZ amino acid


<400>    47
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
  1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
             20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
         35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
     50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175
```

```
Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ile Glu
        195                 200                 205

Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser Asn Gly Thr
    210                 215                 220

Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser Pro Leu Phe Pro
225                 230                 235                 240

Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly Val Leu
                245                 250                 255

Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val
            260                 265                 270

Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr
        275                 280                 285

Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
    290                 295                 300

Pro Arg Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu
305                 310                 315                 320

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
                325                 330                 335

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
            340                 345                 350

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
        355                 360                 365

Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
    370                 375                 380

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
385                 390                 395                 400

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
                405                 410                 415
```

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
420 425 430

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
435 440 445

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
450 455 460

Pro Pro Arg
465

<210> 48
<211> 1386
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-28(H)OX40Z nucleotide

<400> 48
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctgggat cgaggtcatg taccccctc catatctgga caacgaaaag
660

tccaatggaa ctatcattca cgtgaagggc aaacatctgt gcccatctcc cctgttccct
720

gggccaagta aacctttttg ggtcctggtg gtcgtgggag gggtgctggc atgttactca
780

ctgctggtca ccgtggcctt catcatcttc tgggtgcgga gcaagaggtc ccgcctgctg
840

cacagcgact atatgaacat gacccccacgg agacccggcc ctacacggaa acattaccag
900

ccctatgctc caccccggga cttcgcagct tacagaagtc gggaccagag actgccacct
960

gatgcacaca agccaccagg aggaggcagc ttcaggaccc ccatccagga ggaacaggcc
1020

gacgctcatt ccacactggc caaaattcga gtgaagttca gcaggtccgc cgacgctcct
1080

gcataccagc agggacagaa ccagctgtat aacgagctga atctgggccg gagagaggaa
1140

tacgacgtgc tggacaaaag gcggggccgg gaccccgaaa tgggagggaa gccacgacgg
1200

aaaaaccccc aggagggcct gtacaatgag ctgcaaaagg acaaaatggc cgaggcttat
1260

tctgaaatcg ggatgaaggg agagagaagg cgcggaaaag gccacgatgg cctgtaccag
1320

gggctgagca ccgctacaaa ggacacctat gatgcactgc acatgcaggc cctgccccct
1380

cggtga
1386

<210> 49
<211> 461
<212> PRT
<213> Artificial Sequence

<220>
<223> CD16V-28(H)OX40Z amino acid

<400> 49
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1 5 10 15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
20 25 30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
50 55 60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65 70 75 80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
85 90 95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
100 105 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
115 120 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
130 135 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145 150 155 160

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Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ile Glu
        195                 200                 205

Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser Asn Gly Thr
    210                 215                 220

Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser Pro Leu Phe Pro
225                 230                 235                 240

Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly Val Leu
                245                 250                 255

Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val
            260                 265                 270

Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr
        275                 280                 285

Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
    290                 295                 300

Pro Arg Asp Phe Ala Ala Tyr Arg Ser Arg Asp Gln Arg Leu Pro Pro
305                 310                 315                 320

Asp Ala His Lys Pro Pro Gly Gly Gly Ser Phe Arg Thr Pro Ile Gln
                325                 330                 335

Glu Glu Gln Ala Asp Ala His Ser Thr Leu Ala Lys Ile Arg Val Lys
            340                 345                 350

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
        355                 360                 365

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
    370                 375                 380

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
385                 390                 395                 400
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Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
405 410 415

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
420 425 430

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
435 440 445

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
450 455 460

<210> 50
<211> 1344
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-28(H)OX40LZ nucleotide

<400> 50
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctgggat cgaggtcatg tacccccctc catatctgga caacgaaaag
660

tccaatggaa ctatcattca cgtgaagggc aaacatctgt gcccatctcc cctgttccct
720

gggccaagta aacctttttg ggtcctggtg gtcgtgggag gggtgctggc atgttactca
780

ctgctggtca ccgtggcctt catcatcttc tgggtgcgga gcaagaggtc ccgcctgctg
840

cacagcgact atatgaacat gaccccacgg agacccggcc ctacacggaa acattaccag
900

ccctatgctc caccccggga cttcgcagct tacagaagtg aaagagtgca gcccctggaa
960

gagaatgtcg ggaatgccgc tcgcccaaga tttgaaagga acaaacgagt gaagttcagc
1020

aggtccgccg acgctcctgc ataccagcag ggacagaacc agctgtataa cgagctgaat
1080

ctgggccgga gagaggaata cgacgtgctg gacaaaaggc ggggccggga ccccgaaatg
1140

ggagggaagc cacgacggaa aaacccccag gagggcctgt acaatgagct gcaaaaggac
1200

aaaatggccg aggcttattc tgaaatcggg atgaagggag agagaaggcg cggaaaaggc
1260

cacgatggcc tgtaccaggg gctgagcacc gctacaaagg acacctatga tgcactgcac
1320

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a t g c a g g c c c           t g c c c c c t c g           g t g a
1344


<210>    51
<211>    447
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    CD16V-28(H)OX40LZ amino acid


<400>    51
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
  1               5                   10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
           100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
       115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
   130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160
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Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ile Glu
        195                 200                 205

Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser Asn Gly Thr
    210                 215                 220

Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser Pro Leu Phe Pro
225                 230                 235                 240

Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly Val Leu
                245                 250                 255

Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val
            260                 265                 270

Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr
        275                 280                 285

Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
    290                 295                 300

Pro Arg Asp Phe Ala Ala Tyr Arg Ser Glu Arg Val Gln Pro Leu Glu
305                 310                 315                 320

Glu Asn Val Gly Asn Ala Ala Arg Pro Arg Phe Glu Arg Asn Lys Arg
                325                 330                 335

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln
            340                 345                 350

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
        355                 360                 365

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
    370                 375                 380

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
385                 390                 395                 400
```

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
405 410 415

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
420 425 430

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
435 440 445

<210> 52
<211> 1365
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-BBOX40LZ nucleotide

<400> 52
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc
660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc
720

ggcggggccg tgcataccag gggcctggac ttcgcctgtg atatctacat ttgggctcca
780

ctggctggga cttgcggcgt gctgctgctg tctctggtca ttactctgta ttgtaagcgg
840

ggaagaaaga aactgctgta catcttcaaa cagcccttta tgaggcctgt gcagaccaca
900

caggaggaag acggctgctc ctgccggttc cccgaggaag aggaaggcgg gtgcgagctg
960

gaaagagtgc agcccctgga agagaatgtc gggaatgccg ctcgcccaag atttgaaagg
1020

aacaaacgag tgaagttcag caggtccgcc gacgctcctg cataccagca gggacagaac
1080

cagctgtata acgagctgaa tctgggccgg agagaggaat acgacgtgct ggacaaaagg
1140

cggggccggg accccgaaat gggagggaag ccacgacgga aaaacccca ggagggcctg
1200

tacaatgagc tgcaaaagga caaaatggcc gaggcttatt ctgaaatcgg gatgaaggga
1260

gagagaaggc gcggaaaagg ccacgatggc ctgtaccagg ggctgagcac cgctacaaag
1320

gacacctatg atgcactgca catgcaggcc ctgcccctc ggtga
1365

<210> 53
<211> 454
<212> PRT
<213> Artificial Sequence

<220>
<223> CD16V-BBOX40LZ amino acid

<400> 53
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1 5 10 15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
20 25 30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
50 55 60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65 70 75 80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
85 90 95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
100 105 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
115 120 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
130 135 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145 150 155 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
165 170 175

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Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
        195                 200                 205

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
    210                 215                 220

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
                245                 250                 255

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
            260                 265                 270

Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile
        275                 280                 285

Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp
    290                 295                 300

Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
305                 310                 315                 320

Glu Arg Val Gln Pro Leu Glu Glu Asn Val Gly Asn Ala Ala Arg Pro
                325                 330                 335

Arg Phe Glu Arg Asn Lys Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
            340                 345                 350

Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
        355                 360                 365

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
    370                 375                 380

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
385                 390                 395                 400

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
                405                 410                 415
```

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
            420   425   430

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
        435   440   445

Gln Ala Leu Pro Pro Arg
    450

<210> 54
<211> 1239
<212> DNA
<213> Artificial Sequence

<220>
<223> CD16V-ZOX40L nucleotide

<400> 54
atgtggcagc tgctgctgcc taccgctctg ctgctgctgg tctccgctgg gatgcgaacc
60

gaggatctgc ctaaagccgt ggtcttcctg gagcctcagt ggtacagagt gctggagaag
120

gactctgtga cactgaaatg ccagggcgct tattcaccag aggataacag cactcagtgg
180

ttccacaatg aatccctgat cagctcccag gcatctagtt actttattga cgccgctaca
240

gtggacgatt ctggagagta tcgatgccag actaacctga gcaccctgtc cgatcccgtg
300

cagctggaag tccacatcgg atggctgctg ctccaggcac caagatgggt cttcaaggag
360

gaagacccca ttcacctgcg ctgtcatagc tggaagaata ccgctctgca taaagtgaca
420

tacctccaga acggaaaggg ccgaaaatac ttccaccata attccgactt ttatatcccc
480

aaggcaaccc tgaaagatag tgggtcatat ttttgtcggg ggctggtggg aagtaaaaac
540

gtctcaagcg agactgtgaa tatcaccatt acacagggcc tggctgtcag caccatctcc
600

tctttctttc cccctggggc caaacctacc acaactcctg ctccaagacc acccacaccc
660

gctcctacta ttgcatctca gccactgagt ctgcgaccag aggcctgccg gcccgccgcc
720

ggcggggccg tgcataccag gggcctggac ttcgcctgtg atatctacat ttgggctcca
780

ctggctggga cttgcggcgt gctgctgctg tctctggtca ttactctgta ttgtcgagtg
840

aagttcagca ggtccgccga cgctcctgca taccagcagg gacagaacca gctgtataac
900

gagctgaatc tgggccggag agaggaatac gacgtgctgg acaaaaggcg gggccgggac
960

cccgaaatgg gagggaagcc acgacggaaa aacccccagg agggcctgta caatgagctg
1020

caaaaggaca aaatggccga ggcttattct gaaatcggga tgaagggaga gagaaggcgc
1080

ggaaaaggcc acgatggcct gtaccagggg ctgagcaccg ctacaaagga cacctatgat
1140

gcactgcaca tgcaggccct gccccctcgg gaaagagtgc agcccctgga agagaatgtc
1200

gggaatgccg ctcgcccaag atttgaaagg aacaaatga
1239

<210> 55
<211> 412
<212> PRT
<213> Artificial Sequence

<220>
<223> CD16V-ZOX40L amino acid

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<400>    55
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
  1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
                 20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
         35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
     50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
 65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                 85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Ala Lys
        195                 200                 205

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
    210                 215                 220
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Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
225                 230                 235                 240

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
                245                 250                 255

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
            260                 265                 270

Val Ile Thr Leu Tyr Cys Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
        275                 280                 285

Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
    290                 295                 300

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
305                 310                 315                 320

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
                325                 330                 335

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
            340                 345                 350

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
        355                 360                 365

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
    370                 375                 380

Gln Ala Leu Pro Pro Arg Glu Arg Val Gln Pro Leu Glu Glu Asn Val
385                 390                 395                 400

Gly Asn Ala Ala Arg Pro Arg Phe Glu Arg Asn Lys
                405                 410


<210>  56
<211>  63
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  CD8 alpha nucleotide
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<400> 56
atggccttac cagtgaccgc cttgctcctg ccgctggcct tgctgctcca cgccgccagg
60

c c g
63

<210> 57
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<223> CD8 alpha nucleotide codon optimization

<400> 57
atggctctgc cagtgactgc actgctgctg ccactggccc tgctgctgca cgcagctcga
60

c c t
63

<210> 58
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 alpha amino acid

<400> 58
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
20

<210> 59
<211> 405

<212>   DNA
<213>   Artificial Sequence

<220>
<223>   NKG2D nucleotide

<400>   59
ttattcaacc aagaagttca aattcccttg accgaaagtt actgtggccc atgtcctaaa
60

aactggatat gttacaaaaa taactgctac caattttttg atgagagtaa aaactggtat
120

gagagccagg cttcttgtat gtctcaaaat gccagccttc tgaaagtata cagcaaagag
180

gaccaggatt tacttaaact ggtgaagtca tatcattgga tgggactagt acacattcca
240

acaaatggat cttggcagtg ggaagatggc tccattctct cacccaacct actaacaata
300

attgaaatgc agaagggaga ctgtgcactc tatgcctcga gctttaaagg ctatatagaa
360

aactgttcaa ctccaaatac atacatctgc atgcaaagga ctgtg
405

<210>   60
<211>   405
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   NKG2D nucleotide codon optimization

<400>   60
ctgttcaacc aggaggtcca gatcccactg accgaaagtt actgcggacc atgtcccaag
60

aactggatct gctacaagaa caactgttac cagttctttg acgagtctaa gaactggtat
120

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gaatctcagg ccagttgcat gtcacagaat gcttcactgc tgaaggtgta cagcaaagag
180

gaccaggatc tgctgaagct ggtgaaatcc tatcactgga tgggcctggt ccatatccca
240

accaacgggt cttggcagtg ggaggacgga agcattctgt cccccaatct gctgacaatc
300

attgaaatgc agaagggcga ttgtgctctg tacgcaagct ccttcaaagg gtatatcgag
360

aactgctcca cccccaatac atacatttgt atgcagagga cagtg
405


<210>   61
<211>   135
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   NKG2D amino acid


<400>   61
Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr Glu Ser Tyr Cys Gly
  1               5                  10                  15

Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn Asn Cys Tyr Gln Phe
             20                  25                  30

Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln Ala Ser Cys Met Ser
         35                  40                  45

Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys Glu Asp Gln Asp Leu
     50                  55                  60

Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly Leu Val His Ile Pro
 65                  70                  75                  80

Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser Ile Leu Ser Pro Asn
                 85                  90                  95
```

Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp Cys Ala Leu Tyr Ala
            100   105   110

Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser Thr Pro Asn Thr Tyr
        115   120   125

Ile Cys Met Gln Arg Thr Val
    130   135

<210>   62
<211>   1023
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   NKG2D-Z nucleotide

<400>   62
atggctctgc cagtgactgc actgctgctg ccactggccc tgctgctgca cgcagctcga
60

cctctgttca accaggaggt ccagatccca ctgaccgaaa gttactgcgg accatgtccc
120

aagaactgga tctgctacaa gaacaactgt taccagttct ttgacgagtc taagaactgg
180

tatgaatctc aggccagttg catgtcacag aatgcttcac tgctgaaggt gtacagcaaa
240

gaggaccagg atctgctgaa gctggtgaaa tcctatcact ggatgggcct ggtccatatc
300

ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccacccccaa tacatacatt tgtatgcaga ggacagtggc aaaacctacc
480

acaactcctg caccacgccc ccctactcca gcacctacca tcgcatctca gccactgagt
540

ctgcgaccag aggcctgccg gcccgccgcc ggcggggccg tccataccag agggctggac
600

tttgcctgcg atatctacat ttgggcccct ctggctggaa catgtggcgt gctgctgctg
660

tccctggtca ttactctgta ttgtcgagtg aagttcagca ggtccgccga cgctcctgca
720

taccagcagg gacagaacca gctgtataac gagctgaatc tgggccggag agaggaatac
780

gacgtgctgg acaaaaggcg gggccgggac cccgaaatgg gagggaagcc acgacggaaa
840

aacccccagg agggcctgta caatgagctg caaaaggaca aaatggccga ggcttattct
900

gaaatcggga tgaagggaga gagaaggcgc ggaaaaggcc acgatggcct gtaccagggg
960

ctgagcaccg ctacaaagga cacctatgat gcactgcaca tgcaggccct gccccctcgg
1020

t g a
1023

<210> 63
<211> 340
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-Z amino acid

<400> 63
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
20 25 30

```
Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
         35                  40                  45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
     50                  55                  60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Lys Pro Thr
145                 150                 155                 160

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                165                 170                 175

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            180                 185                 190

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
        195                 200                 205

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
    210                 215                 220

Thr Leu Tyr Cys Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
225                 230                 235                 240

Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
                245                 250                 255

Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
            260                 265                 270
```

```
Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
        275                 280                 285

Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
    290                 295                 300

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
305                 310                 315                 320

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
                325                 330                 335

Leu Pro Pro Arg
            340


<210>    64
<211>    1149
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    NKG2D-BBZ nucleotide


<400>    64
atggctctgc  cagtgactgc  actgctgctg  ccactggccc  tgctgctgca  cgcagctcga
60

cctctgttca  accaggaggt  ccagatccca  ctgaccgaaa  gttactgcgg  accatgtccc
120

aagaactgga  tctgctacaa  gaacaactgt  taccagttct  ttgacgagtc  taagaactgg
180

tatgaatctc  aggccagttg  catgtcacag  aatgcttcac  tgctgaaggt  gtacagcaaa
240

gaggaccagg  atctgctgaa  gctggtgaaa  tcctatcact  ggatgggcct  ggtccatatc
300

ccaaccaacg  ggtcttggca  gtgggaggac  ggaagcattc  tgtcccccaa  tctgctgaca
360

atcattgaaa  tgcagaaggg  cgattgtgct  ctgtacgcaa  gctccttcaa  agggtatatc
420
```

gagaactgct ccaccccaa tacatacatt tgtatgcaga ggacagtggc aaaacctacc
480

acaactcctg caccacgccc ccctactcca gcacctacca tcgcatctca gccactgagt
540

ctgcgaccag aggcctgccg gcccgccgcc ggcggggccg tccataccag agggctggac
600

tttgcctgcg atatctacat ttgggcccct ctggctggaa catgtggcgt gctgctgctg
660

tccctggtca ttactctgta ttgtaagcgg ggaagaaaga aactgctgta catcttcaaa
720

cagcccttta tgaggcctgt gcagaccaca caggaggaag acggctgctc ctgccggttc
780

cccgaggaag aggaaggcgg gtgcgagctg cgagtgaagt tcagcaggtc cgccgacgct
840

cctgcatacc agcagggaca gaaccagctg tataacgagc tgaatctggg ccggagagag
900

gaatacgacg tgctggacaa aaggcggggc cgggaccccg aaatgggagg gaagccacga
960

cggaaaaacc cccaggaggg cctgtacaat gagctgcaaa aggacaaaat ggccgaggct
1020

tattctgaaa tcgggatgaa gggagagaga aggcgcggaa aaggccacga tggcctgtac
1080

caggggctga gcaccgctac aaaggacacc tatgatgcac tgcacatgca ggccctgccc
1140

c c t c g g t g a
1149

<210> 65
<211> 382
<212> PRT
<213> Artificial Sequence

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<220>
<223>   NKG2D-BBZ amino acid


<400>   65
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
             20                  25                  30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
         35                  40                  45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
     50                  55                  60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Lys Pro Thr
145                 150                 155                 160

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                165                 170                 175

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            180                 185                 190

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
        195                 200                 205
```

```
Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
    210                 215                 220

Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
225                 230                 235                 240

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
                245                 250                 255

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
            260                 265                 270

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn
        275                 280                 285

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
    290                 295                 300

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
305                 310                 315                 320

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
                325                 330                 335

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
            340                 345                 350

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
        355                 360                 365

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
    370                 375                 380



<210>    66
<211>    1131
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    NKG2D-OX40Z nucleotide
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<400>   66
atggctctgc cagtgactgc actgctgctg ccactggccc tgctgctgca cgcagctcga
60

cctctgttca accaggaggt ccagatccca ctgaccgaaa gttactgcgg accatgtccc
120

aagaactgga tctgctacaa gaacaactgt taccagttct ttgacgagtc taagaactgg
180

tatgaatctc aggccagttg catgtcacag aatgcttcac tgctgaaggt gtacagcaaa
240

gaggaccagg atctgctgaa gctggtgaaa tcctatcact ggatgggcct ggtccatatc
300

ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccacccccaa tacatacatt tgtatgcaga ggacagtggc aaaacctacc
480

acaactcctg caccacgccc ccctactcca gcacctacca tcgcatctca gccactgagt
540

ctgcgaccag aggcctgccg gcccgccgcc ggcggggccg tccataccag agggctggac
600

tttgcctgcg atatctacat ttgggcccct ctggctggaa catgtggcgt gctgctgctg
660

tccctggtca ttactctgta ttgtcgggac cagagactgc cacctgatgc acacaagcca
720

ccaggaggag gcagcttcag gacccccatc caggaggaac aggccgacgc tcattccaca
780

ctggccaaaa ttcgagtgaa gttcagcagg tccgccgacg ctcctgcata ccagcaggga
840

cagaaccagc tgtataacga gctgaatctg ggccggagag aggaatacga cgtgctggac
900

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aaaaggcggg gccgggaccc cgaaatggga gggaagccac gacggaaaaa cccccaggag
960

ggcctgtaca atgagctgca aaaggacaaa atggccgagg cttattctga aatcgggatg
1020

aagggagaga gaaggcgcgg aaaaggccac gatggcctgt accaggggct gagcaccgct
1080

acaaaggaca cctatgatgc actgcacatg caggccctgc cccctcggtg a
1131


<210>   67
<211>   376
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   NKG2D-OX40Z amino acid


<400>   67
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
             20                  25                  30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
         35                  40                  45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
     50                  55                  60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110
```

```
Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Lys Pro Thr
145                 150                 155                 160

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                165                 170                 175

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            180                 185                 190

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
        195                 200                 205

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
    210                 215                 220

Thr Leu Tyr Cys Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro
225                 230                 235                 240

Pro Gly Gly Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp
                245                 250                 255

Ala His Ser Thr Leu Ala Lys Ile Arg Val Lys Phe Ser Arg Ser Ala
            260                 265                 270

Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
        275                 280                 285

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
    290                 295                 300

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
305                 310                 315                 320

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
                325                 330                 335

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
            340                 345                 350
```

```
Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
        355                 360                 365

His Met Gln Ala Leu Pro Pro Arg
    370                 375


<210>    68
<211>    1089
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    NKG2D-ZOX40L nucleotide


<400>    68
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60

cctctgttca  accaggaggt  ccagatccca  ctgaccgaaa  gttactgcgg  accatgtccc
120

aagaactgga  tctgctacaa  gaacaactgt  taccagttct  ttgacgagtc  taagaactgg
180

tatgaatctc  aggccagttg  catgtcacag  aatgcttcac  tgctgaaggt  gtacagcaaa
240

gaggaccagg  atctgctgaa  gctggtgaaa  tcctatcact  ggatgggcct  ggtccatatc
300

ccaaccaacg  ggtcttggca  gtgggaggac  ggaagcattc  tgtcccccaa  tctgctgaca
360

atcattgaaa  tgcagaaggg  cgattgtgct  ctgtacgcaa  gctccttcaa  agggtatatc
420

gagaactgct  ccacccccaa  tacatacatt  tgtatgcaga  ggacagtggc  aaaacctacc
480

acaactcctg  caccacgccc  ccctactcca  gcacctacca  tcgcatctca  gccactgagt
540

ctgcgaccag  aggcctgccg  gcccgccgcc  ggcggggccg  tccataccag  agggctggac
600
```

tttgcctgcg atatctacat ttgggcccct ctggctggaa catgtggcgt gctgctgctg
660

tccctggtca ttactctgta ttgtcgagtg aagttcagca ggtccgccga cgctcctgca
720

taccagcagg gacagaacca gctgtataac gagctgaatc tgggccggag agaggaatac
780

gacgtgctgg acaaaaggcg gggccgggac cccgaaatgg gagggaagcc acgacggaaa
840

aacccccagg agggcctgta caatgagctg caaaaggaca aaatggccga ggcttattct
900

gaaatcggga tgaagggaga gagaaggcgc ggaaaaggcc acgatggcct gtaccagggg
960

ctgagcaccg ctacaaagga cacctatgat gcactgcaca tgcaggccct gccccctcgg
1020

gaaagagtgc agcccctgga agagaatgtc gggaatgccg ctcgcccaag atttgaaagg
1080

a a c a a a t g a
1089

<210> 69
<211> 362
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-ZOX40L amino acid

<400> 69
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
20 25 30

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Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
         35                  40                  45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
     50                  55                  60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Lys Pro Thr
145                 150                 155                 160

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                165                 170                 175

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            180                 185                 190

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
        195                 200                 205

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
    210                 215                 220

Thr Leu Tyr Cys Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
225                 230                 235                 240

Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
                245                 250                 255

Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
            260                 265                 270
```

Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
        275   280   285

Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
    290   295   300

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
305   310   315   320

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
                325   330   335

Leu Pro Pro Arg Glu Arg Val Gln Pro Leu Glu Glu Asn Val Gly Asn
            340   345   350

Ala Ala Arg Pro Arg Phe Glu Arg Asn Lys
        355   360

<210> 70
<211> 1155
<212> DNA
<213> Artificial Sequence

<220>
<223> NKG2D-28Z nucleotide

<400> 70
atggctctgc cagtgactgc actgctgctg ccactggccc tgctgctgca cgcagctcga
60

cctctgttca accaggaggt ccagatccca ctgaccgaaa gttactgcgg accatgtccc
120

aagaactgga tctgctacaa gaacaactgt taccagttct ttgacgagtc taagaactgg
180

tatgaatctc aggccagttg catgtcacag aatgcttcac tgctgaaggt gtacagcaaa
240

gaggaccagg atctgctgaa gctggtgaaa tcctatcact ggatgggcct ggtccatatc
300

ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccaccccaa tacatacatt tgtatgcaga ggacagtggc aaaacctacc
480

acaactcctg caccacgccc ccctactcca gcacctacca tcgcatctca gccactgagt
540

ctgcgaccag aggcctgccg gcccgccgcc ggcggggccg tccataccag agggctggac
600

tttgcctgcg atttttgggt cctggtggtc gtgggagggg tgctggcatg ttactcactg
660

ctggtcaccg tggccttcat catcttctgg gtgcggagca agaggtcccg cctgctgcac
720

agcgactata tgaacatgac cccacggaga cccggcccta cacggaaaca ttaccagccc
780

tatgctccac cccgggactt cgcagcttac agaagtcgag tgaagttcag caggtccgcc
840

gacgctcctg cataccagca gggacagaac cagctgtata acgagctgaa tctgggccgg
900

agagaggaat acgacgtgct ggacaaaagg cggggccggg accccgaaat gggagggaag
960

ccacgacgga aaaacccca ggagggcctg tacaatgagc tgcaaaagga caaaatggcc
1020

gaggcttatt ctgaaatcgg gatgaaggga gagagaaggc gcggaaaagg ccacgatggc
1080

ctgtaccagg ggctgagcac cgctacaaag gacacctatg atgcactgca catgcaggcc
1140

c t g c c c c c t c g g t g a
1155

<210> 71

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<211>    384
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    NKG2D-28Z amino acid


<400>    71
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
             20                  25                  30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
         35                  40                  45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
     50                  55                  60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Lys Pro Thr
145                 150                 155                 160

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                165                 170                 175

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            180                 185                 190
```

```
Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp Val Leu
        195                 200                 205

Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val
    210                 215                 220

Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His
225                 230                 235                 240

Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys
                245                 250                 255

His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
            260                 265                 270

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
        275                 280                 285

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
    290                 295                 300

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
305                 310                 315                 320

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
                325                 330                 335

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
            340                 345                 350

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
        355                 360                 365

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
    370                 375                 380
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<210> 72
<211> 1128
<212> DNA
<213> Artificial Sequence

<220>

<223> NKG2D-28(H)Z nucleotide

<400> 72
atggctctgc cagtgactgc actgctgctg ccactggccc tgctgctgca cgcagctcga
60

cctctgttca accaggaggt ccagatccca ctgaccgaaa gttactgcgg accatgtccc
120

aagaactgga tctgctacaa gaacaactgt taccagttct ttgacgagtc taagaactgg
180

tatgaatctc aggccagttg catgtcacag aatgcttcac tgctgaaggt gtacagcaaa
240

gaggaccagg atctgctgaa gctggtgaaa tcctatcact ggatgggcct ggtccatatc
300

ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccacccccaa tacatacatt tgtatgcaga ggacagtgat cgaggtcatg
480

tacccccctc catatctgga caacgaaaag tccaatggaa ctatcattca cgtgaagggc
540

aaacatctgt gcccatctcc cctgttccct gggccaagta aacctttttg ggtcctggtg
600

gtcgtgggag gggtgctggc atgttactca ctgctggtca ccgtggcctt catcatcttc
660

tgggtgcgga gcaagaggtc ccgcctgctg cacagcgact atatgaacat gaccccacgg
720

agacccggcc ctacacggaa acattaccag ccctatgctc caccccggga cttcgcagct
780

tacagaagtc gagtgaagtt cagcaggtcc gccgacgctc ctgcatacca gcagggacag
840

aaccagctgt ataacgagct gaatctgggc cggagagagg aatacgacgt gctggacaaa
900

aggcggggcc gggaccccga aatgggaggg aagccacgac ggaaaaaccc ccaggagggc
960

ctgtacaatg agctgcaaaa ggacaaaatg gccgaggctt attctgaaat cgggatgaag
1020

ggagagagaa ggcgcggaaa aggccacgat ggcctgtacc aggggctgag caccgctaca
1080

aaggacacct atgatgcact gcacatgcag gccctgcccc ctcggtga
1128

<210> 73
<211> 375
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-28(H)Z amino acid

<400> 73
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
20 25 30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
35 40 45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
50 55 60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
65 70 75 80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
85 90 95

```
Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ile Glu Val Met
145                 150                 155                 160

Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser Asn Gly Thr Ile Ile
                165                 170                 175

His Val Lys Gly Lys His Leu Cys Pro Ser Pro Leu Phe Pro Gly Pro
            180                 185                 190

Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
        195                 200                 205

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
    210                 215                 220

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
225                 230                 235                 240

Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
                245                 250                 255

Asp Phe Ala Ala Tyr Arg Ser Arg Val Lys Phe Ser Arg Ser Ala Asp
            260                 265                 270

Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
        275                 280                 285

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
    290                 295                 300

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
305                 310                 315                 320

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
                325                 330                 335
```

```
Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
            340                 345                 350

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
        355                 360                 365

Met Gln Ala Leu Pro Pro Arg
    370                 375
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<210>    74
<211>    1257
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    NKG2D-BBOX40Z nucleotide


<400>    74
atggctctgc  cagtgactgc  actgctgctg  ccactggccc  tgctgctgca  cgcagctcga
60

cctctgttca  accaggaggt  ccagatccca  ctgaccgaaa  gttactgcgg  accatgtccc
120

aagaactgga  tctgctacaa  gaacaactgt  taccagttct  ttgacgagtc  taagaactgg
180

tatgaatctc  aggccagttg  catgtcacag  aatgcttcac  tgctgaaggt  gtacagcaaa
240

gaggaccagg  atctgctgaa  gctggtgaaa  tcctatcact  ggatgggcct  ggtccatatc
300

ccaaccaacg  ggtcttggca  gtgggaggac  ggaagcattc  tgtcccccaa  tctgctgaca
360

atcattgaaa  tgcagaaggg  cgattgtgct  ctgtacgcaa  gctccttcaa  agggtatatc
420

gagaactgct  ccaccccaa  tacatacatt  tgtatgcaga  ggacagtggc  aaaacctacc
480

acaactcctg  caccacgccc  ccctactcca  gcacctacca  tcgcatctca  gccactgagt
540
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ctgcgaccag aggcctgccg gcccgccgcc ggcggggccg tccataccag agggctggac
600

tttgcctgcg atatctacat ttgggcccct ctggctggaa catgtggcgt gctgctgctg
660

tccctggtca ttactctgta ttgtaagcgg ggaagaaaga aactgctgta catcttcaaa
720

cagcccttta tgaggcctgt gcagaccaca caggaggaag acggctgctc ctgccggttc
780

cccgaggaag aggaaggcgg gtgcgagctg cgggaccaga gactgccacc tgatgcacac
840

aagccaccag gaggaggcag cttcaggacc cccatccagg aggaacaggc cgacgctcat
900

tccacactgg ccaaaattcg agtgaagttc agcaggtccg ccgacgctcc tgcataccag
960

cagggacaga accagctgta taacgagctg aatctgggcc ggagagagga atacgacgtg
1020

ctggacaaaa ggcggggccg ggaccccgaa atgggaggga agccacgacg gaaaaacccc
1080

caggagggcc tgtacaatga gctgcaaaag gacaaaatgg ccgaggctta ttctgaaatc
1140

gggatgaagg gagagagaag gcgcggaaaa ggccacgatg gcctgtacca ggggctgagc
1200

accgctacaa aggacaccta tgatgcactg cacatgcagg ccctgccccc tcggtga
1257

<210> 75
<211> 418
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-BBOX40Z amino acid

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<400>    75
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
             20                  25                  30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
         35                  40                  45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
     50                  55                  60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Lys Pro Thr
145                 150                 155                 160

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                165                 170                 175

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            180                 185                 190

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
        195                 200                 205

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
    210                 215                 220
```

```
Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
225                 230                 235                 240

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
                245                 250                 255

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Asp
            260                 265                 270

Gln Arg Leu Pro Pro Asp Ala His Lys Pro Pro Gly Gly Gly Ser Phe
        275                 280                 285

Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp Ala His Ser Thr Leu Ala
    290                 295                 300

Lys Ile Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln
305                 310                 315                 320

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
                325                 330                 335

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
            340                 345                 350

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
        355                 360                 365

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
    370                 375                 380

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
385                 390                 395                 400

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
                405                 410                 415

Pro Arg


<210>    76
<211>    1215
<212>    DNA
<213>    Artificial Sequence
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<220>
<223>   NKG2D-BBOX40LZ nucleotide

<400>   76
atggctctgc cagtgactgc actgctgctg ccactggccc tgctgctgca cgcagctcga
60

cctctgttca accaggaggt ccagatccca ctgaccgaaa gttactgcgg accatgtccc
120

aagaactgga tctgctacaa gaacaactgt taccagttct ttgacgagtc taagaactgg
180

tatgaatctc aggccagttg catgtcacag aatgcttcac tgctgaaggt gtacagcaaa
240

gaggaccagg atctgctgaa gctggtgaaa tcctatcact ggatgggcct ggtccatatc
300

ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccacccccaa tacatacatt tgtatgcaga ggacagtggc aaaacctacc
480

acaactcctg caccacgccc ccctactcca gcacctacca tcgcatctca gccactgagt
540

ctgcgaccag aggcctgccg gcccgccgcc ggcggggccg tccataccag agggctggac
600

tttgcctgcg atatctacat ttgggcccct ctggctggaa catgtggcgt gctgctgctg
660

tccctggtca ttactctgta ttgtaagcgg ggaagaaaga aactgctgta catcttcaaa
720

cagcccttta tgaggcctgt gcagaccaca caggaggaag acggctgctc ctgccggttc
780

cccgaggaag aggaaggcgg gtgcgagctg gaaagagtgc agcccctgga agagaatgtc
840

gggaatgccg ctcgcccaag atttgaaagg aacaaacgag tgaagttcag caggtccgcc 900

gacgctcctg cataccagca gggacagaac cagctgtata acgagctgaa tctgggccgg 960

agagaggaat acgacgtgct ggacaaaagg cggggccggg accccgaaat gggagggaag 1020

ccacgacgga aaaacccca ggagggcctg tacaatgagc tgcaaaagga caaaatggcc 1080

gaggcttatt ctgaaatcgg gatgaaggga gagagaaggc gcggaaaagg ccacgatggc 1140

ctgtaccagg ggctgagcac cgctacaaag gacacctatg atgcactgca catgcaggcc 1200

ctgcccccctc ggtga 1215

<210> 77
<211> 404
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-BBOX40LZ amino acid

<400> 77
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
20 25 30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
35 40 45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
50 55 60

```
Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Lys Pro Thr
145                 150                 155                 160

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                165                 170                 175

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            180                 185                 190

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
        195                 200                 205

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
    210                 215                 220

Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
225                 230                 235                 240

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
                245                 250                 255

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Glu Arg
            260                 265                 270

Val Gln Pro Leu Glu Glu Asn Val Gly Asn Ala Ala Arg Pro Arg Phe
        275                 280                 285

Glu Arg Asn Lys Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
    290                 295                 300
```

```
Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
305                 310                 315                 320

Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
                325                 330                 335

Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
            340                 345                 350

Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
        355                 360                 365

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
    370                 375                 380

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
385                 390                 395                 400

Leu Pro Pro Arg



<210>    78
<211>    1257
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    NKG2D-OX40BBZ nucleotide


<400>    78
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60

cctctgttca  accaggaggt  ccagatccca  ctgaccgaaa  gttactgcgg  accatgtccc
120

aagaactgga  tctgctacaa  gaacaactgt  taccagttct  ttgacgagtc  taagaactgg
180

tatgaatctc  aggccagttg  catgtcacag  aatgcttcac  tgctgaaggt  gtacagcaaa
240

gaggaccagg  atctgctgaa  gctggtgaaa  tcctatcact  ggatgggcct  ggtccatatc
300
```

ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccacccccaa tacatacatt tgtatgcaga ggacagtggc aaaacctacc
480

acaactcctg caccacgccc ccctactcca gcacctacca tcgcatctca gccactgagt
540

ctgcgaccag aggcctgccg gcccgccgcc ggcggggccg tccataccag agggctggac
600

tttgcctgcg atatctacat ttgggcccct ctggctggaa catgtggcgt gctgctgctg
660

tccctggtca ttactctgta ttgtcgggac cagagactgc cacctgatgc acacaagcca
720

ccaggaggag gcagcttcag gacccccatc caggaggaac aggccgacgc tcattccaca
780

ctggccaaaa ttaagcgggg aagaaagaaa ctgctgtaca tcttcaaaca gccctttatg
840

aggcctgtgc agaccacaca ggaggaagac ggctgctcct gccggttccc cgaggaagag
900

gaaggcgggt gcgagctgcg agtgaagttc agcaggtccg ccgacgctcc tgcataccag
960

cagggacaga accagctgta taacgagctg aatctgggcc ggagagagga atacgacgtg
1020

ctggacaaaa ggcggggccg ggaccccgaa atgggaggga agccacgacg gaaaaacccc
1080

caggagggcc tgtacaatga gctgcaaaag gacaaaatgg ccgaggctta ttctgaaatc
1140

gggatgaagg gagagagaag gcgcggaaaa ggccacgatg gcctgtacca ggggctgagc
1200

accgctacaa aggacaccta tgatgcactg cacatgcagg ccctgccccc tcggtga
1257

<210> 79
<211> 418
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-OX40BBZ amino acid

<400> 79
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
20 25 30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
35 40 45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
50 55 60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
65 70 75 80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
85 90 95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
100 105 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
115 120 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
130 135 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Lys Pro Thr
145 150 155 160

```
Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                165                 170                 175

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            180                 185                 190

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
        195                 200                 205

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
    210                 215                 220

Thr Leu Tyr Cys Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro
225                 230                 235                 240

Pro Gly Gly Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp
                245                 250                 255

Ala His Ser Thr Leu Ala Lys Ile Lys Arg Gly Arg Lys Lys Leu Leu
            260                 265                 270

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
        275                 280                 285

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
    290                 295                 300

Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln
305                 310                 315                 320

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
                325                 330                 335

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
            340                 345                 350

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
        355                 360                 365

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
    370                 375                 380

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
385                 390                 395                 400
```

```
Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
                405                 410                 415

Pro Arg




<210>    80
<211>    1281
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    NKG2D-28BBZ nucleotide


<400>    80
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60

cctctgttca  accaggaggt  ccagatccca  ctgaccgaaa  gttactgcgg  accatgtccc
120

aagaactgga  tctgctacaa  gaacaactgt  taccagttct  ttgacgagtc  taagaactgg
180

tatgaatctc  aggccagttg  catgtcacag  aatgcttcac  tgctgaaggt  gtacagcaaa
240

gaggaccagg  atctgctgaa  gctggtgaaa  tcctatcact  ggatgggcct  ggtccatatc
300

ccaaccaacg  ggtcttggca  gtgggaggac  ggaagcattc  tgtcccccaa  tctgctgaca
360

atcattgaaa  tgcagaaggg  cgattgtgct  ctgtacgcaa  gctccttcaa  agggtatatc
420

gagaactgct  ccacccccaa  tacatacatt  tgtatgcaga  ggacagtggc  aaaacctacc
480

acaactcctg  caccacgccc  ccctactcca  gcacctacca  tcgcatctca  gccactgagt
540

ctgcgaccag  aggcctgccg  gcccgccgcc  ggcggggccg  tccataccag  agggctggac
600
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tttgcctgcg attttgggt cctggtggtc gtgggagggg tgctggcatg ttactcactg
660

ctggtcaccg tggccttcat catcttctgg gtgcggagca agaggtcccg cctgctgcac
720

agcgactata tgaacatgac cccacggaga cccggcccta cacggaaaca ttaccagccc
780

tatgctccac cccgggactt cgcagcttac agaagtaagc ggggaagaaa gaaactgctg
840

tacatcttca aacagccctt tatgaggcct gtgcagacca cacaggagga agacggctgc
900

tcctgccggt tccccgagga agaggaaggc gggtgcgagc tgcgagtgaa gttcagcagg
960

tccgccgacg ctcctgcata ccagcaggga cagaaccagc tgtataacga gctgaatctg
1020

ggccggagag aggaatacga cgtgctggac aaaaggcggg gccgggaccc cgaaatggga
1080

gggaagccac gacggaaaaa cccccaggag ggcctgtaca atgagctgca aaaggacaaa
1140

atggccgagg cttattctga aatcgggatg aagggagaga gaaggcgcgg aaaaggccac
1200

gatggcctgt accaggggct gagcaccgct acaaaggaca cctatgatgc actgcacatg
1260

caggccctgc cccctcggtg a
1281

<210> 81
<211> 426
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-28BBZ amino acid

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<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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
             20                  25                  30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
         35                  40                  45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
     50                  55                  60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Lys Pro Thr
145                 150                 155                 160

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                165                 170                 175

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            180                 185                 190

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp Val Leu
        195                 200                 205

Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val
    210                 215                 220
```

Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His
225   230   235   240

Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys
                245   250   255

His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
            260   265   270

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
        275   280   285

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
    290   295   300

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
305   310   315   320

Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn
                325   330   335

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
            340   345   350

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
        355   360   365

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
    370   375   380

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
385   390   395   400

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
                405   410   415

Ala Leu His Met Gln Ala Leu Pro Pro Arg
            420   425

<210> 82
<211> 1263
<212> DNA
<213> Artificial Sequence

<220>
<223> NKG2D-28OX40Z nucleotide

<400> 82
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60

cctctgttca accaggaggt ccagatccca ctgaccgaaa gttactgcgg accatgtccc
120

aagaactgga tctgctacaa gaacaactgt taccagttct ttgacgagtc taagaactgg
180

tatgaatctc aggccagttg catgtcacag aatgcttcac tgctgaaggt gtacagcaaa
240

gaggaccagg atctgctgaa gctggtgaaa tcctatcact ggatgggcct ggtccatatc
300

ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccacccccaa tacatacatt tgtatgcaga ggacagtggc aaaacctacc
480

acaactcctg caccacgccc ccctactcca gcacctacca tcgcatctca gccactgagt
540

ctgcgaccag aggcctgccg gcccgccgcc ggcggggccg tccataccag agggctggac
600

tttgcctgcg atttttgggt cctggtggtc gtgggagggg tgctggcatg ttactcactg
660

ctggtcaccg tggccttcat catcttctgg gtgcggagca agaggtcccg cctgctgcac
720

agcgactata tgaacatgac cccacggaga cccggcccta cacggaaaca ttaccagccc
780

tatgctccac cccgggactt cgcagcttac agaagtcggg accagagact gccacctgat
840

gcacacaagc caccaggagg aggcagcttc aggaccccca tccaggagga acaggccgac
900

gctcattcca cactggccaa aattcgagtg aagttcagca ggtccgccga cgctcctgca
960

taccagcagg gacagaacca gctgtataac gagctgaatc tgggccggag agaggaatac
1020

gacgtgctgg acaaaaggcg gggccgggac cccgaaatgg gagggaagcc acgacggaaa
1080

aacccccagg agggcctgta caatgagctg caaaaggaca aaatggccga ggcttattct
1140

gaaatcggga tgaagggaga gagaaggcgc ggaaaaggcc acgatggcct gtaccagggg
1200

ctgagcaccg ctacaaagga cacctatgat gcactgcaca tgcaggccct gccccctcgg
1260

t g a
1263

<210> 83
<211> 420
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-28OX40Z amino acid

<400> 83
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
20 25 30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
35 40 45

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Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
     50                  55                  60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Lys Pro Thr
145                 150                 155                 160

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                165                 170                 175

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            180                 185                 190

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp Val Leu
        195                 200                 205

Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val
    210                 215                 220

Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His
225                 230                 235                 240

Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys
                245                 250                 255

His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
            260                 265                 270

Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro Pro Gly Gly Gly
        275                 280                 285
```

Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp Ala His Ser Thr
290 295 300

Leu Ala Lys Ile Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
305 310 315 320

Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
325 330 335

Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
340 345 350

Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
355 360 365

Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
370 375 380

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
385 390 395 400

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
405 410 415

Leu Pro Pro Arg
420

<210> 84
<211> 1221
<212> DNA
<213> Artificial Sequence

<220>
<223> NKG2D-28OX40LZ nucleotide

<400> 84
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60

cctctgttca accaggaggt ccagatccca ctgaccgaaa gttactgcgg accatgtccc
120

aagaactgga tctgctacaa gaacaactgt taccagttct ttgacgagtc taagaactgg
180

tatgaatctc aggccagttg catgtcacag aatgcttcac tgctgaaggt gtacagcaaa
240

gaggaccagg atctgctgaa gctggtgaaa tcctatcact ggatgggcct ggtccatatc
300

ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccaccccca a tacatacatt tgtatgcaga ggacagtggc aaaacctacc
480

acaactcctg caccacgccc ccctactcca gcacctacca tcgcatctca gccactgagt
540

ctgcgaccag aggcctgccg gcccgccgcc ggcggggccg tccataccag agggctggac
600

tttgcctgcg atttttgggt cctggtggtc gtgggagggg tgctggcatg ttactcactg
660

ctggtcaccg tggccttcat catcttctgg gtgcggagca agaggtcccg cctgctgcac
720

agcgactata tgaacatgac cccacggaga cccggcccta cacggaaaca ttaccagccc
780

tatgctccac cccgggactt cgcagcttac agaagtgaaa gagtgcagcc cctggaagag
840

aatgtcggga atgccgctcg cccaagattt gaaaggaaca aacgagtgaa gttcagcagg
900

tccgccgacg ctcctgcata ccagcaggga cagaaccagc tgtataacga gctgaatctg
960

ggccggagag aggaatacga cgtgctggac aaaaggcggg gccgggaccc cgaaatggga
1020

gggaagccac gacggaaaaa cccccaggag ggcctgtaca atgagctgca aaaggacaaa
1080

atggccgagg cttattctga aatcgggatg aagggagaga gaaggcgcgg aaaaggccac
1140

gatggcctgt accaggggct gagcaccgct acaaaggaca cctatgatgc actgcacatg
1200

caggccctgc cccctcggtg a
1221

<210> 85
<211> 406
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-28OX40LZ amino acid

<400> 85
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
20 25 30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
35 40 45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
50 55 60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
65 70 75 80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
85 90 95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
100 105 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
115 120 125

```
Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Lys Pro Thr
145                 150                 155                 160

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                165                 170                 175

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            180                 185                 190

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp Val Leu
        195                 200                 205

Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val
    210                 215                 220

Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His
225                 230                 235                 240

Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys
                245                 250                 255

His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
            260                 265                 270

Glu Arg Val Gln Pro Leu Glu Glu Asn Val Gly Asn Ala Ala Arg Pro
        275                 280                 285

Arg Phe Glu Arg Asn Lys Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    290                 295                 300

Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
305                 310                 315                 320

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                325                 330                 335

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            340                 345                 350

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        355                 360                 365
```

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
370 375 380

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
385 390 395 400

Gln Ala Leu Pro Pro Arg
405

<210> 86
<211> 1254
<212> DNA
<213> Artificial Sequence

<220>
<223> NKG2D-28(H)BBZ nucleotide

<400> 86
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60

cctctgttca accaggaggt ccagatccca ctgaccgaaa gttactgcgg accatgtccc
120

aagaactgga tctgctacaa gaacaactgt taccagttct ttgacgagtc taagaactgg
180

tatgaatctc aggccagttg catgtcacag aatgcttcac tgctgaaggt gtacagcaaa
240

gaggaccagg atctgctgaa gctggtgaaa tcctatcact ggatgggcct ggtccatatc
300

ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccacccccaa tacatacatt tgtatgcaga ggacagtgat cgaggtcatg
480

tacccccctc catatctgga caacgaaaag tccaatggaa ctatcattca cgtgaagggc
540

aaacatctgt gcccatctcc cctgttccct gggccaagta aaccttttg ggtcctggtg 600

gtcgtgggag gggtgctggc atgttactca ctgctggtca ccgtggcctt catcatcttc 660

tgggtgcgga gcaagaggtc ccgcctgctg cacagcgact atatgaacat gaccccacgg 720

agacccggcc ctacacggaa acattaccag ccctatgctc caccccggga cttcgcagct 780

tacagaagta agcggggaag aaagaaactg ctgtacatct tcaaacagcc ctttatgagg 840

cctgtgcaga ccacacagga ggaagacggc tgctcctgcc ggttccccga ggaagaggaa 900

ggcgggtgcg agctgcgagt gaagttcagc aggtccgccg acgctcctgc ataccagcag 960

ggacagaacc agctgtataa cgagctgaat ctgggccgga gagaggaata cgacgtgctg 1020

gacaaaaggc ggggccggga ccccgaaatg ggagggaagc cacgacggaa aaacccccag 1080

gagggcctgt acaatgagct gcaaaaggac aaaatggccg aggcttattc tgaaatcggg 1140

atgaagggag agagaaggcg cggaaaaggc cacgatggcc tgtaccaggg gctgagcacc 1200

gctacaaagg acacctatga tgcactgcac atgcaggccc tgccccctcg gtga 1254

<210> 87
<211> 417
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-28(H)BBZ amino acid

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<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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
             20                  25                  30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
         35                  40                  45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
     50                  55                  60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ile Glu Val Met
145                 150                 155                 160

Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser Asn Gly Thr Ile Ile
                165                 170                 175

His Val Lys Gly Lys His Leu Cys Pro Ser Pro Leu Phe Pro Gly Pro
            180                 185                 190

Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
        195                 200                 205

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
    210                 215                 220
```

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
225   230   235   240

Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
                245   250   255

Asp Phe Ala Ala Tyr Arg Ser Lys Arg Gly Arg Lys Lys Leu Leu Tyr
            260   265   270

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
        275   280   285

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
    290   295   300

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln
305   310   315   320

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
                325   330   335

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
            340   345   350

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
        355   360   365

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
    370   375   380

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
385   390   395   400

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
                405   410   415

Arg

<210> 88
<211> 1236
<212> DNA
<213> Artificial Sequence

<220>
<223>   NKG2D-28(H)OX40Z nucleotide

<400>   88
atggctctgc cagtgactgc actgctgctg ccactggccc tgctgctgca cgcagctcga
60

cctctgttca accaggaggt ccagatccca ctgaccgaaa gttactgcgg accatgtccc
120

aagaactgga tctgctacaa gaacaactgt taccagttct ttgacgagtc taagaactgg
180

tatgaatctc aggccagttg catgtcacag aatgcttcac tgctgaaggt gtacagcaaa
240

gaggaccagg atctgctgaa gctggtgaaa tcctatcact ggatgggcct ggtccatatc
300

ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccacccccaa tacatacatt tgtatgcaga ggacagtgat cgaggtcatg
480

taccccctc catatctgga caacgaaaag tccaatggaa ctatcattca cgtgaagggc
540

aaacatctgt gcccatctcc cctgttccct gggccaagta aacctttttg ggtcctggtg
600

gtcgtgggag gggtgctggc atgttactca ctgctggtca ccgtggcctt catcatcttc
660

tgggtgcgga gcaagaggtc ccgcctgctg cacagcgact atatgaacat gaccccacgg
720

agacccggcc ctacacggaa acattaccag ccctatgctc caccccggga cttcgcagct
780

tacagaagtc gggaccagag actgccacct gatgcacaca agccaccagg aggaggcagc
840

ttcaggaccc ccatccagga ggaacaggcc gacgctcatt ccacactggc caaaattcga
900

gtgaagttca gcaggtccgc cgacgctcct gcataccagc agggacagaa ccagctgtat
960

aacgagctga atctgggccg gagagaggaa tacgacgtgc tggacaaaag gcggggccgg
1020

gaccccgaaa tgggagggaa gccacgacgg aaaaaccccc aggagggcct gtacaatgag
1080

ctgcaaaagg acaaaatggc cgaggcttat tctgaaatcg ggatgaaggg agagagaagg
1140

cgcggaaaag gccacgatgg cctgtaccag ggctgagca ccgctacaaa ggacacctat
1200

gatgcactgc acatgcaggc cctgccccct cggtga
1236

<210> 89
<211> 411
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-28(H)OX40Z amino acid

<400> 89
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
20 25 30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
35 40 45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
50 55 60

```
Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ile Glu Val Met
145                 150                 155                 160

Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser Asn Gly Thr Ile Ile
                165                 170                 175

His Val Lys Gly Lys His Leu Cys Pro Ser Pro Leu Phe Pro Gly Pro
            180                 185                 190

Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
        195                 200                 205

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
    210                 215                 220

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
225                 230                 235                 240

Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
                245                 250                 255

Asp Phe Ala Ala Tyr Arg Ser Arg Asp Gln Arg Leu Pro Pro Asp Ala
            260                 265                 270

His Lys Pro Pro Gly Gly Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu
        275                 280                 285

Gln Ala Asp Ala His Ser Thr Leu Ala Lys Ile Arg Val Lys Phe Ser
    290                 295                 300
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Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr
305                 310                 315                 320

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                325                 330                 335

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            340                 345                 350

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        355                 360                 365

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    370                 375                 380

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
385                 390                 395                 400

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                405                 410


<210>    90
<211>    1194
<212>    DNA
<213>    Artificial Sequence

<220>
<223>    NKG2D-28(H)OX40LZ nucleotide


<400>    90
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60

cctctgttca  accaggaggt  ccagatccca  ctgaccgaaa  gttactgcgg  accatgtccc
120

aagaactgga  tctgctacaa  gaacaactgt  taccagttct  ttgacgagtc  taagaactgg
180

tatgaatctc  aggccagttg  catgtcacag  aatgcttcac  tgctgaaggt  gtacagcaaa
240

gaggaccagg  atctgctgaa  gctggtgaaa  tcctatcact  ggatgggcct  ggtccatatc
300
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ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccacccccaa tacatacatt tgtatgcaga ggacagtgat cgaggtcatg
480

taccccccctc catatctgga caacgaaaag tccaatggaa ctatcattca cgtgaagggc
540

aaacatctgt gcccatctcc cctgttccct gggccaagta aacctttttg ggtcctggtg
600

gtcgtgggag gggtgctggc atgttactca ctgctggtca ccgtggcctt catcatcttc
660

tgggtgcgga gcaagaggtc ccgcctgctg cacagcgact atatgaacat gaccccacgg
720

agacccggcc ctacacggaa acattaccag ccctatgctc caccccggga cttcgcagct
780

tacagaagtg aaagagtgca gcccctggaa gagaatgtcg ggaatgccgc tcgcccaaga
840

tttgaaagga acaaacgagt gaagttcagc aggtccgccg acgctcctgc ataccagcag
900

ggacagaacc agctgtataa cgagctgaat ctgggccgga gagaggaata cgacgtgctg
960

gacaaaaggc ggggccggga ccccgaaatg ggagggaagc cacgacggaa aaacccccag
1020

gagggcctgt acaatgagct gcaaaaggac aaaatggccg aggcttattc tgaaatcggg
1080

atgaagggag agagaaggcg cggaaaaggc cacgatggcc tgtaccaggg gctgagcacc
1140

gctacaaagg acacctatga tgcactgcac atgcaggccc tgccccctcg gtga
1194

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<210>    91
<211>    397
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    NKG2D-28(H)OX40LZ amino acid


<400>    91
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
             20                  25                  30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
         35                  40                  45

Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
     50                  55                  60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ile Glu Val Met
145                 150                 155                 160

Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser Asn Gly Thr Ile Ile
                165                 170                 175
```

His Val Lys Gly Lys His Leu Cys Pro Ser Pro Leu Phe Pro Gly Pro
180 185 190

Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys
195 200 205

Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser
210 215 220

Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg
225 230 235 240

Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg
245 250 255

Asp Phe Ala Ala Tyr Arg Ser Glu Arg Val Gln Pro Leu Glu Glu Asn
260 265 270

Val Gly Asn Ala Ala Arg Pro Arg Phe Glu Arg Asn Lys Arg Val Lys
275 280 285

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
290 295 300

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
305 310 315 320

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
325 330 335

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
340 345 350

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
355 360 365

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
370 375 380

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
385 390 395

<210> 92
<211> 1203

<212>   DNA
<213>   Artificial Sequence

<220>
<223>   NKG2D-AAA-28(H)OX40LZ nucleotide

<400>   92
atggctctgc cagtgactgc actgctgctg ccactggccc tgctgctgca cgcagctcga
60

cctctgttca accaggaggt ccagatccca ctgaccgaaa gttactgcgg accatgtccc
120

aagaactgga tctgctacaa gaacaactgt taccagttct ttgacgagtc taagaactgg
180

tatgaatctc aggccagttg catgtcacag aatgcttcac tgctgaaggt gtacagcaaa
240

gaggaccagg atctgctgaa gctggtgaaa tcctatcact ggatgggcct ggtccatatc
300

ccaaccaacg ggtcttggca gtgggaggac ggaagcattc tgtcccccaa tctgctgaca
360

atcattgaaa tgcagaaggg cgattgtgct ctgtacgcaa gctccttcaa agggtatatc
420

gagaactgct ccacccccaa tacatacatt tgtatgcaga ggacagtggc cgccgctatc
480

gaggtcatgt acccccctcc atatctggac aacgaaaagt ccaatggaac tatcattcac
540

gtgaagggca aacatctgtg cccatctccc ctgttccctg ggccaagtaa acctttttgg
600

gtcctggtgg tcgtgggagg ggtgctggca tgttactcac tgctggtcac cgtggccttc
660

atcatcttct gggtgcggag caagaggtcc cgcctgctgc acagcgacta tatgaacatg
720

accccacgga gacccggccc tacacggaaa cattaccagc cctatgctcc accccgggac
780

ttcgcagctt acagaagtga aagagtgcag cccctggaag agaatgtcgg gaatgccgct
840

cgcccaagat ttgaaaggaa caaacgagtg aagttcagca ggtccgccga cgctcctgca
900

taccagcagg gacagaacca gctgtataac gagctgaatc tgggccggag agaggaatac
960

gacgtgctgg acaaaaggcg gggccgggac cccgaaatgg gagggaagcc acgacggaaa
1020

aacccccagg agggcctgta caatgagctg caaaaggaca aaatggccga ggcttattct
1080

gaaatcggga tgaagggaga gagaaggcgc ggaaaaggcc acgatggcct gtaccagggg
1140

ctgagcaccg ctacaaagga cacctatgat gcactgcaca tgcaggccct gccccctcgg
1200

t g a
1203

<210> 93
<211> 400
<212> PRT
<213> Artificial Sequence

<220>
<223> NKG2D-AAA-28(H)OX40LZ amino acid

<400> 93
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 Leu Phe Asn Gln Glu Val Gln Ile Pro Leu Thr
20 25 30

Glu Ser Tyr Cys Gly Pro Cys Pro Lys Asn Trp Ile Cys Tyr Lys Asn
35 40 45

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Asn Cys Tyr Gln Phe Phe Asp Glu Ser Lys Asn Trp Tyr Glu Ser Gln
     50                  55                  60

Ala Ser Cys Met Ser Gln Asn Ala Ser Leu Leu Lys Val Tyr Ser Lys
 65                  70                  75                  80

Glu Asp Gln Asp Leu Leu Lys Leu Val Lys Ser Tyr His Trp Met Gly
                 85                  90                  95

Leu Val His Ile Pro Thr Asn Gly Ser Trp Gln Trp Glu Asp Gly Ser
            100                 105                 110

Ile Leu Ser Pro Asn Leu Leu Thr Ile Ile Glu Met Gln Lys Gly Asp
        115                 120                 125

Cys Ala Leu Tyr Ala Ser Ser Phe Lys Gly Tyr Ile Glu Asn Cys Ser
    130                 135                 140

Thr Pro Asn Thr Tyr Ile Cys Met Gln Arg Thr Val Ala Ala Ala Ile
145                 150                 155                 160

Glu Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser Asn Gly
                165                 170                 175

Thr Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser Pro Leu Phe
            180                 185                 190

Pro Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly Val
        195                 200                 205

Leu Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp
    210                 215                 220

Val Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met
225                 230                 235                 240

Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala
                245                 250                 255

Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser Glu Arg Val Gln Pro Leu
            260                 265                 270

Glu Glu Asn Val Gly Asn Ala Ala Arg Pro Arg Phe Glu Arg Asn Lys
        275                 280                 285
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Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
    290   295   300

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
305   310   315   320

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
                325   330   335

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
            340   345   350

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
        355   360   365

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
    370   375   380

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
385   390   395   400