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(54) Benævnelse: **MAGE-A1-GENKENDENDE BINDINGSMOLEKYLER MED HØJ AVIDITET**

(56) Fremdragne publikationer:
CHAMES P ET AL: "Direct selection of a human antibody fragment directed against the tumor T-cell epitope HLA-A1-MAGE-A1 from a nonimmunized phage-Fab library", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, NATIONAL ACADEMY OF SCIENCES, US, vol. 97, no. 14, 5 July 2000 (2000-07-05), pages 7969-7974, XP002967292, ISSN: 0027-8424, DOI: 10.1073/PNAS.97.14.7969
MATKOVIC BOZICA ET AL: "Expression of MAGE-A and NY-ESO-1 cancer/testis antigens in medullary breast cancer: retrospective immunohistochemical study", CROATIAN MEDICAL JOURNAL, vol. 52, no. 2, April 2011 (2011-04), pages 171-177, XP002699807, ISSN: 0353-9504
SOMMERMEYER DANIEL ET AL: "Designer T cells by T cell receptor replacement", EUROPEAN JOURNAL OF IMMUNOLOGY NOV 2006,, vol. 36, no. 11, 1 November 2006 (2006-11-01), pages 3052-3059, XP002550367, DOI: 10.1002/EJI.200636539
ORENTAS RIMAS J ET AL: "Retroviral transduction of a T cell receptor specific for an Epstein-Barr virus-encoded peptide", CLINICAL IMMUNOLOGY, ACADEMIC PRESS, US, vol. 98, no. 2, 1 February 2001 (2001-02-01), pages 220-228, XP002414017, ISSN: 1521-6616, DOI: 10.1006/CLIM.2000.4977
ENGELS BORIS ET AL: "Redirecting human T lymphocytes toward renal cell carcinoma specificity by retroviral transfer of T cell receptor genes", HUMAN GENE THERAPY, MARY ANN LIEBERT, NEW YORK ,NY, US, vol. 16,

Fortsættes ...

no. 7, 1 July 2005 (2005-07-01), pages 799-810, XP002460992, ISSN: 1043-0342, DOI: 10.1089/HUM.2005.16.799
OTTAVIANI, S.; ZHANG, Y; BOON, T; VAN DER BRUGGEN, P.: "A MAGE-1 antigenic peptide recognized by human cytolytic T lymphocytes on HLA-A2 tumor cells", CANCER IMMUNOLOGY, IMMUNOTHERAPY: CII, vol. 54, no. 12, 2005, pages 1214-1220, XP019333091, cited in the application
Jeffrey Ishizuka ET AL: "The Structural Dynamics and Energetics of an Immunodominant T Cell Receptor Are Programmed by Its V[beta] Domain", IMMUNITY., vol. 28, no. 2, 1 February 2008 (2008-02-01), pages 171-182, XP55488302, US ISSN: 1074-7613, DOI: 10.1016/j.immuni.2007.12.018
PREETI SHARMA ET AL: "Subtle changes at the variable domain interface of the T-cell receptor can strongly increase affinity", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 293, no. 5, 11 December 2017 (2017-12-11), pages 1820-1834, XP055460242, US ISSN: 0021-9258, DOI: 10.1074/jbc.M117.814152

DESCRIPTION

FIELD OF THE INVENTION

[0001] The present invention pertains to novel high avidity antigen recognizing constructs according to the appended set of claims, which are T cell receptors and which specifically bind to the melanoma associated antigen (MAGE) A1. The constructs of the invention are particularly useful for the diagnosis, prevention or therapy of tumorous diseases which are characterized by the specific expression of the MAGE-A1 antigen. Furthermore provided are nucleic acids, vectors and host cells - such as CD4 or CD8 positive T cells - which encode, comprise or present the antigen recognizing constructs of the invention. The invention thus provides new means for immune therapy, specifically adoptive T cell therapy, for treating cancer.

DESCRIPTION

[0002] Despite remarkable technological advancements in the diagnosis and treatment options available to patients diagnosed with cancer, the prognosis still often remains poor and many patients cannot be cured. Immunotherapy holds the promise of offering a potent, yet targeted, treatment to patients diagnosed with various tumors, with the potential to eradicate the malignant tumor cells without damaging normal tissues. In theory the T cells of the immune system are capable of recognizing protein patterns specific for tumor cells and to mediate their destruction through a variety of effector mechanisms. Adoptive T-cell therapy is an attempt to harness and amplify the tumor-eradicating capacity of a patient's own T cells and then return these effectors to the patient in such a state that they effectively eliminate residual tumor, however without damaging healthy tissue. Although this approach is not new to the field of tumor immunology, still many drawbacks in the clinical use of adoptive T cell therapy impair the full use of this approach in cancer treatments.

[0003] A TCR is a heterodimeric cell surface protein of the immunoglobulin super-family which is associated with invariant proteins of the CD3 complex involved in mediating signal transduction. TCRs exist in αβ and γδ forms, which are structurally similar but have quite distinct anatomical locations and probably functions. The extracellular portion of native heterodimeric αβTCR consists of two polypeptides, each of which has a membrane-proximal constant domain, and a membrane-distal variable domain. Each of the constant and variable domains includes an intra-chain disulfide bond. The variable domains contain the highly polymorphic loops analogous to the complementarity determining regions (CDRs) of antibodies. The use of TCR gene therapy overcomes a number of current hurdles. It allows equipping patients' own T cells with desired specificities and generation of sufficient numbers of T cells in a short period of time, avoiding their exhaustion. The TCR will be transduced into central memory T cells or T cells with stem cell characteristics, which may ensure better

persistence and function upon transfer. TCR-engineered T cells will be infused into cancer patients rendered lymphopenic by chemotherapy or irradiation, allowing efficient engraftment but inhibiting immune suppression. Transgenic mice expressing human MHC molecules and a diverse human TCR repertoire serve as a tool to rapidly analyze whether peptide antigens are immunogenic, i.e. are they efficiently processed and presented by MHC molecules, do they efficiently induce T cell responses following immunization (Li et al. 2010 Nat Med). The concept of adoptive T cell therapy using the AB*ab*DII mouse published by Li et al is shown in Figure 1.

[0004] In brief, CD8+ T cells in AB*ab*DII mice harbor human T cell receptors (TCRs) which recognize antigens presented by human MHC class I molecules. As opposed to humans, AB*ab*DII mice are not tolerant to human tumor associated antigens (TAAs). Therefore, when vaccinated with a human TAA, AB*ab*DII mice generate an efficient adaptive immune response against those foreign antigens including the expansion of high avidity antigen specific T cells (Figure 1, right side). After immunization with a suitable human TAA the genetic information coding for the high avidity TCRs of the AB*ab*DII mice can be extracted (Figure 1, center). These TCRs can subsequently be re-expressed in T cells from tumor patients through retroviral transduction. Those re-targeted T cells can be transferred back into the patient fighting the tumor (Figure 1, left side).

[0005] Using the human TCR transgenic mouse, any human peptide sequence not encoded by the mouse genome is thus suitable for immunization and will yield TCRs with optimal affinity. Optimal affinity means that the T cells are restricted to human self-MHC molecules and recognize the peptide antigen as foreign, e.g. represent the non-tolerant repertoire. By using peptide/MHC multimers, specific T cells of the transgenic mice can be sorted, human TCRs isolated, e.g. by single cell PCR, the TCRs optimized for efficient expression while avoiding mispairing with endogenous TCR and used for transduction of patients' T cells with viral vectors (Uckert et al. 2008 Cancer Immunol Immunother; Kammertoens T et al. 2009 Eur J Immunol).

[0006] The melanoma antigen genes (MAGE-A) were found to be expressed in a variety of tumors of different histological origin. Proteins encoded by the MAGE genes are tumor rejection antigens, which can induce specific cytotoxic T-lymphocytes (CTL) having the ability to recognize and kill cancerous cells. MAGE genes and proteins are thus a preferential target for the development of novel drugs to fight cancer by immunotherapy. MAGE-A proteins constitute a sub-family of Cancer-Testis Antigens which are expressed mainly, but not exclusively, in the germ line. They are however also expressed in various human cancers where they are associated with, and may drive, malignancy. This specific expression of MAGE antigens in tumors and not the normal surrounding healthy tissue makes this family of antigens very interesting for targeted adoptive T cell transfer. However, to date no satisfactory immune therapy is known due to the lack of specific and highly avid antibodies or T cell receptors targeting the MAGE antigen.

[0007] Ottavani S. et al, 2005 (CANCER IMMUNOLOGY, IMMUNOTHERAPY: CII, (2005), vol. 54, no. 12, pages 1214 - 1220) disclose cytotoxic T lymphocyte (CTL) clones having specificity

to a HLA-A*0201 restricted Mage A1 antigenic peptide.

[0008] In view of the above described major drawbacks in the background art, it is the objective of the present invention to provide new antigen recognizing constructs with high avidity and specificity against the MAGE-A antigen. Furthermore, the present invention intends to provide novel methods that allow for the production of such constructs. In more general terms the invention seeks to provide novel means for immuno cancer therapy.

[0009] The above problem is solved in a first aspect by an antigen recognizing construct which is a T cell receptor (TCR), comprising (i) an alpha chain variable region with CDR1, CDR2 and CDR3 that comprise an amino acid sequence shown in SEQ ID NO: 40, 41, and 1 respectively; and comprising (ii) a beta chain variable region with CDR1, CDR2 and CDR3 that comprise an amino acid sequence shown in SEQ ID NO: 46, 47, and 4 respectively; wherein said TCR binds specifically to the MAGE-A1 antigen. It was surprisingly discovered that the TCRs provided in the examples of the present invention are highly avid compared to state of the art TCRs directed at MAGE antigens.

[0010] Preferred in the context of the invention is also that the antigen recognizing construct further comprises a V element selected from TRAV5, TRAV13-1, TRAV12-3, TRBV28, TRBV29-1, TRBV13, TRBV20, TRBV12, and/or a J element selected from TRAJ41, TRAJ29, TRAJ31, TRAJ49, TRAJ34, TRBJ2-7, TRBJ2-2, TRBJ2-6, TRBJ7, TRBJ1-2; preferably in the combination as depicted in table 1.

[0011] The antigen recognizing construct in accordance with the invention is specific for and/or binds specifically to a MAGE-A1 antigen. Various proteins are known to be part of the MAGE family which includes also some pseudo genes. One region of homology shared by all of the members of the MAGE family is a stretch of about 200 amino acids which has been named the MAGE conserved domain. The MAGE conserved domain is usually located close to the C-terminal, although it can also be found in a more central position in some proteins. The MAGE conserved domain is generally present as a single copy but it is duplicated in some proteins. MAGE genes which are detectable by the antigen recognizing constructs of the invention are selected from MAGE-B1, MAGE-A1, MAGE-A10, MAGE-A11, MAGE-A12, MAGE-A2B, MAGE-A3, MAGE-A4, MAGE-A6, MAGE-A8, MAGE-A9, MAGE-B1, MAGE-B10, MAGE-B16, MAGE-B18, MAGE-B2, MAGE-B3, MAGE-B4, MAGE-B5, MAGE-B6, MAGE-B6B, MAGE-C1, MAGE-C2, MAGE-C3, MAGE-D1, MAGE-D2, MAGE-D4, MAGE-E1, MAGE-E2, MAGE-F1, MAGE-H1, MAGE-L2, NDN, NDNL2. Preferred in the context of the present invention are the 12 homologous MAGE proteins selected from MAGE-A1, MAGE-A2, MAGE-A3, MAGE-A4, MAGE-A5, MAGE-A6, MAGE-A7, MAGE-A8, MAGE-A9, MAGE-A10, MAGE-A11, or MAGE-A12.

[0012] The term "specificity" or "antigen specificity" or "specific for" a given antigen, as used herein means that the antigen recognizing construct can specifically bind to and immunologically recognize said MAGE-A1 antigen, more preferably with high avidity. For example, a TCR may be considered to have "antigenic specificity" for MAGE-A1 if T cells

expressing the TCR secrete at least about 200 pg/ml or more (e.g., 250 pg/ml or more, 300 pg/ml or more, 400 pg/ml or more, 500 pg/ml or more, 600 pg/ml or more, 700 pg/ml or more, 1000 pg ml or more, 2,000 pg/ml or more, 2,500 pg/ml or more, 5,000 pg/ml or more) of interferon γ (IFN-γ) upon co-culture with target cells pulsed with a low concentration of a MAGE peptide, such as the MAGE-A1 HLA-A02 restricted MAGE-$A1_{278-286}$ peptide (e.g., about 10^{-11} mol/l, 10^{-10} mol/l, 10^{-9} mol/l, 10^{-8} mol/l, 10^{-7} mol/l, 10^{-6} mol/l, 10^{-5} mol/l). Alternatively or additionally, a TCR may be considered to have "antigenic specificity" for MAGE- A1 if T cells expressing the TCR secrete at least twice as much IFN-γ as the untransduced background level of IFN-γ upon co-culture with target cells pulsed with a low concentration of HLA-A02 restricted MAGE-A1. Such a "specificity" as described above can - for example - be analyzed with an ELISA.

[0013] Native alpha-beta heterodimeric TCRs have an alpha chain and a beta chain. Each chain comprises variable, joining and constant regions, and the beta chain also usually contains a short diversity region between the variable and joining regions, but this diversity region is often considered as part of the joining region. Each variable region comprises three CDRs (Complementarity Determining Regions) embedded in a framework sequence, one being the hyper-variable region named CDR3. There are several types of alpha chain variable (Vα) regions and several types of beta chain variable (Vβ) regions distinguished by their framework, CDR1 and CDR2 sequences, and by a partly defined CDR3 sequence. The Vα types are referred to in IMGT nomenclature by a unique TRAV number.

[0014] CDR 1 and CDR2 regions of the respective known Vα and Vβ types are according to the IMGT database:

TRAV5:	CDR1: DSSSTY (SEQ ID NO: 40), CDR2: IFSNMDM (SEQ ID NO: 41)
TRAV13-1	CDR1: DSASNY (SEQ ID NO: 42), CDR2: IRSNVGE (SEQ ID NO: 43)
TRAV12-3	CDR1: NSAFQY (SEQ ID NO: 44), CDR2: TYSSGN (SEQ ID NO: 45)
TRBV28:	CDR1: MDHEN (SEQ ID NO: 46), CDR2: SYDVKM (SEQ ID NO: 47).
TRBV29-1:	CDR1: SQVTM (SEQ ID NO: 48), CDR2: ANQGSEA (SEQ ID NO: 49)
TRBV13:	CDR1: PRHDT (SEQ ID NO: 50), CDR2: FYEKMQ (SEQ ID NO: 51).

[0015] For the purposes of the present invention, a TCR is a moiety having at least one TCR alpha and/or TCR beta variable domain. Generally they comprise both a TCR alpha variable domain and a TCR beta variable domain. They may be αβ heterodimers or may be single chain format. For use in adoptive therapy, an αβ heterodimeric TCR may, for example, be

transfected as full length chains having both cytoplasmic and transmembrane domains. If desired, an introduced disulfide bond between residues of the respective constant domains may be present.

[0016] SEQ ID Nos. 13 to 21 depict the nucleotide sequences of the vector maps of figures 8 to 16. Each of these vectors comprise an alpha and a beta chain of a TCR of the present invention. In the figures the beta chain is located upstream of the alpha chain sequence. As also described below, the invention exemplary describes three isolated TCRs, which were to different degrees optimized by murinization of the original sequence of the constant domain of the TCR chains. The abbreviation in the vector designation "hc" stands for the complete human variant of the TCR, "mc" for a complete murinized constant domain in the TCR chain, whereas "mmc" depicts minimal murinization in the constant domain of the TCR chain. The exact location of the alpha and beta chains in the vector maps (and thus in the corresponding sequences) can be derived from the figure legend.

[0017] In one additional preferred embodiment of the first aspect of the invention, the antigen recognizing construct is as described above a TCR. The TCR preferably comprises at least one alpha and/or beta TCR chain, wherein said TCR chain comprises an amino acid sequence according to any one of the TCR chains shown in SEQ ID Nos. 22 - 25, 34 or 35, or an amino acid sequence having at least 90%, 95%, 98%, 99% or 100% identity to an amino acid sequence shown in SEQ ID No. 22 to 25, 34 or 35.

[0018] An scTCR can comprise a polypeptide of a variable region of a first TCR chain (e.g., an alpha chain) and a polypeptide of an entire (full-length) second TCR chain (e.g., a beta chain), or *vice versa.* Furthermore, the scTCR can optionally comprise one or more linkers which join the two or more polypeptides together. The linker can be, for instance, a peptide which joins together two single chains, as described herein.

[0019] Also provided is such a scTCR of the invention, which is fused to a human cytokine, such as IL-2, IL-7 or IL-15.

[0020] The antigen recognizing construct according to the invention can also be provided in the form of a multimeric complex, comprising at least two scTCR molecules, wherein said scTCR molecules are each fused to at least one biotin moiety, and wherein said scTCRs are interconnected by biotin-strepavidin interaction to allow the formation of said multimeric complex. Also provided are multimeric complexes of a higher order, comprising more than two scTCR of the invention.

[0021] In an embodiment of the invention the antigen recognizing construct binds to a human leucocyte antigen (HLA) presented peptide, preferably by HLA-A02, of MAGE. In a preferred embodiment the antigen recognizing construct specifically binds to the human MAGE-$A1_{278-286}$ epitope.

[0022] In a preferred embodiment the antigen recognizing construct is a human TCR, or

fragment or derivative thereof. A human TCR or fragment or derivative thereof is a TCR which comprises over 50% of the corresponding human TCR sequence. Preferably only a small part of the TCR sequence is of artificial origin or derived from other species. It is known however, that chimeric TCRs e.g. from human origin with murine sequences in the constant domains, are advantageous. Particularly preferred are therefore TCRs in accordance with the present invention, which contain murine sequences in the extracellular part of their constant domains.

[0023] Thus, it is also preferred that the inventive antigen recognizing construct is able to recognize its antigen in a human leucocyte antigen (HLA) dependent manner, preferably in a HLA-A02 dependent manner. The term "HLA dependent manner" in the context of the present invention means that the antigen recognizing construct binds to the antigen only in the event that the antigenic peptide is presented by HLA.

[0024] The antigen recognizing construct in accordance with the invention in one embodiment preferably induces an immune response, preferably wherein the immune response is characterized by the increase in interferon (IFN) γ levels.

[0025] Furthermore preferred is that the antigen recognizing construct of the invention, which is a T cell receptor, comprises an amino acid sequence having at least 90%, 95%, 98%, 99% or 100% sequence identity to an amino acid sequence shown in SEQ ID No. 22 to 25, and 34, 35. Particularly preferred are TCRs having at least 90%, 95%, 98%, 99% or 100% sequence identity to a TCR selected from TCR1367hc, TCR1367mc, or TCR1367mmc. Most preferred is a TCR selected from the group consisting of TCR1367hc, TCR1367mc, or TCR1367mmc. The amino acid sequences of the above referenced TCRs of the invention are depicted in SEQ ID No. 22 to 25, and 34, 35.

[0026] The antigen recognizing construct in accordance with the invention are high avidity TCRs.

[0027] The problem of the invention is solved in another aspect by providing a nucleic acid encoding for an antigen recognizing construct in accordance with the present invention. The nucleic acid preferably (a) has a strand encoding for an antigen recognizing construct according to the invention; (b) has a strand complementary to the strand in (a); or (c) has a strand that hybridizes under stringent conditions with a molecule as described in (a) or (b). Stringent conditions are known to the person of skill in the art, specifically from Sambrook et al, "Molecular Cloning". In addition to that, the nucleic acid optionally has further sequences which are necessary for expressing the nucleic acid sequence corresponding to the protein, specifically for expression in a mammalian/human cell. The nucleic acid used can be contained in a vector suitable for allowing expression of the nucleic acid sequence corresponding to the peptide in a cell. However, the nucleic acids can also be used to transform a presenting cell, which shall not be restricted to classical antigen-presenting cells such as dendritic cells, in such a way that they themselves produce the corresponding proteins on their cellular surface.

[0028] By "nucleic acid" as used herein includes "polynucleotide," "oligonucleotide," and

"nucleic acid molecule," and generally means a polymer of DNA or RNA, which can be single-stranded or double-stranded, synthesized or obtained (e.g., isolated and/or purified) from natural sources, which can contain natural, non-natural or altered nucleotides, and which can contain a natural, non-natural or altered internucleotide linkage, such as a phosphoroamidate linkage or a phosphorothioate linkage, instead of the phosphodiester found between the nucleotides of an unmodified oligonucleotide.

[0029] Preferably, the nucleic acids of the invention are recombinant. As used herein, the term "recombinant" refers to (i) molecules that are constructed outside living cells by joining natural or synthetic nucleic acid segments to nucleic acid molecules that can replicate in a living cell, or (ii) molecules that result from the replication of those described in (i) above. For purposes herein, the replication can be *in vitro* replication or in vivo replication. The nucleic acid can comprise any nucleotide sequence which encodes any of the TCRs, polypeptides, or proteins, or functional portions or functional variants thereof described herein.

[0030] Furthermore, the invention provides a vector comprising a nucleic acid in accordance to the invention as described above. Desirably, the vector is an expression vector or a recombinant expression vector. The term "recombinant expression vector" refers in context of the present invention to a nucleic acid construct that allows for the expression of an mRNA, protein or polypeptide in a suitable host cell. The recombinant expression vector of the invention can be any suitable recombinant expression vector, and can be used to transform or transfect any suitable host. Suitable vectors include those designed for propagation and expansion or for expression or both, such as plasmids and viruses. Examples of animal expression vectors include pEUK-Cl, pMAM and pMAMneo. Preferably, the recombinant expression vector is a viral vector, e.g., a retroviral vector. The recombinant expression vector comprises regulatory sequences, such as transcription and translation initiation and termination codons, which are specific to the type of host cell (e.g., bacterium, fungus, plant, or animal) into which the vector is to be introduced and in which the expression of the nucleic acid of the invention shall be performed. Furthermore, the vector of the invention may include one or more marker genes, which allow for selection of transformed or transfected hosts. The recombinant expression vector can comprise a native or normative promoter operably linked to the nucleotide sequence encoding the constructs of the invention, or to the nucleotide sequence which is complementary to or which hybridizes to the nucleotide sequence encoding the constructs of the invention. The selection of promoters include, e.g., strong, weak, inducible, tissue-specific and developmental-specific promoters. The promoter can be a non-viral promoter or a viral promoter. The inventive recombinant expression vectors can be designed for either transient expression, for stable expression, or for both. Also, the recombinant expression vectors can be made for constitutive expression or for inducible expression.

[0031] The invention also pertains to a host cell comprising an antigen recognizing construct in accordance with the invention. Specifically the host cell of the invention comprises a nucleic acid, or a vector as described herein above. The host cell can be a eukaryotic cell, e.g., plant, animal, fungi, or algae, or can be a prokaryotic cell, e.g., bacteria or protozoa. The host cell

can be a cultured cell or a primary cell, i.e., isolated directly from an organism, e.g., a human. The host cell can be an adherent cell or a suspended cell, i.e., a cell that grows in suspension. For purposes of producing a recombinant TCR, polypeptide, or protein, the host cell is preferably a mammalian cell. Most preferably, the host cell is a human cell. While the host cell can be of any cell type, can originate from any type of tissue, and can be of any developmental stage, the host cell preferably is a peripheral blood leukocyte (PBL) or a peripheral blood mononuclear cell (PBMC). More preferably, the host cell is a T cell. The T cell can be any T cell, such as a cultured T cell, e.g., a primary T cell, or a T cell from a cultured T cell line, e.g., Jurkat, SupTl, etc., or a T cell obtained from a mammal, preferably a T cell or T cell pre-curser from a human patient. If obtained from a mammal, the T cell can be obtained from numerous sources, including but not limited to blood, bone marrow, lymph node, the thymus, or other tissues or fluids. T cells can also be enriched for or purified. Preferably, the T cell is a human T cell. More preferably, the T cell is a T cell isolated from a human. The T cell can be any type of T cell and can be of any developmental stage, including but not limited to, CD4positive and/or CD8positive, CD4 positive helper T cells, e.g., Th1 and Th2 cells, CD8 positive T cells (e.g., cytotoxic T cells), tumor infiltrating cells (TILs), memory T cells, naive T cells, and the like. Preferably, the T cell is a CD8 positive T cell or a CD4 positive T cell.

[0032] Preferably, the host cell of the invention is a lymphocyte, preferably a T lymphocyte, such as a CD4 or CD8 positive T-cell. The host cell furthermore preferably is a tumor reactive T cell specific for MAGE-A1 expressing tumor cells.

[0033] One further aspect of the present invention relates to the herein disclosed antigen recognizing constructs, nucleic acids, vectors and/or host cell for use in medicine. The use in medicine in one preferred embodiment includes the use in the diagnosis, prevention and/or treatment of a proliferative disease, such as a malignant or benign tumor disease.

[0034] Thus also disclosed by the present invention is a method for treating a subject suffering from a tumor or tumor disease comprising the administration of the antigen recognizing constructs, nucleic acids, vectors and/or host cell as disclosed by the present invention. Preferably the subject is a subject in need of such a treatment. The subject in preferred embodiments is a mammalian subject, preferably a human patient, suffering from a tumor or tumor disease.

[0035] In one preferred aspect of the invention the tumor or tumor disease is a disease characterized by the expression of a MAGE antigen as described herein above. Most preferably the tumor or tumor disease expresses the MAGE-A1 antigen, even more preferably wherein the tumor or tumor disease presents via HLA the MAGE-$A1_{278-286}$ epitope. Further preferred is that the tumor or tumor disease is characterized by the differential expression of the MAGE-A1 antigen compared to healthy tissue. The MAGE-A1 antigen may be expressed to a low extend in normal (non-cancerous) cells, whereas the antigen is significantly stronger expressed in the tumor cells.

[0036] Also, in one preferred aspect of the invention the expression of MAGE-A1 in the tumor

is induced or enhanced by prior pharmacologic treatment, e.g. with 5-aza-2-deoxycitabine.

[0037] The term "tumor" or "tumor disease" in the context of the present invention denotes a disease selected from melanomas, hepatocellular carcinomas, intra- and extrahepatic cholangiocellular carcinomas, squamous cell carcinomas, adenocarcinomas as well as undifferentiated carcinomas of the head, neck, lung or esophagus, colorectal carcinomas, chondrosarcomas, osteo-sarcomas, medulloblastomas, neuroblastomas, non-squamous cell carcinomas of the head or neck, ovarian tumors, lymphomas, acute and chronic lymphocytic leukemias, acute and chronic myeloid leukemia, bladder carcinomas, prostate carcinomas, pancreatic adenocarcinomas, mammary carcinomas and gastric carcinomas. Preferred diseases to be treated by the products and/or methods of the invention include melanoma, non-small-cell lung cancer, pancreatic adenocarcinoma and cholangiocellular carcinoma.

[0038] One preferred medicinal use of the invention relates to immune therapy, preferably adoptive T cell therapy. The product and methods of the invention are particularly useful in the context of adoptive T cell therapy. The administration of the compounds of the invention can for example involve the infusion of T cells of the invention into said patient. Preferably such T cells are autologous T cells of the patient which were in vitro transduced with a nucleic acid or antigen recognizing constructs of the present invention.

[0039] The invention in one further aspect discloses a method for the manufacturing of a MAGE-A1 specific antigen recognizing construct (ARC) expressing cell line, the ARC being a T cell receptor (TCR), comprising:

1. a. Providing a suitable host cell,
2. b. Providing a genetic construct encoding for an ARC according of the invention,
3. c. Introducing into said suitable host cell said genetic construct,
4. d. Expressing said genetic construct by said suitable host cell.

[0040] The above method may in one preferred embodiment further comprise the step of including a cell surface presentation of said ARC.

[0041] Of course it is that in context of this aspect of the invention said ARC is an ARC according to the inventive aspects as described herein above. In this respect it is also additionally or alternatively preferred that said ARC is of mammalian origin, preferably of human origin.

[0042] The preferred suitable host cell for use in the method of the invention is a mammalian, in particular a human cell, such as a human T-cell. T cells for use in the invention are described in detail herein above.

[0043] The ARC produced according to the method of the invention is a TCR. For example also included are TCRs with additional (functional) domains or a TCR provided with alternative

domains, e.g. a TCR provided with a foreign transmembrane-domain as membrane anchor. A TCR produced in accordance with the present invention is for example an alpha/beta TCR, gamma/delta TCR or a single chain TCR (scTCR). Also, TCR forms which are included by the present invention are generally any TCR known in the art, specifically those described herein above.

[0044] Desirably, the transfection system for use in the method in accordance with the invention is a retroviral vector system. Such systems are well known to the skilled artisan.

[0045] Also comprised by the present invention is in one embodiment the additional method step of purification of the ARC from the cell and, optionally, the reconstitution of the translated ARC-fragments in a T-cell.

[0046] Disclosed is also a T-cell obtained or obtainable by a method for the production of a T cell receptor (TCR), which is specific for tumorous cells and has high avidity as described herein above. Such a T cell is depending on the host cell used in the method of the invention for example a human or non-human T-cell, preferably a human TCR.

[0047] Thus also provided is a pharmaceutical composition, comprising any of the herein described products of the invention, specifically any proteins, nucleic acids or host cells. In a preferred embodiment the pharmaceutical composition is for immune therapy.

[0048] Examples of pharmaceutically acceptable carriers or diluents useful in the present invention include stabilizers such as SPGA, carbohydrates (e.g. sorbitol, mannitol, starch, sucrose, glucose, dextran), proteins such as albumin or casein, protein containing agents such as bovine serum or skimmed milk and buffers (e.g. phosphate buffer).

[0049] The present invention will now be further described in the following examples with reference to the accompanying figures and sequences, nevertheless, without being limited thereto. For the purposes of the present invention, all references as cited herein are incorporated by reference in their entireties. In the Figures and Sequences:

Figure 1:
shows the concept of adoptive T cell therapy

Figure 2:
shows MAGE-A1 and its epitope localization

Figure 3:
shows the immune response against MAGE-A1 in AB*ab*DII mice

Figure 4:
shows a schematic representation of the TCR vectors

Figure 5:
shows FACS results of TCR transduced Jurkat 76 cells

Figure 6:
shows the functional avidity of MAGE-A1 specific T cells

Figure 7:

shows the tumor cell recognition MAGE-A1 by T cells transduced with the MAGE-A1 specific TCRs of the invention.

Figure 8:

Vector map of pMP71-TCR1367hc. The TCR encoding sequence is located between nucleotides 1041 and 2864 of SEQ ID No. 13. The TCR beta chain is located between nucleotides 1041 and 1970, the alpha chain between 2037 and 2864.

Figure 9:

Vector map of pMP71-TCR1367mc. The TCR encoding sequence is located between nucleotides 1041 and 2834 of SEQ ID No. 14.. The TCR beta chain is located between nucleotides 1041 and 1952, the alpha chain between 2019 and 2834.

Figure 10:

Vector map of pMP71-TCR1367mmc. The TCR encoding sequence is located between nucleotides 1041 and 2864 of SEQ ID No. 15. The TCR beta chain is located between nucleotides 1041 and 1970, the alpha chain between 2037 and 2864.

Figure 11:

Vector map of pMP71-TCR1405hc. The TCR encoding sequence is located between nucleotides 1041 and 2855 of SEQ ID No. 16. The TCR beta chain is located between nucleotides 1041 and 1967, the alpha chain between 2034 and 2855.

Figure 12:

Vector map of pMP71-TCR1405mc. The TCR encoding sequence is located between nucleotides 1041 and 2825 of SEQ ID No. 17. The TCR beta chain is located between nucleotides 1041 and 1949, the alpha chain between 2016 and 2825.

Figure 13:

Vector map of pMP71-TCR1405mmc. The TCR encoding sequence is located between nucleotides 1041 and 2854 of SEQ ID No. 18. The TCR beta chain is located between nucleotides 1041 and 1967, the alpha chain between 2034 and 2854.

Figure 14:

Vector map of pMP71-TCR1705hc. The TCR encoding sequence is located between nucleotides 1041 and 2894 of SEQ ID No. 19. The TCR beta chain is located between nucleotides 1041 and 2006, the alpha chain between 2073 and 2894.

Figure 15:

Vector map of pMP71-TCR1705mc. The TCR encoding sequence is located between nucleotides 1041 and 2864 of SEQ ID No. 20. The TCR beta chain is located between nucleotides 1041 and 1988, the alpha chain between 2055 and 2864.

Figure 16:

Vector map of pMP71-TCR1705mmc. The TCR encoding sequence is located between nucleotides 1041 and 2894 of SEQ ID No. 21. The TCR beta chain is located between nucleotides 1041 and 2006, the alpha chain between 2073 and 2894.

Figure 17:

T2 cells were incubated with increasing concentrations of MAGE-A1278 and cocultured with human T cells that had been transduced with different TCRs as indicated. After 12 hours, functional response was assessed by measuring IFNγ in the cultures.

Figure 18:

T2 cells were loaded with 10-5 mol/l MAGE-A1278 or the 2 most similar epitopes in the human proteome (MAGE-B16 and MAGE-B5) differing in only 2 amino acids from MAGE-A1278 and co-cultured with TCR modified T cells. Functional response was assessed based on IFNγ production.

Figure 19:

T2 cells were loaded with one of 114 different HLA-A2 restricted self-peptides at a concentration of 10-5 mol/l and co-cultured with T cells from 2 different donors that were transduced with TCR 1367. The results of donor 1 are shown as black dots, the results of donor 2 by white dots.

SEQ ID No 1 to 6: show alpha and beta CDR3 sequences of the TCRs of the invention.

SEQ ID No 7 to 10: show alpha and beta chain CDR3 sequences of healthy humans.

SEQ ID No 11 to 12: show the epitope sequences of human (11) and mouse (12) MAGE-A1.

SEQ ID No 13 to 21: show the vector nucleotide sequences of figures 8 to 16.

SEQ ID No 22 to 39: show the complete amino acid sequences of the alpha and beta chains of the TCRs of the invention

SEQ ID No 40 to 51: show alpha and beta CDR1 and CDR2 sequences of Vα and Vβ genes.

EXAMPLES

Example 1: Generation of T-cells with a MAGE epitope using the AB*ab*DII mouse

[0050] Figure 2 shows the location of the HLA-A2 restricted epitope MAGE-$A1_{278-286}$ is shown in relation to the full-length MAGE-A1 protein (top). The human MAGE-$A1_{278-286}$ epitope is sufficiently different from its mouse homologue to prevent tolerance against human MAGE-$A1_{278-286}$ in AB*ab*DII mice (bottom).

[0051] MAGE-A1 is expressed in a variety of human tumors, whereas its expression on normal human tissue is believed to be restricted to the testes. Therefore, specific targeting of MAGE-A1 expressing cells should limit toxicity to a minimum.

[0052] AB*ab*DII mice were immunized with a 30mer peptide encompassing the nonamer MAGE-$A1_{278-286}$ plus CpG in incomplete Freund's adjuvant. Boosts were performed with the nonamer MAGE-$A_{1278-286}$ plus CpG in incomplete Freund's adjuvant. On the day of analysis, blood was taken and stained with a MAGE-A1/HLA-A2 specific tetramer and with antibodies for certain TRBV chains (IMGT nomenclature). After several boosts a monoclonal population of

MAGE-A1 specific T cells is detectable in the blood of AB*ab*DII mice. Figure 3 shows the immune response of the immunized animal and the immunization scheme. A significant shift in FACS analysis of the immunized cells is observed with the tetramer staining indicating that MAGE specific T cells were generated.

Example 2: Isolation and characterization of T cell receptors

[0053] The cDNA from MAGE-A1 specific T cell clones as generated in Example 1 was amplified by 5'-RACE and sequenced.

[0054] The table 1 shows the amino acid sequences of complementary determining region 3 (CDR3) of the alpha and beta chains for three different TCRs from AB*ab*DII mice and two TCRs obtained from healthy humans (Ottaviani, S., Zhang, Y., Boon, T., & van der Bruggen, P. (2005). A MAGE-1 antigenic peptide recognized by human cytolytic T lymphocytes on HLA-A2 tumor cells. Cancer Immunology, Immunotherapy: CII, 54(12), 1214-1220.*)*.

T**able 1:** Amino acid sequences of the CDR3-regions for three different MAGE-A1 specific TCRs.

TCR	**alpha chain CDR3**	**beta chain CDR3**
1367	TRAV5-CAESIGSNSGYALNF-TRAJ41 (SEQ ID No. 1)	TRBV28-CASRGLAGYEQYF-TRBJ2-7(SEQ ID No. 4)
1405	TRAV13-1-CAARPNSGNTPLVF-TRAJ29 (SEQ ID No. 2)	TRBV29-1-CSVEQDTNTGELFF-TRBJ2-2(SEQ ID No. 5)
1705	TRAV12-3-CAMSDTGNQFYF-TRAJ49(SEQ ID No. 3)	TRBV13-CASSFRGGGANVLTF-TRBJ2-6(SEQ ID No. 6)
CTL27*	TRAV5-CAESYNARLMF-TRAJ31 (SEQ ID No. 7)	TRBV20-CSAREPGQGPYEQYFG-TRBJ7 (SEQ ID No. 9)
CTL89*	TRAV5-CAGSGGGTDKLIF-TRAJ34 (SEQ ID No. 8)	TRBV12-CASLSGVYTFG-TRBJ1-2 (SEQ ID No. 10)
**human repertoire see:* Ottaviani et al. (2005). Cancer Immunology, Immunotherapy, 54(12), 1214-1220		

[0055] The isolated TCR which comprise the above CDR3 sequences were then cloned. The retroviral vector MP71 is used for transduction of primary human peripheral blood lymphocytes (hPBLs). The alpha and beta genes of each TCR are linked with a P2A element which is cut by a cellular protease during translation of the transduced TCR ensuring equimolar expression of both chains (Figure 4).

[0056] All genes are codon optimized for optimal expression. In order to further optimize expression in hPBLs additional modifications were introduced into the wild-type TCR constant

regions. Complete (A) and minimal (B) murinization of the constant regions of the TCR chains usually result in higher expression levels in hPBLs than the unmodified human constant region (C).

[0057] Then hCD8+ Jurkat 76 cells were transduced with different TCRs derived from AB*ab*DII mice and human volunteers. Transduced cells stain positive for CD3. All transduced cells specifically bind the MAGE-A1/HLA-A2 tetramer (Figure 5).

[0058] Surprisingly, the TCRs of the present invention provide an unusually high avidity compared to the TCRs of the state of the art. hPBLs were transduced with different MAGE-A1 specific TCRs. The transduced PBLs were then incubated with T2 cells, which had been pulsed with different concentrations of MAGE-$A1_{278-286}$ peptide. After overnight incubation IFNγ-production was measured by ELISA.

[0059] In response to stimulation with peptide pulsed T2 cells the TCRs from AB*ab*DII mice (Figure 6, closed circles) show a response at lower peptide concentrations and a higher amount of IFNy-production than the TCRs derived from the tolerant human system (Figure 6, open circles) .

[0060] This was further confirmed by testing tumor cell recognition using the TCRs of the invention (Figure 7). Transduced hBLs were incubated with different tumor cell lines. After overnight incubation IFNy-production was measured by ELISA. The transduced hPBLs specifically recognize MAGE-A1 in the context of HLA-A2 restricted presentation. PBLs transduced with TCRs from ABabDII mice (full bars) produce higher amounts of IFNγ than those transduced with TCRs from the human repertoire (shaded bars) when incubated with MAGE-A1 expressing tumor cell lines.

Example 3: Sensitivity and Specificity of the TCR of the Invention

[0061] MAGE-$A1_{278}$ antigen was presented on T2 cells. The antigen presenting T2 cells were co-cultured with T-cells expressing the TCR of the invention or a control TCR (CTL27). As shown in figure 17 T cells modified with inventive TCRs from ABabDII mice (solid lines) respond to lower amounts of antigen than those modified with a human TCR (dash-dotted line). (One representative example out of 3 independent experiments is shown). These results indicate the surprisingly improved (by at least one order of magnitude) sensitivity of the TCR of the invention compared to state of the art TCR.

[0062] In order to test the specificity of the TCR of the invention over closely related MAGE antigenic epitopes, the TCRs were brought into contact with the MAGE antigens KVLEFVAKV (MAGE-B16) and KVLEYLAKV (MAGE-B5). The antigens were presented by T2 cells which were then co-cultured with T-cells expressing the TCR of the invention and a control. Interferon-y release was measured. As can be seen from figure 18, the TCR of the invention

significantly recognized the MAGE-$A1_{278}$ antigen and not the varients of the epitope. The specificity was much better compared to the control TCR.

[0063] The high specificity of the TCR of the invention was confirmed in an experiment testing 144 human HLA-A2 restricted self-antigens. Figure 19 shows that donor T cells transfected with TCR 1367 specifically detected MAGE-A1 and not any other tested self-antigen, demonstrating the surprisingly high degree of specificity of the TCR of the invention.

[0064] Furthermore 10^6 murine MAGE-A1 expressing fibrosarcoma cells were injected into immunodeficient mice and grown to a clinically relevant size of approximately 500 mm^3 tumor volume. To treat the tumors 10^6 MAGE-A1 specific T cells bearing the either one of 2 TCRs from ABabDII mice (1367, 1405) or a human TCR (CTL27) were injected. In the control group, 10^6 T cells bearing an irrelevant TCR were injected.

[0065] Treatment response was assessed 14 days after T-cell injection based on tumor volume. The results are provided in table 2 below. In the groups treated with ABabDII TCRs 100% and 67% of the animals responded to treatment. On the contrary, none of the animals treated with T cells transduced with a human TCR or an irrelevant TCR responded.

Table 2:

Treatment group	Response rate
1367	5/5 (100%)
1405	4/6 (67%)
CTL27 (human)	0/6 (0%)
Irrelevant TCR	0/3 (0%)

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cccagtcacg acgttgtaaa acgacggcca gtgaattagt actctagctt aagtaacgcc     7260
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<210> 22

<211> 275

<212> PRT

<213> Artificial

<220>

<223> TCR1367hc - TCRa15

<400> 22

```
Met Lys Thr Phe Ala Gly Phe Ser Phe Leu Phe Leu Trp Leu Gln Leu
1               5                   10                  15

Asp Cys Met Ser Arg Gly Glu Asp Val Glu Gln Ser Leu Phe Leu Ser
            20                  25                  30

Val Arg Glu Gly Asp Ser Ser Val Ile Asn Cys Thr Tyr Thr Asp Ser
        35                  40                  45

Ser Ser Thr Tyr Leu Tyr Trp Tyr Lys Gln Glu Pro Gly Ala Gly Leu
    50                  55                  60

Gln Leu Leu Thr Tyr Ile Phe Ser Asn Met Asp Met Lys Gln Asp Gln
65                  70                  75                  80

Arg Leu Thr Val Leu Leu Asn Lys Lys Asp Lys His Leu Ser Leu Arg
                85                  90                  95

Ile Ala Asp Thr Gln Thr Gly Asp Ser Ala Ile Tyr Phe Cys Ala Glu
            100                 105                 110
```

```
Ser Ile Gly Ser Asn Ser Gly Tyr Ala Leu Asn Phe Gly Lys Gly Thr
        115                 120                 125

Ser Leu Leu Val Thr Pro His Ile Gln Asn Pro Asp Pro Ala Val Tyr
    130                 135                 140

Gln Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr
145                 150                 155                 160

Asp Phe Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser Asp Val
                165                 170                 175

Tyr Ile Thr Asp Lys Thr Val Leu Asp Met Arg Ser Met Asp Phe Lys
            180                 185                 190

Ser Asn Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala Cys Ala
        195                 200                 205

Asn Ala Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser
    210                 215                 220

Pro Glu Ser Ser Cys Asp Val Lys Leu Val Glu Lys Ser Phe Glu Thr
225                 230                 235                 240

Asp Thr Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe Arg Ile
                245                 250                 255

Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu
            260                 265                 270

Trp Ser Ser
        275
```

<210> 23

<211> 310

<212> PRT

<213> Artificial

<220>

<223> TCR1367hc - TCRb3

<400> 23

```
Met Gly Ile Arg Leu Leu Cys Arg Val Ala Phe Cys Phe Leu Ala Val
1               5                   10                  15

Gly Leu Val Asp Val Lys Val Thr Gln Ser Ser Arg Tyr Leu Val Lys
            20                  25                  30

Arg Thr Gly Glu Lys Val Phe Leu Glu Cys Val Gln Asp Met Asp His
        35                  40                  45

Glu Asn Met Phe Trp Tyr Arg Gln Asp Pro Gly Leu Gly Leu Arg Leu
    50                  55                  60

Ile Tyr Phe Ser Tyr Asp Val Lys Met Lys Glu Lys Gly Asp Ile Pro
```

```
65                  70                  75                  80

Glu Gly Tyr Ser Val Ser Arg Glu Lys Lys Glu Arg Phe Ser Leu Ile
                85                  90                  95

Leu Glu Ser Ala Ser Thr Asn Gln Thr Ser Met Tyr Leu Cys Ala Ser
            100                 105                 110

Arg Gly Leu Ala Gly Tyr Glu Gln Tyr Phe Gly Pro Gly Thr Arg Leu
        115                 120                 125

Thr Val Thr Glu Asp Leu Lys Asn Val Phe Pro Pro Glu Val Ala Val
    130                 135                 140

Phe Glu Pro Ser Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr Leu
145                 150                 155                 160

Val Cys Leu Ala Thr Gly Phe Tyr Pro Asp His Val Glu Leu Ser Trp

                165                 170                 175

Trp Val Asn Gly Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln
            180                 185                 190

Pro Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser
        195                 200                 205

Ser Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His
    210                 215                 220

Phe Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp
225                 230                 235                 240

Thr Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala
                245                 250                 255

Trp Gly Arg Ala Asp Cys Gly Phe Thr Ser Glu Ser Tyr Gln Gln Gly
            260                 265                 270

Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr
        275                 280                 285

Leu Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys
    290                 295                 300

Arg Lys Asp Ser Arg Gly
305                 310
```

<210> 24

<211> 275

<212> PRT

<213> Artificial

<220>

<223> TCR1367mmc - TCRa15mmc

<400> 24

```
Met Lys Thr Phe Ala Gly Phe Ser Phe Leu Phe Leu Trp Leu Gln Leu
1               5                  10                  15

Asp Cys Met Ser Arg Gly Glu Asp Val Glu Gln Ser Leu Phe Leu Ser
            20                  25                  30

Val Arg Glu Gly Asp Ser Ser Val Ile Asn Cys Thr Tyr Thr Asp Ser
        35                  40                  45

Ser Ser Thr Tyr Leu Tyr Trp Tyr Lys Gln Glu Pro Gly Ala Gly Leu
    50                  55                  60

Gln Leu Leu Thr Tyr Ile Phe Ser Asn Met Asp Met Lys Gln Asp Gln
65                  70                  75                  80

Arg Leu Thr Val Leu Leu Asn Lys Lys Asp Lys His Leu Ser Leu Arg
                85                  90                  95

Ile Ala Asp Thr Gln Thr Gly Asp Ser Ala Ile Tyr Phe Cys Ala Glu
            100                 105                 110

Ser Ile Gly Ser Asn Ser Gly Tyr Ala Leu Asn Phe Gly Lys Gly Thr
        115                 120                 125

Ser Leu Leu Val Thr Pro His Ile Gln Asn Pro Asp Pro Ala Val Tyr
    130                 135                 140

Gln Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr
145                 150                 155                 160

Asp Phe Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser Asp Val
                165                 170                 175

Tyr Ile Thr Asp Lys Cys Val Leu Asp Met Arg Ser Met Asp Phe Lys
            180                 185                 190

Ser Asn Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala Cys Ala
        195                 200                 205

Asn Ala Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser
    210                 215                 220

Ser Asp Val Pro Cys Asp Val Lys Leu Val Glu Lys Ser Phe Glu Thr
225                 230                 235                 240

Asp Thr Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe Arg Ile
                245                 250                 255

Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu
            260                 265                 270

Trp Ser Ser
        275
```

<210> 25

<211> 310

<212> PRT

<213> Artificial

<220>

<223> TCR1367mmc - TCRb3mmc

<400> 25

```
Met Gly Ile Arg Leu Leu Cys Arg Val Ala Phe Cys Phe Leu Ala Val
1               5                  10                  15

Gly Leu Val Asp Val Lys Val Thr Gln Ser Ser Arg Tyr Leu Val Lys
            20                  25                  30

Arg Thr Gly Glu Lys Val Phe Leu Glu Cys Val Gln Asp Met Asp His
        35                  40                  45

Glu Asn Met Phe Trp Tyr Arg Gln Asp Pro Gly Leu Gly Leu Arg Leu
    50                  55                  60

Ile Tyr Phe Ser Tyr Asp Val Lys Met Lys Glu Lys Gly Asp Ile Pro
65                  70                  75                  80

Glu Gly Tyr Ser Val Ser Arg Glu Lys Lys Glu Arg Phe Ser Leu Ile
                85                  90                  95

Leu Glu Ser Ala Ser Thr Asn Gln Thr Ser Met Tyr Leu Cys Ala Ser
            100                 105                 110

Arg Gly Leu Ala Gly Tyr Glu Gln Tyr Phe Gly Pro Gly Thr Arg Leu
        115                 120                 125

Thr Val Thr Glu Asp Leu Lys Asn Val Phe Pro Pro Glu Val Ala Val
    130                 135                 140

Phe Glu Pro Ser Lys Ala Glu Ile Ala His Thr Gln Lys Ala Thr Leu
145                 150                 155                 160

Val Cys Leu Ala Thr Gly Phe Tyr Pro Asp His Val Glu Leu Ser Trp
                165                 170                 175

Trp Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln
            180                 185                 190

Pro Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser
        195                 200                 205

Ser Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His
    210                 215                 220

Phe Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp
225                 230                 235                 240
```

```
Thr Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala
                245                 250                 255

Trp Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr His Gln Gly
            260                 265                 270

Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr
        275                 280                 285

Leu Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys
    290                 295                 300

Arg Lys Asp Ser Arg Gly
305                 310
```

<210> 26

<211> 273

<212> PRT

<213> Artificial

<220>

<223> TCR1405hc - TCRa8

<400> 26

```
Met Thr Ser Ile Arg Ala Val Phe Ile Phe Leu Trp Leu Gln Leu Asp
1               5                   10                  15

Leu Val Asn Gly Glu Asn Val Glu Gln His Pro Ser Thr Leu Ser Val
            20                  25                  30

Gln Glu Gly Asp Ser Ala Val Ile Lys Cys Thr Tyr Ser Asp Ser Ala
        35                  40                  45

Ser Asn Tyr Phe Pro Trp Tyr Lys Gln Glu Leu Gly Lys Gly Pro Gln
    50                  55                  60

Leu Ile Ile Asp Ile Arg Ser Asn Val Gly Glu Lys Lys Asp Gln Arg
65                  70                  75                  80

Ile Ala Val Thr Leu Asn Lys Thr Ala Lys His Phe Ser Leu His Ile
                85                  90                  95

Thr Glu Thr Gln Pro Glu Asp Ser Ala Val Tyr Phe Cys Ala Ala Arg
            100                 105                 110

Pro Asn Ser Gly Asn Thr Pro Leu Val Phe Gly Lys Gly Thr Arg Leu
        115                 120                 125

Ser Val Ile Ala Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr Gln Leu
    130                 135                 140

Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp Phe
145                 150                 155                 160
```

```
Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser Asp Val Tyr Ile
                165                 170                 175

Thr Asp Lys Thr Val Leu Asp Met Arg Ser Met Asp Phe Lys Ser Asn
            180                 185                 190

Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala Cys Ala Asn Ala
        195                 200                 205

Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser Pro Glu
    210                 215                 220

Ser Ser Cys Asp Val Lys Leu Val Glu Lys Ser Phe Glu Thr Asp Thr
225                 230                 235                 240

Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe Arg Ile Leu Leu
                245                 250                 255

Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser
            260                 265                 270

Ser
```

<210> 27

<211> 309

<212> PRT

<213> Artificial

<220>

<223> TCR1405hc - TCRb4

<400> 27

```
Met Leu Ser Leu Leu Leu Leu Leu Leu Gly Leu Gly Ser Val Phe Ser
1               5                   10                  15

Ala Val Ile Ser Gln Lys Pro Ser Arg Asp Ile Cys Gln Arg Gly Thr
            20                  25                  30

Ser Leu Thr Ile Gln Cys Gln Val Asp Ser Gln Val Thr Met Met Phe
        35                  40                  45

Trp Tyr Arg Gln Gln Pro Gly Gln Ser Leu Thr Leu Ile Ala Thr Ala
    50                  55                  60

Asn Gln Gly Ser Glu Ala Thr Tyr Glu Ser Gly Phe Val Ile Asp Lys
65                  70                  75                  80

Phe Pro Ile Ser Arg Pro Asn Leu Thr Phe Ser Thr Leu Thr Val Ser
                85                  90                  95

Asn Met Ser Pro Glu Asp Ser Ser Ile Tyr Leu Cys Ser Val Glu Gln
            100                 105                 110

Asp Thr Asn Thr Gly Glu Leu Phe Phe Gly Glu Gly Ser Arg Leu Thr
        115                 120                 125
```

```
Val Leu Glu Asp Leu Lys Asn Val Phe Pro Pro Glu Val Ala Val Phe
    130                 135                 140

Glu Pro Ser Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr Leu Val
145                 150                 155                 160

Cys Leu Ala Thr Gly Phe Tyr Pro Asp His Val Glu Leu Ser Trp Trp
                165                 170                 175

Val Asn Gly Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln Pro
            180                 185                 190

Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser Ser
        195                 200                 205

Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His Phe
    210                 215                 220

Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr
225                 230                 235                 240

Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala Trp
                245                 250                 255

Gly Arg Ala Asp Cys Gly Phe Thr Ser Glu Ser Tyr Gln Gln Gly Val
            260                 265                 270

Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu
        275                 280                 285

Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys Arg
    290                 295                 300

Lys Asp Ser Arg Gly
305
```

<210> 28

<211> 273

<212> PRT

<213> Artificial

<220>

<223> TCR1405mmc - TCRa8mmc

<400> 28

```
Met Thr Ser Ile Arg Ala Val Phe Ile Phe Leu Trp Leu Gln Leu Asp
1               5                   10                  15

Leu Val Asn Gly Glu Asn Val Glu Gln His Pro Ser Thr Leu Ser Val
            20                  25                  30

Gln Glu Gly Asp Ser Ala Val Ile Lys Cys Thr Tyr Ser Asp Ser Ala
        35                  40                  45

Ser Asn Tyr Phe Pro Trp Tyr Lys Gln Glu Leu Gly Lys Gly Pro Gln
    50                  55                  60
```

```
    50                  55                  60

Leu Ile Ile Asp Ile Arg Ser Asn Val Gly Glu Lys Lys Asp Gln Arg
65                  70                  75                  80

Ile Ala Val Thr Leu Asn Lys Thr Ala Lys His Phe Ser Leu His Ile
                85                  90                  95

Thr Glu Thr Gln Pro Glu Asp Ser Ala Val Tyr Phe Cys Ala Ala Arg
            100                 105                 110

Pro Asn Ser Gly Asn Thr Pro Leu Val Phe Gly Lys Gly Thr Arg Leu
        115                 120                 125

Ser Val Ile Ala Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr Gln Leu
    130                 135                 140

Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp Phe
145                 150                 155                 160

Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser Asp Val Tyr Ile
                165                 170                 175

Thr Asp Lys Cys Val Leu Asp Met Arg Ser Met Asp Phe Lys Ser Asn
            180                 185                 190

Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala Cys Ala Asn Ala
        195                 200                 205

Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser Ser Asp
    210                 215                 220

Val Pro Cys Asp Val Lys Leu Val Glu Lys Ser Phe Glu Thr Asp Thr
225                 230                 235                 240

Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe Arg Ile Leu Leu
                245                 250                 255

Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser
            260                 265                 270

Ser
```

<210> 29

<211> 309

<212> PRT

<213> Artificial

<220>

<223> TCR1405mmc - TCRb4mmc

<400> 29

```
Met Leu Ser Leu Leu Leu Leu Leu Leu Gly Leu Gly Ser Val Phe Ser
1               5                   10                  15
```

```
Ala Val Ile Ser Gln Lys Pro Ser Arg Asp Ile Cys Gln Arg Gly Thr
            20                  25                  30

Ser Leu Thr Ile Gln Cys Gln Val Asp Ser Gln Val Thr Met Met Phe
        35                  40                  45

Trp Tyr Arg Gln Gln Pro Gly Gln Ser Leu Thr Leu Ile Ala Thr Ala
    50                  55                  60

Asn Gln Gly Ser Glu Ala Thr Tyr Glu Ser Gly Phe Val Ile Asp Lys
65                  70                  75                  80

Phe Pro Ile Ser Arg Pro Asn Leu Thr Phe Ser Thr Leu Thr Val Ser
                85                  90                  95

Asn Met Ser Pro Glu Asp Ser Ser Ile Tyr Leu Cys Ser Val Glu Gln
            100                 105                 110

Asp Thr Asn Thr Gly Glu Leu Phe Phe Gly Glu Gly Ser Arg Leu Thr

        115                 120                 125

Val Leu Glu Asp Leu Lys Asn Val Phe Pro Pro Glu Val Ala Val Phe
    130                 135                 140

Glu Pro Ser Lys Ala Glu Ile Ala His Thr Gln Lys Ala Thr Leu Val
145                 150                 155                 160

Cys Leu Ala Thr Gly Phe Tyr Pro Asp His Val Glu Leu Ser Trp Trp
                165                 170                 175

Val Asn Gly Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Pro
            180                 185                 190

Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser Ser
        195                 200                 205

Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His Phe
    210                 215                 220

Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr
225                 230                 235                 240

Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala Trp
                245                 250                 255

Gly Arg Ala Asp Cys Gly Ile Thr Ser Ala Ser Tyr His Gln Gly Val
            260                 265                 270

Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu
        275                 280                 285

Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys Arg
    290                 295                 300
```

Lys Asp Ser Arg Gly
305

<210> 30

<211> 273

<212> PRT

<213> Artificial

<220>

<223> TCR1705hc - TCRa2

<400> 30

Met Met Lys Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu
1 5 10 15

Ser Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asp Pro Gly Pro
20 25 30

Leu Ser Val Pro Glu Gly Ala Ile Val Ser Leu Asn Cys Thr Tyr Ser
35 40 45

Asn Ser Ala Phe Gln Tyr Phe Met Trp Tyr Arg Gln Tyr Ser Arg Lys
50 55 60

Gly Pro Glu Leu Leu Met Tyr Thr Tyr Ser Ser Gly Asn Lys Glu Asp
65 70 75 80

Gly Arg Phe Thr Ala Gln Val Asp Lys Ser Ser Lys Tyr Ile Ser Leu
85 90 95

Phe Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala
100 105 110

Met Ser Asp Thr Gly Asn Gln Phe Tyr Phe Gly Thr Gly Thr Ser Leu
115 120 125

Thr Val Ile Pro Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr Gln Leu
130 135 140

Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp Phe
145 150 155 160

Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser Asp Val Tyr Ile
165 170 175

Thr Asp Lys Thr Val Leu Asp Met Arg Ser Met Asp Phe Lys Ser Asn
180 185 190

Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala Cys Ala Asn Ala
195 200 205

Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser Pro Glu
210 215 220

Ser Ser Cys Asp Val Lys Leu Val Glu Lys Ser Phe Glu Thr Asp Thr
225 230 235 240

Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe Arg Ile Leu Leu
245 250 255

Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser
260 265 270

Ser

<210> 31
<211> 322
<212> PRT
<213> Artificial

<220>
<223> TCR1705hc - TCRb13

<400> 31
Met Leu Ser Pro Asp Leu Pro Asp Ser Ala Trp Asn Thr Arg Leu Leu
1 5 10 15

Cys His Val Met Leu Cys Leu Leu Gly Ala Val Ser Val Ala Ala Gly
20 25 30

Val Ile Gln Ser Pro Arg His Leu Ile Lys Glu Lys Arg Glu Thr Ala
35 40 45

Thr Leu Lys Cys Tyr Pro Ile Pro Arg His Asp Thr Val Tyr Trp Tyr
50 55 60

Gln Gln Gly Pro Gly Gln Asp Pro Gln Phe Leu Ile Ser Phe Tyr Glu
65 70 75 80

Lys Met Gln Ser Asp Lys Gly Ser Ile Pro Asp Arg Phe Ser Ala Gln
85 90 95

Gln Phe Ser Asp Tyr His Ser Glu Leu Asn Met Ser Ser Leu Glu Leu
100 105 110

Gly Asp Ser Ala Leu Tyr Phe Cys Ala Ser Ser Phe Arg Gly Gly Gly
115 120 125

Ala Asn Val Leu Thr Phe Gly Ala Gly Ser Arg Leu Thr Val Leu Glu
130 135 140

Asp Leu Lys Asn Val Phe Pro Pro Glu Val Ala Val Phe Glu Pro Ser
145 150 155 160

Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr Leu Val Cys Leu Ala
165 170 175

Thr Gly Phe Tyr Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly
180 185 190

```
Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln Pro Leu Lys Glu
        195                 200                 205

Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser Ser Arg Leu Arg
    210                 215                 220

Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His Phe Arg Cys Gln
225                 230                 235                 240

Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr Gln Asp Arg
                245                 250                 255

Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala Trp Gly Arg Ala
            260                 265                 270

Asp Cys Gly Phe Thr Ser Glu Ser Tyr Gln Gln Gly Val Leu Ser Ala
        275                 280                 285

Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val
    290                 295                 300

Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys Arg Lys Asp Ser
305                 310                 315                 320

Arg Gly
```

<210> 32

<211> 273

<212> PRT

<213> Artificial

<220>

<223> TCR1705mmc - TCRa2mmc

<400> 32

```
Met Met Lys Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu
1               5                   10                  15

Ser Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asp Pro Gly Pro
            20                  25                  30

Leu Ser Val Pro Glu Gly Ala Ile Val Ser Leu Asn Cys Thr Tyr Ser
        35                  40                  45

Asn Ser Ala Phe Gln Tyr Phe Met Trp Tyr Arg Gln Tyr Ser Arg Lys
    50                  55                  60

Gly Pro Glu Leu Leu Met Tyr Thr Tyr Ser Ser Gly Asn Lys Glu Asp
65                  70                  75                  80

Gly Arg Phe Thr Ala Gln Val Asp Lys Ser Ser Lys Tyr Ile Ser Leu
                85                  90                  95
```

```
Phe Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala
            100                 105                 110

Met Ser Asp Thr Gly Asn Gln Phe Tyr Phe Gly Thr Gly Thr Ser Leu
        115                 120                 125

Thr Val Ile Pro Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr Gln Leu
    130                 135                 140

Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp Phe
145                 150                 155                 160

Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser Asp Val Tyr Ile
                165                 170                 175

Thr Asp Lys Cys Val Leu Asp Met Arg Ser Met Asp Phe Lys Ser Asn
            180                 185                 190

Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala Cys Ala Asn Ala
        195                 200                 205

Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser Ser Asp
    210                 215                 220

Val Pro Cys Asp Val Lys Leu Val Glu Lys Ser Phe Glu Thr Asp Thr
225                 230                 235                 240

Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe Arg Ile Leu Leu
                245                 250                 255

Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser
            260                 265                 270

Ser
```

<210> 33

<211> 322

<212> PRT

<213> Artificial

<220>

<223> TCR1705mmc - TCRb13mmc

<400> 33

```
Met Leu Ser Pro Asp Leu Pro Asp Ser Ala Trp Asn Thr Arg Leu Leu
1               5                   10                  15

Cys His Val Met Leu Cys Leu Leu Gly Ala Val Ser Val Ala Ala Gly
            20                  25                  30

Val Ile Gln Ser Pro Arg His Leu Ile Lys Glu Lys Arg Glu Thr Ala
        35                  40                  45

Thr Leu Lys Cys Tyr Pro Ile Pro Arg His Asp Thr Val Tyr Trp Tyr
    50                  55                  60
```

```
Gln Gln Gly Pro Gly Gln Asp Pro Gln Phe Leu Ile Ser Phe Tyr Glu
65                  70                  75                  80

Lys Met Gln Ser Asp Lys Gly Ser Ile Pro Asp Arg Phe Ser Ala Gln
                85                  90                  95

Gln Phe Ser Asp Tyr His Ser Glu Leu Asn Met Ser Ser Leu Glu Leu
            100                 105                 110

Gly Asp Ser Ala Leu Tyr Phe Cys Ala Ser Ser Phe Arg Gly Gly Gly
        115                 120                 125

Ala Asn Val Leu Thr Phe Gly Ala Gly Ser Arg Leu Thr Val Leu Glu
    130                 135                 140

Asp Leu Lys Asn Val Phe Pro Pro Glu Val Ala Val Phe Glu Pro Ser
145                 150                 155                 160

Lys Ala Glu Ile Ala His Thr Gln Lys Ala Thr Leu Val Cys Leu Ala
                165                 170                 175

Thr Gly Phe Tyr Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly
            180                 185                 190

Lys Glu Val His Ser Gly Val Cys Thr Asp Pro Gln Pro Leu Lys Glu
        195                 200                 205

Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser Ser Arg Leu Arg
    210                 215                 220

Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His Phe Arg Cys Gln
225                 230                 235                 240

Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr Gln Asp Arg
                245                 250                 255

Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala Trp Gly Arg Ala
            260                 265                 270

Asp Cys Gly Ile Thr Ser Ala Ser Tyr His Gln Gly Val Leu Ser Ala
        275                 280                 285

Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val
    290                 295                 300

Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys Arg Lys Asp Ser
305                 310                 315                 320

Arg Gly
```

<210> 34

<211> 271

<212> PRT

<213> Artificial

<220>

<223> 1367_mc - TCRa15mc

<400> 34

```
Met Lys Thr Phe Ala Gly Phe Ser Phe Leu Phe Leu Trp Leu Gln Leu
1               5                  10                  15

Asp Cys Met Ser Arg Gly Glu Asp Val Glu Gln Ser Leu Phe Leu Ser
            20                  25                  30

Val Arg Glu Gly Asp Ser Ser Val Ile Asn Cys Thr Tyr Thr Asp Ser
        35                  40                  45

Ser Ser Thr Tyr Leu Tyr Trp Tyr Lys Gln Glu Pro Gly Ala Gly Leu
    50                  55                  60

Gln Leu Leu Thr Tyr Ile Phe Ser Asn Met Asp Met Lys Gln Asp Gln
65                  70                  75                  80

Arg Leu Thr Val Leu Leu Asn Lys Lys Asp Lys His Leu Ser Leu Arg
                85                  90                  95

Ile Ala Asp Thr Gln Thr Gly Asp Ser Ala Ile Tyr Phe Cys Ala Glu
            100                 105                 110

Ser Ile Gly Ser Asn Ser Gly Tyr Ala Leu Asn Phe Gly Lys Gly Thr
        115                 120                 125

Ser Leu Leu Val Thr Pro His Ile Gln Asn Pro Glu Pro Ala Val Tyr
    130                 135                 140

Gln Leu Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr
145                 150                 155                 160

Asp Phe Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr
                165                 170                 175

Phe Ile Thr Asp Lys Thr Val Leu Asp Met Lys Ala Met Asp Ser Lys
            180                 185                 190

Ser Asn Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln
        195                 200                 205

Asp Ile Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro
    210                 215                 220

Cys Asp Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu
225                 230                 235                 240

Asn Phe Gln Asn Leu Ser Val Met Gly Leu Arg Ile Leu Leu Leu Lys
                245                 250                 255

Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser
```

260 265 270

<210> 35

<211> 304

<212> PRT

<213> Artificial

<220>

<223> 1367_mc - TCRb3mc

<400> 35

```
Met Gly Ile Arg Leu Leu Cys Arg Val Ala Phe Cys Phe Leu Ala Val
1               5                  10                  15

Gly Leu Val Asp Val Lys Val Thr Gln Ser Ser Arg Tyr Leu Val Lys
            20                  25                  30

Arg Thr Gly Glu Lys Val Phe Leu Glu Cys Val Gln Asp Met Asp His
        35                  40                  45

Glu Asn Met Phe Trp Tyr Arg Gln Asp Pro Gly Leu Gly Leu Arg Leu
    50                  55                  60

Ile Tyr Phe Ser Tyr Asp Val Lys Met Lys Glu Lys Gly Asp Ile Pro
65                  70                  75                  80

Glu Gly Tyr Ser Val Ser Arg Glu Lys Lys Glu Arg Phe Ser Leu Ile
                85                  90                  95

Leu Glu Ser Ala Ser Thr Asn Gln Thr Ser Met Tyr Leu Cys Ala Ser
            100                 105                 110

Arg Gly Leu Ala Gly Tyr Glu Gln Tyr Phe Gly Pro Gly Thr Arg Leu
        115                 120                 125

Thr Val Thr Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu
    130                 135                 140

Phe Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu
145                 150                 155                 160

Val Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp
                165                 170                 175

Trp Val Asn Gly Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln
            180                 185                 190

Ala Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg
        195                 200                 205

Val Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln
    210                 215                 220

Val Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser
```

```
225                 230                 235                 240

Pro Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala
                245                 250                 255

Asp Cys Gly Ile Thr Ser Ala Ser Tyr His Gln Gly Val Leu Ser Ala
            260                 265                 270

Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val
        275                 280                 285

Leu Val Ser Gly Leu Val Leu Met Ala Met Val Lys Lys Lys Asn Ser
    290                 295                 300
```

<210> 36

<211> 269

<212> PRT

<213> Artificial

<220>

<223> 1405_mc - TCRa8mc

<400> 36

```
Met Thr Ser Ile Arg Ala Val Phe Ile Phe Leu Trp Leu Gln Leu Asp
1               5                   10                  15

Leu Val Asn Gly Glu Asn Val Glu Gln His Pro Ser Thr Leu Ser Val
            20                  25                  30

Gln Glu Gly Asp Ser Ala Val Ile Lys Cys Thr Tyr Ser Asp Ser Ala
        35                  40                  45

Ser Asn Tyr Phe Pro Trp Tyr Lys Gln Glu Leu Gly Lys Gly Pro Gln
    50                  55                  60

Leu Ile Ile Asp Ile Arg Ser Asn Val Gly Glu Lys Lys Asp Gln Arg
65                  70                  75                  80

Ile Ala Val Thr Leu Asn Lys Thr Ala Lys His Phe Ser Leu His Ile
                85                  90                  95

Thr Glu Thr Gln Pro Glu Asp Ser Ala Val Tyr Phe Cys Ala Ala Arg
            100                 105                 110

Pro Asn Ser Gly Asn Thr Pro Leu Val Phe Gly Lys Gly Thr Arg Leu
        115                 120                 125

Ser Val Ile Ala Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu
    130                 135                 140

Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe
145                 150                 155                 160

Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile
                165                 170                 175
```

```
Thr Asp Lys Thr Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn
            180                 185                 190

Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile
        195                 200                 205

Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp

    210                 215                 220

Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe
225                 230                 235                 240

Gln Asn Leu Ser Val Met Gly Leu Arg Ile Leu Leu Leu Lys Val Ala
                245                 250                 255

Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser
            260                 265
```

<210> 37

<211> 303

<212> PRT

<213> Artificial

<220>

<223> 1405_mc - TCRb4mc

<400> 37

```
Met Leu Ser Leu Leu Leu Leu Leu Leu Gly Leu Gly Ser Val Phe Ser
1               5                   10                  15

Ala Val Ile Ser Gln Lys Pro Ser Arg Asp Ile Cys Gln Arg Gly Thr
            20                  25                  30

Ser Leu Thr Ile Gln Cys Gln Val Asp Ser Gln Val Thr Met Met Phe
        35                  40                  45

Trp Tyr Arg Gln Gln Pro Gly Gln Ser Leu Thr Leu Ile Ala Thr Ala
    50                  55                  60

Asn Gln Gly Ser Glu Ala Thr Tyr Glu Ser Gly Phe Val Ile Asp Lys
65                  70                  75                  80

Phe Pro Ile Ser Arg Pro Asn Leu Thr Phe Ser Thr Leu Thr Val Ser
                85                  90                  95

Asn Met Ser Pro Glu Asp Ser Ser Ile Tyr Leu Cys Ser Val Glu Gln
            100                 105                 110

Asp Thr Asn Thr Gly Glu Leu Phe Phe Gly Glu Gly Ser Arg Leu Thr
        115                 120                 125

Val Leu Glu Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe
```

```
    130                 135                 140

Glu Pro Ser Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val
145                 150                 155                 160

Cys Leu Ala Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp
                165                 170                 175

Val Asn Gly Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln Ala
            180                 185                 190

Tyr Lys Glu Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val
        195                 200                 205

Ser Ala Thr Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val
    210                 215                 220

Gln Phe His Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro
225                 230                 235                 240

Lys Pro Val Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp
                245                 250                 255

Cys Gly Ile Thr Ser Ala Ser Tyr His Gln Gly Val Leu Ser Ala Thr
            260                 265                 270

Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu
        275                 280                 285

Val Ser Gly Leu Val Leu Met Ala Met Val Lys Lys Lys Asn Ser
    290                 295                 300
```

<210> 38

<211> 269

<212> PRT

<213> Artificial

<220>

<223> 1705_mc - TCRa2mc

<400> 38

```
Met Met Lys Ser Leu Arg Val Leu Leu Val Ile Leu Trp Leu Gln Leu
1               5                   10                  15

Ser Trp Val Trp Ser Gln Gln Lys Glu Val Glu Gln Asp Pro Gly Pro
            20                  25                  30

Leu Ser Val Pro Glu Gly Ala Ile Val Ser Leu Asn Cys Thr Tyr Ser
        35                  40                  45

Asn Ser Ala Phe Gln Tyr Phe Met Trp Tyr Arg Gln Tyr Ser Arg Lys
    50                  55                  60

Gly Pro Glu Leu Leu Met Tyr Thr Tyr Ser Ser Gly Asn Lys Glu Asp
65                  70                  75                  80
```

```
Gly Arg Phe Thr Ala Gln Val Asp Lys Ser Ser Lys Tyr Ile Ser Leu
                85                  90                  95

Phe Ile Arg Asp Ser Gln Pro Ser Asp Ser Ala Thr Tyr Leu Cys Ala
            100                 105                 110

Met Ser Asp Thr Gly Asn Gln Phe Tyr Phe Gly Thr Gly Thr Ser Leu
        115                 120                 125

Thr Val Ile Pro Asn Ile Gln Asn Pro Glu Pro Ala Val Tyr Gln Leu
    130                 135                 140

Lys Asp Pro Arg Ser Gln Asp Ser Thr Leu Cys Leu Phe Thr Asp Phe
145                 150                 155                 160

Asp Ser Gln Ile Asn Val Pro Lys Thr Met Glu Ser Gly Thr Phe Ile
                165                 170                 175

Thr Asp Lys Thr Val Leu Asp Met Lys Ala Met Asp Ser Lys Ser Asn
            180                 185                 190

Gly Ala Ile Ala Trp Ser Asn Gln Thr Ser Phe Thr Cys Gln Asp Ile
        195                 200                 205

Phe Lys Glu Thr Asn Ala Thr Tyr Pro Ser Ser Asp Val Pro Cys Asp
    210                 215                 220

Ala Thr Leu Thr Glu Lys Ser Phe Glu Thr Asp Met Asn Leu Asn Phe
225                 230                 235                 240

Gln Asn Leu Ser Val Met Gly Leu Arg Ile Leu Leu Leu Lys Val Ala
                245                 250                 255

Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser
            260                 265
```

<210> 39

<211> 316

<212> PRT

<213> Artificial

<220>

<223> 1705_mc - TCRb13mc

<400> 39

```
Met Leu Ser Pro Asp Leu Pro Asp Ser Ala Trp Asn Thr Arg Leu Leu
1               5                   10                  15

Cys His Val Met Leu Cys Leu Leu Gly Ala Val Ser Val Ala Ala Gly
            20                  25                  30

Val Ile Gln Ser Pro Arg His Leu Ile Lys Glu Lys Arg Glu Thr Ala
        35                  40                  45
```

```
Thr Leu Lys Cys Tyr Pro Ile Pro Arg His Asp Thr Val Tyr Trp Tyr
    50                  55                  60

Gln Gln Gly Pro Gly Gln Asp Pro Gln Phe Leu Ile Ser Phe Tyr Glu
65                  70                  75                  80

Lys Met Gln Ser Asp Lys Gly Ser Ile Pro Asp Arg Phe Ser Ala Gln
                85                  90                  95

Gln Phe Ser Asp Tyr His Ser Glu Leu Asn Met Ser Ser Leu Glu Leu
            100                 105                 110

Gly Asp Ser Ala Leu Tyr Phe Cys Ala Ser Ser Phe Arg Gly Gly Gly
        115                 120                 125

Ala Asn Val Leu Thr Phe Gly Ala Gly Ser Arg Leu Thr Val Leu Glu
    130                 135                 140

Asp Leu Arg Asn Val Thr Pro Pro Lys Val Ser Leu Phe Glu Pro Ser
145                 150                 155                 160

Lys Ala Glu Ile Ala Asn Lys Gln Lys Ala Thr Leu Val Cys Leu Ala
                165                 170                 175

Arg Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly
            180                 185                 190

Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln Ala Tyr Lys Glu
        195                 200                 205

Ser Asn Tyr Ser Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr
    210                 215                 220

Phe Trp His Asn Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe His
225                 230                 235                 240

Gly Leu Ser Glu Glu Asp Lys Trp Pro Glu Gly Ser Pro Lys Pro Val
                245                 250                 255

Thr Gln Asn Ile Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Ile
            260                 265                 270

Thr Ser Ala Ser Tyr His Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr
        275                 280                 285

Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Gly
    290                 295                 300

Leu Val Leu Met Ala Met Val Lys Lys Lys Asn Ser
305                 310                 315
```

<210> 40

<211> 6

<212> PRT

<213> Homo sapiens

<400> 40
Asp Ser Ser Ser Thr Tyr
1 5

<210> 41
<211> 7
<212> PRT
<213> Homo sapiens

<400> 41
Ile Phe Ser Asn Met Asp Met
1 5

<210> 42
<211> 6
<212> PRT
<213> Homo sapiens

<400> 42
Asp Ser Ala Ser Asn Tyr
1 5

<210> 43
<211> 7
<212> PRT
<213> Homo sapiens

<400> 43
Ile Arg Ser Asn Val Gly Glu
1 5

<210> 44
<211> 6
<212> PRT
<213> Homo sapiens

<400> 44
Asn Ser Ala Phe Gln Tyr
1 5

<210> 45
<211> 6
<212> PRT
<213> Homo sapiens

<400> 45
Thr Tyr Ser Ser Gly Asn
1 5

<210> 46
<211> 5
<212> PRT

<213> Homo sapiens

<400> 46
Met Asp His Glu Asn
1 5

<210> 47
<211> 6
<212> PRT
<213> Homo sapiens

<400> 47
Ser Tyr Asp Val Lys Met
1 5

<210> 48
<211> 5
<212> PRT
<213> Homo sapiens

<400> 48
Ser Gln Val Thr Met
1 5

<210> 49
<211> 7
<212> PRT
<213> Homo sapiens

<400> 49
Ala Asn Gln Gly Ser Glu Ala
1 5

<210> 50
<211> 5
<212> PRT
<213> Homo sapiens

<400> 50
Pro Arg His Asp Thr
1 5

<210> 51
<211> 6
<212> PRT
<213> Homo sapiens

<400> 51
Phe Tyr Glu Lys Met Gln
1 5

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- EP14702238 [0066]
- EP13153081 [0066]

Non-patent literature cited in the description

- **LI et al.**Nat Med, 2010, [0003]
- **UCKERT et al.**Cancer Immunol Immunother, 2008, [0005]
- **KAMMERTOENS T et al.**Eur J Immunol, 2009, [0005]
- **OTTAVANI S. et al.**CANCER IMMUNOLOGY, IMMUNOTHERAPY: CII, 2005, vol. 54, 121214-1220 [0007]
- **SAMBROOK et al.**Molecular Cloning, [0027]
- **OTTAVIANI, S.ZHANG, Y.BOON, T.VAN DER BRUGGEN, P.**A MAGE-1 antigenic peptide recognized by human cytolytic T lymphocytes on HLA-A2 tumor cellsCancer Immunology, Immunotherapy: CII, 2005, vol. 54, 121214-1220 [0054]
- **OTTAVIANI et al.**Cancer Immunology, Immunotherapy, 2005, vol. 54, 121214-1220 [0054]

Patentkrav

1. Antigengenkendende konstrukt, der er en T-cellereceptor (TCR), og som omfatter (i) et variabelt alpha-kædeområde med CDR1, CDR2 og CDR3, der omfatter en aminosyresekvens vist i henholdsvis SEQ ID NO: 40, 41 og 1; og som omfatter (ii) et variabelt beta-kædeområde med CDR1, CDR2 og CDR3, der omfatter en aminosyresekvens vist i henholdsvis SEQ ID NO: 46, 47 og 4; hvor TCR'en specifikt binder til MAGE-A1-antigenet.

2. Antigengenkendende konstrukt ifølge krav 1, hvor det antigengenkendende konstrukt inducerer et immunrespons.

3. Antigengenkendende konstrukt ifølge krav 1 eller 2, der omfatter det variable alpha-kædeelement TRAV5-CAESIGSNSGYALNF-TRAJ41 og det variable beta-kædeelement: TRBV28-CASRGLAGYEQYF-TRBJ2-7.

4. Antigengenkendende konstrukt ifølge krav 1 eller 2, der omfatter en alpha-kæde med mindst 90 % sekvensidentitet med sekvensen vist i SEQ ID NO: 22 eller 24; og som omfatter en beta-kæde med mindst 90 % sekvensidentitet med sekvensen vist i SEQ ID NO: 23 eller 25.

5. Nukleinsyre, der koder for et antigengenkendende konstrukt ifølge et hvilket som helst af kravene 1 til 4.

6. Vektor, der omfatter en nukleinsyre ifølge krav 5.

7. Værtscelle, der omfatter et antigengenkendende konstrukt ifølge et hvilket som helst af kravene 1 til 4, eller en nukleinsyre ifølge krav 5, eller en vektor ifølge krav 6.

8. Værtscelle ifølge krav 7, der er en T-lymfocyt.

9. Antigengenkendende konstrukt ifølge et hvilket som helst af kravene 1 til 4, eller nukleinsyre ifølge krav 5, eller vektor ifølge krav 6, eller værtscelle ifølge et hvilket som helst af kravene 7 eller 8, til anvendelse i medicin.

10. Antigengenkendende konstrukt, eller nukleinsyre, eller vektor, eller værtscelle ifølge krav 9, til anvendelse i diagnose, forebyggelse og/eller behandling af en ondartet eller godartet tumorsygdom.

11. Antigengenkendende konstrukt, eller nukleinsyre, eller vektor, eller værtscelle til anvendelsen ifølge krav 9 eller 10, hvor anvendelsen i medicin er en anvendelse i immunterapi.

12. Fremgangsmåde til fremstilling af en cellelinje, der udtrykket et MAGE-A1-specifikt antigengenkendende konstrukt (ARC), hvilket ARC er en T-cellereceptor (TCR), omfattende

a. tilvejebringelse af en egnet værtscelle,

b. tilvejebringelse af et genetisk konstrukt, der koder for et ARC ifølge et hvilket som helst af kravene 1 til 4,

c. indføring i den egnede værtscelle af det genetiske konstrukt,

d. ekspression af det genetiske konstrukt ved den egnede værtscelle.

13. Fremgangsmåde ifølge krav 12, der endvidere omfatter oprensningen af ARC'et fra cellen.

14. Fremgangsmåde ifølge krav 13, der endvidere omfatter rekonstitutionen af de translaterede ARC-fragmenter i en T-celle.

DRAWINGS

FIGURES

Figure 1:

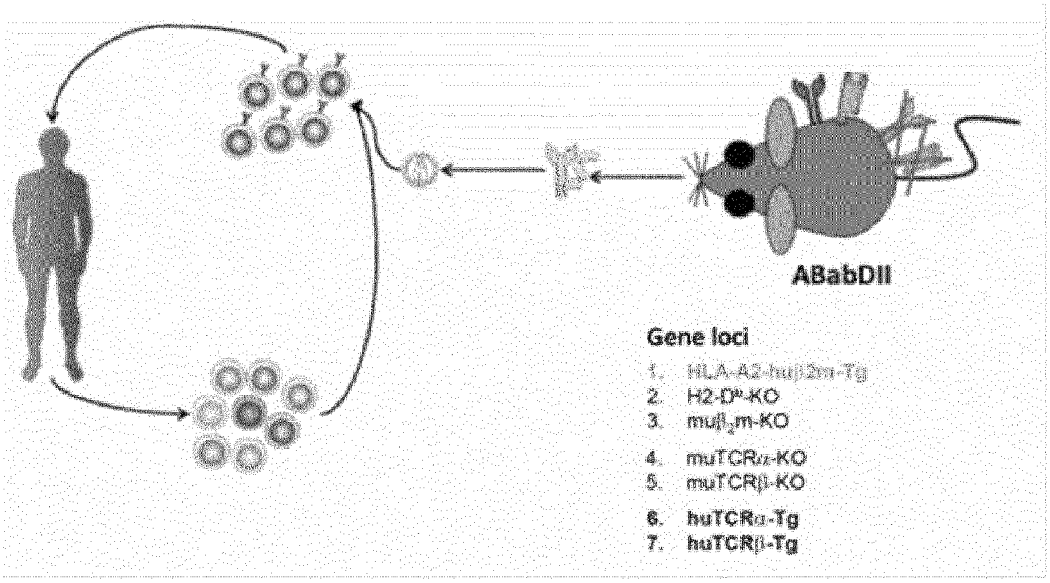


Figure 2:

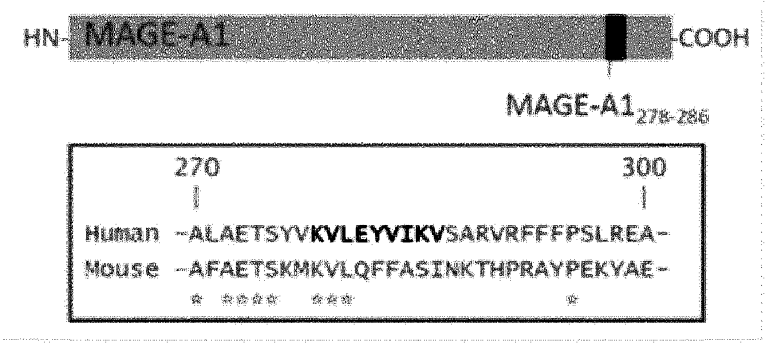


Figure 3:

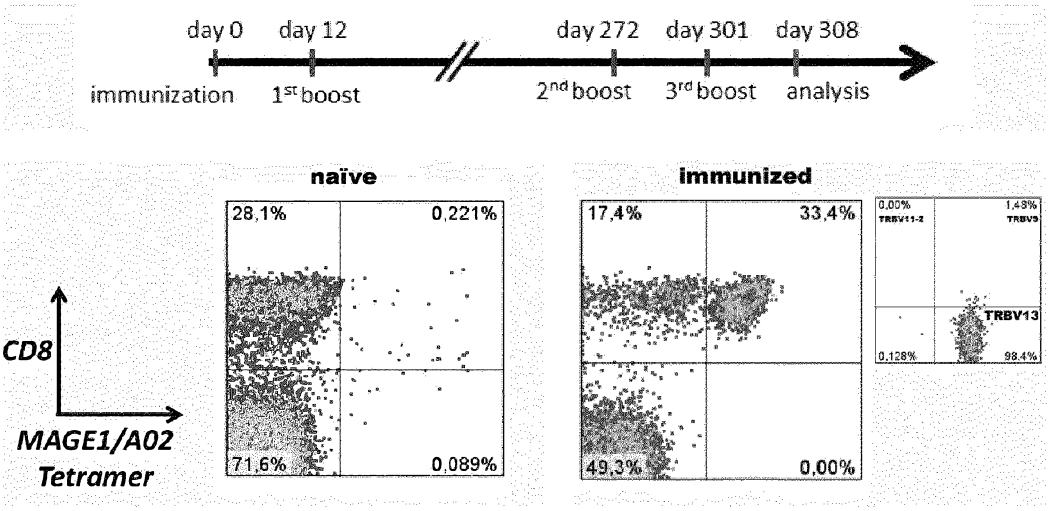


Figure 4:

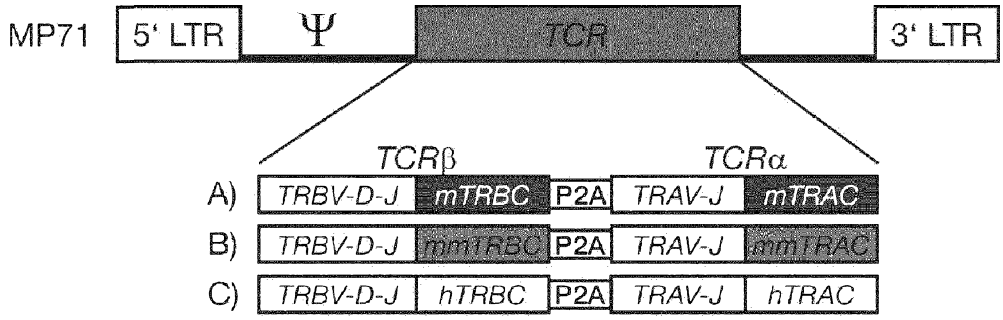
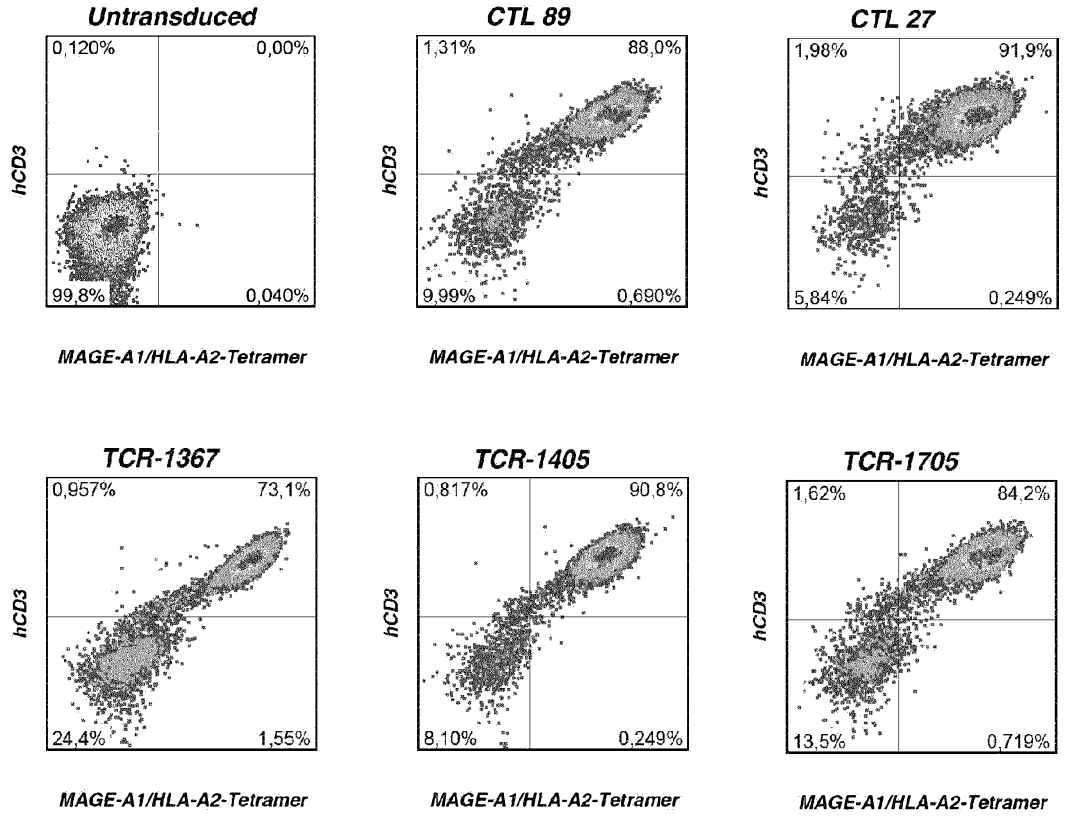


Figure 5: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0,00%
99,8%
0,040%
hCD3
MAGE-A1/HLA-A2-Tetramer
CTL 89
1,31%
88,0%
9,99%
0,690%
hCD3
MAGE-A1/HLA-A2-Tetramer
CTL 27
1,98%
91,9%
5,84%
0,249%
hCD3
MAGE-A1/HLA-A2-Tetramer
TCR-1367
0,957%
73,1%
24,4%
1,55%
hCD3
MAGE-A1/HLA-A2-Tetramer
TCR-1405
0,817%
90,8%
8,10%
0,249%
hCD3
MAGE-A1/HLA-A2-Tetramer
TCR-1705
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hCD3
MAGE-A1/HLA-A2-Tetramer

Figure 6:

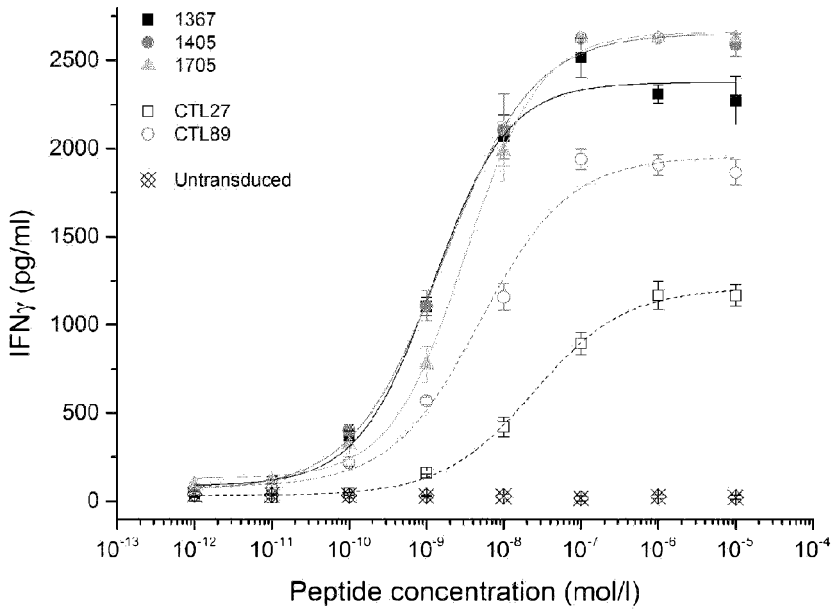
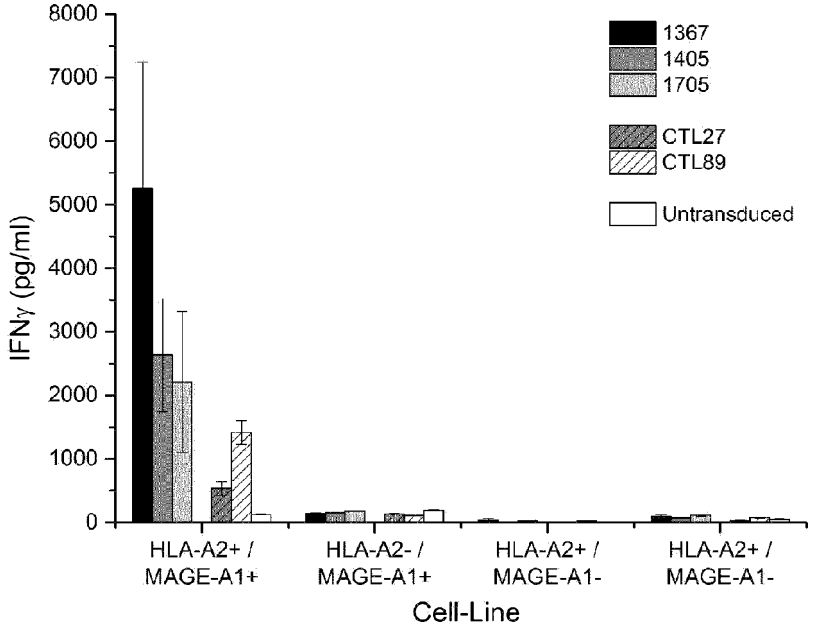


Figure 7:



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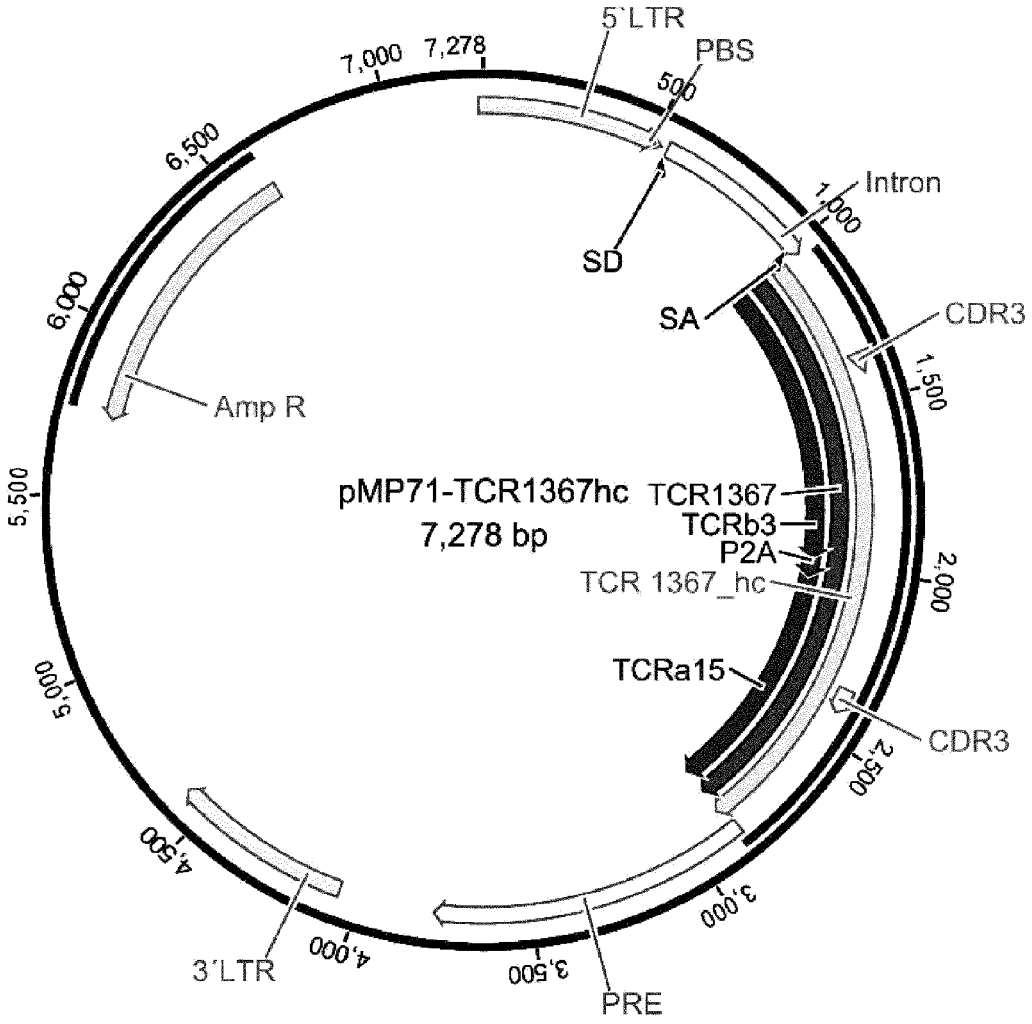
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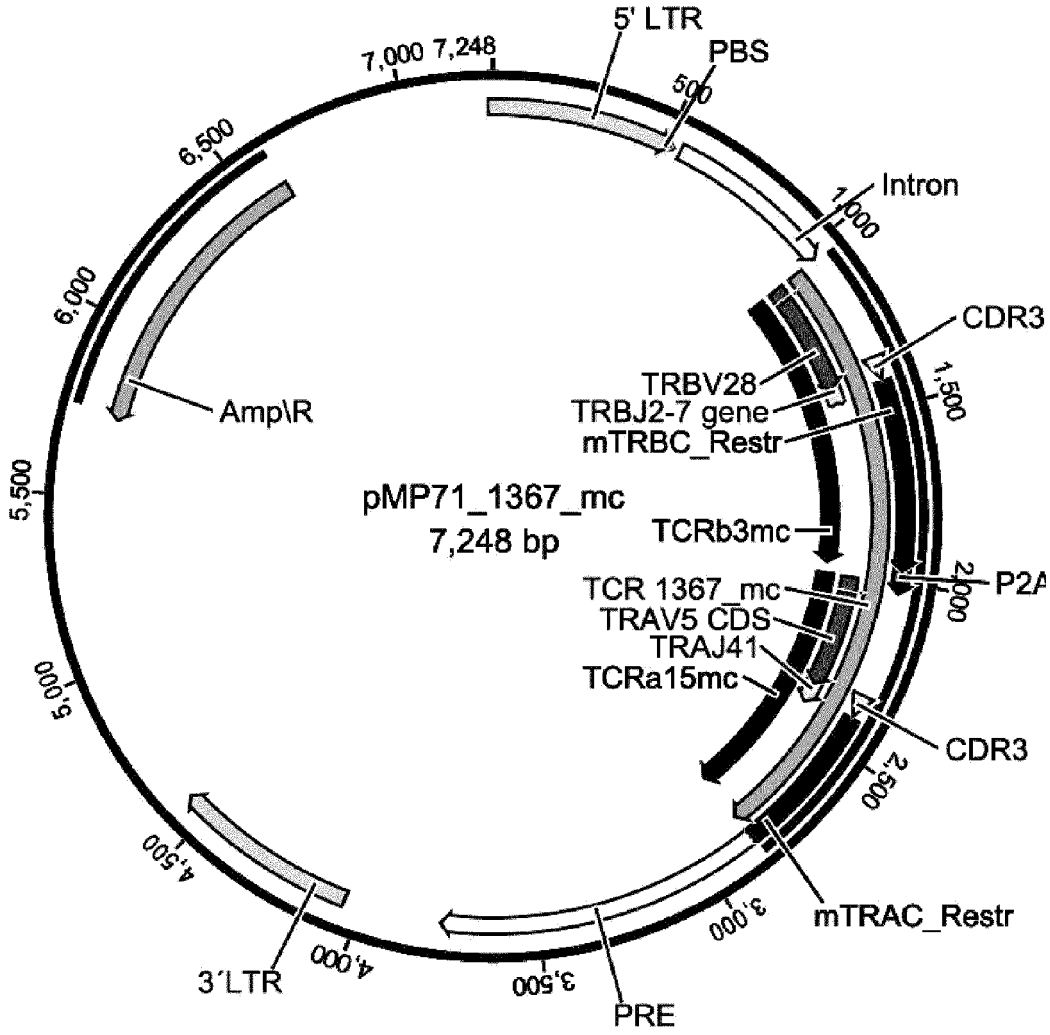
5,000
4,500
4,000
3,500
3,000
2,500
2,000
1,500
1,000
Intron
SD
SA
CDR3
Amp R
pMP71-TCR1367hc
7,278 bp
TCR1367
TCRb3
P2A
TCR 1367_hc
TCRa15
CDR3
3´LTR
PRE

Figure 9: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TRBJ2-7 gene
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pMP71_1367_mc
7,248 bp
TCRb3mc
TCR 1367_mc
TRAV5 CDS
TRAJ41
TCRa15mc
P2A
2,000
CDR3
2,500
mTRAC_Restr
3,000
PRE
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4,000
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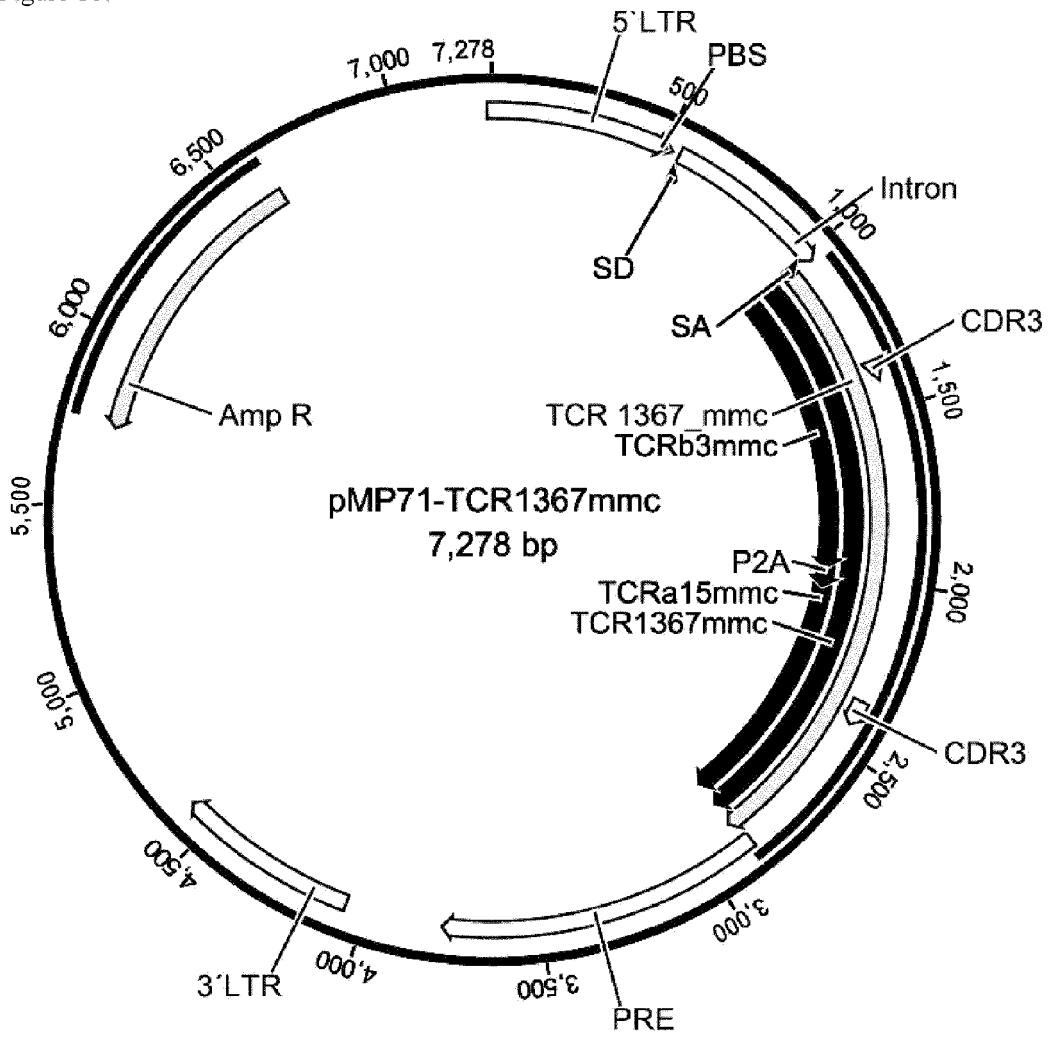
5,500
6,000
6,500
7,000
7,248
Amp\R

Figure 10: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4,000
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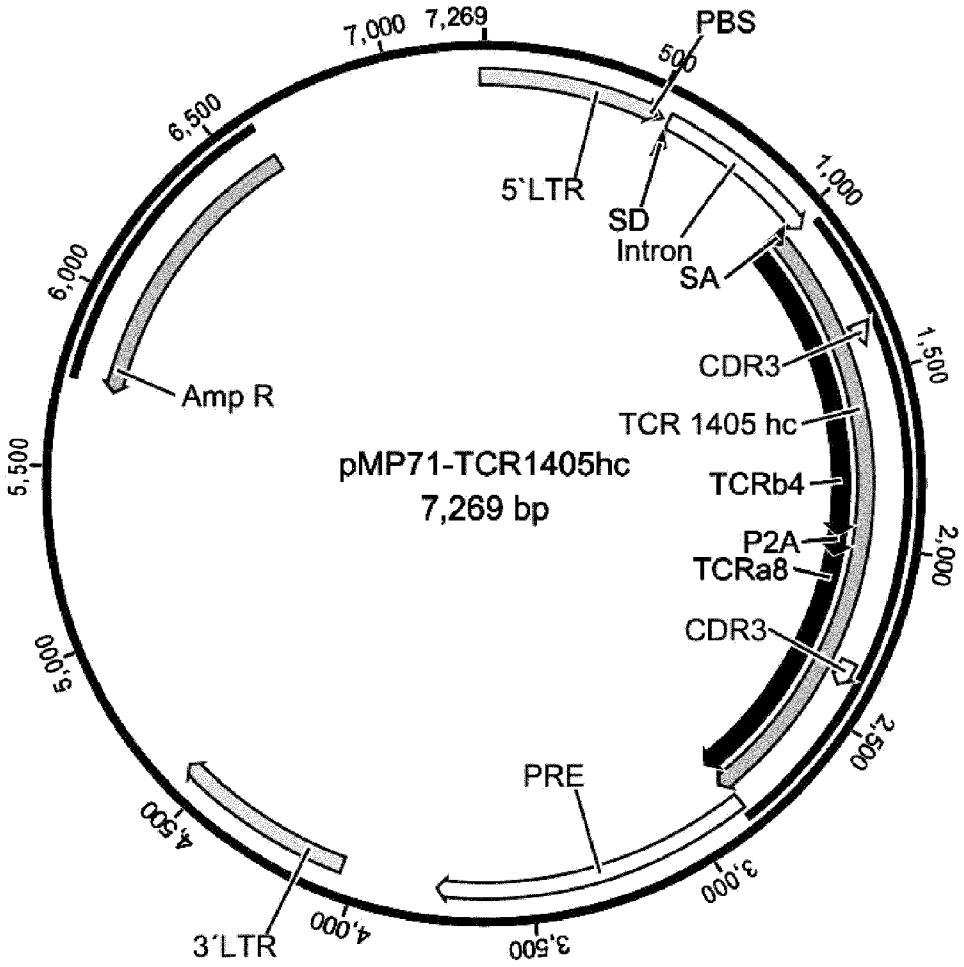
2,500
2,000
1,500
1,000
Intron
SD
SA
CDR3
Amp R
TCR 1367_mmc
TCRb3mmc
pMP71-TCR1367mmc
7,278 bp
P2A
TCRa15mmc
TCR1367mmc
CDR3
3´LTR
PRE

Figure 11: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SD
Intron
SA
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2,000
2,500
3,000
3,500
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7,000
CDR3
TCR 1405 hc
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CDR3
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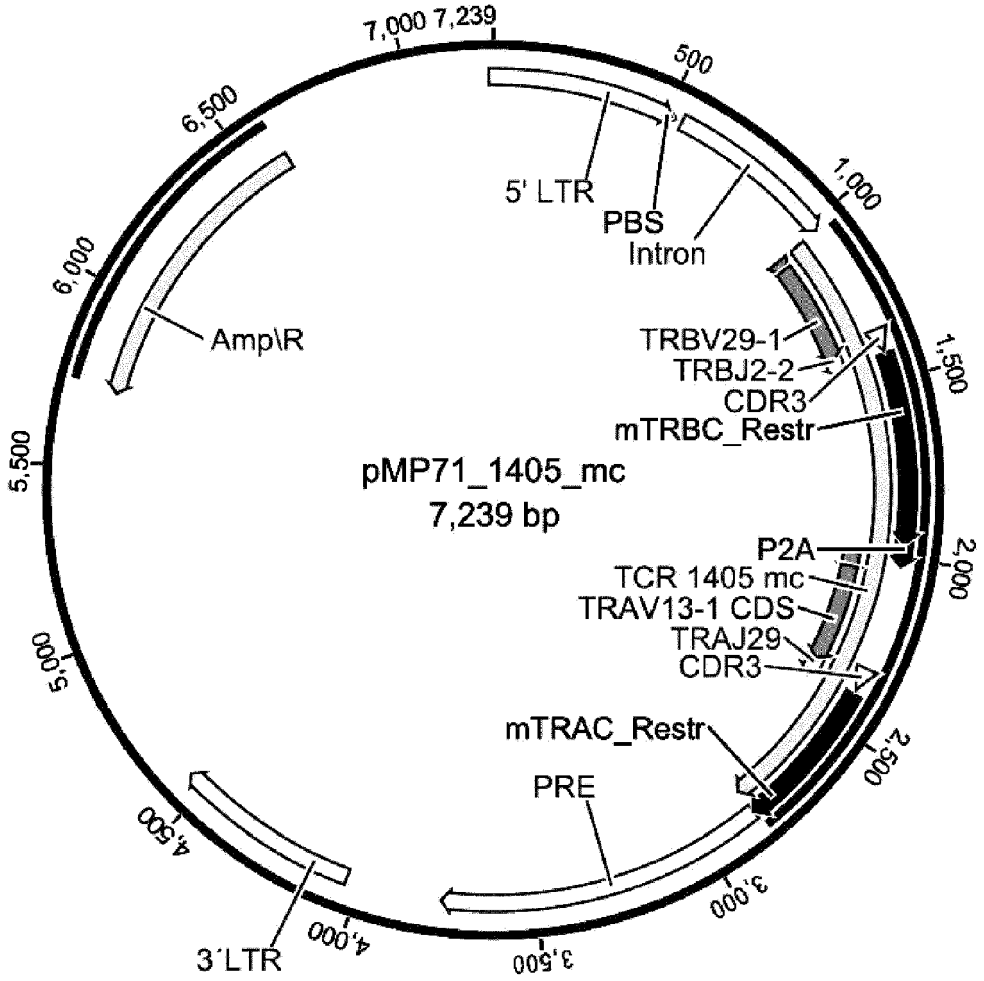
7,269 bp
Amp R
PRE
3´LTR

Figure 12: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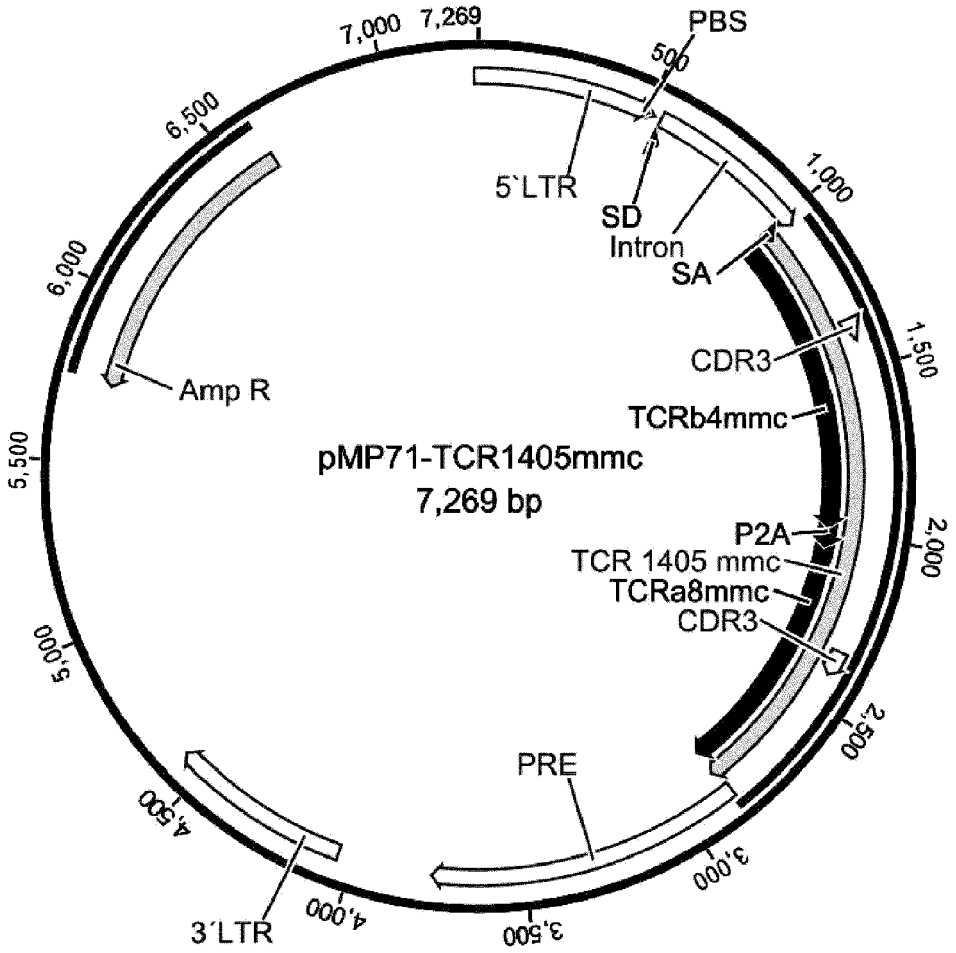
3,000
3,500
4,000
4,500
5,000
5,500
6,000
6,500
5' LTR
PBS
Intron
TRBV29-1
TRBJ2-2
CDR3
mTRBC_Restr
P2A
TCR 1405 mc
TRAV13-1 CDS
TRAJ29
CDR3
mTRAC_Restr
PRE
3´LTR
Amp\R
pMP71_1405_mc
7,239 bp

Figure 13: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6,000
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7,000
5`LTR
SD
Intron
SA
CDR3
TCRb4mmc
P2A
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TCRa8mmc
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PRE
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Amp R
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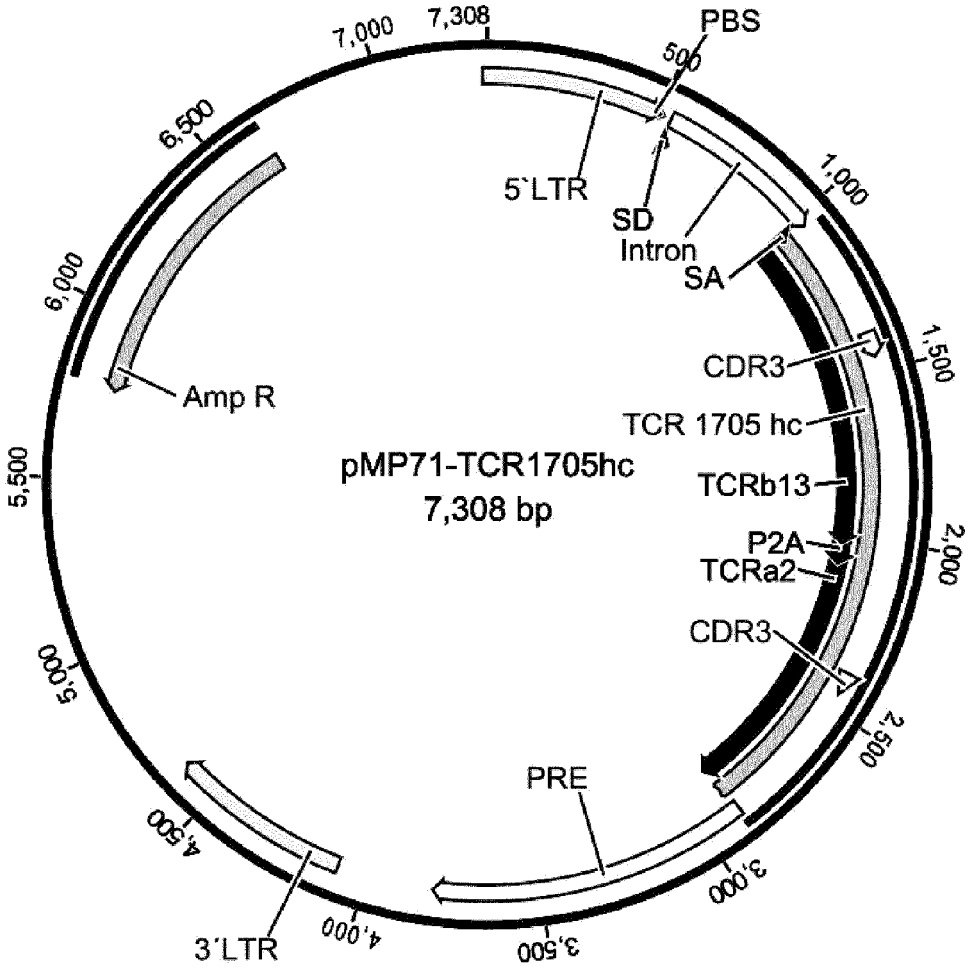
7,269 bp

Figure 14: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6,000
6,500
7,000
5`LTR
SD
Intron
SA
CDR3
TCR 1705 hc
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TCRa2
CDR3
PRE
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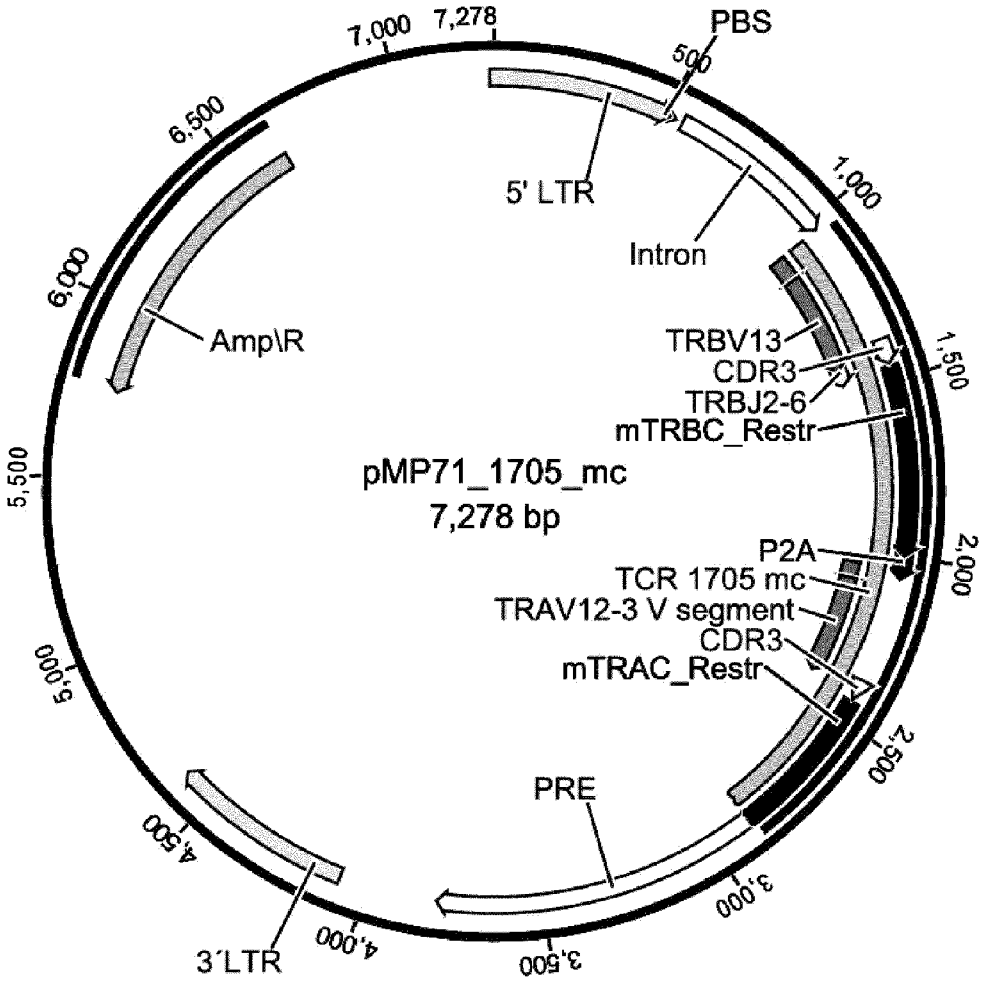
Amp R
pMP71-TCR1705hc
7,308 bp

Figure 15: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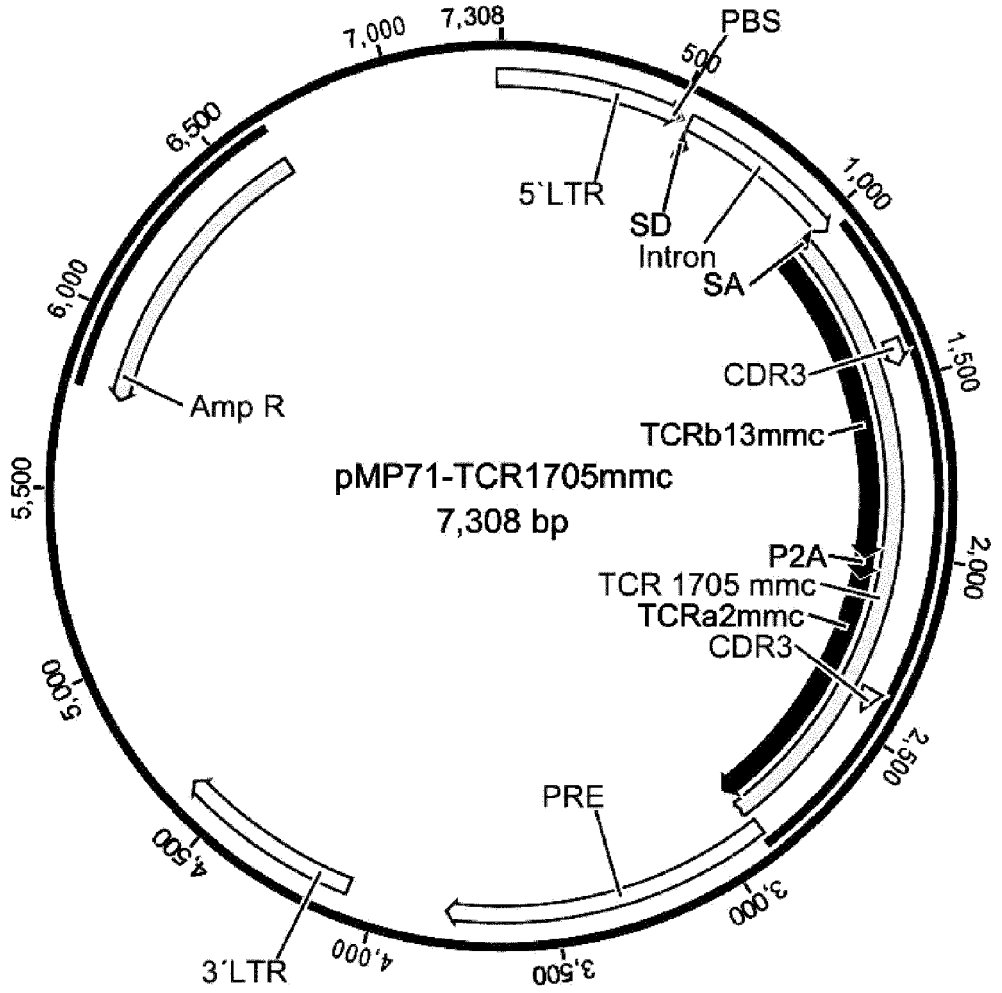
3,500
4,000
4,500
5,000
5,500
6,000
6,500
7,000
5' LTR
Intron
TRBV13
CDR3
TRBJ2-6
mTRBC_Restr
pMP71_1705_mc
7,278 bp
P2A
TCR 1705 mc
TRAV12-3 V segment
CDR3
mTRAC_Restr
PRE
3´LTR
Amp\R

Figure 16: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4,000
4,500
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6,000
6,500
7,000
5`LTR
SD
Intron
SA
CDR3
TCRb13mmc
pMP71-TCR1705mmc
7,308 bp
P2A
TCR 1705 mmc
TCRa2mmc
CDR3
PRE
3´LTR
Amp R

Figure 17:

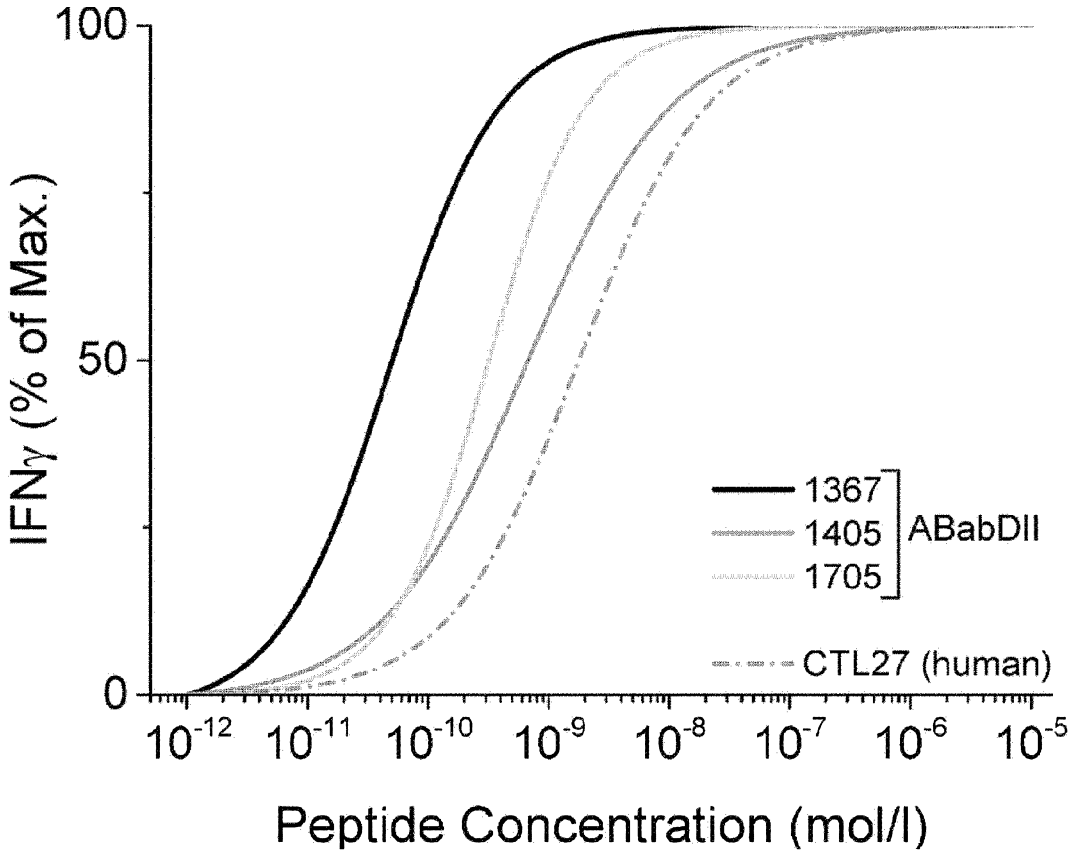
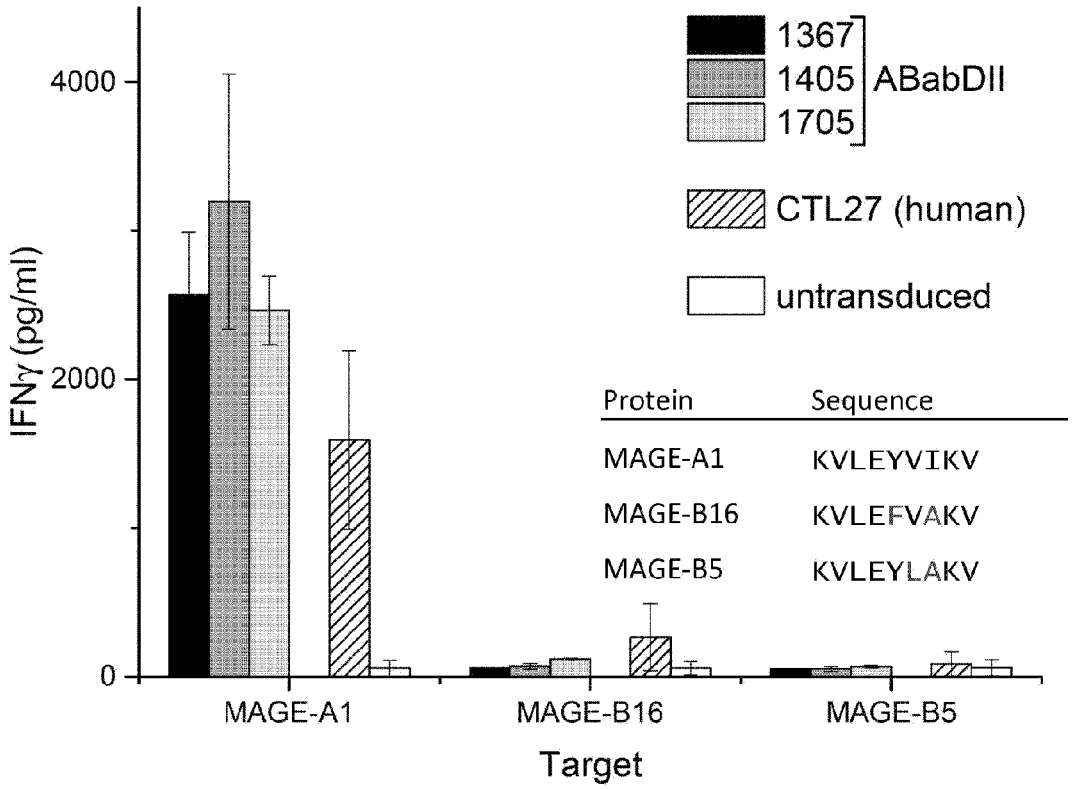

100
50
0
IFNγ (% of Max.)
1367
1405
1705
ABabDII
CTL27 (human)
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
Peptide Concentration (mol/l)

Figure 18: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2000
0
IFNγ (pg/ml)
1367
1405
1705
ABabDII
CTL27 (human)
untransduced
Protein
Sequence
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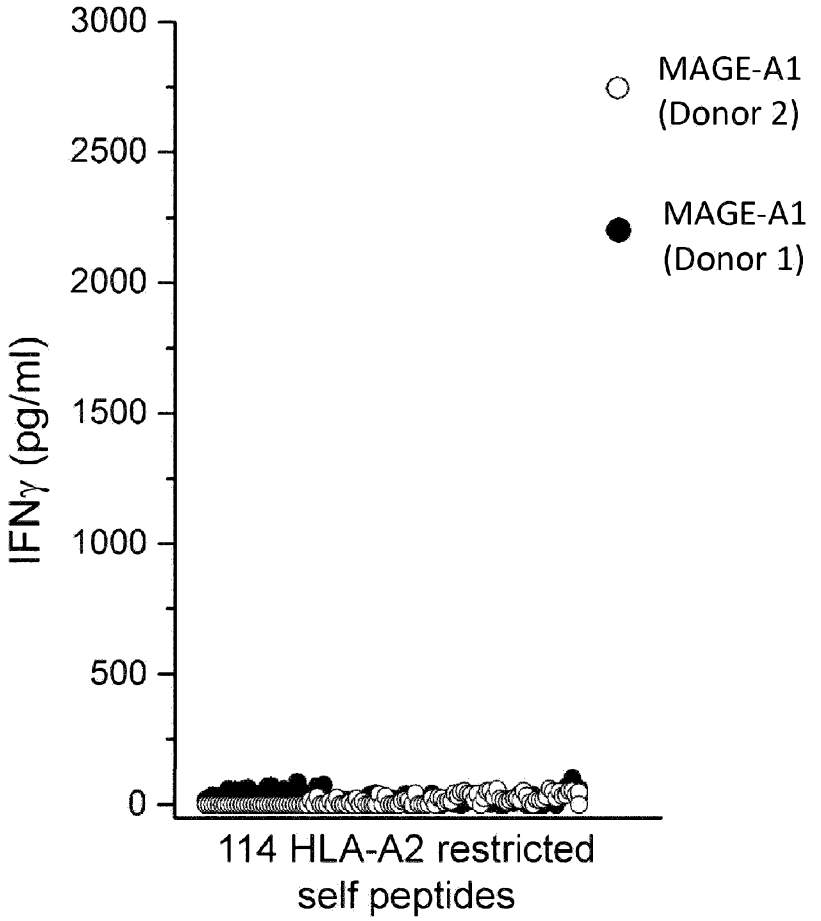
KVLEYVIKV
MAGE-B16
KVLEFVAKV
MAGE-B5
KVLEYLAKV
MAGE-A1
MAGE-B16
MAGE-B5
Target

Figure 19:


3000
2500
2000
1500
1000
500
0
IFNγ (pg/ml)
MAGE-A1
(Donor 2)
MAGE-A1
(Donor 1)
114 HLA-A2 restricted
self peptides