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The figure of the drawing to which the abstract refers is attached.

ABSTRACT

The present invention provides a cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain. Furthermore, a nucleic acid sequence encoding a CD3 specific binding construct of the invention is provided. Further aspects of the invention are vectors and host cells comprising said nucleic acid sequence, a process for the production of the construct of the invention and composition comprising said construct. The invention also provides the use of said constructs for the preparation of pharmaceutical compositions for the treatment of particular diseases, a method for the treatment of particular diseases and a kit comprising the binding construct of the invention.

Multispecific deimmunized CD3-binders

The present invention relates to a cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain. Furthermore, a nucleic acid sequence encoding a CD3 specific binding construct of the invention is provided. Further aspects of the invention are vectors and host cells comprising said nucleic acid sequence, a process for the production of the construct of the invention and composition comprising said construct. The invention also provides the use of said constructs for the preparation of pharmaceutical compositions for the treatment of particular diseases, a method for the treatment of particular diseases and a kit comprising the binding construct of the invention.

Human CD3 denotes an antigen which is expressed on T cells as part of the multimolecular T cell complex and which consists of three different chains: CD3- ϵ , CD3- δ and CD3- γ . Clustering of CD3 on T cells, e.g. by immobilized anti-CD3 antibodies leads to T cell activation similar to the engagement of the T cell receptor but independent of its clone-typical specificity; see WO 99/54440 or Hoffman (1985) J. Immunol. 135:5-8.

Antibodies which specifically recognize CD3 antigen are described in the prior art, e.g. in Traunecker, EMBO J 10 (1991), 3655-9 and Kipriyanov, Int. J. Cancer 77 (1998), 763-772. Lately, antibodies directed against CD3 have been proposed in the treatment of a variety of diseases. These antibodies or antibody constructs act as either T-cell depleting agents or as mitogenic agents, as disclosed in EP 1 025 854. Human/rodent hybrid antibodies which specifically bind to the human CD3 antigen complex are disclosed in WO 00/05268 and are proposed as immunosuppressive agents, for example for the treatment of rejection episodes following the transplantation of the renal, septic and cardiac allografts. WO 03/04648 discloses a bispecific antibody directed to CD3 and to an ovarian cancer antigen. Furthermore,

Kufer (1997) *Cancer Immunol Immunother* 45:193-7 relates to a bispecific antibody specific for CD3 and EpCAM for the therapy of minimal residual cancer.

However, prior art antibodies directed against CD3 are derived from non-human sources. This leads to several serious problems when using such anti-CD3 antibodies as part of a therapeutic regimen in humans.

One such problem is "cytokine release syndrome (CRS)". CRS is a clinical syndrome which has been observed following the administration of the first few doses of anti-CD3 antibodies and is related to the fact that many antibodies directed against CD3 are mitogenic. In vitro, mitogenic antibodies directed against CD3 induce T cell proliferation and cytokine production. In vivo this mitogenic activity leads to the large-scale release of cytokines, including many T cell-derived cytokines, within the initial hours after the first injection of antibody. The mitogenic capacity of CD3-specific antibodies is monocyte/macrophage dependent and it involves the production of IL-6 and IL-1 β by these cells.

CRS symptoms range from frequently reported mild "flu-like" symptoms to less frequently reported severe "shock-like" reactions (which may include cardiovascular and central nervous system manifestations). Symptoms include, inter alia, headache, tremor, nausea/vomiting, diarrhoea, abdominal pain, malaise and muscle/joint aches and pains, generalized weakness, cardiorespiratory events as well as neuro-psychiatric events. Severe pulmonary oedema has occurred in patients with fluid overload and in those who appeared not to have a fluid overload. Another serious problem hampering the therapeutic use of, especially, murine monoclonal antibodies is the mounting of a humoral immune response against such antibodies, resulting in the production of human anti-mouse antibodies ("HAMAs") (Schroff (1985) *Cancer Res.* 45:879-885, Shawler (1985) *J. Immunol.* 135:1530-1535). HAMAs are typically generated during the second week of treatment with the murine antibody and neutralize the murine antibodies, thereby blocking their ability to bind to their intended target. The HAMA response can depend on the murine constant ("Fc") antibody regions or/and the nature of the murine variable ("V") regions.

The prior art contains various approaches to reducing or preventing the production of HAMAs by modifying monoclonal antibodies of non-human origin.

One approach to reducing the immunogenicity of such antibodies is by humanization, as for example described in WO 91/09968 and US 6,407,213. In general, humanization entails substitutions of non-human antibody sequences for corresponding human sequences, as for example is the case with CDR-grafting.

Another approach to reducing the immunogenicity of such antibodies is by deimmunization, as for example described in WO 00/34317, WO 98/52976, WO 02/079415, WO 02/012899 and WO 02/069232. In general, deimmunization entails carrying out substitutions of amino acids within potential T cell epitopes. In this way, the likelihood that a given sequence will give rise to T cell epitopes upon intracellular protein processing is reduced. Moreover, WO 92/10755 describes an approach in which antigenic determinants on proteins are engineered. Particularly, proteins are epitope mapped and their amino acid sequence is changed through genetic engineering.

However, humanized antibodies often exhibit a decreased binding affinity with respect to their target as compared to their non-humanized parent antibodies and also often are still somewhat immunogenic in a human host.

Therefore, the technical problem of the present invention was the provision of means and methods for the treatment of and/or the amelioration of tumorous diseases, proliferative disorders as well as B-cell related diseases by induction of T cell mediated immune response. The above-mentioned means and methods should overcome the recited disadvantages of known antibody-based therapies.

The solution to said technical problem is achieved by providing the embodiments characterized in the claims.

Accordingly, the present invention relates to a cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain,

wherein said first domain is deimmunized and comprises a CDR-H1 region, a CDR-H2 region and a CDR-H3 region, said CDR-H3 region comprising an amino acid sequence as depicted in SEQ ID NO.: 96, 108, 119, 120, 121, 122, 123, 124, 125, 126, or 127; and

wherein said first domain further comprises in its framework H1 the sequence VKK (Val-Lys-Lys) and wherein the transition sequence between framework H1 and CDR-H1 region comprises the sequence Ala-Ser-Gly-Tyr-Thr-Phe (ASGYTF; SEQ ID NO.: 233).

It was surprisingly found that the above-recited, specific modifications to known CDR regions as well as framework regions and their corresponding transition sequences lead to deimmunized, CD3 specific binding molecules which show reduced immunogenicity but retain their cytotoxic activity compared to original non-deimmunized sequences. This finding was in particular surprising since not all possible deimmunization protocols led to bioactive, functional constructs which show distinct cytotoxic activity; see appended examples. Furthermore, surprisingly the deimmunized cytotoxically active CD3 binding molecules showed increased productivity. In accordance with this invention, specific sequences of non-deimmunized antibodies have been replaced by/modified to the sequences recited herein above. In particular, in framework H1 regions the original sequence Leu-Ala-Arg (LAR) has been replaced by the sequence Val-Lys-Lys (VKK). Furthermore, the sequence Thr-Ser-Gly-Tyr-Thr-Phe (TSGYTF) comprised in the transition region of framework H1 and CDR-H1 of some non-modified/non-deimmunized CD3specific antibodies has been modified in accordance with the invention to Ala-Ser-Gly-Tyr-Thr-Phe (ASGYTF) (SEQ ID NO.:233) (see Figure 14). A desired, inventive CD3-specific binding construct is characterized as comprising at least two binding specificities whereby a second binding specificity is Ig-derived. Furthermore, said desired constructs are characterized by the specific amino acid sequences shown herein above. As documented in the appended examples the constructs as provided herein still retain bioactivity in their modified/deimmunized form. The examples also document that not all deimmunizations, determined by methods known in the art (WO 92/10755, WO 00/34317, WO 98/52976, WO 02/079415 or WO 02/012899), lead to bioactive molecules; see in particular the examples 2 and 5.

The term "cytotoxically active CD3 binding construct" as used herein relates to a CD3 specific construct capable of binding to human CD3 complex expressed on T cells and capable of inducing elimination/lysis of target cells. Binding of CD3 specific binders of the CD3/CD3 complex (e.g. antibodies, antibody derivatives or antibody fragments) leads to activation of T cells as known in the art; see WO 99/54440. Accordingly, an inventive construct has to be able to eliminate/lyse target cells in vivo and/or in vitro. Corresponding target cells comprise cells expressing a surface molecule, which is recognized by the second Ig-derived binding domain of the inventive constructs. Such surface molecules are characterized herein below. Cytotoxicity can be detected by methods known in the art and methods as illustrated herein below and in the appended examples. Accordingly, such methods comprise, inter alia, physiological in vitro assays. Such physiological assays may monitor cell death, for example by loss of cell membrane integrity (e.g. FACS based propidium iodide assay, trypan Blue influx assay, photometric enzyme release assays (LDH), radiometric ^{51}Cr release assay, fluorometric Europium release and CalceinAM release assays). Further assays comprise monitoring of cell viability, for example by photometric MTT, XTT, WST-1 and alamarBlue assays, radiometric ^3H -Thd incorporation assay, clonogenic assay measuring cell division activity, and fluorometric Rhodamine ^{123} assay measuring mitochondrial transmembrane gradient. In addition, apoptosis may be monitored for example by FACS-based phosphatidylserin exposure assay, ELISA-based TUNEL test, caspase activity assay (photometric, fluorometric or ELISA-based) or analysing changed cell morphology (shrinking, membrane blebbing). It is preferred that cytotoxic activity is analysed by FACS-based measurements of release of fluorescence-based dyes. In such an assay fluorescence labelled cells, which carry a molecule which binds to the second domain of the cytotoxically active bispecific CD3 binding construct of the invention (preferably, NALM-6 cells for CD19 and Kato cells for the EpCAM antigen) are incubated with isolated PBMCs of random donors or with a standardized T-cell line in the presence of the cytotoxically active bispecific CD3 binding construct of the invention. After incubation, the release of the dye from the fluorescent target cells into the supernatant is determined by a spectrofluorimeter. A cytotoxically active deimmunized bispecific CD3 binding construct of the present invention is characterized by comparing values obtained by measuring the bioactivity of a similar construct which is not deimmunized or has no specificity to the target cells.

The term "binding to/interacting with" as used in the context with the present invention defines a binding/interaction of at least two "antigen-interaction-sites" with each other. The term "antigen-interaction-site" defines, in accordance with the present invention, a motif of a polypeptide which shows the capacity of specific interaction with a specific antigen or a specific group of antigens. Said binding/interaction is also understood to define a "specific recognition". The term "specifically recognizing" means in accordance with this invention that the antibody molecule is capable of specifically interacting with and/or binding to at least two amino acids of each of the human target molecules as defined herein. Antibodies can recognize, interact and/or bind to different epitopes on the same target molecule. Said term relates to the specificity of the antibody molecule, i.e. to its ability to discriminate between the specific regions of the human target molecule as defined herein. The specific interaction of the antigen-interaction-site with its specific antigen may result in an initiation of a signal, e.g. due to the induction of a change of the conformation of the antigen, an oligomerization of the antigen, etc. Thus, a specific motif in the amino acid sequence of the antigen-interaction-site and the antigen bind to each other as a result of their primary, secondary or tertiary structure as well as the result of secondary modifications of said structure.

The term "specific interaction" as used in accordance with the present invention means that the CD3 specific binding construct of the invention does not or essentially does not cross-react with (poly)peptides of similar structures. Accordingly, the construct of the invention specifically binds to/interacts with human CD3 and is capable, due to its second, Ig-derived domain to interact with specific, selected other compounds, antigens, cell surface markers, tumor markers, etc. Specific examples of such molecules against which said second, Ig-derived domain is directed are given herein below.

Cross-reactivity of a panel of constructs under investigation may be tested, for example, by assessing binding of said panel of bispecific single chain constructs under conventional conditions (see, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, 1988 and *Using Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, 1999) to the (poly)peptide of interest as well as to a number of more or less (structurally and/or functionally) closely related (poly)peptides. Only those constructs (i.e. antibodies, (bispecific)

scFvs and the like) that bind to the (poly)peptide/protein of interest but do not or do not essentially bind to any of the other (poly)peptides which are preferably expressed by the same tissue as the (poly)peptide of interest, e.g. by the cells of the heart tissue, are considered specific for the (poly)peptide/protein of interest and selected for further studies in accordance with the method provided herein and illustrated in the appended examples. These methods may comprise, inter alia, binding studies, blocking and competition studies with structurally and/or functionally closely related molecules. These binding studies also comprise FACS analysis, surface plasmon resonance (SPR, e.g. with BIAcore®), analytical ultracentrifugation, isothermal titration calorimetry, fluorescence anisotropy, fluorescence spectroscopy or by radiolabeled ligand binding assays. Furthermore, physiological assays, like cytotoxic assays (as illustrated in the examples) and assays mentioned above may be performed. Accordingly, examples for the specific interaction of an antigen-interaction-site with a specific antigen may comprise the specificity of a ligand for its receptor. Said definition particularly comprises the interaction of ligands which induce a signal upon binding to its specific receptor. Examples for corresponding ligands comprise cytokines which interact/bind with/to its specific cytokine-receptors. Also particularly comprised by said definition is the binding of an antigen-interaction-site to antigens such as antigens of the selectin family, integrins and of the family of growth factors like EGF. Another example for said interaction, which is also particularly comprised by said definition, is the interaction of an antigenic determinant (epitope) with the antigenic binding site of an antibody.

The term "binding to/interacting with" relates not only to a linear epitope but may also relate to a conformational epitope, a structural epitope or a discontinuous epitope consisting of two regions of the human target molecules or parts thereof. In context of this invention, a conformational epitope is defined by two or more discrete amino acid sequences separated in the primary sequence which come together on the surface of the molecule when the polypeptide folds to the native protein (Sela, (1969) Science 166, 1365 and Laver, (1990) Cell 61, 553-6).

The term "discontinuous epitope" means in context of the invention non-linear epitopes that are assembled from residues from distant portions of the polypeptide chain. These residues come together on the surface when the polypeptide chain folds into a three-dimensional structure to constitute a conformational/structural epitope.

The constructs of the present invention are also envisaged to specifically bind to/interact with a conformational/structural epitope(s) composed of and/or comprising the two regions of the human CD3 complex described herein or parts thereof as disclosed herein below.

Accordingly, specificity can be determined experimentally by methods known in the art and methods as disclosed and described herein. Such methods comprise, but are not limited to Western blots, ELISA-, RIA-, ECL-, IRMA-tests and peptide scans.

The term "Ig-derived second binding domain" relates to an "immunoglobulin-derived domain", specifically to an antibody or fragments thereof, to single chain antibodies, to synthetic antibodies, to antibody fragments, such as Fab, a F(ab₂)', Fv or scFv fragments etc, or a chemically modified derivative of any of these. These antibodies molecules may be derived from different species or may be of chimeric origin. Most preferably (as documented herein below), said Ig-derived second domain comprised in the CD3 specific binding construct of the invention is a scFv. Antibodies, antibody constructs, antibody fragments, antibody derivatives (all being Ig-derived) to be employed in accordance with the invention or their corresponding immunoglobulin chain(s) can be further modified using conventional techniques known in the art, for example, by using amino acid deletion(s), insertion(s), substitution(s), addition(s), and/or recombination(s) and/or any other modification(s) known in the art either alone or in combination. Methods for introducing such modifications in the DNA sequence underlying the amino acid sequence of an immunoglobulin chain are well known to the person skilled in the art; see, e.g., Sambrook (1989), loc. cit. The term "Ig-derived domain" particularly relates to (poly)peptide constructs comprising at least one CDR. Fragments or derivatives of the recited Ig-derived domains define (poly)peptides which are parts of the above antibody molecules and/or which are modified by chemical/biochemical or molecular biological methods. Corresponding methods are known in the art and described inter alia in laboratory manuals (see Sambrook et al.; Molecular Cloning: A Laboratory Manual; Cold Spring Harbor Laboratory Press, 2nd edition 1989 and 3rd edition 2001; Gerhardt et al.; Methods for General and Molecular Bacteriology; ASM Press, 1994; Lefkovits; Immunology Methods Manual: The Comprehensive Sourcebook of Techniques; Academic Press, 1997; Golemis; Protein-Protein Interactions: A Molecular Cloning Manual; Cold Spring Harbor Laboratory Press, 2002).

The term "deimmunized" as used herein relates to the above-identified first domain of the inventive CD3 binding construct, wherein said first domain is modified compared to an original wildtype construct by rendering said wildtype construct non-immunogenic or less immunogenic in humans. Wildtype constructs according to the invention relate to antibodies or parts thereof (like frameworks and/or CDRs) of non-human origin. Corresponding examples are antibodies or fragments thereof as described in US 4,361,549 or WO 99/54440. The term "deimmunized" also relates to constructs, which show reduced propensity to generate T cell epitopes. In accordance with this invention, the term "reduced propensity to generate T cell epitopes" relates to the removal of T-cell epitopes leading to specific T-cell activation. Furthermore, reduced propensity to generate T cell epitopes means substitution of amino acids contributing to the formation of T cell epitopes, i.e. substitution of amino acids, which are essential for formation of a T cell epitope. In other words, reduced propensity to generate T cell epitopes relates to reduced immunogenicity or reduced capacity to induce antigen independent T cell proliferation. In addition, reduced propensity to generate T cell epitopes relates to deimmunisation, which means loss or reduction of potential T cell epitopes of amino acid sequences inducing antigen independent T cell proliferation. According to the invention, a CD3 binding region, which has reduced propensity to generate T cell epitopes is less or preferably non immunogenic compared to non-deimmunized molecule but which has still retained its capacity to binding to CD3, i.e. a low or non immunogenic antibody construct binding to CD3.

The term "T cell epitope" relates to short peptide sequences which can be released during the degradation of peptides, polypeptides or proteins within cells and subsequently be presented by molecules of the major histocompatibility complex (MHC) in order to trigger the activation of T cells; see inter alia WO 02/066514. For peptides presented by MHC class II such activation of T cells can then give rise to an antibody response by direct stimulation of T cells to produce said antibodies.

Accordingly, a deimmunized first domain specifically binding to a human CD3 comprises at least the above mentioned CDR-H3 located between framework H3 and H4, wherein said first binding domain shows a reduced propensity to generate T-cell epitopes compared to a non-deimmunized first domain comprising the unchanged wildtype (wt)-CDR-H3 located between framework H3 and H4. Furthermore, said

deimmunized first domain comprises at least in the transition region of the framework H1 and CDR-H1 the above mentioned sequence motif which provides a reduced propensity to generate T-cell epitopes compared to a non-deimmunized first domain comprising the unchanged wt-H1 transition region of the framework H1 and CDR-H1. "Reduced propensity to generate T-cell epitopes" and/or "deimmunization" may be measured by techniques known in the art. Preferably, deimmunization of proteins may be tested in vitro by a T cell proliferation assay. In this assay PBMCs from donors representing > 80 % of HLA-DR alleles in the world are screened for proliferation in response to either wildtype or deimmunized peptides. Ideally cell proliferation is only detected upon loading of the antigen-presenting cells with wildtype peptides. Alternatively, one may test deimmunization by expressing HLA-DR tetramers representing all haplotypes. These tetramers may be tested for peptide binding or loaded with peptides substitute for antigen-presenting cells in proliferation assays. In order to test if deimmunized peptides are presented on HLA-DR haplotypes, binding of e.g. fluorescence-labeled peptides on PBMCs can be measured. Furthermore, deimmunization can be proven by determining whether antibodies against the deimmunized molecules have been formed after administration in patients. A particular preferred method is a T-cell proliferation assay as, inter alia, shown in appended example 6.

Preferably, antibody derived molecules are deimmunized in the framework regions and most of the CDR regions are not modified in order to generate reduced propensity to induce T cell epitope so that the binding affinity of the CDR regions is not affected. Even elimination of one T cell epitope results in reduced immunogenicity. Preferably, the molecule is deimmunized in the CDR2 region of the VL chain, more preferably in the CDR2 region of the VH chain, even more preferably in the CDR1 region of the VL chain, even more preferably in the CDR1 region of the VH chain, more preferably in the framework region (FR) of the VL chain and most preferably in the framework region (FR) of the VH chain.

The term "CDR" as employed herein relates to "complementary determining region", which is well known in the art. The CDRs are parts of immunoglobulins and T cell receptors that determine the specificity of said molecules and make contact with specific ligand. The CDRs are the most variable part of the molecule and contribute to the diversity of these molecules. There are three CDR regions CDR1, CDR2 and

CDR3 in each V domain. CDR-H depicts a CDR region of a variable heavy chain and CDR-L relates to a CDR region of a variable light chain. H means the variable heavy chain and L means the variable light chain. The CDR regions of an Ig-derived region may be determined as described in Kabat (1991). Sequences of Proteins of Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Health and Human Services, Chothia (1987). J. Mol. Biol. 196, 901-917 and Chothia (1989) Nature, 342, 877-883.

In general CDR-L1 consists of 10-17 amino acid residues, starts approximately at amino acid residue 24 of the full VL region of an Ig-derived sequence and the residue Cys precedes the CDR-L1. Preferably, the residue Trp follows CDR-L1. CDR-L2 starts preferably, 16 amino acid residues after CDR-L1 and consists preferably of 7 residues. Preferably, the amino acid residues Ile-Tyr, but also, Val-Tyr, Ile-Lys, Ile-Phe precede CDR-L2. CDR-L3 starts, preferably, 33 amino acid residues after CDR-L2 and consists, preferably, of 7-11 residues. CDR-L3 follows, preferably, the residue Cys and, preferably, the residues Phe-Gly-Xaa-Gly follow directly CDR-L3. CDR-H1 consists of, preferably, 10-12 residues and starts, preferably, approximately at residue 26 from the beginning of the VH region. Preferably, the residue Trp follows CDR-H1. CDR-H2 starts, preferably, 15 amino acid residues after the end of CDR-H1 and consists, preferably, of 16 to 19 residues. Preferably, residues Lys/Arg-Leu/Ile/Val/Phe/Thr/Ala-Thr/Ser/Ile/Ala follow CDR-H2. CDR-H3 starts 33 amino acid residues after CDR-H2 and has a length of 3-25 amino acid residues. CDR-H3 follows the sequence Cys-Xaa-Xaa (preferably Cys-Ala-Arg) and the residues Trp-Gly-Xaa-Gly follow CDR-H3. The structure of CDR regions has been described in <http://www.bioinf.org.uk/abs/>.

The above recited CDR-H1 and CDR-H2 regions are derived from antibody molecules which are capable of specifically binding to/interacting with human CD3. Such CD3 specific antibody are known in the art and comprise in particular the monoclonal antibodies OKT-3, TR-66 or X35-3, VIT3, BMA030 (BW264/56), CLB-T3/3, CRIS7, YTH12.5, F111-409, CLB-T3.4.2, TR-66, WT32, SPv-T3b, 11D8, XIII-141, XIII-46, XIII-87, 12F6, T3/RW2-8C8, T3/RW2-4B6, OKT3D, M-T301, SMC2, F101.01, UCHT-1 or WT-31. All the mentioned anti-CD3 antibodies are human specific and in accordance with this invention it is possible to combine various CDR

regions, in particular CDRH regions of the antibodies.

In a more preferred embodiment, said CDR-H1 and CDR-H2 regions of said CD3 specific domain with reduced propensity to generate T cell epitopes are derived from the antibody construct described in WO 99/54440. Even more preferred (and as illustrated in the appended examples) said CDR-H1 and CDR-H2 regions, as well as the CDR-H3 region, are derived from an antibody/antibody derivative with specificity for the CD3 molecule described by Traunecker (1991), EMBO J. 10, 3655-3659. In accordance with this invention, said CDR-H1, CDR-H2 and CDR-H3 regions are derived from antibodies/antibody derivatives and the like which are capable of specifically recognizing the human CD3- ϵ chain in the context of other TCR subunits, e.g. in mouse cells transgenic for human CD3- ϵ chain. These transgenic mouse cells express human CD3- ϵ chain in a native or near native conformation.

In accordance with this invention, a framework region relates to a region in the V domain (VH or VL domain) of immunoglobulins and T-cell receptors that provides a protein scaffold for the hypervariable complementarity determining regions (CDRs) that make contact with the antigen. In each V domain, there are four framework regions designated FR1, FR2, FR3 and FR4. Framework 1 encompasses the region from the N-terminus of the V domain until the beginning of CDR1, framework 2 relates to the region between CDR1 and CDR2, framework 3 encompasses the region between CDR2 and CDR3 and framework 4 means the region from the end of CDR3 until the C-terminus of the V domain; see, inter alia, Janeway, Immunobiology, Garland Publishing, 2001, 5th ed. Thus, the framework regions encompass all the regions outside the CDR regions in VH or VL domains. Furthermore, the term "transition sequence between a framework and a CDR region" relates to a direct junction between the framework and CDR region. In particular, the term "transition sequence between a framework and a CDR region" means the sequence directly located N- and C-terminally of the CDR regions or amino acids surrounding CDR regions. Accordingly, frameworks may also comprise sequences between different CDR regions. The person skilled in the art is readily in a position to deduce from a given sequence the framework regions, the CDRs as well as the corresponding transition sequences; see Kabat (1991) Sequences of Proteins of Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Health and

Human Services, Chothia (1987). J. Mol. Biol. 196, 901-917 and Chothia (1989) Nature, 342, 877-883..

A preferred cytotoxically active CD3 specific binding construct of the invention further comprises in said first domain a framework H3 comprising the sequence Met-Glu-Leu-Ser (MELS; SEQ ID NO.:234). Even more preferred is an inventive construct which comprises in said first domain a framework H3 comprising the sequence Ile-Thr-Thr-Asp-Lys (ITTDK; SEQ ID NO.: 235).

In accordance with the present invention, the first domain of the inventive construct specifically binding to/interacting with human CD3 and having a reduced propensity to generate T cell epitopes, comprises a CDR-H1, CDR-H2 and CDR-H3 regions as defined herein and, in a preferred embodiment, VH-frameworks (frameworks 1, 2, 3, 4) as defined above, in particular as shown in any one of SEQ ID NOs.: 152 or 153, 156 or 157, 160 or 161 and/or 164 or 165. Therefore, the CD3 specific binding construct of the invention comprises a first domain which specifically binds to human CD3 and comprises a framework region 1 as shown in SEQ ID NO.: 152 or 153, a framework region 2 as shown in SEQ ID NO.: 156 or 157, a framework region 3 as shown in SEQ ID NO.: 160 or 161 and/or a framework region 4 as shown in SEQ ID NO.: 164 or 165.

In a particularly preferred embodiment of the invention, the cytotoxically active deimmunized CD3 specific binding construct comprises in its first domain (a) a CDR-H1 as depicted in SEQ ID NO.: 88; and (b) a CDR-H2 as depicted in SEQ ID NO.: 90 or 92.

Accordingly, the modified CDR-H1 and CDR-H2 regions lead to a reduced propensity to generate T cell epitopes and are derived from an CD3- ϵ chain specific antibody. Most preferably in accordance with this invention said (parental) antibodies should be capable of specifically binding epitopes reflecting the native or near native structure or a conformational epitope of human CD3 presented in context of the TCR complex.

Preferably, the CD3 specific binding construct of the invention comprises a VH-region as depicted in SEQ ID NO.:74 or 76. SEQ ID NO.:74 shows an illustrative

deimmunized variable heavy region and, similarly, SEQ ID NO.:76 shows an illustrative deimmunized variable heavy region.

Preferably, the inventive CD3 specific binding construct comprises a CDR-L1 as depicted in SEQ ID NO.: 98 or 100, a CDR-L2 as depicted in SEQ ID NO.:102 and/or a CDR-L3 as depicted in SEQ ID NO.:104.

The CD3 specific binding construct of the invention comprises, in a preferred embodiment, a VL region in its CD3-specific portion, wherein said VL region is selected from the group consisting of SEQ ID NO.: 78 , SEQ ID NO.: 80, SEQ ID NO.: 82 and SEQ ID NO.: 112. VL1 as characterized in SEQ ID NO.:78, VL2 as characterized in SEQ ID NO.:80 and VL 3 as characterized in SEQ ID NO.:82 relate to full deimmunized VL regions in accordance with this invention, and they may be used in various combinations with the above described VH regions. Yet, it is also envisaged that the non-deimmunized VL region may be combined, in accordance with the invention, with deimmunized VH regions defined above. A corresponding non-deimmunized VL-region preferably employed in an cytotoxically active CD3 binding construct of the invention, is shown in SEQ ID NO.: 112. Accordingly, not only heavy chain part of the above recited "first domain" of the inventive CD3 construct may be modified to have a reduced propensity to generate T cell epitopes. It is also envisaged that said domain comprises the corresponding variable light chain parts. SEQ ID NOs.: 78, 80, and 82, for example, depict deimmunized VL1, VL2 and VL3 regions of the CD3 binding part of a construct disclosed in WO 99/54440.

As mentioned above, the CD3 specific binding construct of the invention, most preferably, comprises an Ig-derived second domain which is a scFv. Accordingly, in a most preferred embodiment of the present invention, a deimmunized, bispecific single chain antibody construct is provided with one specificity for human CD3 and a further specificity which is mediated by a second scFv, directed against/capable of interacting with a further molecule/compound. These further molecules/compounds may comprise cell surface molecules, tumor markers, tumor antigens and the like. Such further compounds/molecules are exemplified herein below and specific constructs are also given and provided in the appended examples.

The term "bispecific single chain antibody construct" relates to a construct comprising two antibody derived binding domains, preferably scFvs. One of said binding domains consists of variable regions (or parts thereof) of an antibody, antibody fragment or derivate thereof, capable of specifically binding to/interacting with human CD 3 antigen (target molecule 1). The second binding domain consists of variable regions (or parts thereof) of an antibody, antibody fragment or derivative thereof, capable of specifically binding to/interacting with another (human) antigen (target molecule 2) as defined below. Accordingly, said second binding domain is, in accordance with this invention, the Ig-derived second domain recited above which comprises an antigen-interaction-site with specificity for a cell surface molecule and/or a tumor specific marker. Said two domains/regions in the bispecific construct, preferably said bispecific single chain antibody construct, are preferably covalently connected to one another as a single chain. This connection can be effected either directly (domain 1 [specific for human CD3 antigen, comprising a reduced propensity to generate T cell epitopes and comprising CDR-regions or CDR-regions and framework regions as defined above] – domain 2 [specific for a cell surface molecule and/or a tumor specific marker] or domain 1 [specific for a cell surface molecule and/or a tumor specific marker] – domain 2 [specific for human CD3 antigen, comprising a reduced propensity to generate T cell epitopes and comprising CDR-regions or CDR-regions and framework regions as defined above]) or through an additional polypeptide linker sequence (domain1 – linker sequence – domain2). In the event that a linker is used, this linker is preferably of a length and sequence sufficient to ensure that each of the first and second domains can, independently from one another, retain their differential binding specificities. As mentioned above and as documented in the appended examples, preferably, the CD3 specific binding construct comprising at least two domains as defined herein is a "bispecific single chain antibody construct", most preferably a bispecific single chain Fv (scFv). It is in particular envisaged that said construct is employed in context of a pharmaceutical composition. Bispecific single chain molecules are known in the art and are described in WO 99/54440, Mack, J. Immunol. (1997), 158, 3965-3970, Mack, PNAS, (1995), 92, 7021-7025, Kufer, Cancer Immunol. Immunother., (1997), 45, 193-197, Löffler, Blood, (2000), 95, 6, 2098-2103, Brühl, J. Immunol., (2001), 166, 2420-2426. A particularly preferred molecular format of the invention provides a polypeptide

construct wherein the CD3 specific binding domain of the construct of the invention comprises at least one V_H and one V_L region as defined above. It is of note that in addition to a V_H-region as defined herein and having reduced propensity to generate T cell epitopes, said specific binding construct may comprise additional regions/domains with reduced propensity to generate T cell epitopes. As mentioned above, also the V_L-region and/or the corresponding frameworks may comprise amino acid stretches which have been engineered in accordance with this invention to having reduced propensity for T cell epitope generation. The intramolecular orientation of the V_H-domain and the V_L-domain, which are linked to each other by a linker-domain, in the scFv format is not decisive for the recited bispecific single chain constructs. Thus, scFvs with both possible arrangements (V_H-domain – linker domain – V_L-domain; V_L-domain – linker domain – V_H-domain) are particular embodiments of the recited bispecific single chain construct. A CD3 specific domain can be located N- or C-terminally in the bispecific molecule. V_H and V_L regions of each domain can be arranged in different orders (V_H-V_L or V_L-V_H).

The term "single-chain" as used in accordance with the present invention means that said first and second domain of the bispecific single chain construct are covalently linked, preferably in the form of a co-linear amino acid sequence encoded by a single nucleic acid molecule.

It is of note that the construct of the invention may comprise, in addition to the herein defined first domain and the Ig-derived second domain (an) additional domain(s), e.g. for the isolation and/or preparation of recombinantly produced constructs.

It is of note that, in accordance with this invention, not only the above described first domain which specifically binds to human CD3 of the inventive CD3 construct may have reduced propensity to generate T cell epitopes. It is also envisaged that the Ig-derived second domain and/or (a) connecting linker-region(s) is (are) modified, for example humanized and/or also deimmunized.

As mentioned above, deimmunization approaches are in particular illustrated in WO 00/34317, WO 98/52976, WO 02/079415 or WO 02/012899 and the appended examples. These approaches entail carrying out substitutions of amino acids within

potential T cell epitopes. In this way, the likelihood that a given sequence will give rise to T cell epitopes upon intracellular protein processing is reduced. In addition, WO 92/10755 describes an approach in which antigenic determinants on proteins are engineered. Particularly, proteins are epitope mapped and their amino acid sequence is changed through genetic engineering.

Furthermore, "humanization approaches" are well known in the art and in particular described for antibody molecules, e.g. Ig-derived molecules. The term "humanized" refers to humanized forms of non-human (e.g., murine) antibodies or fragments thereof (such as Fv, Fab, Fab', F(ab'), scFvs, or other antigen-binding partial sequences of antibodies) which contain some portion of the sequence derived from non-human antibody. Humanized antibodies include human immunoglobulins in which residues from a complementary determining region (CDR) of the human immunoglobulin are replaced by residues from a CDR of a non-human species such as mouse, rat or rabbit having the desired binding specificity, affinity and capacity. In general, the humanized antibody will comprise substantially all of at least one, and generally two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin; see, inter alia, Jones et al., *Nature* 321:522-525 (1986), Presta, *Curr. Op. Struct. Biol.* 2:593-596 (1992). Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acids introduced into it from a source which is non-human in order to more closely resemble a human antibody, while still retaining the original binding activity of the antibody. Methods for humanization of antibodies/antibody molecules are further detailed in Jones et al., *Nature* 321:522-525 (1986); Riechmann et al., *Nature* 332:323-327 (1988); and Verhoeyen et al., *Science* 239:1534-1536 (1988). Specific examples of humanized antibodies, e.g. antibodies directed against EpCAM, are known in the art, see e.g. (LoBuglio, Proceedings of the American Society of Clinical Oncology (Abstract), 1997, 1562 and Khor, Proceedings of the American Society of Clinical Oncology (Abstract), 1997, 847).

Accordingly, in the context of this invention, in particular bispecific single chain antibody constructs are provided, which are deimmunized and can successfully be employed in pharmaceutical compositions.

As mentioned above, the Ig-derived second domain of the above-described CD3 specific binding construct may comprise an antigen-interaction-site with specificity for a cell surface molecule.

The term "cell surface molecule", as used herein, also denotes molecules which are presented on the surface of cells. The term "cell surface molecule", relates to molecules, which are presented on the surface of cells and comprise domains or epitopes accessible (in vitro or in vivo) to Ig-derived binding domains, preferably antibodies, antibody fragments or derivatives. As illustrated above, most preferably said Ig-derived domain is a scFv. Examples for said cell surface molecules are membrane and transmembrane proteins, molecules adapted to said proteins or the cell surface etc. According to a further preferred embodiment of the invention said cell surface molecule is a tumor specific marker. In context of this invention, the term "tumor specific marker" relate to molecules, which are presented and/or located on the surface of tumor cells or which are ubiquitously expressed but are only accessible for binding of antibodies, antibody fragments or antibody derivatives on the surface of tumor cells. Examples of tumor markers are given herein below and comprise, but are not limited to, EpCAM, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, MUC5_{AC}, MUC5_B, MUC7, Lewis-Y, CD20, CD33, CD30, CD44v6, Wue-1, Plasma Cell Antigen (see WO 01/47953), (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), STEAP, mesothelin, Prostate Stem Cell Antigen (PSCA), sTn (sialylated Tn antigen), FAP (fibroblast activation antigen), EGFRvIII, Ig α , Ig β , MT-MMPs, Cora antigen, EphA2, L6 and CO-29.

The Ig-derived second domain of the CD3 specific binding construct of the invention may also comprise an antigen-interaction site with a specificity for a molecule selected from the group consisting of EpCAM, CCR5, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, MUC5_{AC}, MUC5_B, MUC7, β hCG, Lewis-Y, CD20, CD33, CD30, ganglioside GD3, 9-O-Acetyl-GD3, GM2, Globo H, fucosyl GM1, Poly SA, GD2, Carboanhydrase IX

(MN/CA IX), CD44v6, Sonic Hedgehog (Shh), Wue-1, Plasma Cell Antigen, (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), CCR8, TNF-alpha precursor, STEAP, mesothelin, A33 Antigen, Prostate Stem Cell Antigen (PSCA), Ly-6; desmoglein 4, E-cadherin neoepitope, Fetal Acetylcholine Receptor, CD25, CA19-9 marker, CA-125 marker and Muellerian Inhibitory Substance (MIS) Receptor type II, sTn (sialylated Tn antigen), FAP (fibroblast activation antigen), endosialin, EGFRvIII, L6, SAS, CD63, TAG72, TF-antigen, Cora antigen, CD7, CD22, Ig α (CD79a), Ig β (CD79b), G250, gp100, MT-MMPs, F19-antigen, CO-29 and EphA2.

The constructs provided herein are particularly useful in medical setting. For example, tumorous diseases and/or lymphomas, preferably non-Hodgkin's B-cell lymphoma, may be treated with an inventive deimmunized (bispecific) construct directed against human CD3 and CD20 (CD3xCD20 or CD20xCD3). Autoimmune diseases may be treated by the administration of deimmunized (bispecific) constructs directed against human CD3 and CD30 or CD19 (i.e. CD3xCD30 or CD30xCD3 or CD3xCD19 or CD19xCD3). Rheumatoid arthritis, as well as other inflammatory diseases may be treated with an inventive deimmunized (bispecific) construct directed against human CD3 and CCR5 (CD3xCCR5 or CCR5xCD3). A deimmunized CD3 specific binding construct as defined herein and comprising a second Ig-derived domain directed to/binding with TNF-alpha precursor may also be useful in the treatment or prevention of inflammatory disorders. CD3 constructs as provided herein and comprising a second, Ig-derived domain directed against/binding to/interacting with EpCAM, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, MUC5_{AC}, MUC5_B, MUC7, Lewis-Y, CD20, CD33, CD30, CD44v6, Wue-1, Plasma Cell Antigen (see WO 01/47953), (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), STEAP, mesothelin, Prostate Stem Cell Antigen (PSCA), sTn (sialylated Tn antigen), FAP (fibroblast activation antigen), EGFRvIII, Ig α , Ig β , MT-MMPs, Cora antigen, EphA2, L6 and CO-29 may be particularly useful in the medical intervention of tumorous diseases like breast cancer, colon cancer, prostate cancer, head and neck cancer, skin cancer (melanoma), cancers of the genito-urinary tract, e.g. ovarian cancer, endometrial cancer, cervix cancer and kidney cancer, lung cancer, gastric cancer, cancer of the small intestine, liver cancer, pancreas cancer, gall bladder cancer,

cancers of the bile duct, esophagus cancer, cancer of the salivatory glands and cancer of the thyroid gland or other tumorous diseases like hematological tumors, gliomas, sarcomas or osteosarcomas. The administration of the CD3 binding constructs is also indicated for minimal residual disease, preferably for early solid tumors, advanced solid tumors or metastatic solid tumors.

As also illustrated in the appended examples, a particularly preferred CD3 specific binding construct of the invention comprises the above defined first domain with reduced propensity to generate T cell epitopes and a second, Ig-derived domain comprising an antigen-interaction site with a specificity for EpCAM.

Epithelial cell adhesion molecule (EpCAM, also called 17-1A antigen, KSA, EGP40, GA733-2, ks1-4 or esa) is a 40-kDa membrane-integrated glycoprotein of 314 amino acids with specific expression in certain epithelia and on many human carcinomas (reviewed in Balzar, J. Mol. Med. 1999, 77, 699-712). EpCAM was discovered and subsequently cloned through its recognition by the murine monoclonal antibody 17-1A/edrecolomab (Goettlinger, Int J Cancer. 1986; 38, 47-53 and Simon, Proc. Natl. Acad. Sci. USA. 1990; 87, 2755-2759). EpCAM serves to adhere epithelial cells in an oriented and highly ordered fashion (Litvinov, J Cell Biol. 1997, 139, 1337-1348). Upon malignant transformation of epithelial cells the rapidly growing tumor cells are abandoning the high cellular order of epithelia. Consequently, the surface distribution of EpCAM becomes less restricted and the molecule better exposed on tumor cells and accessible for binding of antibodies, antibody fragments or antibody derivatives on the surface of tumor cells. Due to their epithelial cell origin, tumor cells from most carcinomas still express EpCAM on their surface.

In vivo, expression of EpCAM is related to increased epithelial proliferation and negatively correlates with cell differentiation (for review see Balzar, 1999, J. Mol. Med. 77, 699-712). Expression of EpCAM is essentially seen with all major carcinomas (reviewed in Balzar, J Mol Med. 1999, 77, 699-712 or documented, inter alia, in De Bree, Nucl Med Commun. 1994, 15, 613-27; Zhang, Clin Cancer Res. 1998, 4, 295-302). Because of its widespread expression, EpCAM is referred to as a "pan-carcinoma" antigen. In many cases, tumor cells were observed to express EpCAM to a much higher degree than their parental epithelium or less aggressive

forms of said cancers. For example, increased EpCAM expression represents an early event in the development of prostate cancer (Poczatek, J Urol., 1999, 162, 1462-1644). In addition, in the majority of both squamous and adenocarcinomas of the cervix a strong EpCAM expression correlates with an increased proliferation and the disappearance of markers for terminal differentiation (Litvinov, Am. J. Pathol. 1996, 148, 865-75). In breast cancer, overexpression of EpCAM on tumor cells is a predictor of survival (Gastl, Lancet. 2000, 356, 1981-1982). EpCAM is a marker for the detection of disseminated tumor cells in patients suffering from squamous cell carcinoma of the head, neck and lung (Chaubal, Anticancer Res 1999, 19, 2237-2242, Piyathilake, Hum Pathol. 2000, 31, 482-487). Normal squamous epithelium, as found in epidermis, oral cavity, epiglottis, pharynx, larynx and esophagus did not significantly express EpCAM (Quak, Hybridoma, 1990, 9, 377-387). EpCAM has been shown to be expressed on the majority of primary, metastatic, and disseminated NSCLC (non small cell lung cancer cells (Passlick, Int J Cancer, 2000, 87, 548-552)), on gastric and gastro-oesophageal junction adenocarcinomas (Martin, J Clin Pathol 1999, 52, 701-4) and in cell lines derived from colorectal, pancreatic carcinomas and breast carcinomas (Szala, Proc Natl Acad Sci U S A 1990, 87, 3542-6, Packeisen, Hybridoma, 1999, 18, 37-40).

In a most preferred embodiment, the CD3 specific binding construct of the invention which comprises a second Ig-derived domain directed against/binding to EpCAM, comprises an amino acid sequence selected from the group of

- (a) an amino acid sequence as shown in any one of SEQ ID NO.: 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 and 325;
- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of SEQ ID NO.: 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 and 324; and
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b).

Accordingly, the present invention provides, in a particularly preferred embodiment for specific CD3 constructs which comprise a CD3 binding/interaction part ("anti-CD3") which has reduced propensity to generate T cell epitopes and a further single chain part (an Ig-derived domain) which specifically interacts with/binds to EpCAM ("anti-EpCAM"). The following tables 1A, 1B, 2A, 2B, 3A, 3B, 4A, 4B, 5A and 5B relate to preferred configurations of such CD3 and EpCAM binding constructs.

EpCAM 3-1, EpCAM 3-5, EpCAM 4-1, EpCAM 4-7 and EpCAM 5-10 relate to specific single chain antibodies against EpCAM isolated by phage display in WO99/25818.

Each protein construct in Tables 1A, 2A, 3A, 4A and 5A comprises 7 distinct protein modules, denoted A-G. Protein modules A-G are directly and covalently linked to one another in a single contiguous polypeptide chain by peptide bonds in the order A-B-C-D-E-F-G, with protein module A at the N-terminus and protein module G at the C-terminus. Protein modules A, C, E and G denote antibody variable domains which can be either VH or VL domains of antibodies having specificity for the human CD3 or EpCAM antigen. The modules B, D and F are linkers connecting the VH and VL domains.

If protein module A is a VH antibody domain, then protein module C is a VL protein domain, and vice versa. If protein module E is a VH antibody domain, then protein module G is a VL protein domain, and vice versa.

Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 78, 80 or 82. The VH protein domain of human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO.: 137, 141, 145, 149 and 133, respectively. The VL protein domain of human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO.: 139, 143, 147, 151 and 135, respectively.

Pairs of antibody variable domains denoted by the protein module pairs A/C and E/G are joined by additional linking protein modules, wherein protein module B serves to directly link the module pair A/C and protein module F serves to directly link the module pair E/G. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human

CD3 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO.: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the EpCAM antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO.: 168. The module D connects the ABC and EFG module groups.

The combination of protein modules A-B-C and the combination of protein modules E-F-G each respectively constitute one scFv fragment of an antibody having specificity for either the human CD3 antigen or for the EpCAM antigen. If the modules A and C show the CD3 binding sequence, the respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO.: 176. On the other hand, if the modules A and C show the EpCAM binding sequence, the respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO.: 174. Thus, an additional serine may be inserted after the VL chain for cloning purposes. However, the skilled artisan may also use the linker as shown in SEQ ID NO.:174 in order to link a VL domain with the subsequent V domain instead of SEQ ID NO.:176. Protein module D serves to connect the C-terminal end of protein module C with the N-terminal end of protein module E.

Each nucleic acid construct in Tables 1B, 2B, 3B, 4B and 5B comprises 7 distinct nucleic acid modules, denoted A-G. Nucleic acid modules A-G are directly and covalently linked to one another in a single contiguous nucleotide chain by phosphate glycoside bonds in the order A-B-C-D-E-F-G, with nucleic acid module A at the 5'-end and nucleic acid module G at the 3'-end of a respective nucleic acid construct. Nucleic acid modules A, C, E and G denote encoding regions for antibody variable domains which can be either VH or VL domains of antibodies having specificity for the human CD3 or EpCAM antigen.

If nucleic acid module A encodes a VH antibody domain, then nucleic acid module C encodes a VL protein domain, and vice versa. If nucleic acid module E encodes a VH antibody domain, then nucleic acid module G encodes a VL protein domain, and vice versa.

Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 77, 79 or 81. The nucleic acid molecule encoding the VH protein domain of the human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO.: 136, 140, 144, 148 and 132 respectively. The nucleic acid molecule encoding the VL protein domain of the human EpCAM 3-1, 3-5, 4-1, 4-7 and 5-10 antibody is as set out in SEQ ID NO.: 138, 142, 146, 150 and 134, respectively.

Pairs of nucleic acids encoding antibody variable domains denoted by the nucleic acid module pairs A/C and E/G are joined by additional linking nucleic acid modules, wherein nucleic acid module B serves to directly link the module pair A/C and nucleic acid module F serves to directly link the module pair E/G. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the nucleotide sequence as set out in SEQ ID NO.: 202. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of VH/VL or VL/VH from an antibody having specificity for the human EpCAM antigen, nucleic acid module B or F, respectively, has the nucleotide sequence as set out in SEQ ID NO.: 201.

The combination of nucleic acid modules A-B-C and the combination of nucleic acid modules E-F-G each respectively constitute one scFv fragment of an antibody having specificity for either the human CD3 antigen or for the EpCAM antigen. If the A and C modules comprise CD3 binding sequences, the respective groups of nucleic acid modules A-B-C and E-F-G are connected to each other through nucleic acid module D, having the nucleotide sequence as set out in SEQ ID NO.: 175. If the A and C modules comprise EpCAM binding sequences, the respective groups of nucleic acid modules A-B-C and E-F-G are connected to each other through nucleic acid module D, having the nucleotide sequence as set out in SEQ ID NO.: 173. However, as mentioned above, the additional codon encoding a serine (in SEQ ID NO.: 175) may be inserted for cloning purposes. The skilled person may link the nucleotide

sequence encoding the VL chain directly with the subsequent V domain with the linker as depicted in SEQ ID NO.:173 without the additional codon encoding serine at the 5' end of the linker. Nucleic acid module D serves to connect the 3'-end of nucleic acid module C with the 5'-end of nucleic acid module E.

Table 1A
Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-1 variable regions: amino acid sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	137	168	139	CD3 (VL2/ VH5)xEPCAM(3-1)	LHHL
2	74	3	80	176	137	168	139	CD3 (VH5/VL2)xEPCAM(3-1)	HLHL
3	80	3	74	176	139	168	137	CD3 (VL2/ VH5)xEPCAM(3-1)	LHLH
4	74	3	80	176	139	168	137	CD3 (VH5/VL2)xEPCAM(3-1)	HLLH
5	139	168	137	174	74	3	80	EPCAM(3-1)xCD3 (VH5/VL2)	LHHL
6	137	168	139	174	74	3	80	EPCAM(3-1)xCD3(VH5/VL2)	HLHL
7	139	168	137	174	80	3	74	EPCAM(3-1)xCD3 (VL2/ VH5)	LHLH
8	137	168	139	174	80	3	74	EPCAM(3-1)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	137	168	139	CD3 (VL2/ VH7)xEPCAM(3-1)	LHHL
10	76	3	80	176	137	168	139	CD3 (VH7/VL2)xEPCAM(3-1)	HLHL
11	80	3	76	176	139	168	137	CD3 (VL2/VH7)xEPCAM(3-1)	LHLH
12	76	3	80	176	139	168	137	CD3 (VH7/VL2)xEPCAM(3-1)	HLLH
13	139	168	137	174	76	3	80	EPCAM(3-1)xCD3 (VH7/VL2)	LHHL
14	137	168	139	174	76	3	80	EPCAM(3-1)xCD3(VH7/VL2)	HLHL
15	139	168	137	174	80	3	76	EPCAM(3-1)xCD3 (VL2/ VH7)	LHLH
16	137	168	139	174	80	3	76	EPCAM(3-1)xCD3(VL2/ VH7)	HLLH

Table 1B
Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-1 variable regions: nucleotide sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	136	201	138	CD3 (VL2/ VH5)xEPCAM(3-1)	LHHL
2	73	202	79	175	136	201	138	CD3 (VH5/VL2)xEPCAM(3-1)	HLHL
3	79	202	73	175	138	201	136	CD3 (VL2/ VH5)xEPCAM(3-1)	LHLH
4	73	202	79	175	138	201	136	CD3 (VH5/VL2)xEPCAM(3-1)	HLLH
5	138	201	136	173	73	202	79	EPCAM(3-1)xCD3 (VH5/VL2)	LHHL
6	136	201	138	173	73	202	79	EPCAM(3-1)xCD3 (VH5/VL2)	HLHL
7	138	201	136	173	79	202	73	EPCAM(3-1)xCD3 (VL2/ VH5)	LHLH
8	136	201	138	173	79	202	73	EPCAM(3-1)xCD3 (VL2/ VH5)	HLLH
9	79	202	75	175	136	201	138	CD3 (VL2/ VH7)xEPCAM(3-1)	LHHL
10	75	202	79	175	136	201	138	CD3 (VH7/VL2)xEPCAM(3-1)	HLHL
11	79	202	75	175	138	201	136	CD3 (VL2/ VH7)xEPCAM(3-1)	LHLH
12	75	202	79	175	138	201	136	CD3 (VH7/VL2)xEPCAM(3-1)	HLLH
13	138	201	136	173	75	202	79	EPCAM(3-1)xCD3 (VH7/VL2)	LHHL
14	136	201	138	173	75	202	79	EPCAM(3-1)xCD3 (VH7/VL2)	HLHL
15	138	201	136	173	79	202	75	EPCAM(3-1)xCD3 (VL2/ VH7)	LHLH
16	136	201	138	173	79	202	75	EPCAM(3-1)xCD3 (VL2/ VH7)	HLLH

Table 2A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-5 variable regions: amino acid sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	141	168	143	CD3 (VL2/VH5)xEPICAM(3-5)	LHHL
2	74	3	80	176	141	168	143	CD3 (VH5/VL2)xEPICAM(3-5)	HLHL
3	80	3	74	176	143	168	141	CD3 (VL2/VH5)xEPICAM(3-5)	LHLH
4	74	3	80	176	143	168	141	CD3 (VH5/VL2)xEPICAM(3-5)	HLLH
5	143	168	141	174	74	3	80	EPICAM(3-5)xCD3 (VH5/VL2)	LHHL
6	141	168	143	174	74	3	80	EPICAM(3-5)xCD3 (VH5/VL2)	HLHL
7	143	168	141	174	80	3	74	EPICAM(3-5)xCD3 (VL2/VH5)	LHLH
8	141	168	143	174	80	3	74	EPICAM(3-5)xCD3 (VL2/VH5)	HLLH
9	80	3	76	176	141	168	143	CD3 (VL2/VH7)xEPICAM(35)	LHHL
10	76	3	80	176	141	168	143	CD3 (VH7/VL2)xEPICAM(3-5)	HLHL
11	80	3	76	176	143	168	141	CD3 (VL2/VH7)xEPICAM(3-5)	LHLH
12	76	3	80	176	143	168	141	CD3 (VH7/VL2)xEPICAM(3-5)	HLLH
13	143	168	141	174	76	3	80	EPICAM(3-5)xCD3 (VH7/VL2)	LHHL
14	141	168	143	174	76	3	80	EPICAM(3-5)xCD3 (VH7/VL2)	HLHL
15	143	168	141	174	80	3	76	EPICAM(3-5)xCD3 (VL2/VH7)	LHLH
16	141	168	143	174	80	3	76	EPICAM(3-5)xCD3 (VL2/VH7)	HLLH

Table 2B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 3-5 variable regions: nucleotide sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	140	201	142	CD3 (VL2/ VH5)xEPCAM(3-5)	LHHL
2	73	202	79	175	140	201	142	CD3 (VH5/VL2)xEPCAM(3-5)	HLHL
3	79	202	73	175	142	201	140	CD3 (VL2/ VH5)xEPCAM(3-5)	LHLH
4	73	202	79	175	142	201	140	CD3 (VH5/VL2)xEPCAM(3-5)	HLLH
5	142	201	140	173	73	202	79	EPCAM(3-5)xCD3(VH5/VL2)	LHHL
6	140	201	142	173	73	202	79	EPCAM(3-5)xCD3(VH5/VL2)	HLHL
7	142	201	140	173	79	202	73	EPCAM(3-5)xCD3 (VL2/VH5)	LHLH
8	140	201	142	173	79	202	73	EPCAM(3-5)xCD3(VL2/VH5)	HLLH
9	79	202	75	175	140	201	142	CD3 (VL2/ VH7)xEPCAM(3-5)	LHHL
10	75	202	79	175	140	201	142	CD3 (VH7/VL2)xEPCAM(3-5)	HLHL
11	79	202	75	175	142	201	140	CD3 (VL2/ VH7)xEPCAM(3-5)	LHLH
12	75	202	79	175	142	201	140	CD3 (VH7/VL2)xEPCAM(3-5)	HLLH
13	142	201	140	173	75	202	79	EPCAM(3-5)xCD3 (VH7/VL2)	LHHL
14	140	201	142	173	75	202	79	EPCAM(3-5)xCD3(VH7/VL2)	HLHL
15	142	201	140	173	79	202	75	EPCAM(3-5)xCD3 (VL2/VH7)	LHLH
16	140	201	142	173	79	202	75	EPCAM(3-5)xCD3(VL2/VH7)	HLLH

Table 3A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-1 variable regions: amino acid sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N → C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	145	168	147	CD3 (VL2/ VH5)xEPCCAM(4-1)	LHHL
2	74	3	80	176	145	168	147	CD3 (VH5/VL2)xEPCCAM(4-1)	HLHL
3	80	3	74	176	147	168	145	CD3 (VL2/ VH5)xEPCCAM(4-1)	LHLH
4	74	3	80	176	147	168	145	CD3 (VH5/VL2)xEPCCAM(4-1)	HLLH
5	147	168	145	174	74	3	80	EPCCAM(4-1)xCD3 (VH5/VL2)	LHHL
6	145	168	147	174	74	3	80	EPCCAM(4-1)xCD3 (VH5/VL2)	HLHL
7	147	168	145	174	80	3	74	EPCCAM(4-1)xCD3 (VL2/ VH5)	LHLH
8	145	168	147	174	80	3	74	EPCCAM(4-1)xCD3 (VL2/ VH5)	HLLH
9	80	3	76	176	145	168	147	CD3 (VL2/ VH7)xEPCCAM(4-1)	LHHL
10	76	3	80	176	145	168	147	CD3 (VH7/VL2)xEPCCAM(4-1)	HLHL
11	80	3	76	176	147	168	145	CD3 (VL2/ VH7)xEPCCAM(4-1)	LHLH
12	76	3	80	176	147	168	145	CD3 (VH7/VL2)xEPCCAM(4-1)	HLLH
13	147	168	145	174	76	3	80	EPCCAM(4-1)xCD3 (VH7/VL2)	LHHL
14	145	168	147	174	76	3	80	EPCCAM(4-1)xCD3 (VH7/VL2)	HLHL
15	147	168	145	174	80	3	76	EPCCAM(4-1)xCD3 (VL2/ VH7)	LHLH
16	145	168	147	174	80	3	76	EPCCAM(4-1)xCD3 (VL2/ VH7)	HLLH

Table 3B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-1 variable regions: nucleotide sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	144	201	146	CD3 (VL2/ VH5)xEPCAM(4-1)	LHHL
2	73	202	79	175	144	201	146	CD3 (VH5/VL2)xEPCAM(4-1)	HLHL
3	79	202	73	175	146	201	144	CD3 (VL2/ VH5)xEPCAM(4-1)	LHLH
4	73	202	79	175	146	201	144	CD3 (VH5/VL2)xEPCAM(4-1)	HLLH
5	146	201	144	173	73	202	79	EPCAM(4-1)xCD3 (VH5/VL2)	LHHL
6	144	201	146	173	73	202	79	EPCAM(4-1)xCD3(VH5/VL2)	HLHL
7	146	201	144	173	79	202	73	EPCAM(4-1)xCD3 (VL2/ VH5)	LHLH
8	144	201	146	173	79	202	73	EPCAM(4-1)xCD3(VL2/ VH5)	HLLH
9	79	202	75	175	144	201	146	CD3 (VL2/ VH7)xEPCAM(4-1)	LHHL
10	75	202	79	175	144	201	146	CD3 (VH7/VL2)xEPCAM(4-1)	HLHL
11	79	202	75	175	146	201	144	CD3 (VL2/ VH7)xEPCAM(4-1)	LHLH
12	75	202	79	175	146	201	144	CD3 (VH7/VL2)xEPCAM(4-1)	HLLH
13	146	201	144	173	75	202	79	EPCAM(4-1)xCD3 (VH7/VL2)	LHHL
14	144	201	146	173	75	202	79	EPCAM(4-1)xCD3(VH7/VL2)	HLHL
15	146	201	144	173	79	202	75	EPCAM(4-1)xCD3 (VL2/ VH7)	LHLH
16	144	201	146	173	79	202	75	EPCAM(4-1)xCD3(VL2/ VH7)	HLLH

Table 4A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-7 variable regions: amino acid sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	149	168	151	CD3 (VL2/ VH5)xEPcAM(4-7)	LHHL
2	74	3	80	176	149	168	151	CD3 (VH5/VL2)xEPcAM(4-7)	HLHL
3	80	3	74	176	151	168	149	CD3 (VL2/ VH5)xEPcAM(4-7)	LHLH
4	74	3	80	176	151	168	149	CD3 (VH5/VL2)xEPcAM(4-7)	HLLH
5	151	168	149	174	74	3	80	EPcAM(4-7)xCD3 (VH5/VL2)	LHHL
6	149	168	151	174	74	3	80	EPcAM(4-7)xCD3(VH5/VL2)	HLHL
7	151	168	149	174	80	3	74	EPcAM(4-7)xCD3 (VL2/ VH5)	LHLH
8	149	168	151	174	80	3	74	EPcAM(4-7)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	149	168	151	CD3 (VL2/ VH7)xEPcAM(4-7)	LHHL
10	76	3	80	176	149	168	151	CD3 (VH7/VL2)xEPcAM(4-7)	HLHL
11	80	3	76	176	151	168	149	CD3 (VL2/ VH7)xEPcAM(4-7)	LHLH
12	76	3	80	176	151	168	149	CD3 (VH7/VL2)xEPcAM(4-7)	HLLH
13	151	168	149	174	76	3	80	EPcAM(4-7)xCD3 (VH7/VL2)	LHHL
14	149	168	151	174	76	3	80	EPcAM(4-7)xCD3(VH7/VL2)	HLHL
15	151	168	149	174	80	3	76	EPcAM(4-7)xCD3 (VL2/ VH7)	LHLH
16	149	168	151	174	80	3	76	EPcAM(4-7)xCD3(VL2/ VH7)	HLLH

Table 4B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 4-7 variable regions: nucleotide sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	148	201	150	CD3 (VL2/ VH5)xEPcAM(4-7)	LHHL
2	73	202	79	175	148	201	150	CD3 (VH5/VL2)xEPcAM(4-7)	HLHL
3	79	202	73	175	150	201	148	CD3 (VL2/ VH5)xEPcAM(4-7)	LHLH
4	73	202	79	175	150	201	148	CD3 (VH5/VL2)xEPcAM(4-7)	HLLH
5	150	201	148	173	73	202	79	EPcAM(4-7)xCD3 (VH5/VL2)	LHHL
6	148	201	150	173	73	202	79	EPcAM(4-7)xCD3 (VH5/VL2)	HLHL
7	150	201	148	173	79	202	73	EPcAM(4-7)xCD3 (VL2/ VH5)	LHLH
8	148	201	150	173	79	202	73	EPcAM(4-7)xCD3 (VL2/ VH5)	HLLH
9	79	202	75	175	148	201	150	CD3 (VL2/ VH7)xEPcAM(4-7)	LHHL
10	75	202	79	175	148	201	150	CD3 (VH7/VL2)xEPcAM(4-7)	HLHL
11	79	202	75	175	150	201	148	CD3 (VL2/ VH7)xEPcAM(4-7)	LHLH
12	75	202	79	175	150	201	148	CD3 (VH7/VL2)xEPcAM(4-7)	HLLH
13	150	201	148	173	75	202	79	EPcAM(4-7)xCD3 (VH7/VL2)	LHHL
14	148	201	150	173	75	202	79	EPcAM(4-7)xCD3 (VH7/VL2)	HLHL
15	150	201	148	173	79	202	75	EPcAM(4-7)xCD3 (VL2/ VH7)	LHLH
16	148	201	150	173	79	202	75	EPcAM(4-7)xCD3 (VL2/ VH7)	HLLH

Table 5A

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 5-10 variable regions: amino acid sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	176	133	168	135	CD3 (VL2/ VH5)xEPCAM(5-10)	LHHL
2	74	3	80	176	133	168	135	CD3 (VH5/VL2)xEPCAM(5-10)	HLHL
3	80	3	74	176	135	168	133	CD3 (VL2/ VH5)xEPCAM(5-10)	LHLH
4	74	3	80	176	135	168	133	CD3 (VH5/VL2)xEPCAM(5-10)	HLLH
5	135	168	133	174	74	3	80	EPCAM(5-10)xCD3 (VH5/VL2)	LHHL
6	133	168	135	174	74	3	80	EPCAM(5-10)xCD3(VH5/VL2)	HLHL
7	135	168	133	174	80	3	74	EPCAM(5-10)xCD3 (VL2/ VH5)	LHLH
8	133	168	135	174	80	3	74	EPCAM(5-10)xCD3(VL2/ VH5)	HLLH
9	80	3	76	176	133	168	135	CD3(VL2/ VH7) xEPCAM(5-10)	LHHL
10	76	3	80	176	133	168	135	CD3 (VH7/VL2) xEPCAM(5-10)	HLHL
11	80	3	76	176	135	168	133	CD3(VL2/VH7) xEPCAM(5-10)	LHLH
12	76	3	80	176	135	168	133	CD3 (VH7/VL2) xEPCAM(5-10)	HLLH
13	135	168	133	174	76	3	80	EPCAM(5-10)xCD3 (VH7/VL2)	LHHL
14	133	168	135	174	76	3	80	EPCAM(5-10)xCD3(VH7/VL2)	HLHL
15	135	168	133	174	80	3	76	EPCAM(5-10)xCD3 (VL2/ VH7)	LHLH
16	133	168	135	174	80	3	76	EPCAM(5-10)xCD3(VL2/ VH7)	HLLH

Table 5B

Deimmunized anti-human CD3 constructs comprising single chain anti-EpCAM 5-10 variable regions: nucleotide sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	175	132	201	134	CD3 (VL2/ VH5) xEPCAM(5-10)	LHHL
2	73	202	79	175	132	201	134	CD3 (VH5/VL2) xEPCAM(5-10)	HLHL
3	79	202	73	175	134	201	132	CD3 (VL2/ VH5) xEPCAM(5-10)	LHLH
4	73	202	79	175	134	201	132	CD3 (VH5/VL2) xEPCAM(5-10)	HLLH
5	134	201	132	173	73	202	79	EPCAM(5-10)xCD3 (VH5/VL2)	LHHL
6	132	201	134	173	73	202	79	EPCAM(5-10)xCD3(VH5/VL2)	HLHL
7	134	201	132	173	79	202	73	EPCAM(5-10)xCD3 (VL2/ VH5)	LHLH
8	132	201	134	173	79	202	73	EPCAM(5-10)xCD3(VL2/ VH5)	HLLH
9	79	202	75	175	132	201	134	CD3 (VL2/ VH7) xEPCAM(5-10)	LHHL
10	75	202	79	175	132	201	134	CD3 (VH7/VL2) xEPCAM(5-10)	HLHL
11	79	202	75	175	134	201	132	CD3 (VL2/ VH7) xEPCAM(5-10)	LHLH
12	75	202	79	175	134	201	132	CD3 (VH7/VL2) xEPCAM(5-10)	HLLH
13	134	201	132	173	75	202	79	EPCAM(5-10)xCD3 (VH7/VL2)	LHHL
14	132	201	134	173	75	202	79	EPCAM(5-10)xCD3(VH7/VL2)	HLHL
15	134	201	132	173	79	202	75	EPCAM(5-10)xCD3 (VL2/ VH7)	LHLH
16	132	201	134	173	79	202	75	EPCAM(5-10)xCD3(VL2/ VH7)	HLLH

Most preferably, the invention provides bispecific antibody constructs comprising a specificity binding to CD3 and EpCAM and having the SEQ ID NO.: 30, 31 (construct 2 of Table 1A and 1B), Seq ID NO.: 48, 49 (construct 5 of the Table 1A, 1B), SEQ ID NO.: 64, 65 (construct 2 of Table 2A, 2B), SEQ ID NO.: 54, 55 (construct 5 of Table 2A, 2B), Seq ID NO.: 66, 67 (construct 2 of Table 3A, 3B), SEQ ID NO.: 32, 33 (construct 2 of Table 4A, 4B), SEQ ID NO.: 34, 35 (construct 4 of Table 4A, 4B), SEQ ID NO.: 60, 61 (construct 5 of Table 4A, 4B), SEQ ID NO.: 36, 37 (construct 2 of Table 5A, 5B), SEQ ID NO.: 38, 39 (construct 4 of Table 5A, 5B) or SEQ ID NO.: 62, 63 (construct 5 of Table 5A, 5B).

In accordance with constructs provided herein above, particularly preferred CD3 and EpCAM binding constructs of the invention, comprising at least the above described first domain with reduced propensity for T cell epitope generation and specificity for human CD3 and a second, Ig-derived domain which is specific for EpCAM are shown in SEQ ID NOs.: 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 and 325. Corresponding nucleic acid molecules encoding said preferred CD3 and EpCAM binding constructs as defined herein comprise SEQ ID NOs.: 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 and 324.

Accordingly, the present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/capable of binding to EpCAM, selected from the group consisting of

- (a) an amino acid sequence as shown in any one of SEQ ID NO.: 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 or 325;

- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of SEQ ID NO.: 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 or 324;
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);
- (d) an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridization conditions.

The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to EpCAM, which comprise an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence as shown in any one of SEQ ID NO.: 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 or 324 under stringent hybridization conditions.

The term "hybridizing" as used herein refers to polynucleotides/nucleic acid sequences which are capable of hybridizing to the polynucleotides encoding the deimmunized constructs as defined herein. Therefore, said polynucleotides may be useful as probes in Northern or Southern Blot analysis of RNA or DNA preparations, respectively, or can be used as oligonucleotide primers in PCR analysis dependent on their respective size. Preferably, said hybridizing polynucleotides comprise at least 10, more preferably at least 15 nucleotides in length while a hybridizing polynucleotide of the present invention to be used as a probe preferably comprises at least 100, more preferably at least 200, or most preferably at least 500 nucleotides in length.

It is well known in the art how to perform hybridization experiments with nucleic acid molecules, i.e. the person skilled in the art knows what hybridization conditions s/he

has to use in accordance with the present invention. Such hybridization conditions are referred to in standard text books such as *Molecular Cloning A Laboratory Manual*, Cold Spring Harbor Laboratory (2001) N.Y. Preferred in accordance with the present inventions are polynucleotides which are capable of hybridizing to the polynucleotides of the invention or parts thereof, under stringent hybridization conditions.

"Stringent hybridization conditions" refer, i.e. to an overnight incubation at 42°C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1 x SSC at about 65°C. Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH₂PO₄; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 µg/ml salmon sperm blocking DNA; followed by washes at 50°C with 1 X SSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC). It is of note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

The recited nucleic acid molecules may be, e.g., DNA, cDNA, RNA or synthetically produced DNA or RNA or a recombinantly produced chimeric nucleic acid molecule comprising any of those polynucleotides either alone or in combination.

The deimmunized CD3 and EpCAM binding constructs provided in this invention are particularly useful in medical settings, for example in the prevention, treatment and/or the amelioration of tumorous diseases, in particular, breast cancer, colon cancer,

prostate cancer, head and neck cancer, skin cancer (melanoma), cancers of the genito-urinary tract, e.g. ovarian cancer, endometrial cancer, cervix cancer and kidney cancer, lung cancer, gastric cancer, cancer of the small intestine, liver cancer, pancreas cancer, gall bladder cancer, cancers of the bile duct, esophagus cancer, cancer of the salivatory glands and cancer of the thyroid gland. In particular, the deimmunized constructs binding CD3 and EpCAM can be used for the treatment of epithelial cancer, preferably adenocarcinomas, or minimal residual disease, more preferably early solid tumor, advanced solid tumor or metastatic solid tumor.

In a more particularly preferred embodiment of the CD3 specific binding construct described herein, said construct comprises a second Ig-derived domain which comprises an antigen-interaction site with a specificity for CCR5.

The chemokine receptor CCR5 is a member of a large family of G protein coupled seven transmembrane domain receptors that binds the proinflammatory chemokines RANTES, MIP1- α , MIP1- β and MCP-2. Chemokines act in concert with adhesion molecules to induce the extravasation of leukocytes and to direct their migration to sites of tissue injury. CCR5 is expressed on a minority of T-cells and monocytes and is further the major co-receptor for M-trophic HIV-1 strains that predominate early in the course of an HIV-infection.

Human immunodeficiency virus (HIV) cannot enter human cells unless it first binds to two key molecules on the cell surface, CD4 and a co-receptor. The co-receptor that is initially recognized is CCR5, later in the life cycle of the virus another chemokine receptor CXCR4 becomes the co-receptor for HIV-1 (D'Souza, Nature Med. 2, 1293 (1996); Premack, Nature Med. 2, 1174; Fauci, Nature 384, 529 (1996)). The HIV-1 strains that cause most transmissions of viruses by sexual contact are called M-tropic viruses. These HIV-1 strains (also known as non-syncytia inducing (NSI) primary viruses) can replicate in primary CD4⁺ T-cells and macrophages and use the chemokine receptor CCR5 (and, less often, CCR3) as their coreceptor. The T-tropic viruses (sometimes called syncytia inducing (SI) primary viruses) can also replicate in primary CD4⁺ T-cells but can in addition infect established CD4⁺ T-cell lines in vitro, which they do via the chemokine receptor CXCR4 (fusin). Many of these T-tropic strains can use CCR5 in addition to CXCR4, and some can enter macrophages via CCR5, at least under certain in vitro conditions (D'Souza, Nature Med. 2, 1293 (1996); Premack, Nature Med. 2, 1174; Fauci, Nature 384, 529 (1996)).

Whether other coreceptors contribute to HIV-1 pathogenesis is unresolved, but the existence of another coreceptor for some T-tropic strains can be inferred from in vitro studies. Because M-tropic HIV-1 strains are implicated in about 90% of sexual transmissions of HIV, CCR5 is the predominant coreceptor for the virus in patients; transmission (or systemic establishment) of CXCR4-using (T-tropic) strains is rare (D'Souza, *Nature Med.* 2, 1293 (1996); Premack, *Nature Med.* 2, 1174; Fauci, *Nature* 384, 529 (1996), Paxton, *Nature Med.* 2, 412 (1996); Liu, *Cell* 86, 367 (1996); Samson, *Nature* 382, 722 (1996); Dean, *Science* 273, 1856 (1996); Huang, *Nature Med.* 2, 1240 (1996)). However, once SI viruses evolve in vivo (or if they are transmitted), they are especially virulent and cause faster disease progression (D'Souza, *Nature Med.* 2, 1293 (1996); Premack, *Nature Med.* 2, 1174; Fauci, *Nature* 384, 529 (1996), Schuitemaker, *J. Virol.* 66, 1354 (1992); Connor, *J. Virol.* 67, 1772 (1993); Richman, *J. Infect. Dis.* 169, 968 (1994); R. I. Connor et al., *J. Exp. Med.* 185, 621 (1997); Trkola, *Nature* 384, 184 (1996)).

The numbers and identity of coreceptor molecules on target cells, and the ability of HIV-1 strains to likely enter cells via the different coreceptors, seem to be critical determinants of disease progression. These factors are major influences on both host- and virus-dependent aspects of HIV-1 infection. For example, a homozygous defect ($\Delta 32$) in CCR5 correlates strongly with resistance to HIV-1 infection in vivo and in vitro. Individuals who are heterozygous for a defective CCR5 allele are at best weakly protected against infection and have only a modestly slowed disease progression (Paxton, *Nature Med.* 2, 412 (1996); Liu, *Cell* 86, 367 (1996); Samson, *Nature* 382, 722 (1996); Dean, *Science* 273, 1856 (1996); Huang et al., *Nature Med.* 2, 1240 (1996)). However, other factors can influence the level of CCR5 expression on activated CD4⁺ T-cells and thereby affect the efficiency of HIV-1 infection in vitro (Trkola, *Nature* 384, 184 (1996); Bleul, *Proc. Natl. Acad. Sci. U.S.A.* 94, 1925 (1997)).

For multiple sclerosis it was shown that CCR5 and CXCR3 are predominantly expressed on T-cells infiltrating demyelinating brain lesions, as well as in the peripheral blood of affected patients. Elimination of the T-cells would block the T-cell arm of this autoimmune disease.

High expression of CCR3 and CCR5 was also observed in T cells and B cells of lymph nodes derived from patients with Hodgkin's disease.

Diabetes type I is considered to be a T-cell mediated autoimmune disease. The expression of CCR5 receptor in the pancreas was associated with the progression of type I diabetes in relevant animal models (Cameron (2000) *J. Immunol.* 165, 1102-1110). In particular, the CCR5 expression was associated with the development of insulinitis and spontaneous type I diabetes.

Several antibodies specifically binding to (human) CCR5 are known in the art and comprise, MC-1 (Mack (1998) *J. Exp. Med.* 187, 1215-1224 or MC-5 (Blanpain (2002) *Mol Biol Cell.* 13:723-37, Segerer (1999) *Kidney Int.* 56:52-64, Kraft (2001) *J Biol Chem.* 14;276:34408-18). The CCR-5 antibodies, in particular MC-1 and MC-5 may serve as a source for Ig-derived second domain of the CD3 specific construct of the invention. Accordingly, in a preferred embodiment, the invention relates to a bispecific construct comprising at least two domains, wherein the first domain provides for the specificity to human CD3 and has a reduced propensity to generate T cell epitopes and whereby said Ig-derived second domain is derived from an antibody specific for (human) CCR5. Most preferably, such a construct is a single chain scFV as defined herein .

MC-1 was shown to bind specifically to the first part of the second extracellular loop of human CCR5 and did not crossreact with CCR5 derived from rhesus macaques as shown in the appended examples. Therefore, it is preferred that the CD3 specific construct of this invention comprises, for example, VL and VH domains of an antibody (i.e. an Ig-derived second domain) specific for CCR5, preferably the human CCR5, and VH and VL domains of an antibody specific for the CD3 antigen. Said antibody specific for the human CCR5 is the murine anti-human CCR5 antibody MC-1, described, inter alia, in Mack (1998), *J. Exp. Med.* 187, 1215-1224 and in the appended examples. Yet, it is envisaged that other anti-CCR5 antibodies, like MC-5 (as characterized in the appended examples and disclosed in Blanpain (2002) *Mol Biol Cell.* 13:723-37, Segerer (1999) *Kidney Int.* 56:52-64 and Kraft (2001) *J Biol Chem.* 14;276:34408-18 may be employed in the context of this invention.

In a particularly preferred embodiment of the present invention, CD3-specific binding constructs are provided, which comprise a deimmunized domain directed against/binding to/interacting with human CD3 and a second Ig-derived domain which specifically binds to/interacts with CCR5. Such constructs are shown in Table 6A and 6B. The modules A-G in Tables 6A and 6B can be defined as mentioned

above for Tables 1-5. Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 78, 80 or 82. The VH protein domain of human CCR5 antibody is as set out in SEQ ID NO.: 129. The VL protein domain of human CCR5 antibody is as set out in SEQ ID NO.: 131. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO.: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the EpCAM antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO.: 168. The respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO.: 174. However, as mentioned above an additional serine may be introduced for cloning purposes (linker as depicted in SEQ ID NO.:176) between the VL and subsequent V domain.

Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 77, 79 or 81. The nucleic acid molecule encoding the VH protein domain of the human CCR5 antibody is as set out in SEQ ID NO.: 128. The nucleic acid molecule encoding the VL protein domain of the human CCR5 antibody is as set out in SEQ ID NO.: 130. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO.: 202. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of VH/VL or VL/VH from an antibody having specificity for the CCR5 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO.: 201. The groups of nucleic acid modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO.: 173. An alternative linker SEQ ID NO.:175 may

also be used to conjugate VL domain with a subsequent V domain (including an additional codon encoding a serine residue for cloning purposes).

Table 6A Deimmunized anti-human CD3 constructs comprising single chain anti-CCR5 variable regions: amino acid sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	174	129	168	131	CD3 (VL2/VH5) xCCR5	LHHL
2	74	3	80	174	129	168	131	CD3 (VH5/ML2) xCCR5	HLHL
3	80	3	74	174	131	168	129	CD3 (VL2/VH5) xCCR5	LHLH
4	74	3	80	174	131	168	129	CD3 (VH5/ML2) xCCR5	HLLH
5	131	168	129	174	74	3	80	CCR5xCD3 (VH5/ML2)	LHHL
6	129	168	131	174	74	3	80	CCR5xCD3(VH5/ML2)	HLHL
7	131	168	129	174	80	3	74	CCR5xCD3 (VL2/VH5)	LHLH
8	129	168	131	174	80	3	74	CCR5xCD3(VL2/VH5)	HLLH
9	80	3	76	174	129	168	131	CD3 (VL2/VH7) xCCR5	LHHL
10	76	3	80	174	129	168	131	CD3 (VH7/ML2) xCCR5	HLHL
11	80	3	76	174	131	168	129	CD3 (VL2/VH7) xCCR5	LHLH
12	76	3	80	174	131	168	129	CD3 (VH7/ML2) xCCR5	HLLH
13	131	168	129	174	76	3	80	CCR5xCD3 (VH7/ML2)	LHHL
14	129	168	131	174	76	3	80	CCR5xCD3(VH7/ML2)	HLHL
15	131	168	129	174	80	3	76	CCR5xCD3 (VL2/VH7)	LHLH
16	129	168	131	174	80	3	76	CCR5xCD3(VL2/VH7)	HLLH

Table 6B Deimmunized anti-human CD3 constructs comprising single chain anti-CCR5 variable regions: nucleic acid sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	173	128	201	130	CD3 (VL2/ VH5) xCCR5	LHHL
2	73	202	79	173	128	201	130	CD3 (VH5/ML2) xCCR5	HLHL
3	79	202	73	173	130	201	128	CD3 (VL2/ VH5) xCCR5	LHLH
4	73	202	79	173	130	201	128	CD3 (VH5/ML2) xCCR5	HLLH
5	130	201	128	173	73	202	79	CCR5xCD3 (VH5/ML2)	LHHL
6	128	201	130	173	73	202	79	CCR5xCD3 (VH5/ML2)	HLHL
7	130	201	128	173	79	202	73	CCR5xCD3 (VL2/ VH5)	LHLH
8	128	201	130	173	79	202	73	CCR5xCD3 (VL2/ VH5)	HLLH
9	79	202	75	173	128	201	130	CD3 (VL2/ VH7) xCCR5	LHHL
10	75	202	79	173	128	201	130	CD3 (VH7/ML2) xCCR5	HLHL
11	79	202	75	173	130	201	128	CD3 (VL2/ VH7) xCCR5	LHLH
12	75	202	79	173	130	201	128	CD3 (VH7/ML2) xCCR5	HLLH
13	130	201	128	173	75	202	79	CCR5xCD3 (VH7/ML2)	LHHL
14	128	201	130	173	75	202	79	CCR5xCD3 (VH7/ML2)	HLHL
15	130	201	128	173	79	202	75	CCR5xCD3 (VL2/ VH7)	LHLH
16	128	201	130	173	79	202	75	CCR5xCD3 (VL2/ VH7)	HLLH

Preferably, said constructs comprise an amino acid sequence selected from the group of

- (a) an amino acid sequence as shown in any one of SEQ ID NO.: 206, 208, 210, 212, 214 or 216;
- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO.: 205, 207, 209, 211, 213 or 215; and
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);
- (d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

The CCR5 and CD3 binding constructs SEQ ID NO.:206, 208, 210 represent construct 5 and SEQ ID NO.:212, 214 and 216 represent construct 13 of Table 6 and have the three different VL regions (VL1 (SEQ ID NO.:78), VL2 (SEQ ID NO.:80), or VL3 (SEQ ID NO.:82).

The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/ capable of binding to CCR5, which comprise an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence as shown in any one of SEQ ID NO.: 205, 207, 209, 211, 213 or 215 under stringent hybridization conditions. The terms "hybridization" and "stringent conditions" have been described herein above. The corresponding definitions and embodiments apply here mutatis mutandis.

The deimmunized CD3 and CCR5 binding constructs provided herein are particularly useful in the medical intervention of viral disease, in particular HIV infections and AIDS, or of autoimmune diseases and/or inflammatory diseases, like rheumatoid arthritis.

In another embodiment, the present invention provides for CD3 specific binding constructs as defined herein above, wherein the Ig-derived second domain of the inventive construct comprises an antigen-interaction site with specificity for CD19.

CD19 has proved to be a very useful medical target. CD19 is expressed in the whole B cell lineage from the pro B cell to the mature B cell, it is not shed, is uniformly expressed on all lymphoma cells, and is absent from stem cells (Haagen, Clin Exp Immunol 90 (1992), 368-75; Uckun, Proc. Natl. Acad. Sci. USA 85 (1988), 8603-7). Combination therapy employing both an antibody directed against CD19 and an additional immunoregulatory antibody has been disclosed for the treatment of B cell malignancies (WO 02/04021, US2002006404, US2002028178) and autoimmune diseases (WO 02/22212, US2002058029). WO 00/67795 discloses the use i.a. of antibodies directed against CD19 for the treatment of indolent and aggressive forms of B-cell lymphomas, as well as acute and chronic forms of lymphatic leukemias. WO 02/80987 discloses the therapeutic use of immunotoxins based on antibodies against the antigen CD19 for the treatment of such diseases as B cell non-Hodgkin's lymphoma, Hodgkin's lymphoma or B cell leukemias (e.g. B cell acute lymphatic leukemia (B-ALL), (e.g. hairy cell lymphoma) B cell precursor acute lymphatic leukemia (pre-B-ALL), B cell chronic lymphatic leukemia (B-CLL)) .

In a particularly preferred embodiment of the present invention, CD3-specific binding constructs are provided, which comprise an deimmunized domain directed against/binding to/interacting with human CD3. and a second Ig-derived domain which specifically binds to/interacts with CD19. Such constructs are shown in Tables 7A and 7B. The modules A-G in Tables 7A and 7B can be defined as mentioned above for Tables 1-5. Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 78, 80 or 82. The VH protein domain of human CD19 antibody is as set out in SEQ ID NO.: 114. The VL protein domain of human CCR5 antibody is as set out in SEQ ID NO.: 116. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, protein module B or F, respectively, has the amino acid sequence as

set out in SEQ ID NO.: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the CD19 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO.: 168. The respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO.: 174. However, as mentioned above an additional serine may be introduced for cloning purposes (linker as depicted in SEQ ID NO.:176) between the VL and subsequent V domain.

Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 77, 79 or 81. The nucleic acid molecule encoding the VH protein domain of the human CD19 antibody is as set out in SEQ ID NO.: 113. The nucleic acid molecule encoding the VL protein domain of the human CCR5 antibody is as set out in SEQ ID NO.: 115. When either the module pair A/C or E/G denotes nucleic acid encoding a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO.: 202. When either the module pair A/C or E/G denotes a nucleic acid encoding a pair of VH/VL or VL/VH from an antibody having specificity for the CD19 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO.: 201. The groups of nucleic acid modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO.: 173. An alternative linker SEQ ID NO.:175 may also be used to conjugate VL domain with a subsequent V domain (including an additional codon encoding a serine residue for cloning purposes).

Table 7A Deimmunized anti-human CD3 constructs comprising single chain anti-CD19 variable regions: amino acid sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	174	114	168	116	CD3 (VL2/ VH5) xCD19	LHHL
2	74	3	80	174	114	168	116	CD3 (VH5/ML2) xCD19	HLHL
3	80	3	74	174	116	168	114	CD3 (VL2/ VH5) xCD19	LHLH
4	74	3	80	174	116	168	114	CD3 (VH5/ML2) xCD19	HLLH
5	116	168	114	174	74	3	80	CD19xCD3 (VH5/ML2)	LHHL
6	114	168	116	174	74	3	80	CD19xCD3(VH5/ML2)	HLHL
7	116	168	114	174	80	3	74	CD19xCD3 (VL2/ VH5)	LHLH
8	114	168	116	174	80	3	74	CD19xCD3(VL2/ VH5)	HLLH
9	80	3	76	174	114	168	116	CD3 (VL2/ VH7) xCD19	LHHL
10	76	3	80	174	114	168	116	CD3 (VH7/ML2) xCD19	HLHL
11	80	3	76	174	116	168	114	CD3 (VL2/ VH7) xCD19	LHLH
12	76	3	80	174	116	168	114	CD3 (VH7/ML2) xCD19	HLLH
13	116	168	114	174	76	3	80	CD19xCD3 (VH7/ML2)	LHHL
14	114	168	116	174	76	3	80	CD19xCD3(VH7/ML2)	HLHL
15	116	168	114	174	80	3	76	CD19xCD3 (VL2/ VH7)	LHLH
16	114	168	116	174	80	3	76	CD19xCD3(VL2/ VH7)	HLLH

Table 7B Deimmunized anti-human CD3 constructs comprising single chain anti-CD19 variable regions: Nucleic acid sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	173	113	201	115	CD3 (VL2/VH5) xCD19	LHHL
2	73	202	79	173	113	201	115	CD3 (VH5/ML2) xCD19	HLHL
3	79	202	73	173	115	201	113	CD3 (VL2/VH5) xCD19	LHLH
4	73	202	79	173	115	201	113	CD3 (VH5/ML2) xCD19	HLLH
5	115	201	113	173	73	202	79	CD19xCD3 (VH5/ML2)	LHHL
6	113	201	115	173	73	202	79	CD19xCD3 (VH5/ML2)	HLHL
7	115	201	113	173	79	202	73	CD19xCD3 (VL2/VH5)	LHLH
8	113	201	115	173	79	202	73	CD19xCD3 (VL2/VH5)	HLLH
9	79	202	75	173	113	201	115	CD3 (VL2/VH7) xCD19	LHHL
10	75	202	79	173	113	201	115	CD3 (VH7/ML2) xCD19	HLHL
11	79	202	75	173	115	201	113	CD3 (VL2/VH7) xCD19	LHLH
12	75	202	79	173	115	201	113	CD3 (VH7/ML2) xCD19	HLLH
13	115	201	113	173	75	202	79	CD19xCD3 (VH7/ML2)	LHHL
14	113	201	115	173	75	202	79	CD19xCD3 (VH7/ML2)	HLHL
15	115	201	113	173	79	202	75	CD19xCD3 (VL2/VH7)	LHLH
16	113	201	115	173	79	202	75	CD19xCD3 (VL2/VH7)	HLLH

In a more preferred embodiment, the present invention provides for a deimmunized CD3-specific binding construct which comprises a CD3-binding domain as defined above and a second, Ig-derived domain which specifically binds to/interacts with CD19, preferably human CD19, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

- (a) an amino acid sequence as shown in any one of SEQ ID NO.: 190, 192, 194, 196, 198, 200, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407 or 409;
- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO.: 189, 191, 193, 195, 197, 199, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398, 400, 402, 404, 406 or 408; and
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);
- (d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

Preferred CD19 and CD3 binding constructs according to the invention are SEQ ID NO.:190, 192, 194 representing construct 5 and SEQ ID NO.:196, 198 and 200 representing construct 13 of Table 7 and having the three different VL regions (VL1 (SEQ ID NO.:78), VL2 (SEQ ID NO.:80), or VL3 (SEQ ID NO.:82)).

The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/capable of binding to CD19, which comprise an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence as shown in any one of SEQ ID NOs.: 189, 191, 193, 195, 197, 199, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398,

400, 402, 404, 406 or 408, under stringent hybridization conditions. The terms "hybridization" and "stringent conditions" have been described herein above. The corresponding definitions and embodiments apply here *mutatis mutandis*.

The herein disclosed deimmunized CD3 and CD19 binding constructs are particularly useful in the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, a viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases, host-versus-graft diseases or B-cell malignancies, in particular B cell non-Hodgkin's lymphoma, Hodgkin's lymphoma or B cell leukemias (e.g. B cell acute lymphocytic leukemia (B-ALL), (e.g. hairy cell lymphoma) B cell precursor acute lymphatic leukemia (pre-B-ALL), B cell chronic lymphatic leukemia (B-CLL)) leukemia.

In a further embodiment, the present invention relates to a CD3 specific binding construct as defined above comprising a first domain specifically binding to human CD3 and having reduced propensity to generate T cell epitopes and a second domain, wherein said second domain is Ig-derived and comprises an antigen-interaction site with a specificity for CD20.

CD20 is one of the cell surface proteins present on B-lymphocytes. CD20 antigen is found in normal and malignant pre-B and mature B lymphocytes, including those in over 90% of B-cell non-Hodgkin's lymphomas (NHL). The antigen is absent in hematopoietic stem cells, activated B lymphocytes (plasma cells) and normal tissue. Several antibodies mostly of murine origin have been described: 1F5 (Press et al., 1987, Blood 69/2, 584-591), 2B8 / C2B8, 2H7, 1H4 (Liu et al., 1987, J Immunol 139, 3521-3526; Anderson et al., 1998, US patent No. 5,736,137; Haisma et al., 1998, Blood 92, 184-190; Shan et al., 1999, J. Immunol 162, 6589-6595).

CD20 has been described in immunotherapeutic strategies for the treatment of plasma cell malignancies using vaccination with DNA encoding scFv linked to carrier protein (Treon et al., 2000, Semin Oncol 27(5), 598) and in immunotherapeutic treatment using CD20 antibodies (IDEC-C2B8) have been shown to be effective in the treatment of non-Hodgkin's B-cell lymphoma. CD20 antibodies have proven

efficacy and tolerability in non-Hodgkin's lymphoma, achieving response rates of 73% and 48% in previously untreated or relapsed/refractory indolent non-Hodgkin's lymphoma, respectively (Montserrat, 2003, *Semin Oncol* 30(1suppl2), 34-39). Furthermore, CD20 antibodies have been widely used to treat relapsing or advanced stage B-cell neoplasms with an efficacy of about 50%.

In a particularly preferred embodiment of the present invention, CD3-specific binding constructs are provided, which comprise a deimmunized domain directed against/binding to/interacting with human CD3 and a second Ig-derived domain which specifically binds to/interacts with CD20. Such constructs are shown in Tables 8A and 8B. The modules A-G in Tables 8A and 8B can be defined as mentioned above for Tables 1-5. Deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 74 or 76. Deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 78, 80 or 82. The VH protein domain of human CD20 antibody is as set out in SEQ ID NO.: 170. The VL protein domain of human CD20 antibody is as set out in SEQ ID NO.: 172. When either the module pair A/C or E/G is a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO.: 3. When either the module pair A/C or E/G is a pair of VH/VL or VL/VH from an antibody having specificity for the CD20 antigen, protein module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO.: 168. The respective groups of protein modules A-B-C and E-F-G are connected to each other through protein module D, having the sequence as set out in SEQ ID NO.: 174. However, as mentioned above an additional serine may be introduced for cloning purposes (linker as depicted in SEQ ID NO.: 176) between the VL and subsequent V domain.

Nucleic acid molecules encoding deimmunized VH domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 73 or 75. Nucleic acid molecules encoding deimmunized VL domains of antibodies having specificity for the human CD3 antigen can be selected from the sequences as set out in SEQ ID NOs.: 77, 79 or 81. The nucleic acid

molecule encoding the VH protein domain of the human CD20 antibody is as set out in SEQ ID NO.: 169. The nucleic acid molecule encoding the VL protein domain of the human CD20 antibody is as set out in SEQ ID NO.: 171. When either the module pair A/C or E/G denotes a nucleic acid encoding a pair of deimmunized VH/VL or VL/VH protein domains from an antibody having specificity for the human CD3 antigen, nucleic acid module B or F, respectively, has the amino acid sequence as set out in SEQ ID NO.: 202. When either the module pair A/C or E/G denotes a nucleic acid encoding a pair of VH/VL or VL/VH from an antibody having specificity for the CD20 antigen, nucleic acid module B or F, respectively, has the nucleic acid sequence as set out in SEQ ID NO.: 201. The groups of nucleic acid modules A-B-C and E-F-G are connected to each other through nucleic acid module D, having the sequence as set out in SEQ ID NO.: 173. An alternative linker SEQ ID NO.: 175 may also be used to conjugate VL domain with a subsequent V domain (including an additional codon encoding a serine residue for cloning purposes).

Table 8A Deimmunized anti-human CD3 constructs comprising single chain anti-CD20 variable regions: amino acid sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	80	3	74	174	170	168	172	CD3 (VL2/ VH5) xCD20	LHHL
2	74	3	80	174	170	168	172	CD3 (VH5/ML2) xCD20	HLHL
3	80	3	74	174	172	168	170	CD3 (VL2/ VH5) xCD20	LHLH
4	74	3	80	174	172	168	170	CD3 (VH5/ML2) xCD20	HLLH
5	172	168	170	174	74	3	80	CD20xCD3 (VH5/ML2)	LHHL
6	170	168	172	174	74	3	80	CD20xCD3 (VH5/ML2)	HLHL
7	172	168	170	174	80	3	74	CD20xCD3 (VL2/ VH5)	LHLH
8	170	168	172	174	80	3	74	CD20xCD3 (VL2/ VH5)	HLLH
9	80	3	76	174	170	168	172	CD3 (VL2/ VH7) xCD20	LHHL
10	76	3	80	174	170	168	172	CD3 (VH7/ML2) xCD20	HLHL
11	80	3	76	174	172	168	170	CD3 (VL2/ VH7) xCD20	LHLH
12	76	3	80	174	172	168	170	CD3 (VH7/ML2) xCD20	HLLH
13	172	168	170	174	76	3	80	CD20xCD3 (VH7/ML2)	LHHL
14	170	168	172	174	76	3	80	CD20xCD3 (VH7/ML2)	HLHL
15	172	168	170	174	80	3	76	CD20xCD3 (VL2/ VH7)	LHLH
16	170	168	172	174	80	3	76	CD20xCD3 (VL2/ VH7)	HLLH

Table 8B Deimmunized anti-human CD3 constructs comprising single chain anti-CD20 variable regions: Nucleotide sequence

Construct	SEQ ID NO.: in construct portion ...							deimmunized anti-CD3 construct / Specificity (N -> C)	Domain Arrangement
	A	B	C	D	E	F	G		
1	79	202	73	173	169	201	171	CD3 (VL2/ VH5) xCD20	LHHL
2	73	202	79	173	169	201	171	CD3 (VH5/ML2) xCD20	HLHL
3	79	202	73	173	171	201	169	CD3 (VL2/ VH5) xCD20	LHLH
4	73	202	79	173	171	201	169	CD3 (VH5/ML2) xCD20	HLLH
5	171	201	169	173	73	202	79	CD20xCD3 (VH5/ML2)	LHHL
6	169	201	171	173	73	202	79	CD20xCD3(VH5/ML2)	HLHL
7	171	201	169	173	79	202	73	CD20xCD3 (VL2/ VH5)	LHLH
8	169	201	171	173	79	202	73	CD20xCD3(VL2/ VH5)	HLLH
9	79	202	75	173	169	201	171	CD3 (VL2/ VH7) xCD20	LHHL
10	75	202	79	173	169	201	171	CD3 (VH7/ML2) xCD20	HLHL
11	79	202	75	173	171	201	169	CD3 (VL2/ VH7) xCD20	LHLH
12	75	202	79	173	171	201	169	CD3 (VH7/ML2) xCD20	HLLH
13	171	201	169	173	75	202	79	CD20xCD3 (VH7/ML2)	LHHL
14	169	201	171	173	75	202	79	CD20xCD3(VH7/ML2)	HLHL
15	171	201	169	173	79	202	75	CD20xCD3 (VL2/ VH7)	LHLH
16	169	201	171	173	79	202	75	CD20xCD3(VL2/ VH7)	HLLH

More preferably, the deimmunized CD3 and CD20 binding constructs of the present invention comprises an amino acid sequence which is selected from the group consisting of

- (a) an amino acid sequence as shown in any one of SEQ ID NO.: 218, 220, 222, 224, 226, or 228 ;
- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO.: 217, 219, 221, 223, 225 or 227; and
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b) ;
- (d) and amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridization conditions.

The present invention also provides for CD3 specific binding constructs comprising a first domain which specifically binds to human CD3 and has reduced propensity to generate T cell epitopes and comprising an Ig-derived second domain directed against/capable of binding to CD20, which comprise an amino acid sequence encoded by a nucleic acid sequence hybridizing with the complementary strand of a nucleic acid sequence as defined in (b) herein above, i.e. to a nucleic acid sequence as shown in any one of SEQ ID NO.: 217, 219, 221, 223, 225 or 227, under stringent hybridization conditions. The terms "hybridization" and "stringent conditions" have been described herein above. The corresponding definitions and embodiments apply here mutatis mutandis.

The herein described deimmunized CD3 and CD20 binding constructs are envisaged for use in the treatment, prevention and/or amelioration of B-cell related disorders, preferably in the medical intervention of lymphoma, more preferably in the treatment of non-Hodgkin lymphoma.

The invention also provides for nucleic acid sequence encoding a CD3 specific binding molecule of the invention.

It is evident to the person skilled in the art that regulatory sequences may be added to the nucleic acid molecule of the invention. For example, promoters, transcriptional

enhancers and/or sequences which allow for induced expression of the polynucleotide of the invention may be employed. A suitable inducible system is for example tetracycline-regulated gene expression as described, e.g., by Gossen and Bujard (Proc. Natl. Acad. Sci. USA 89 (1992), 5547-5551) and Gossen et al. (Trends Biotech. 12 (1994), 58-62), or a dexamethasone-inducible gene expression system as described, e.g. by Crook (1989) EMBO J. 8, 513-519 .

Furthermore, it is envisaged for further purposes that nucleic acid molecules may contain, for example, thioester bonds and/or nucleotide analogues. Said modifications may be useful for the stabilization of the nucleic acid molecule against endo- and/or exonucleases in the cell. Said nucleic acid molecules may be transcribed by an appropriate vector containing a chimeric gene which allows for the transcription of said nucleic acid molecule in the cell. In this respect, it is also to be understood that such polynucleotide can be used for "gene targeting" or "gene therapeutic" approaches. In another embodiment said nucleic acid molecules are labeled. Methods for the detection of nucleic acids are well known in the art, e.g., Southern and Northern blotting, PCR or primer extension. This embodiment may be useful for screening methods for verifying successful introduction of the nucleic acid molecules described above during gene therapy approaches.

Said nucleic acid molecule(s) may be a recombinantly produced chimeric nucleic acid molecule comprising any of the aforementioned nucleic acid molecules either alone or in combination. Preferably, the nucleic acid molecule is part of a vector.

The present invention therefore also relates to a vector comprising the nucleic acid molecule described in the present invention.

Many suitable vectors are known to those skilled in molecular biology, the choice of which would depend on the function desired and include plasmids, cosmids, viruses, bacteriophages and other vectors used conventionally in genetic engineering. Methods which are well known to those skilled in the art can be used to construct various plasmids and vectors; see, for example, the techniques described in Sambrook et al. (loc cit.) and Ausubel, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. (1989), (1994). Alternatively, the polynucleotides and vectors of the invention can be reconstituted into liposomes for

delivery to target cells. As discussed in further details below, a cloning vector was used to isolate individual sequences of DNA. Relevant sequences can be transferred into expression vectors where expression of a particular polypeptide is required. Typical cloning vectors include pBluescript SK, pGEM, pUC9, pBR322 and pGBT9. Typical expression vectors include pTRE, pCAL-n-EK, pESP-1, pOP13CAT. Preferably said vector comprises a nucleic acid sequence which is a regulatory sequence operably linked to said nucleic acid sequence encoding a bispecific single chain antibody constructs defined herein.

Such regulatory sequences (control elements) are known to the artisan and may include a promoter, a splice cassette, translation initiation codon, translation and insertion site for introducing an insert into the vector. Preferably, said nucleic acid molecule is operatively linked to said expression control sequences allowing expression in eukaryotic or prokaryotic cells.

It is envisaged that said vector is an expression vector comprising the nucleic acid molecule encoding a bispecific single chain antibody constructs defined herein.

The term "regulatory sequence" refers to DNA sequences, which are necessary to effect the expression of coding sequences to which they are ligated. The nature of such control sequences differs depending upon the host organism. In prokaryotes, control sequences generally include promoter, ribosomal binding site, and terminators. In eukaryotes generally control sequences include promoters, terminators and, in some instances, enhancers, transactivators or transcription factors. The term "control sequence" is intended to include, at a minimum, all components the presence of which are necessary for expression, and may also include additional advantageous components.

The term "operably linked" refers to a juxtaposition wherein the components so described are in a relationship permitting them to function in their intended manner. A control sequence "operably linked" to a coding sequence is ligated in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequences. In case the control sequence is a promoter, it is obvious for a skilled person that double-stranded nucleic acid is preferably used.

Thus, the recited vector is preferably an expression vector. An "expression vector" is a construct that can be used to transform a selected host and provides for expression of a coding sequence in the selected host. Expression vectors can for instance be cloning vectors, binary vectors or integrating vectors. Expression comprises

transcription of the nucleic acid molecule preferably into a translatable mRNA. Regulatory elements ensuring expression in prokaryotes and/or eukaryotic cells are well known to those skilled in the art. In the case of eukaryotic cells they comprise normally promoters ensuring initiation of transcription and optionally poly-A signals ensuring termination of transcription and stabilization of the transcript. Possible regulatory elements permitting expression in prokaryotic host cells comprise, e.g., the P_L , *lac*, *trp* or *lac* promoter in *E. coli*, and examples of regulatory elements permitting expression in eukaryotic host cells are the *AOX1* or *GAL1* promoter in yeast or the CMV-, SV40-, RSV-promoter (Rous sarcoma virus), CMV-enhancer, SV40-enhancer or a globin intron in mammalian and other animal cells.

Beside elements which are responsible for the initiation of transcription such regulatory elements may also comprise transcription termination signals, such as the SV40-poly-A site or the tk-poly-A site, downstream of the polynucleotide. Furthermore, depending on the expression system used leader sequences capable of directing the polypeptide to a cellular compartment or secreting it into the medium may be added to the coding sequence of the recited nucleic acid sequence and are well known in the art; see also, e.g., appended example 1. The leader sequence(s) is (are) assembled in appropriate phase with translation, initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein, or a portion thereof, into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an N-terminal identification peptide imparting desired characteristics, e.g., stabilization or simplified purification of expressed recombinant product; see supra. In this context, suitable expression vectors are known in the art such as Okayama-Berg cDNA expression vector pcDV1 (Pharmacia), pCDM8, pRc/CMV, pcDNA1, pcDNA3 (In-vitrogene), pEF-DHFR, pEF-ADA or pEF-neo (Raum et al. Cancer Immunol Immunother (2001) 50(3), 141-150) or pSPORT1 (GIBCO BRL).

Preferably, the expression control sequences will be eukaryotic promoter systems in vectors capable of transforming or transfecting eukaryotic host cells, but control sequences for prokaryotic hosts may also be used. Once the vector has been incorporated into the appropriate host, the host is maintained under conditions suitable for high level expression of the nucleotide sequences, and as desired, the collection and purification of the polypeptide of the invention may follow; see, e.g.,

the appended examples.

An alternative expression system which could be used is an insect system. In one such system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The coding sequence of a recited nucleic acid molecule may be cloned into a nonessential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of said coding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein coat. The recombinant viruses are then used to infect *S. frugiperda* cells or *Trichoplusia* larvae in which the protein of the invention is expressed (Smith, J. Virol. 46 (1983), 584; Engelhard, Proc. Nat. Acad. Sci. USA 91 (1994), 3224-3227).

Additional regulatory elements may include transcriptional as well as translational enhancers. Advantageously, the above-described vectors of the invention comprises a selectable and/or scorable marker.

Selectable marker genes useful for the selection of transformed cells and, e.g., plant tissue and plants are well known to those skilled in the art and comprise, for example, antimetabolite resistance as the basis of selection for dhfr, which confers resistance to methotrexate (Reiss, Plant Physiol. (Life Sci. Adv.) 13 (1994), 143-149); npt, which confers resistance to the aminoglycosides neomycin, kanamycin and paromycin (Herrera-Estrella, EMBO J. 2 (1983), 987-995) and hygromycin (Marsh, Gene 32 (1984), 481-485). Additional selectable genes have been described, namely trpB, which allows cells to utilize indole in place of tryptophan; hisD, which allows cells to utilize histinol in place of histidine (Hartman, Proc. Natl. Acad. Sci. USA 85 (1988), 8047); mannose-6-phosphate isomerase which allows cells to utilize mannose (WO 94/20627) and ODC (ornithine decarboxylase) which confers resistance to the ornithine decarboxylase inhibitor, 2-(difluoromethyl)-DL-ornithine, DFMO (McConlogue, 1987, In: Current Communications in Molecular Biology, Cold Spring Harbor Laboratory ed.) or deaminase from *Aspergillus terreus* which confers resistance to Blasticidin S (Tamura, Biosci. Biotechnol. Biochem. 59 (1995), 2336-2338).

Useful scorable markers are also known to those skilled in the art and are commercially available. Advantageously, said marker is a gene encoding luciferase (Giacomin, Pl. Sci. 116 (1996), 59-72; Scikantha, J. Bact. 178 (1996), 121), green fluorescent protein (Gerdes, FEBS Lett. 389 (1996), 44-47) or β -glucuronidase

(Jefferson, EMBO J. 6 (1987), 3901-3907). This embodiment is particularly useful for simple and rapid screening of cells, tissues and organisms containing a recited vector.

As described above, the recited nucleic acid molecule can be used alone or as part of a vector to express the encoded CD3 specific construct in cells, for, e.g., purification but also for gene therapy purposes. The nucleic acid molecules or vectors containing the DNA sequence(s) encoding any one of the above described (bispecific) CD3 constructs is introduced into the cells which in turn produce the polypeptide of interest. Gene therapy, which is based on introducing therapeutic genes into cells by ex-vivo or in-vivo techniques is one of the most important applications of gene transfer. Suitable vectors, methods or gene-delivery systems for in-vitro or in-vivo gene therapy are described in the literature and are known to the person skilled in the art; see, e.g., Giordano, *Nature Medicine* 2 (1996), 534-539; Schaper, *Circ. Res.* 79 (1996), 911-919; Anderson, *Science* 256 (1992), 808-813; Verma, *Nature* 389 (1994), 239; Isner, *Lancet* 348 (1996), 370-374; Muhlhauser, *Circ. Res.* 77 (1995), 1077-1086; Onodera, *Blood* 91 (1998), 30-36; Verma, *Gene Ther.* 5 (1998), 692-699; Nabel, *Ann. N.Y. Acad. Sci.* 811 (1997), 289-292; Verzeletti, *Hum. Gene Ther.* 9 (1998), 2243-51; Wang, *Nature Medicine* 2 (1996), 714-716; WO 94/29469; WO 97/00957, US 5,580,859; US 5,589,466; or Schaper, *Current Opinion in Biotechnology* 7 (1996), 635-640. The recited nucleic acid molecules and vectors may be designed for direct introduction or for introduction via liposomes, or viral vectors (e.g., adenoviral, retroviral) into the cell. Preferably, said cell is a germ line cell, embryonic cell, or egg cell or derived therefrom, most preferably said cell is a stem cell. An example for an embryonic stem cell can be, inter alia, a stem cell as described in, Nagy, *Proc. Natl. Acad. Sci. USA* 90 (1993), 8424-8428.

In accordance with the above, the present invention relates to methods to derive vectors, particularly plasmids, cosmids, viruses and bacteriophages used conventionally in genetic engineering that comprise a nucleic acid molecule encoding the polypeptide sequence of a bispecific single chain antibody construct defined herein. Preferably, said vector is an expression vector and/or a gene transfer or targeting vector. Expression vectors derived from viruses such as retroviruses, vaccinia virus, adeno-associated virus, herpes viruses, or bovine papilloma virus, may be used for delivery of the recited polynucleotides or vector into targeted cell

populations. Methods which are well known to those skilled in the art can be used to construct recombinant vectors; see, for example, the techniques described in Sambrook et al. (loc cit.), Ausubel (1989, loc cit.) or other standard text books. Alternatively, the recited nucleic acid molecules and vectors can be reconstituted into liposomes for delivery to target cells. The vectors containing the nucleic acid molecules of the invention can be transferred into the host cell by well-known methods, which vary depending on the type of cellular host. For example, calcium chloride transfection is commonly utilized for prokaryotic cells, whereas calcium phosphate treatment or electroporation may be used for other cellular hosts; see Sambrook, supra.

The recited vector may, inter alia, be the pEF-DHFR, pEF-ADA or pEF-neo. The vectors pEF-DHFR, pEF-ADA and pEF-neo have been described in the art, e.g. in Mack et al. (PNAS (1995) 92, 7021-7025) and Raum et al. (Cancer Immunol Immunother (2001) 50(3), 141-150).

The invention also provides for a host transformed or transfected with a vector as described herein. Said host may be produced by introducing said at least one of the above described vector or at least one of the above described nucleic acid molecules into the host. The presence of said at least one vector or at least one nucleic acid molecule in the host may mediate the expression of a gene encoding the above described bispecific single chain antibody constructs.

The described nucleic acid molecule or vector which is introduced in the host may either integrate into the genome of the host or it may be maintained extrachromosomally.

The host can be any prokaryotic or eukaryotic cell.

The term "prokaryote" is meant to include all bacteria which can be transformed or transfected with DNA or RNA molecules for the expression of a protein of the invention. Prokaryotic hosts may include gram negative as well as gram positive bacteria such as, for example, *E. coli*, *S. typhimurium*, *Serratia marcescens* and *Bacillus subtilis*. The term "eukaryotic" is meant to include yeast, higher plant, insect and preferably mammalian cells. Depending upon the host employed in a recombinant production procedure, the protein encoded by the polynucleotide of the present invention may be glycosylated or may be non-glycosylated. Especially preferred is the use of a plasmid or a virus containing the coding sequence of the

polypeptide of the invention and genetically fused thereto an N-terminal FLAG-tag and/or C-terminal His-tag. Preferably, the length of said FLAG-tag is about 4 to 8 amino acids, most preferably 8 amino acids. An above described polynucleotide can be used to transform or transfect the host using any of the techniques commonly known to those of ordinary skill in the art. Furthermore, methods for preparing fused, operably linked genes and expressing them in, e.g., mammalian cells and bacteria are well-known in the art (Sambrook, loc cit.).

Preferably, said the host is a bacteria, an insect, fungal, plant or animal cell.

It is particularly envisaged that the recited host may be a mammalian cell, more preferably a human cell or human cell line.

Particularly preferred host cells comprise CHO cells, COS cells, myeloma cell lines like SP2/0 or NS/0. As illustrated in the appended examples, particularly preferred are CHO-cells as hosts.

In a further embodiment, the present invention thus relates to a process for the preparation of a CD3 specific construct described above comprising cultivating a cell and/or the host of the invention under conditions suitable for the expression of said construct and isolating the construct from the cell or the culture medium.

The transformed hosts can be grown in fermentors and cultured according to techniques known in the art to achieve optimal cell growth. The polypeptide of the invention can then be isolated from the growth medium, cellular lysates, or cellular membrane fractions. The isolation and purification of the, e.g., microbially expressed polypeptides of the invention may be by any conventional means such as, for example, preparative chromatographic separations and immunological separations such as those involving the use of monoclonal or polyclonal antibodies directed, e.g., against a tag of the polypeptide of the invention or as described in the appended examples.

Furthermore, the invention provides for a composition comprising a (human) CD3-specific binding construct as defined herein or a (human) CD3-specific binding construct as produced by the process disclosed above, a nucleic acid molecule of the invention, a vector or a host of the invention. Said composition may, optionally, also comprise a proteinaceous compound capable of providing an activation signal for immune effector cells. Most preferably, said composition is a pharmaceutical

composition further comprising, optionally, suitable formulations of carrier, stabilizers and/or excipients.

In accordance with this invention, the term "pharmaceutical composition" relates to a composition for administration to a patient, preferably a human patient. In a preferred embodiment, the pharmaceutical composition comprises a composition for parenteral, transdermal, intraluminal, intra arterial, intrathecal administration or by direct injection into the tissue or tumour. It is in particular envisaged that said pharmaceutical composition is administered to a patient via infusion or injection. Administration of the suitable compositions may be effected by different ways, e.g., by intravenous, intraperitoneal, subcutaneous, intramuscular, topical or intradermal administration. The pharmaceutical composition of the present invention may further comprise a pharmaceutically acceptable carrier. Examples of suitable pharmaceutical carriers are well known in the art and include phosphate buffered saline solutions, water, emulsions, such as oil/water emulsions, various types of wetting agents, sterile solutions, etc. Compositions comprising such carriers can be formulated by well known conventional methods. These pharmaceutical compositions can be administered to the subject at a suitable dose. The dosage regimen will be determined by the attending physician and clinical factors. As is well known in the medical arts, dosages for any one patient depends upon many factors, including the patient's size, body surface area, age, the particular compound to be administered, sex, time and route of administration, general health, and other drugs being administered concurrently. Generally, the regimen as a regular administration of the pharmaceutical composition should be in the range of 1 μg to 5 g units per day. However, a more preferred dosage for continuous infusion might be in the range of 0.01 μg to 2 mg, preferably 0.01 μg to 1 mg, more preferably 0.01 μg to 100 μg , even more preferably 0.01 μg to 50 μg and most preferably 0.01 μg to 10 μg units per kilogram of body weight per hour. Particularly preferred dosages are recited herein below. Progress can be monitored by periodic assessment. Dosages will vary but a preferred dosage for intravenous administration of DNA is from approximately 10^6 to 10^{12} copies of the DNA molecule. The compositions of the invention may be administered locally or systemically. Administration will generally be parenterally, e.g., intravenously; DNA may also be administered directed to the target site, e.g., by biolistic delivery to an internal or external target site or by catheter to a site in an

artery. Preparations for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. Parenteral vehicles include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's, or fixed oils. Intravenous vehicles include fluid and nutrient replenishes, electrolyte replenishers (such as those based on Ringer's dextrose), and the like. Preservatives and other additives may also be present such as, for example, antimicrobials, anti-oxidants, chelating agents, and inert gases and the like. In addition, the pharmaceutical composition of the present invention might comprise proteinaceous carriers, like, e.g., serum albumine or immunoglobuline, preferably of human origin. It is envisaged that the pharmaceutical composition of the invention might comprise, in addition to the proteinaceous bispecific single chain antibody constructs or nucleic acid molecules or vectors encoding the same (as described in this invention), further biologically active agents, depending on the intended use of the pharmaceutical composition. Such agents might be drugs acting on the gastro-intestinal system, drugs acting as cytostatica, drugs preventing hyperurikemia, drugs inhibiting immunereactions (e.g. corticosteroids), drugs acting on the circulatory system and/or agents such as T-cell co-stimulatory molecules or cytokines known in the art.

Possible indications for administration of the composition(s) of the invention are tumorous diseases especially epithelial cancers/carcinomas such as breast cancer, colon cancer, prostate cancer, head and neck cancer, skin cancer (melanoma), cancers of the genito-urinary tract, e.g. ovarian cancer, endometrial cancer, cervix cancer and kidney cancer, lung cancer, gastric cancer, cancer of the small intestine, liver cancer, pancreas cancer, gall bladder cancer, cancers of the bile duct, esophagus cancer, cancer of the salivary glands and cancer of the thyroid gland or other tumorous diseases like haematological tumors, gliomas, sarcomas or osteosarcomas. The administration of the composition(s) of the invention is especially indicated for minimal residual disease, preferably early solid tumors, advanced solid tumors or metatatic solid tumors, which is characterized by the local and non-local reoccurrence of the tumor caused by the survival of single cells.

The invention further envisages the co-administration protocols with other compounds, e.g. molecules capable of providing an activation signal for immune effector cells, for cell proliferation or for cell stimulation. Said molecule may be, e.g. a further primary activation signal for T cells (e.g. a further costimulatory molecule: molecules of B7 family, Ox40L, 4.1 BBL), or a further cytokine: interleukin (e.g. IL-2) or NKG-2D engaging compound.

The composition of the invention as described above may also be a diagnostic composition further comprising, optionally, means and methods for detection.

The CD3-specific constructs provided herein are also suited for use in immunoassays in which they can be utilized in liquid phase or bound to a solid phase carrier. Examples of immunoassays which can utilize the polypeptide of the invention are competitive and non-competitive immunoassays in either a direct or indirect format. Examples of such immunoassays are the enzyme linked immunosorbent assay (ELISA), enzyme immunoassay (EIA), radioimmunoassay (RIA), the sandwich (immunometric assay) and the Western blot assay.

The CD3 specific binding constructs of the invention can be bound to many different carriers and used to isolate cells specifically bound to said polypeptides. Examples of well-known carriers include glass, polystyrene, polyvinyl chloride, polypropylene, polyethylene, polycarbonate, dextran, nylon, amyloses, natural and modified celluloses, polyacrylamides, agaroses, and magnetite. The nature of the carrier can be either soluble or insoluble, e.g. as beads, for the purposes of the invention.

There are many different labels and methods of labeling known to those of ordinary skill in the art. Examples of the types of labels which can be used in the present invention include enzymes, radioisotopes, colloidal metals, fluorescent compounds, chemiluminescent compounds, and bioluminescent compounds; see also the embodiments discussed hereinabove.

In a most preferred embodiment of the present invention, the use of a CD3 specific binding molecule of the invention, of a vector or of a host of the invention for the preparation of a pharmaceutical composition is envisaged. Said pharmaceutical composition may be employed in the prevention, treatment or amelioration of a

proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases.

Furthermore, in accordance to the invention, the deimmunized constructs comprising CD19 and CD3 binding domains, preferably SEQ ID NO.:190, 192, 194, 196, 198, 200, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407 or 409, can be used for the treatment of immunological disorders (various B cell malignancies) or autoimmune diseases, the deimmunized constructs comprising CCR5 and CD3 binding domains, preferably SEQ ID NO.:206, 208, 210, 212, 214 or 216, can be used for the treatment of viral diseases (HIV), autoimmune diseases and/or of inflammatory diseases (like rheumatoid arthritis), the deimmunized constructs comprising CD20 and CD3 binding domains, preferably SEQ ID NO.:218, 220, 222, 224, 226, 228, can be used for the treatment of tumorous diseases, preferably lymphoma, more preferably non-Hodgkin's B-cell lymphoma and the deimmunized constructs comprising EpCAM and CD3 binding domains, preferably SEQ ID NO.:31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 or 325 can be used for the treatment of tumorous diseases, preferably epithelial cancers.

The invention also relates to a method for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases comprising the administration of a (bispecific) CD3 specific binding molecule of the invention or a (bispecific) CD3 specific binding molecule as produced by the process described herein, of a nucleic acid molecule, a vector or a host of the invention to a subject in need of such a prevention, treatment or amelioration. Preferably, said subject is a human.

The method for the prevention, treatment or amelioration may also, in addition, comprise the administration of a proteinaceous compound capable of providing an activation signal for immune effector cells. Said proteinaceous compound may be administered simultaneously or non-simultaneously with the CD3 binding molecule, a nucleic acid molecule, a vector or a host of the invention. The proteinaceous compound may, inter alia, selected from the group consisting of a further costimulatory molecule: molecules of B7 family, Ox40L, 4.1 BBL), or a further cytokine: interleukin (e.g. IL-2) or NKG-2D engaging compounds.

Finally, the invention provides for a kit comprising the CD3 specific binding molecule, a nucleic acid molecule, a vector or a host of the invention.

Said kit is particularly useful in the preparation of the pharmaceutical composition of the present invention and may, inter alia, consist of a container useful for injections or infusions. Advantageously, the kit of the present invention further comprises, optionally (a) buffer(s), storage solutions and/or remaining reagents or materials required for the conduct of medical or scientific purposes. Furthermore, parts of the kit of the invention can be packaged individually in vials or bottles or in combination in containers or multicontainer units. The kit of the present invention may be advantageously used, inter alia, for carrying out the method of the invention and could be employed in a variety of applications referred herein, e.g., as research tools or medical tools. The manufacture of the kits preferably follows standard procedures which are known to the person skilled in the art.

These and other embodiments are disclosed and encompassed by the description and Examples of the present invention. Further literature concerning any one of the antibodies, methods, uses and compounds to be employed in accordance with the present invention may be retrieved from public libraries and databases, using for example electronic devices. For example, the public database "Medline", available on the Internet, may be utilized, for example under <http://www.ncbi.nlm.nih.gov/PubMed/medline.html>. Further databases and addresses, such as <http://www.ncbi.nlm.nih.gov/>, <http://www.infobiogen.fr/>, http://www.fmi.ch/biology/research_tools.html, <http://www.tigr.org/>, are known to the person skilled in the art and can also be obtained using, e.g., <http://www.lycos.com>.

The figures show:

Figure 1. DNA and amino acid sequences of the non-deimmunized anti-CD3 cassette (SEQ ID NOs.: 1 and 2).

Figure 2. A) Amino acid sequences of the heavy chains VH2 (SEQ ID NO.:70), VH3 (SEQ ID NO.:72), VH5 (SEQ ID NO.:74) and VH7 (SEQ ID NO.:76) and light chains VL1 (SEQ ID NO.:78), VL2 (SEQ ID NO.:80) and VL3 (SEQ ID NO.:82), respectively, B) Nucleotide sequences of the heavy chains VH2 (SEQ ID NO.:69), VH3 (SEQ ID NO.:71), VH5 (SEQ ID NO.:73) and VH7 (SEQ ID NO.:75) and light chains VL1 (SEQ ID NO.:77), VL2 (SEQ ID NO.:79) and VL3 (SEQ ID NO.:81), respectively, C) Amino acid sequences of the CDRs 1, 2 and 3 of the heavy chains of the non-deimmunized anti-CD3 (SEQ ID NO.:84, 90, 96, respectively), VH2 (SEQ ID NO.:86, 94, 96, respectively), VH3 (SEQ ID NO.:86, 94, 96, respectively), VH5 (SEQ ID NO.:88, 92, 96, respectively) and VH7 (SEQ ID NO.:88, 90, 96, respectively) and of the light chains of the non-deimmunized anti-CD3 (SEQ ID NO.:98, 102, 104, respectively), chains VL1 (SEQ ID NO.:100, 102, 104, respectively), VL2 (SEQ ID NO.:100, 102, 104, respectively) and VL3 (SEQ ID NO.:98, 102, 104, respectively) and D) Nucleotide sequences of the CDRs 1, 2 and 3 of the heavy chains of the non-deimmunized anti-CD3 (SEQ ID NO.:83, 89, 95, respectively), VH2 (SEQ ID NO.:85, 93, 95, respectively), VH3 (SEQ ID NO.:85, 93, 95, respectively), VH5 (SEQ ID NO.:87, 91, 95, respectively) and VH7 (SEQ ID NO.:87, 89, 95, respectively) and of the light chains of the non-deimmunized anti-CD3 (SEQ ID NO.:97, 101, 103, respectively), chains VL1 (SEQ ID NO.:99, 101, 103, respectively), VL2 (SEQ ID NO.:99, 101, 103, respectively) and VL3 (SEQ ID NO.:97, 101, 103, respectively).

Figure 3. A) Nucleotide sequence of anti-CD3 (VH2/VL1) (SEQ ID NO.:4) B) Amino acid sequence of anti-CD3 (VH2/VL1) (SEQ ID NO.:5) C) Nucleotide sequence of anti-CD3 (VH2/VL2) (SEQ ID NO.:6) D) Amino acid sequence of anti-CD3 (VH2/VL2) (SEQ ID NO.:7) E) Nucleotide sequence of anti-CD3 (VH2/VL3) (SEQ ID NO.:8) F) Amino acid sequence of anti-CD3 (VH2/VL3) (SEQ ID NO.:9).

Figure 4. A) Nucleotide sequence of anti-CD3 (VH3/VL1) (SEQ ID NO.:10) B) Amino acid sequence of anti-CD3 (VH3/VL1) (SEQ ID NO.:11) C) Nucleotide sequence of anti-CD3 (VH3/VL2) (SEQ ID NO.:12) D) Amino acid sequence of anti-CD3 (VH3/VL2) (SEQ ID NO.:13) E) Nucleotide sequence of anti-CD3 (VH3/VL3) (SEQ ID NO.:14) F) Amino acid sequence of anti-CD3 (VH3/VL3) (SEQ ID NO.:15).

Figure 5. A) Nucleotide sequence of anti-CD3 (VH5/VL1) (SEQ ID NO.:16) B) Amino acid sequence of anti-CD3 (VH5/VL1) (SEQ ID NO.:17) C) Nucleotide sequence of anti-CD3 (VH5/VL2) (SEQ ID NO.:18) D) Amino acid sequence of anti-CD3 (VH5/VL2) (SEQ ID NO.:19) E) Nucleotide sequence of anti-CD3 (VH5/VL3) (SEQ ID NO.:20) F) Amino acid sequence of anti-CD3 (VH5/VL3) (SEQ ID NO.:21).

Figure 6. A) Nucleotide sequence of anti-CD3 (VH7/VL1) (SEQ ID NO.:22) B) Amino acid sequence of anti-CD3 (VH7/VL1) (SEQ ID NO.:23) C) Nucleotide sequence of anti-CD3 (VH7/VL2) (SEQ ID NO.:24) D) Amino acid sequence of anti-CD3 (VH7/VL2) (SEQ ID NO.:25) E) Nucleotide sequence of anti-CD3 (VH7/VL3) (SEQ ID NO.:26) F) Amino acid sequence of anti-CD3 (VH7/VL3) (SEQ ID NO.:27).

Figure 7. Binding of bispecific anti-CD19 constructs with different deimmunized anti-CD3 parts: the anti-CD3 (VH2/VL1) (SEQ ID NO.:178), anti-CD3 (VH2/VL2) (SEQ ID NO.:180), anti-CD3 (VH2/VL3) (SEQ ID NO.:182), anti-CD3 (VH3/VL1) (SEQ ID NO.:184), anti-CD3 (VH3/VL2) (SEQ ID NO.:186), anti-CD3 (VH3/VL3) (SEQ ID NO.:188), anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198), anti-CD3 (VH7/VL3) (SEQ ID NO.:200) A) CD3 and B) CD19. Binding was measured by a FACS-based assay using CD3 enriched PBMCs (A) or CD19-positive NALM-cells (B). CD3 and a secondary FITC labeled anti-mouse Ig antibody was used as a negative control in (A) and CD19 and a secondary FITC labeled anti-mouse Ig antibody was used as a negative control in (B). Constructs anti-CD19xanti-CD3 and anti-EpCAM (M79)xanti-CD3 were used as controls. MFI indicates mean fluorescence intensity.

Figure 8: A representative elution pattern of a deimmunized variant of anti-CD19xanti-CD3 protein fraction from a HIC column at 280 nm. The bottom line

showing a major step at 700 ml indicates the theoretical gradient of the elution buffer containing 20 mM acetate, pH3.5. High adsorption at 280 nm was due to non-bound protein in the column flow-through. The arrow at 810,98 ml indicates the eluted deimmunized anti-CD3 fraction.

Figure 9: A representative elution pattern of a deimmunized variant of anti-CD19xanti-CD3 protein fraction from a Ni-Chelating His Trap® column at 280 nm. The bottom line showing a first step at 85 ml and a second major step at 90 ml indicates the theoretical gradient of the elution buffer (dotted line). The arrow at 93,16 ml indicates the protein fraction containing the antiCD19 x antiCD3 construct.

Figure 10: A representative protein elution pattern from a Sephadex S200 gelfiltration column. Fractions were collected from 0-130 ml retention time. The protein peak at 80.44 ml corresponds to a MW of ca. 52 kD and contains the deimmunized antiCD19 x antiCD3 construct.

Figure 11: A) SDS-PAGE analysis of deimmunized variants of anti-CD19xanti-CD3 protein fractions. Lane M: Molecular weight marker Lane 1: HCIC flowthrough; lane 2: cell culture supernatant; lane 3: HCIC eluate; lane 4: IMAC flowthrough; lane 5: IMAC wash; lane 6: IMAC eluate; lane 7: gel filtration eluate;

B) Western blot analysis of purified deimmunized variants of anti-CD19xanti-CD3 protein fractions. Western blot analysis of purified bispecific protein was performed with antibodies directed against the His-Tag (PentaHis, Qiagen) and goat anti mouse Ig labeled with alkaline phosphatase. Lane M: Molecular weight marker Lane 1: HCIC flow through; lane 2: cell culture supernatant; lane 3: HCIC eluate; lane 4: IMAC flow through; lane 5: IMAC wash; lane 6: IMAC eluate; lane 7: gel filtration eluate.

Figure 12. Binding of the purified bispecific anti-CD19 constructs with different deimmunized anti-CD3 parts: anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) to A) CD3 and B) CD19 compared to the wild-type anti-CD19xanti-CD3 construct. Binding was measured by a FACS-based assay using CD3 enriched PBMCs (A) or CD19-positive NALM-cells (B). A secondary antibody with CD3 positive cells was used as a negative control in (A) and a secondary

antibody with CD19 positive cells was used as a negative control in (B). Constructs anti-CD19xanti-CD3 and anti-EpCAM (M79)xanti-CD3 were used as controls. Assay was carried out with concentrations of 1 µg/ml and 5 µg/ml. MFI indicates mean fluorescence intensity.

Figure 13. Cytotoxicity assay of bispecific anti-CD19 constructs with different deimmunized anti-CD3 parts anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VK3) (SEQ ID NO.:200) compared to control.

Figure 14. Sequence alignment of variable heavy region of the non-deimmunized CD3 antibody, VH5 (SEQ ID NO.:74), VH7 (SEQ ID NO.:76), VH2 (SEQ ID NO.:70) and VH3 (SEQ ID NO.:72). Framework region 1 (FR1), complementarity determining region 1 (CDR1), Framework region 1 (FR1), complementarity determining region 2 (CDR2), Framework region 3 (FR3), complementarity determining region 3 (CDR3) and Framework region 4 (FR4) have been depicted. The sequence LAR and VKK in FR1, the sequence ASGYTF and ASGYTA at the transition of framework 1 region to CDR1 region and the sequence LTSDK, ITSDK and MTTDT at FR3 and the sequence MQLS, MELS and LQMN at FR3 have been boxed. Alignment was carried out using the AlingnX program of Vector NTI Advance (Informax, Inc., USA).

Figure 15. Binding analysis of bispecific anti EpCAM constructs with different deimmunized anti-CD3 parts: anti-CD3 (VH5/VL2)x5-10 (SEQ ID NO.:37) (A), deimmunized anti-CD3 (VH5/VL2)x4-7 (SEQ ID NO.:33), (B) deimmunized anti-CD3 (VH5/VL2)x3-1 (SEQ ID NO.:31) (C), deimmunized anti-CD3 (VH5/VL2)x4-7 (VL-VH) (SEQ ID NO.:35) (D) and deimmunized anti-CD3 (VH5/VL2)x5-10 (VL-VH) (SEQ ID NO.:39) (E) in CD3-positive Jurkat and EpCAM-positive Kato III cells with a FACS-based assay. A shift to the right shows binding. In Jurkat cells the dotted line indicates the shift of the negative control (only secondary antibody), dashed line shows the binding of an anti-EpCAM-anti-CD3 control antibody, the bold line shows the bispecific construct of interest. In the binding assay using EpCAM-positive Kato III-cells instead of monoclonal antibody to CD3 a monoclonal antibody to EpCAM was used as a positive control.

Figure 16. Binding analysis of bispecific anti EpCAM constructs with different deimmunized anti-CD3 parts: 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49) (A) and 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63) (B) in CD3-positive Jurkat cells and in EpCAM-positive Kato cells with a FACS based assay. A shift to the right shows binding.

Figure 17. Cytotoxicity assay of EpCAM constructs with deimmunized anti-CD3 parts (di anti-CD3) at N-terminal position anti-CD3 (VH5/VL2)x3-1 (SEQ ID NO.:31), anti-CD3 (VH5/VL2)x-5-10 (SEQ ID NO.:37) and anti-CD3 (VH5/VL2)x4-7 (SEQ ID NO.:33) compared to the corresponding non-deimmunized constructs. CB15 T cell clone and CHO-EpCAM cells were used in an E:T ratio of 5:1. CHO-EpCAM cell were stained with PKH26 dye and the cells were counted after bispecific single chain antibody incubation with FACS analysis.

Figure 18. Cytotoxicity assay of EpCAM constructs with deimmunized anti-CD3 parts at the C-terminal position 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49) and 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63) compared to the corresponding non-deimmunized wild-type constructs. Cytotoxicity assay was carried out identically to Figure 17.

The following Examples illustrate the invention:

In the following examples a number of single chain anti-human CD3 antibodies have been engineered to show reduced immunogenicity in man. The different deimmunized anti-human CD3 antibodies comprise 12 combinations of 4 different VH (VH2 (SEQ ID NO.:69, 70), VH3 (SEQ ID NO.:71, 72), VH5 (SEQ ID NO.:73, 74) and VH7 (SEQ ID NO.:75, 76)) and 3 different VL (VL1 (SEQ ID NO.:77, 78), VL2 (SEQ ID NO.:79, 80) and VL3 (SEQ ID NO.:81, 82)) regions joined together. The amino acid and nucleic acid sequences of the above-mentioned VH and VL regions are shown in Figures 3-6. Illustratively, the deimmunized anti-CD3 single chain antibodies were combined with an anti-CD19 single chain antibody or with an anti-EpCAM single chain antibody in order to form a bispecific product.

Example 1. Cloning and expression of deimmunized anti-CD3 constructs

1.1. Transfer of cDNA encoding single chain antibody

The DNA encoding the anti-CD3 single-chain antibody, which was deimmunized, is referred herein as the anti-CD3 cassette. This anti-CD3 cassette consists of a SGGGGS linker (SEQ ID NO.:176), the anti-CD3 VH region (SEQ ID NO.:110), a 14 amino acid GS linker (VEGGSGGSGGSGGSGGVD linker (SEQ ID NO.:68)), and the anti-CD3 VL chains region (SEQ ID NO.:112) followed by 6 histidine residues. The afore-mentioned DNA was cloned into the vector p-PCR-Script-Amp SK(+) (Stratagene) at the Srf1 site. The DNA and amino acid sequence of the anti-CD3 cassette is shown in SEQ ID NO.:1, SEQ ID NO.:2 and Figure 1.

1.2 Computer analysis of sequences for immunogenic T cell epitopes and design of deimmunized single chain antibody sequences

The amino acid sequence of the anti-CD3 cassette (SEQ ID NO.:2) was analyzed by peptide threading program to identify potential T cell epitopes with the method as described in WO 98/52976. SEQ ID NO.3 shows the deimmunized linker sequence and SEQ ID NO.:68 the original linker sequence.

1.3 Construction of deimmunized single chain antibody sequences

The deimmunized versions of the anti-CD3 cassette were constructed by the method of overlapping PCR recombination. The anti-CD3 cassette (SEQ ID NO.:1, 2) in pPCR-S-Amp SK+ was used as the template for mutagenesis to the required deimmunized sequences. Sets of mutagenic primer pairs were synthesized encompassing the regions to be altered. The deimmunized sequences produced, including 4 different VH and 3 different VL regions, were cloned as Not1 to Hind111 fragments into the vector pPCR-S-Amp SK+ and the entire DNA sequence was confirmed to be correct. The 4 different VH and 3 different VK regions were joined in all combinations (a total of 12), either by PCR or using a unique BstE11 site introduced at the 3' end of the VH region. The entire DNA sequence of each combination was confirmed to be correct. The different deimmunized VH regions (SEQ ID NO.:70, 72, 74 and 76) and VL regions (SEQ ID NO.:78, 80 and 82) with the corresponding original non-deimmunized sequences (VH:SEQ ID NO.:110; VL:SEQ ID NO.:112) of the anti-CD3 constructs are summarized in Table 9.

Table 9. SEQ ID NOs.: of deimmunized VH and VL regions

	SEQ ID NO.:		SEQ ID NO.:		SEQ ID NO.:		SEQ ID NO.:	
	Nucleic acid	Amino acid	Nucleic acid	Amino acid	Nucleic acid	Amino acid	Nucleic acid	Amino acid
Deimmunized VH2	69	70	85	86	93	94	95	96
Deimmunized VH3	71	72	85	86	93	94	95	96
Deimmunized VH5	73	74	87	88	91	92	95	96
Deimmunized VH7	75	76	87	88	89	90	95	96
VH of the non-deimmunized CD3	109	110	83	84	89	90	95	96
VH of the non-deimmunized CD3 with Cys→Ser Mutation	105	106	83	84	89	90	107	108
Deimmunized VL1	77	78	99	100	101	102	103	104
Deimmunized VL2	79	80	99	100	101	102	103	104
Deimmunized VL3	81	82	97	98	101	102	103	104
VL of the non-deimmunized CD3	111	112	97	98	101	102	103	104

1.4 Transfer of deimmunized single chain antibody genes into expression vector

The deimmunized anti-CD3 cassettes were excised from pPCR-S-Amp-SK+ with BspE1 and Sal1 and cloned into the expression vector pEF comprising VL_{CD19}-VH_{CD19}-VH_{CD3}-VL_{CD3}. The CD3 part of the pEF-DHFR vector was replaced with each of the deimmunized anti-CD3 cassettes from the BspE1 site to the Sal1 site resulting in the following 12 constructs:

pEF anti-CD19xanti-CD3 (VH2/VL1) (SEQ ID NOs.: 177, 178)
pEF anti-CD19xanti-CD3 (VH2/VL2) (SEQ ID NOs.: 179, 180)
pEF anti-CD19xanti-CD3 (VH2/VL3) (SEQ ID NOs.: 181, 182)
pEF anti-CD19xanti-CD3 (VH3/VL1) (SEQ ID NOs.: 183, 184)
pEF anti-CD19xanti-CD3 (VH3/VL2) (SEQ ID NOs.: 185, 186)
pEF anti-CD19xanti-CD3 (VH3/VL3) (SEQ ID NOs.: 187, 188)
pEF anti-CD19xanti-CD3 (VH5/VL1) (SEQ ID NOs.: 189, 190)

pEF anti-CD19xanti-CD3 (VH5/VL2) (SEQ ID NOs.: 191, 192)
pEF anti-CD19xanti-CD3 (VH5/VL3) (SEQ ID NOs.: 193, 194)
pEF anti-CD19xanti-CD3 (VH7/VL1) (SEQ ID NOs.: 195, 196)
pEF anti-CD19xanti-CD3 (VH7/VL1) (SEQ ID NOs.: 197, 198)
pEF anti-CD19xanti-CD3 (VH7/VL3) (SEQ ID NOs.: 199, 200).

The constructs further comprises a murine IgG heavy chain leader in order to enable the secretion of the protein. The DNA sequences of the deimmunized anti-CD3 cassettes in the expression vector were confirmed using the sequencing primers (SEQ ID NO.: 28 and 29). The DNA and amino acid sequences of the 12 deimmunized anti-CD3 cassettes in the pEF vector from the BspE1 site to the SalI site are shown in SEQ ID NOs.: 177-200.

1.5 Production of antibody constructs

After transformation of the vector into E. coli K12, transfection-grade DNAs of the different expression vectors were prepared. Secreted proteins were produced in CHO-dhfr⁻ cells. For transient production the cell culture supernatants were harvested 2 days after transfection, for the generation of stable transfected cells, cells were put in selection medium two days after transfection. After five passages, stable pools were obtained. Subsequently, single clones were identified in limiting dilutions. To facilitate the purification process, the cells were adapted to serum-free medium. Antibody constructs were purified from about 1 liter of supernatant.

The production levels were tested in ELISA. No major differences in the secreted antibody levels were observed between different constructs comprising anti-CD19 and deimmunized anti-CD3 constructs.

Example 2: Binding Assays

In order to analyze the binding efficacy of the deimmunized constructs to CD3 and CD19 a FACS-based assay was performed. Initially, crude supernatants were tested for binding on CD3-enriched PBMCs or CD19-positive NALM-6 cells. Cells were incubated with non-diluted supernatants for 30 minutes at 8 °C. Upon two wash steps the cells were labeled with an anti-His antibody (Qiagen) under the same conditions. After additional wash steps binding of the constructs was detected with a FITC-conjugated sheep anti-mouse antibody (Sigma). Cells were analyzed with a FACS Calibur cytometer (B&D). As controls supernatants of anti-CD19xanti-CD3 and GFP-transfected cells were included. CD3 and a secondary antibody was used as a

negative control and it showed a mean fluorescence intensity (MFI) of ca. 3.5. The anti-CD19xanti-CD3 constructs comprising anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) had a MFI of at least 90, thus binding about 25 times more strongly. The positive control, which was a non-deimmunized anti-CD19xanti-CD3 construct reached a MFI of around 60 showing that the deimmunized constructs comprising anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) bound CD3 with extremely high efficacy. In a second experiment, the following constructs comprising anti-CD19 and anti-CD3: anti-CD3 (VH2/VL1) (SEQ ID NO.:178), anti-CD3 (VH2/VL2) (SEQ ID NO.:180), anti-CD3 (VH2/VL3) (SEQ ID NO.:182), anti-CD3 (VH3/VL1) (SEQ ID NO.:184), anti-CD3 (VH3/VL2) (SEQ ID NO.:186) and anti-CD3 (VH3/VL3) (SEQ ID NO.:188), showed similar binding as the negative control (MFI ca. 6).

The FACS-based binding assay was also carried out for CD19. In this experiment CD19 and a secondary antibody was as a negative control. In this experiment, all assayed constructs achieved a MFI of at least 80 while the MFI of the negative control was ca. 3.

Thus, the constructs comprising anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) turned out to bind as well CD3 and CD19 as the non-modified anti-CD19xanti-CD3 (SEQ ID NO.:204). However, the constructs anti-CD3 (VH2/VL1) (SEQ ID NO.:178), anti-CD3 (VH2/VL2) (SEQ ID NO.:180), anti-CD3 (VH2/VL3) (SEQ ID NO.:182), anti-CD3 (VH3/VL1) (SEQ ID NO.:184), anti-CD3 (VH3/VL2) (SEQ ID NO.:186), anti-CD3 (VH3/VL3) (SEQ ID NO.:188) had completely lost anti-CD3 binding capacity, while CD19 binding was fully retained (Figure 7).

Thus, it was demonstrated that the deimmunized heavy chains dominated the binding specificity and strength. As a result, the anti-CD3 constructs with VH5 and VH7 groups were purified and analyzed for cytotoxic activity.

Example 3. Expression and purification of the variants showing high binding affinity

The deimmunized anti-CD19xanti-CD3 proteins anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH5/VL2) (SEQ ID NO.:192), anti-CD3 (VH5/VL3) (SEQ ID NO.:194), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) were expressed in chinese hamster ovary cells (CHO).

In order to purify the bispecific single-chain constructs comprising a deimmunized anti-CD3 part CHO-CD19 cells were grown in roller bottles with HiClone CHO modified DMEM medium (HiQ)® for 7 days before harvest. The cells were removed by centrifugation and the supernatant, containing the expressed protein was stored at -20°C.

Äkta FPLC System® (Pharmacia) and Unicorn Software® were used for chromatography. All chemicals were of research grade and purchased from Sigma (Deisenhofen) or Merck (Darmstadt).

Hydrophobic charge induction chromatography was performed on MEP Hypercel® medium loaded to a XK16/60 column (Pharmacia) that was equilibrated with buffer A1 (20 mM Tris pH 7.2). 500ml of cell culture supernatant were applied to the column (10 ml) with a flow rate of 3 ml/min. Unbound sample was washed out with buffer A1 and the bound protein was eluted with 100% buffer B1 (20 mM acetate pH 3.5). Eluted protein fractions were pooled for further purification.

IMAC was performed, using a HisTrap® column (Pharmacia) that was loaded with NiSO₄ according to the manufacturers protocol. The column was equilibrated with buffer A2 (20 mM NaP pH 7.5, 0.4 M NaCl) and the sample was diluted 2:1 with buffer A2 to obtain a pH of 7. The sample was applied to the column (2 ml) with a flow rate of 1 ml/min and the column was washed with buffer A2 to remove unbound sample. Bound protein was eluted using a 2 step gradient of buffer B2 (20 mM NaP pH 7.5, 0.4 M NaCl, 0.5 M Imidazol) Step 1: 20% buffer B2 in 10 column volumes; Step 2: 100% buffer B2 in 10 column volumes. Eluted protein fractions were pooled for further purification.

Gel filtration chromatography was performed on a Sephadex S200 HiPrep® column (Pharmacia) equilibrated with PBS (Gibco). Eluted protein samples (flow rate 1ml/min) were subjected to SDS-Page and Western Blot for detection (Figure 11).

The column was previously calibrated for molecular weight determination (molecular weight marker kit, Sigma MW GF-200).

The deimmunized variants of anti-CD19xanti-CD3 protein were isolated in a three step purification process including hydrophobic charge induction chromatography (HCIC) (Figure 8), immobilized metal affinity chromatography (IMAC) (Figure 9) and gel filtration (Figure 10). The bispecific construct had a molecular weight of 52 kDa under native conditions as determined by gelfiltration in PBS.

The purified bispecific protein was analyzed with SDS-PAGE under reducing conditions using precast 4-12% Bis Tris gels (Invitrogen). Sample preparation and application were according to the manufacturer's protocol. The molecular weight was determined with MultiMark® protein standard (Invitrogen). The gel was stained with colloidal Coomassie (Invitrogen protocol). The purity of the isolated protein was >95% (Figure 11a) and the molecule has a size of 52 kD.

Furthermore, the deimmunized variants of anti-CD19xanti-CD3 protein were specifically detected by Western Blot. Western Blot was performed with an Optitran BA-S83® membrane and the Invitrogen Blot Module® according to the manufacturer's protocol. The antibodies used were Penta His (Quiagen) and Goat-anti-Mouse-Ig labeled with alkaline phosphatase (AP) (Sigma), the staining solution was BCIP/NBT liquid (Sigma). The main signal was shown to correspond to the main band in the SDS-PAGE at 52kD (Figure 11b).

Protein concentrations were determined using protein assay dye (MicroBCA®, Pierce) and IgG (Biorad) as standard protein. A summary of the final yields of purified protein variants is given in Table 10 showing the high productivity of all the constructs and very good yield of construct with anti-CD3 (VH5/VL1) (SEQ ID NO.:190) of 924.8 µg.

Table 10. Protein yields of the deimmunized anti-CD19-anti-CD3 constructs

Deimmunized CD3 construct	Yield [µg/supernatant]
CD19xanti CD3 (VH5/ VL1)(SEQ ID NO.:190)	924.8
CD19xanti CD3 (VH5/ VL2)(SEQ ID NO.:192)	446.7
CD19xanti CD3 (VH5/ VL3)(SEQ ID NO.:194)	218.4
CD19xanti CD3(VH7/ VL1)(SEQ ID NO.:196)	268.5
CD19xanti CD3(VH7/VL2)(SEQ ID NO.:198)	553.4
CD19xanti CD3(VH7/VL3) (SEQ ID NO.:200)	477.3

The productivity of the CD19xanti-CD3 (VH5/ VL2) and CD19xanti-CD3(VH7/VL2) constructs was compared with the corresponding non-deimmunized constructs. The results are shown in Table 11.

Table 11. Yields of the deimmunized bispecific construct compared to the corresponding non-deimmunized construct

Construct	Yield (µg/l)
CD19xanti-CD3	62
CD19xantiCD3(VH5/VL2)	204
CD19xantiCD3(VH7/VL2)	310

Table 11 clearly demonstrates that the bispecific constructs comprising deimmunized CD3 binding domain have much higher (at least three fold) productivity than the corresponding non-deimmunized construct.

Example 4. FACS based binding assays of the anti-CD3 constructs

Binding of selected purified antibody constructs comprising anti-CD19 and anti-CD3 was detected as described above in Example 2 at various concentrations. In the CD3 binding assay, the negative control secondary antibody (anti-His, FITC-conjugated), which was incubated with CD3 positive cells, showed a MFI of about 2.5 and the positive control deimmunized antiCD19xanti-CD3 bispecific single chain antibody of about 70 at 1 µg/ml concentration and 50 at 5 µg/ml concentration (Figure 12A). At the concentration of 1 µg/ml, the anti-CD3 (VH5/VL1) (SEQ ID NO.:190), anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL2) (SEQ ID NO.:198) and anti-CD3 (VH7/VL3) (SEQ ID NO.:200) deimmunized bispecific antibodies showed MFI values of 10-20; anti-CD3 (VH5/VL1) (SEQ ID NO.:190) having the highest (20). At 5 µg/ml anti-CD3 (VH7/VL2) (SEQ ID NO.:198) reached a MFI of 25, while anti-CD3 (VH7/VL1) (SEQ ID NO.:196), anti-CD3 (VH7/VL3) (SEQ ID NO.:200) and anti-CD3 (VH5/VL1) (SEQ ID NO.:190) had an MFI of at least 40 thus, showing the same binding efficacy than the non-deimmunized positive control. At a concentration of 5 µg/ml the strongly binding constructs with deimmunized anti-CD3 part VH5/VL1 (SEQ ID NO.:190), VH7/VL1 (SEQ ID NO.:196), VH7/VL2 (SEQ ID NO.:198), VH7/VL3 (SEQ ID NO.:200) bound to CD3 as well as the non-deimmunized anti-CD19xanti-CD3 (SEQ ID NO.:204).

All the antibody constructs bound to CD19 with a high efficacy, which was at about 200 MFI, while non-deimmunized anti-CD19xanti-CD3 construct (SEQ ID NO.:204)

showed 80 MFI. No differences were observed for CD19 binding at the tested concentrations for the different constructs (Figure 12B).

Example 5. Cytotoxicity Assays

Anti-CD19xanti-CD3 mediates T cell dependent cytotoxicity to CD19-positive target cells. This was analyzed in vitro for the determination of the biological potency of anti-CD19xanti-CD3.

For this purposes fluorescence labeled CD19-positive NALM-6 target cells were incubated with isolated PBMC of random donors or CB15 T-cells (standardized T-cell line) as effector cells in the presence of anti-CD19xanti-CD3. After incubation for 4 h at 37 °C in a humidified incubator, the release of the fluorescent dye from the target cells into the supernatant is determined in a spectrofluorimeter. Target cells incubated without anti-CD19xanti-CD3 and target cells totally lysed by the addition of saponin at the end of the incubation serve as negative and positive controls, respectively. The specific cytotoxicity mediated at a certain anti-CD19xanti-CD3 concentration can be calculated with the following formula:

$$\text{Specific Cytotoxicity [\%]} = \frac{\text{RFU (Sample)} - \text{Mean RFU (control)}}{\text{Mean RFU (total lysis)} - \text{Mean RFU (control)}} \times 100$$

The dose response was analyzed from 0.4 pg/ml anti-CD19xanti-CD3 to 100 ng/ml anti-CD19xanti-CD3 to specify the EC50 value. Although the EC50 value describes the biological potency of anti-CD19xanti-CD3, the absolute value will vary significantly depending on the source of the effector cells. Thus a relative potency is calculated in comparison to an anti-CD19xanti-CD3 reference material based on the following formula:

$$\text{Relative Potency} = \frac{\text{EC50 Sample}}{\text{EC50 Reference}}$$

The cytotoxic activities of the constructs comprising anti-CD19 and deimmunized anti-CD3 are shown in Figure 13. Purified non-deimmunized anti-CD19xanti-CD3 was used as control. The EC50 values of the deimmunized constructs were at a range of 21.9-81.6 pg/ml while the EC50 value of the non-deimmunized anti-CD19xanti-CD3 construct was 22.7 pg/ml. Thus, all deimmunized constructs revealed EC 50 values comparable to the non-deimmunized molecule.

Example 6. T-cell proliferation assay

Twenty healthy donors were selected for screening in T cell assays based on HLA-DR typing (Table 12). This enables the screening of peptides in the T cell assay against greater than 80% of DR alleles expressed in the world population.

Table 12: HLA DR haplotypes of 20 healthy donors used to test the immunogenicity of peptides obtained from deimmunized and non-deimmunized anti-CD3 scAb.

	HLA DR Allotype
1	DRB1*07, DRB1*15, DRB4*01, DRB5
2	DRB1*03, DRB1*04, DRB3, DRB4*01
3	DRB1*04, DRB1*07 and DRB4*01
4	DRB1*07, DRB1*11, DRB4*01
5	DRB1*04, DRB1*07, DRB4*01
6	DRB1*01, DRB1*04, DRB4*01
7	DRB1*03, DRB1*07, DRB3, DRB4*01
8	DRB1*07, DRB1*11, DRB3, DRB4*01
9	DRB1*12, DRB1*15, DRB3, DRB5
10	DRB1*01, DRB1*09, DRB4*01
11	DRB1*03, DRB1*15, DRB3, DRB5
12	DRB1*10, DRB1*13, DRB3
13	DRB1*03, DRB1*15, DRB3, DRB5
14	DRB1*04, DRB1*15, DRB4*01, DRB5
15	DRB1*04, DRB1*13, DRB3, DRB4*01
16	DRB1*01, DRB1*13, DRB3
17	DRB1*01, DRB1*04, DRB4*01
18	DRB1*07, DRB1*13, DRB3, DRB4*01
19	DRB1*07, DRB1*16, DRB4*01, DRB5
20	DRB1*04, DRB1*15, DRB4*01, DRB5

6.1 T-Cell Proliferation Assay

Peptides were obtained from Pepscan (Netherlands) at a purity of greater than 90%. Peripheral blood mononuclear cells (PBMC) from the 20 selected healthy donors (Table 12) were used to screen individual peptides in triplicate wells at 1 and 5 μ M. Two positive control peptides (C32 and C49) and keyhole limpet hemocyanin (KLH) were included in the assay. After 7 days incubation of cells and peptides, an 18 hour pulse with 3H-thymidine at 1 μ Ci/well was used to assess T cell proliferation. These data are expressed as stimulation index where:

Stimulation Index = CPM of test peptide / CPM of untreated control

A T cell epitope is defined as a peptide giving a stimulation index (SI) greater than 2. The results from two independent runs indicated that 5 of the 22 MHC binding peptides in the non-deimmunized anti-CD3 sequence had the capacity to induce human T cell proliferation (SI>2). In contrast, none of the corresponding deimmunized molecules induced T cell proliferation. Table 13 summarizes the T cell proliferation assay results showing Mean SI values of 2 independent runs.

The data also showed a concentration dependent effect whereby each of the non-deimmunized binding molecules showed SI's > 2 in only one of the two concentrations (1µm or 5µm) used. The difference in response at different concentrations is explained by the fact that individual peptides will have optimum concentrations at which they induced T cell proliferation. If this concentration is exceeded, then proliferation can drop off (high peptide concentrations can have an inhibitory effect on T cell proliferation). This explains why, in some instances, proliferation is seen at the lower concentration and not at the higher. From experience, T cell proliferation will be observed at one or two of the peptide concentrations used if a peptide contains a T cell epitope. These data demonstrated that deimmunization had successfully removed T cell epitopes from anti-CD3 (VH5/VL2) (SEQ ID NO.:19) and anti-CD3 (VH7/VL2) (SEQ ID NO.:25). The fact that about 75% of MHC binding peptides from the non-deimmunized anti-CD3 sequence did not induce T cell proliferation can be explained either by tolerance of the human immune system to these peptides or an inability of the human T cell repertoire to recognise these particular peptides.

Table 13: Summary of data comparing positive (SI>2) mouse peptides and corresponding deimmunized peptides.

			Non-deimmunized Anti-CD3	Deimmunized Anti-CD3
Peptide	Allotype	Concentration	Mean SI	Mean SI
Region		(μM)		
6-20	5	5	2.51	0.77
74-86	5	1	2.52	0.97
				0.96
90-102	5	5	2.21	0.56
				1.38
90-102	6	5	2.24	0.90
				0.82
90-102	11	5	2.23	0.83
				0.78
162-174	5	1	3.82	0.59
216-230	10	1	2.12	1.03

Example 7. Homology alignment of anti-CD3 (VH5), anti-CD3 (VH7), anti-CD3 (VH2) and anti-CD3 (VH3) with the non-deimmunized anti-CD3 VH

The variable heavy region of the non-deimmunized CD3 antibody, VH5 (SEQ ID NO.:74), VH7 (SEQ ID NO.:76), VH2 (SEQ ID NO.:70) and VH3 (SEQ ID NO.:72) were aligned using the AlingnX program of Vector NTI Advance (Informax, Inc., USA). The Clustal W algorithm used is described in Nucleic Acid Research, 22 (22): 4673-4860, 1994. The alignment is shown in Figure 14. From the alignment can be seen that the variable regions VH5 and VH7, which show surprisingly good binding have the sequence ASGYTF at the transition region of framework 1 to CDR1. Furthermore, the VH regions showing no binding (VH2 (SEQ ID NO.:70) and VH3 (SEQ ID NO.:72)) comprise the sequence ASGYTA at the transition of framework 1 to CDR1. Thus, for obtaining a construct having reduced propensity to generate T cell epitopes and binding to CD3, the construct has to comprise the sequence ASGYTF at the transition of framework 1 to CDR1. Surprisingly, the variable heavy regions binding to CD3 and showing reduced propensity to generate T cell epitopes comprising the above-mentioned sequence ASGYTF show good binding.

Example 8. Cloning of constructs comprising deimmunized anti-CD3 and anti-EpCAM

In order to demonstrate that the deimmunized anti-CD3 polypeptide of the invention can be a part of a functional construct with other targets, a number of bispecific constructs comprising deimmunized anti-CD3 (VH5/VL2) (SEQ ID NO.:19) and different anti-EpCAM single chain antibodies (3-1 (SEQ ID NO.:137, 139), 3-5 (SEQ ID NO.:141, 143), 4-1 (SEQ ID NO.:145, 147), 4-7 (SEQ ID NO.:149, 151), 5-10 (SEQ ID NO.:133, 135)) were generated.

8.1 Cloning of C-terminal EpCAM binders comprising deimmunized anti-CD3 part (SEQ ID NOs.: 30, 31, 32, 33, 34, 35, 36, 37, 38 and 39)

8.1.1 Amplification of the deimmunized anti-CD3 from the anti-CD19xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:192)

The N-terminal deimmunized anti-CD3(VH5/VL2) was obtained by PCR using the deimmunized (CD19 x anti-CD3 (VH5/VL2) (SEQ ID NO:192) as template and the following primers (DI CD3 5-2 VH BsrGI
AGGTGTACACTCCGACGTCCAAGTGGTGCAGTCAG (SEQ ID NO.:40), DI CD3 5-2 VL BspEI AATCCGGATTTGATCTCCACCTTGGTCCCG (SEQ ID NO.:41).

8.1.2. Cloning and expression of the deimmunized anti-CD3xanti-EpCAM deimmunized constructs in VH_{CD3} - VL_{CD3} x VH_{EpCAM} - VL_{EpCAM} orientation

The above mentioned PCR product containing the deimmunized anti-CD3 was cleaved with the restriction enzymes BsrG1 and BspE1 and subsequently cloned into the bluescript KS vector (Stratagene, La Jolla, CA), containing the amino acid sequence of an eukaryotic secretory signal (leader peptide) as a EcoRI/BsrGI-fragment. After cleavage of this construct with EcoRI and BspEI the resulting DNA fragment comprising the respective anti-CD3 scFv with the leader peptide was cloned into a EcoRI/BspEI cleaved plasmid containing the anti EpCAM scFv 3-1, 4-7, or 5-10 in C-terminal position in pEF-DHFR- vector. After confirmation of the sequence coding for the bispecific single chain by sequencing (Sequiseive, Vaterstetten) the plasmid was transfected into DHFR deficient CHO cells for eukaryotic expression. Eukaryotic protein expression in DHFR deficient CHO cells

was performed as described in Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566).

8.1.3. Cloning and expression of the deimmunized anti-CD3xanti-EpCAM constructs in VH_{CD3} - VL_{CD3} x VL_{EpCAM} - VH_{EpCAM} orientation

Anti-EpCAM 4-7 in VL-VH orientation containing the 15 amino acid standard linker (SEQ ID NO.:168) was obtained by PCR. The 4-7 VH region and the 4-7 VL region were separately amplified by the following primers (4-7 VL: 4-7 VL BspEI FOR CTGAAATCCGGAGGTGGTGGATCCGAGCTCGTGATGACCCAGACTCC (SEQ ID NO.:117), 4-7 VL GS15 REV GGAGCCGCCGCCGCGCCAGAACCACCA CCACCTTTGATCTCAAGCTTGGTCCCC (SEQ ID NO.:118); 4-7 VH: 4-7 VH GS15 FOR

GGCGGCGGCGGCTCCGGTGGTGGTGGTTCTGAGGTGCAGCTGCTCGAGCAG (SEQ ID NO.:42), 4-7 VH Sall REV TTTAAGTCGACCTAATGATGATGATGATGATGTGAGGAGACGGTGACCGTGG (SEQ ID NO.:43)). Overlapping complementary sequences introduced into the PCR products were used to form the coding sequence of a 15-amino acid $(G_4S_1)_3$ (single-letter amino acid code) linker (standard linker) (SEQ ID NO.:168) during the subsequent fusion PCR. This amplification step was performed with the primer pair 4-7 VL BspEI FOR and 4-7 VH Sall REV (SEQ ID Ns. 42 and 43).

Anti-EpCAM 5-10 in VL-VH orientation containing the 15 amino acid standard $((G_4S_1)_3)$ linker was obtained by PCR. The 5-10 VH region and the 5-10 VL region were separately amplified by the following primers (5-10 VL: 5-10 VL BspEI FOR CTGAAATCCGGAGGTGGTGGATCCGAGCTCGTGATGACACAGTCTCCAT (SEQ ID NO.:44), 5-10 VL GS15 REV GGAGCCGCCGCCGCGCCAGAACCACCACCACCTTTGATCTCAAGCTTGGTCCCAG; (SEQ ID NO.:45) 5-10 VH: 5-10 VH GS15 FOR GGCGGCGGCGGCTCCGGTGGTGGTGGTTCTGAGGTGCAGCTGCTCGAGC. (SEQ ID NO.:46), 5-10 VH Sall REV TTTAAGTCGACCTAATGATGATGATGATGATGTGAGGAGACGGTGACCGTGG (SEQ ID NO.:47). Overlapping complementary sequences introduced into the PCR products were used to form the coding sequence of a 15-amino acid $(G_4S_1)_3$ (single-letter amino acid code) linker (standard linker) (SEQ ID NO.:168) during the

subsequent fusion PCR. This amplification step was performed with the primer pair 5-10 VL BspEI FOR and 5-10 VH SalI REV.

The PCR products 5-10 VL-VH and 4-7 VL-VH) were cloned into the pEF-DHFR vector comprising anti-CD3 construct (VH5/VL2). After confirmation of the sequence coding for the bispecific single chain by sequencing the plasmid was transfected into DHFR deficient CHO cells for eukaryotic expression. Eukaryotic protein expression in DHFR deficient CHO cells was performed as described in Kaufmann R.J. (1990) *Methods Enzymol.* 185, 537-566).

8.1.4. Binding of the deimmunized anti-CD3xanti-EpCAM constructs to EpCAM and CD3

Binding of the bispecific single chain molecules with anti-CD3 part in N-terminal orientation to EpCAM and CD3 were confirmed by FACS analyses. For that purpose the EpCAM positive human gastric cancer cell line Kato III (ATCC HTB-103) was used. Binding of the anti-CD3 part was demonstrated on Jurkat cells (ATCC TIB 152).

Cells were cultured according to the recommendations of the supplier and a number of 200000 cells was incubated with 10µg/ml of the construct in 50µl PBS with 2%FCS (fetal calf serum). The binding of the construct was detected with an anti-His antibody (Penta-His Antibody, obtained from Qiagen, Hilden, FRG) at 2µg/ml in PBS with 2%FCS. As a second step R-Phycoerythrin-conjugated affinity purified F(ab')₂ derived from goat anti-mouse IgG, diluted 1:100 in 50µl PBS with 2% FCS (Dianova, Hamburg, FRG) was used. The samples were measured on a FACSScan (BD biosciences, Heidelberg, FRG).

Results of FACS analysis are shown in Fig. 15. All constructs comprising deimmunized anti-CD3 part showed stronger binding than the non-deimmunized anti-EpCAM (M79)xanti-CD3 bispecific single-chain antibody on EpCAM positive KatoIII cells.

8.2 Cloning of N-terminal EpCAM binders comprising deimmunized anti-CD3 part

8.2.1 Cloning of the anti-EpCAM x anti-CD3 constructs

8.2.1.1 Cloning of deimmunized 3-1xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:48, 49):

Deimmunized construct 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.: 48) was derived from non-deimmunized construct anti-EpCAM (3-1)xanti-CD3. The VH and VL regions of the anti-EpCAM antibody 3-1 are shown in SEQ ID NO.:137 and 139. The plasmids pEF-DHFR-3-1x anti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO.:192) were digested with BspEI and Sall (Biolabs) for the isolation of the vector and the insert anti-CD3 (VH5/VL2), respectively. The BspEI-Sall-digested vector was dephosphorylated and purified on 0.7% agarose gel, whereas the insert was purified on 1.5% agarose gel.

The purified fragment (BspEI-Sall) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final 3-1xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:48, 49) was verified by restriction digests and by DNA sequencing of the entire insert.

Cloning of the non-deimmunized 3-1xanti-CD3 construct:

For the cloning of the 3-1xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

The C-terminal 3-1 in VH-VL orientation was obtained by PCR for the construction of non-deimmunized 3-1 x anti-CD3 molecule. Fragments I and II comprising the 3-1 VH-VL in two parts were amplified by PCR using primer pairs me 91a (SEQ ID NO.: 53) /me 90 (SEQ ID NO.: 52) and me 83 (SEQ ID NO.: 50) /me 84 (SEQ ID NO.: 51), respectively. Hot Start PCR was done using the Expand High Fidelity System of Roche Diagnostics. 20 cycles (94°C/30 sec; 60°C/1min;72°C/1min) were used for amplification followed by one cycle of 3 min at 72°C.

PCR fragments I and II were subjected to electrophoresis on a 1.5% agarose gel. Fragments were mixed (1 ng of each) and used as a template for the next PCR reaction performed with primer pair me 91a (SEQ ID NO.: 53) and me 84 (SEQ ID NO.: 51) for amplification of fragment III comprising the entire 3-1. PCR was performed as described above, but with an annealing temperature of 68°C. Fragment III was purified on an agarose gel and digested with BsrGI and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR-anti EpCAM (M79) X anti-CD3 construct. The cloned region was verified by restriction digests and by DNA-sequencing.

Sequences of the Primers used:

Me 83: 5'- GGT TCT GGC GGC GGC GGC TCC GGT GGT GGT GGT TCT
GAG GTG CAG CTG CTC GA CAG TCT G -3' (SEQ ID NO.: 50)

Me 84: 5'- GTG CTC CGG AGG AGA CGG TGA CCG TGG TCC CTT GGC CCC
AG -3' (SEQ ID NO.: 51)

Me 90: 5'- CCG GAG CCG CCG CCG CCA GAA CCA CCA CCA CCT TTG ATC
TCA AGC TTG GTC CC -3' (SEQ ID NO.: 52)

Me 91a: 5'- GGA TTG TAC A CTCC GA GCT CGT CAT GAC CCA GTC TCC ATC
TTA TCT TGC TGC -3' (SEQ ID NO.: 53)

8.2.1.2 Cloning of deimmunized 3-5xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:54, 55):

The C-terminal 3-5 in VH-VL orientation was obtained by PCR for the construction of 3-5 xanti-CD3 molecule. The VH and VL regions of the anti-EpCAM antibody 3-5 are shown in SEQ ID NO.:141 and 143. The plasmids pEF-DHFR-3-5xanti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO.: 192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (3-5) and the vector respectively. The dephosphorylated vector (EcoRI and BspEI digested) and the insert were purified by agarose gel-electrophoresis.

The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final 3-5xanti-CD3 (VH5/VL2) (SEQ ID NO.:54) construct was verified by restriction digests.

Cloning of the non-deimmunized 3-5xanti-CD3 construct:

For cloning of the 3-5xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

Fragments I and II comprising the 3-5 in two parts were amplified by PCR according to the conditions described for 3-1xanti-CD3 using primer pairs me 81 (SEQ ID NO.: 56) /me 90 (SEQ ID NO.: 52) and me 83 (SEQ ID NO.: 50) /me 84 (SEQ ID NO.: 51) respectively. Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 81 (SEQ ID NO.: 56) and me 84 (SEQ ID NO.: 51) for amplification of fragment III comprising the entire 3-5. PCR was performed as described above. Fragment III was purified on an agarose gel and digested with BssHII and BspEI (Biolabs), purified and subsequently cloned into the corresponding

sites of the pEF-DHFRcloning vector. The cloned region was verified by restriction digests and by DNA-sequencing.

Sequence of the Me81 Primer (Seq ID NO.:56):

Me 81: 5'- GGA TGC GCG CGA GCT CGT GAT GAC CCA GAC TCCA CTC
TCC -3'

8.2.1.3 Cloning of the deimmunized 4-1xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:57, 58):

The C-terminal 4-1 in VH-VL orientation was obtained by PCR for the construction of 4-1xanti-CD3 molecule. The VH and VL regions of the anti-EpCAM antibody 4-1 are shown in SEQ ID NO.:145 and 147. The plasmids pEF-DHFR-4-1xanti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO.:192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (4-1) and the vector respectively. The dephosphorylated vector (EcoRI and BspEI digested) and the insert were purified by agarose gel-electrophoresis.

The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the vector. The final construct 4-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:57) was verified by restriction digests.

Cloning of the non-deimmunized 4-1xanti-CD3 construct:

For cloning of the 4-1xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

Fragments I and II comprising the 4-1 in two parts were amplified by PCR using primer pairs me 91a (SEQ ID NO.: 53) /me 90 (SEQ ID NO.: 452) and me 83 (SEQ ID NO.: 50) /me 84 (SEQ ID NO.: 51) with the above-mentioned conditions, respectively.

Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 92a (SEQ ID NO.: 59) and me 84 (SEQ ID NO.: 51) for amplification of fragment III comprising the entire 4-1. PCR was performed as described above but annealing was performed at 68°C. Fragment III was purified on an agarose gel and digested with BsrGI and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR-anti EpCAM (M79) X anti-CD3 cloning vector construct. The cloned region was verified by restriction digests and by DNA-sequencing.

Sequence of the Me92a primer (SEQ ID NO.: 59):

Me 92a: 5'- GGA TTG TAC A CTCC GA GCT CGT GAT GAC ACA GTCTCC ATC
CTC C -3'

8.1.2.4 Cloning of the deimmunized 4-7xanti-CD3 (VH5/VL2) construct (SEQ ID NO.:60, 61):

The C-terminal 4-7 in VH-VL orientation was obtained by PCR for the construction of 4-7 xanti-CD3. The VH and VL regions of the anti-EpCAM antibody 4-7 are shown in SEQ ID NO.:149 and 151. The plasmids pEF-DHFR-4-7xanti-CD3 and pEF anti-CD3 VH5/VL2 (SEQ ID NO.:192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (4-7) and the vector respectively. The de-phosphorylated vector (EcoRI and BspEI digested) and the insert were purified by agarose gel-electrophoresis.

The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final construct 4-7xanti-CD3 (VH5/VL2) (SEQ ID NO.:60) was verified by restriction digests.

Cloning of the non-deimmunized construct 4-7xanti-CD3:

For cloning of the 4-7xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

Fragments I and II comprising the 4-7 in two parts were amplified by PCR using primer pairs me 81 (SEQ ID NO.:56) /me 90 (SEQ ID NO.:52) and me 83 (SEQ ID NO.:50) /me 84 (SEQ ID NO.:51) with the afore mentioned conditions, respectively.

Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 81 (Seq ID NO.:56) and me 84 (Seq ID NO.:51) for amplification of fragment III comprising the entire 4-7 VH and VL chain. PCR was performed as described above. Fragment III was purified on an agarose gel and digested with BssHII and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR cloning vector. The cloned region was verified by restriction digests and by DNA-sequencing.

8.1.2.5 Cloning of the deimmunized 5-10x anti-CD3 (VH5/VL2) construct (SEQ ID NO.: 62, 63):

The C-terminal 5-10 in VH-VL orientation was obtained by PCR for the construction of 5-10 xanti-CD3 molecule. The VH and VL regions of the anti-EpCAM antibody 5-10 are shown in SEQ ID NO.:133 and 135. The plasmids pEF-DHFR-5-10xanti-CD3 and pEF anti-CD3 (VH5/VL2) (SEQ ID NO.:192) were digested with EcoRI and BspEI (Biolabs) for the isolation of the insert (5-10) and the vector respectively. The dephosphorylated vector (EcoRI and BspEI digested) and the insert were purified by agarose gel-electrophoresis.

The purified fragment (EcoRI-BspEI) was subsequently cloned into the corresponding sites of the pEF-DHFR vector. The final construct 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.: 62) was verified by restriction digests and by DNA sequencing.

Cloning of the non-deimmunized 5-10xanti-CD3 construct:

For cloning the 5-10xanti-CD3 (VH5/VL2) construct the corresponding non-deimmunized construct was generated as follows.

Fragments I and II comprising the 5-10 in two parts were amplified by PCR using primer pairs me 92a (SEQ ID NO.: 59) /me 90 (SEQ ID NO.: 52) and me 83 (SEQ ID NO.: 50) /me 84 (SEQ ID NO.: 51) with the above mentioned conditions, respectively. Agarose gel fragments comprising PCR fragments I and II were reamplified with primer pair me 92a SEQ ID NO.: 59) and me 84 (SEQ ID NO.: 51) for amplification of fragment III comprising the entire 5-10. PCR was performed as described above but annealing was performed at 68°C. Fragment III was purified on an agarose gel and digested with BsrGI and BspEI (Biolabs), purified and subsequently cloned into the corresponding sites of the pEF-DHFR-anti EpCAM (M79) x anti-CD3 cloning vector. The cloned region was verified by restriction digests and by DNA-sequencing.

8.2.2 Expression of anti EpCAMxdeimmunized-anti-CD3 molecules with anti-EpCAM at the N-terminal position:

CHO-cells lacking DHFR gene were maintained in alpha MEM medium (Life Technologies, cat.no: 32561) supplemented with 10% fetal calf serum (Life Technologies, heat inactivated at 65°C for 30 minutes) and with HT (Hypoxanthin and Thymidine; Life Technologies). The cells were transfected with pEF-DHFR-3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.: 48) and pEF-DHFR-5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:62), using Lipofectamine 2000 kit® (Invitrogen) according to the

instructions provided by the Manufacturer. After 48 hrs. selection was performed in selection medium (alpha MEM medium containing heat inactivated 10% dialysed fetal calf serum (Life Technologies). After 3-4 weeks cell culture supernatant was collected and centrifuged at 4°C for 10 minutes at 300g to remove cells and cell debris. The supernatant containing the bispecific antibody was stored at -20°C till further analysis.

8.2.3 Binding assays of bispecific anti-EpCAMxanti-CD3 variants:

250000 Jurkat cells (for CD3 binding) and Kato cells (for EpCAM binding) were independently incubated with cell culture supernatants (50µl) containing the bispecific construct (pEF-DHFR-3-1xanti-CD3 (VH5/VL2) (Nr.50, SEQ ID NO.: 48) and pEF-DHFR-5-10xanti-CD3 (VH5/VL2) (Nr.54) (SEQ ID NO.:62), respectively) for 45 min. at 4°C. Thereafter, the cells were washed twice in FACS buffer (phosphate-buffered saline containing 1% fetal calf serum (FCS) and 0.05% sodium azide) and incubated with mouse anti-His antibody (Dianova, DIA910) for 60 min. at 4°C. Washing steps were performed as above.

The cells were finally incubated either with goat anti-mouse Ig-FITC-conjugated antibody (BD 550003) or with anti-mouse IgG conjugated with PE (Sigma, P8547). After washing steps, 10000 events were analysed using FACS Calibur (B&D). The results of the binding assays are shown in Figure 16. The constructs 3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49) and 5-10xanti-CD3 (SEQ ID NO.:63) showed strong binding to CD3 on Jurkat cells and to CD19 on Kato cells.

Example 8.3. Purification of bispecific anti EpCAM constructs with deimmunized anti-CD3 part

The constructs comprising a deimmunized anti-CD3 region and an EpCAM-specific region were purified with a two-step purification process including immobilized metal affinity chromatography (IMAC) and gel filtration. Metal affinity chromatography (IMAC) and gel filtration were carried out as demonstrated in example 3.2.

A further high-resolution cation exchange chromatography was performed on a MiniS column (Amersham), equilibrated with 20mM MES buffer pH 5.5. The sample was diluted 1:3 with the same buffer before loading to the column. Bound protein was eluted with a 0-30% gradient gradient of 1 M NaCl in equilibration buffer. The eluted protein fractions were tested in the bioactivity assay. Table 14 shows the yields of the

purified deimmunized EpCAM constructs. All the constructs could be efficiently produced. Surprisingly, the construct 5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63) had an extremely good yield of 2200 µg/l.

Table 14. Yields of the deimmunized EpCAM constructs

Construct	Yield of the monomer [µg purified protein per liter culture]
anti-CD3 (VH5/VL2)x4-7 (SEQ ID NO.:33)	112.5
3-1xanti-CD3 (VH5/VL2) (SEQ ID NO.:49)	87.5
anti-CD3 (VH5/VL2)x3-1 (SEQ ID NO.:31)	442.5
5-10xanti-CD3 (VH5/VL2) (SEQ ID NO.:63)	2200
anti-CD 3 (VH5/VL2)x5-10 (SEQ ID NO.:37)	80

Example 8.4 Cytotoxic assays of the bispecific anti-EpCAM constructs with deimmunized anti-CD3 part

In order to confirm the high bioactivity of the bispecific antibodies of the invention, a FACS based assay was carried out. CHO cells were transfected with epithelial cell adhesion molecule (EpCAM). A cell clone derived from this transfection, referred to as CHO-EpCAM cells, was used for the experiments.

For the cytotoxicity test, CHO-EpCAM (1.5×10^7) cells were washed free of serum two times with PBS and incubated with PKH26 dye (Sigma-Aldrich Co.) according to the manufacturers instructions. After staining, cells were washed two times with RPMI/10% FCS.

Cells were counted and mixed with CB15 effector cells. The CD4-positive T cell clone CB15 was kindly provided by Dr. Fickenscher, University of Erlangen/Nuernberg, Germany. Cells were cultured as recommended by the suppliers. The resulting cell suspension contained 400.000 target and 2×10^6 effector cells per ml. 50 µl of the mixture was used per well in a 96 well round bottom plate.

Antibodies were diluted in RPMI/10% FCS to the required concentration and 50 µl of this solution was added to the cell suspension. A standard reaction was incubated for 16 h at 37°C / 5% CO₂. Propidium iodide was added to a final concentration of 1 µg/ml. After 10 min of incubation at room temperature cells were analysed by FACS. PKH26 fluorescence was used for positive identification of target cells. Cytotoxicity was measured as ratio of PI positive over all target cells.

Sigmoidal dose response curves typically had R² values >0.97 as determined by Prism Software (GraphPad Software Inc., San Diego, USA). The results of the cytotoxic assays are shown in Figures 17 and 18.

Example 8.5. Comparison of the productivity of bispecific molecules comprising an EpCAM binding part and a deimmunized CD3 binding part in CHO cells

In order to determine the productivity of a deimmunized construct protein L ELISA was performed. The productivity data was calculated from batch cultures.

8.5.1 Cell Culture

CHO cell lines producing deimmunized (CHO-DHFR-) and non-deimmunized (CHO-DHFR- or CHO-K1) were cultivated in HyQ PF CHO LS medium + 4 mM L-Glutamine in a CO₂ incubator at 37°C and 5% CO₂. Cell numbers and viability were determined using Trypan Blue. Cell density was set to $1-2 \times 10^5$ cell/ml.

Cells were transferred to spinner flasks and thus adjusted to conditions of a stirred culture. Operational parameter settings were 80 rpm, 37°C and 5% CO₂ with gassing in a CO₂ incubator. Culture volume was in the 100–500 ml-range and cell density at inoculation in the range of $1-2 \times 10^5$ cells/ml. As for the subcultivation in T-flasks, cultures were centrifuged and resuspended in fresh pre-warmed medium at each passage. Cell density was set to $1-2 \times 10^5$ cells/ml.

For analysis of productivity data (Table 15) cells were cultivated up to 14 days (d) without any medium addition or exchange. Cell numbers and viability were determined daily using Trypan blue stain. Product concentrations in the supernatant were analyzed by Protein L ELISA.

8.5.2 Protein L ELISA

Quantitative binding of the bispecific molecules was carried out with rProtein L-coated microtiter plates. rProtein L is a recombinant form of the immunoglobulin-binding Protein L produced by *Peptostreptococcus magnus*. It has four binding domains and binds immunoglobulin through the light chain (κ). Bispecific molecules, which contain variable domains from two different light chains respectively parent antibodies, are also bound by rProtein L.

Microtiter plates were coated with rProtein L in PBS buffer (2 µg rProtein L/ml PBS buffer) overnight at 2-8°C. Following coating, remaining adsorption sites were blocked with of blocking buffer (2% BSA in PBS buffer). Then, the plates were frozen and stored at ≤18°C. Before use, the plates were thawed and washed with washing buffer (0.05% Tween 20 in PBS buffer) to remove the mixture of coating solution and blocking buffer.

Serial dilutions of cell-free cell culture supernatant in 1% BSA + 0.01% Tween 20 in PBS (dilution buffer) were analyzed. Bispecific anti-EpCAM(M79)xanti-CD3 was used as positive control in comparable dilutions.

Incubation was performed overnight at 2-8°C.

After washing rabbit anti-mouse IgG (1:5,000 in dilution buffer) was added and incubated for 60 min at room temperature. Goat anti-rabbit IgG labeled with alkaline phosphatase was added (1:1,000 in dilution buffer; 60 min at room temperature) after washing. pNPP substrate solution was added and the reaction was stopped by addition of 3 M NaOH. Absorbance was measured with an ELISA reader at 405 nm (reference filter 492 nm).

Table 15. Productivity of an deimmunized anti-EpCAM construct

Construct	M79xanti-anti-CD3		5-10xanti-CD3 (VH5/VL2)
Basic cell line	CHO-K1	CHO-dhfr-	CHO-dhfr-
Specific productivity	0.2-0.6 pg/cell per day	1-3 pg/cell per day	15-20 pg/cell per day
Maximal cell density	3x10 ⁶ c/ml	1.2-1.8x10 ⁶ c/ml	1.5x10 ⁶ c/ml
Doubling time	17-20 h	25-30 h	25-30 h

Thus, the inventive 5-10xanti-CD3 (VH5/VL2) construct demonstrated much higher specific productivity (at least five times higher) than the prior art bispecific non-deimmunized EpCAM and CD3 binding antibody.

Claims

1. A cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain, wherein said first domain is deimmunized and comprises a CDR-H1 region, a CDR-H2 region and a CDR-H3 region, said CDR-H3 region comprising an amino acid sequence as depicted in SEQ ID NO.: 96, 108, 119, 120, 121, 122, 123, 124, 125, 126, or 127; and wherein said first domain further comprises in its framework H1 the sequence VKK and wherein the transition sequence between framework H1 and CDRH1 region comprises the sequence Ala-Ser-Gly-Tyr-Thr-Phe (ASGYTF; SEQ ID NO.: 233).
2. The cytotoxically active CD3 specific binding construct of claim 1 further comprising in said first domain a framework H3 comprising the sequence Met-Glu-Leu-Ser (MELS; SEQ ID NO.: 234).
3. The cytotoxically active CD3 specific binding construct of claim 1 or 2 further comprising in said first domain a framework H3 comprising the sequence Ile-Thr-Thr-Asp-Lys (ITTDK; SEQ ID NO.: 235).
4. The CD3 specific binding construct of any one of claims 1 to 3, wherein said first domain which specifically binds to human CD3 comprises a framework H1 as shown in SEQ ID NO.: 152 or 153.
5. The CD3 specific binding construct of any one of claims 1 to 4, wherein said first domain which specifically binds to human CD3 comprises a framework H2 as shown in SEQ ID NO.: 156 or 157.
6. The CD3 specific binding construct of any one of claims 1 to 5, wherein said first domain which specifically binds to human CD3 comprises a framework H3 as shown in SEQ ID NO.: 160 or 161.

7. The CD3 specific binding construct of any one of claims 1 to 6, wherein said first domain which specifically binds to human CD3 comprises a framework H4 as shown in SEQ ID NO.: 164 or 165.
8. The CD3 specific binding construct of any one of claims 1 to 7, wherein said construct comprises
 - (a) a CDR-H1 as depicted in SEQ ID NO.: 88; and
 - (b) a CDR-H2 as depicted in SEQ ID NO.: 90 or 92.
9. The CD3 specific binding construct of any one of claims 1 to 8, wherein said construct comprises a V_H-region as depicted in SEQ ID NO.: 74 or 76.
10. The CD3 specific binding construct of any one of claims 1 to 9, wherein said construct comprises a CDR-L1 as depicted in SEQ ID NO.: 98 or 100.
11. The CD3 specific binding construct of any one of claims 1 to 10, wherein said construct comprises a CDR-L2 as depicted in SEQ ID NO.: 102.
12. The CD3 specific binding construct of any one of claims 1 to 11, wherein said construct comprises a CDR-L3 as depicted in SEQ ID NO.: 104.
13. The CD3 specific binding construct of any one of claims 1 to 12 comprising a V_L region in its CD3-specific portion, wherein said V_L region is selected from the group consisting of SEQ ID NO.: 78, SEQ ID NO.: 80, SEQ ID NO.: 82 and SEQ ID NO.: 112.
14. The CD3 specific binding construct of any of claims 1 to 13, wherein said Ig-derived second domain is a scFv.
15. The CD3 specific binding construct of any of claims 1 to 14, wherein said Ig-derived second domain and/or (a) connecting linker-region(s) is/are humanized and/or deimmunized.
16. The CD3 specific binding construct of any of claims 1 to 15, wherein said Ig-

derived second domain comprises an antigen-interaction-site with specificity for a cell surface molecule.

17. The CD3 specific binding construct of claim 16, wherein said cell surface molecule is a tumor specific marker.
18. The CD3 specific binding construct of any of claims 16 or 17, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for a molecule selected from the group consisting of EpCAM, CCR5, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, MUC5_{AC}, MUC5_B, MUC7, β hCG, Lewis-Y, CD20, CD33, CD30, ganglioside GD3, 9-O-Acetyl-GD3, GM2, Globo H, fucosyl GM1, Poly SA, GD2, Carboanhydrase IX (MN/CA IX), CD44v6, Sonic Hedgehog (Shh), Wue-1, Plasma Cell Antigen, (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), CCR8, TNF-alpha precursor, STEAP, mesothelin, A33 Antigen, Prostate Stem Cell Antigen (PSCA), Ly-6; desmoglein 4, E-cadherin neo-epitope, Fetal Acetylcholine Receptor, CD25, CA19-9 marker, CA-125 marker and Muellierian Inhibitory Substance (MIS) Receptor type II, sTn (sialylated Tn antigen, TAG72), FAP (fibroblast activation antigen), endosialin, EGFRvIII, L6, SAS, CD63, TAG72, TF-antigen, Cora antigen, CD7, CD22, Ig α , Ig β , G250, gp100, MT-MMPs, F19-antigen, CO-29 and EphA2.
19. The CD3 specific binding construct of any of claims 1 to 18, wherein said second Ig-derived binding domain comprises an antigen-interaction site with a specificity for EpCAM.
20. The CD3 specific binding construct of claim 19, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of
 - (a) an amino acid sequence as shown in any one of SEQ ID NO.: 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275,

- 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 and 325;
- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of SEQ ID NO.: 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 and 324; and
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);
- (d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.
21. The CD3 specific binding construct of any of claims 1 to 18, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity CCR5.
22. The CD3 specific binding construct of claim 21, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of
- (a) an amino acid sequence as shown in any one of SEQ ID NO.: 206, 208, 210, 212, 214 or 216;
- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO.: 205, 207, 209, 211, 213 or 215; and
- (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);
- (d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

23. The CD3 specific binding construct of any of claims 1 to 18, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for CD19.
24. The CD3 specific binding construct of claim 23, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of
- (a) an amino acid sequence as shown in any one of SEQ ID NO.: 190, 192, 194, 196, 198, 200, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407 or 409;
 - (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO.: 189, 191, 193, 195, 197, 199, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398, 400, 402, 404, 406 or 408; and
 - (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);
 - (d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.
25. The CD3 specific binding construct of any of claims 1 to 18, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for CD20.
26. The CD3 specific binding construct of claim 25, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of
- (a) an amino acid sequence as shown in any one of SEQ ID NO.: 218, 220, 222, 224, 226, or 228;

- (b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO.: 217, 219, 221, 223, 225 or 227; and
 - (c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);
 - (d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.
27. A nucleic acid sequence encoding a CD3 specific binding construct according to any of claims 1 to 26.
28. A vector comprising a nucleic acid sequence according to claim 27.
29. The vector of claim 28, which further comprises a nucleic acid sequence which is a regulatory sequence operable linked to said nucleic acid sequence according to claim 27.
30. The vector of claim 28 or 29, wherein the vector is an expression vector.
31. A host transformed or transfected with a vector according to any of claims 28 to 30.
32. A process for the production of a CD3 specific binding construct according to any of claims 1 to 26 said process comprising culturing a host of claim 31 under conditions allowing the expression of the polypeptide construct and recovering the produced polypeptide construct from the culture.
33. A composition comprising a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31 and, optionally, a proteinaceous compound capable of providing an activation signal for immune effector cells.

34. The composition of claim 33, which is a pharmaceutical composition further comprising, optionally, suitable formulations of carrier, stabilizers and/or excipients.
35. The composition of claim 33, which is a diagnostic composition further comprising, optionally, means and methods for detection.
36. Use of a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31 for the preparation of a pharmaceutical composition for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases.
37. A CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31 for use in a method of prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases.
38. The use of claim 37, further comprising the administration of a proteinaceous compound capable of providing an activation signal for immune effector cells.
39. The use of claim 38, wherein said proteinaceous compound is administered simultaneously or non-simultaneously with a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31.
40. A kit comprising a CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule of claim 27, a vector of any one of claims 28 to 30 or a host of claim 31.

Figure 1

Anti-CD3 WT

GATATCAAACTGCAGCAGTCAGGGGCTGAACTGGCAAGACCTGGGGCCTCAGTGAAGATGTCCCT
GCAAGACTTCTGGCTACACCTTTACTAGGTACACGATGCACCTGGGTAAACAGAGCCCTGGACA
GGTCTGGAATGGATTGGATACATTAATCCTAGCCGTGGTTATACTAATTACAATCAGAAGTTC
AAGACAAGGCCACATTGACTACAGACAAATCCTCCAGCACAGCCTACATGCAACTGAGCAGCC
TGACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGATAATTATGATGATCATTTACTGCCTTGA
CTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCAGTCGAAAGTGGAGGTCTCTGGT
GGAAGTGGAGGTTCAAGTGGAGTCGACGACATTCAAGCTGACCCAGTCTCCAGCAATCATGTCTG
CATCTCAGGGGAGAAGTCAACCATGACCTGCAGAGCCAGTTCAAAGTGAAGTTACATGAACTG
GTACCAGCAGAAGTCAGGCACCTCCCCCAAAGATGGATTATGACACATCCAAAGTGGCTTCT
GGAGTCCCTTATCGCTTCAGTGGCAGTGGTCTGGGACCTCATACTCTCACAATCAGCAGCA
TGGAGGCTGAAGATGCTGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCACGTTCCG
TGCTGGGACCAAGCTGGAGCTGAAA

AA Sequence

DIKLQQSGAELARPGASVKMSCKTSGYTFTRYTMHWVKQRPQGLEWIGYINPSRGYTNYNQKF
KDKATLTLDKSSSTAYMQLSLTSEDSAVYYCARYDDHYCLDYWGQGTTLTVSSVEGGSGSG
GSGSGGVDDIQLTQSPAIMASPGEKVTMTCRASSSVSYMNWYQQKSGTSPKRWIYDTSKVAS
GVPIRFSGSGGTSYSLTISSEAEADAATYYCQQWSSNPLTFGAGTKLELK

Fig. 2 A

VH2

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYAQKLQGRVTMTTDTSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWG
QGTTVTVSS

VH3

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYAQKLQGRVTMTTDTSTSTAYLQMNSLKTEDTAVYYCARYYDDHYCLDYWG
QGTTVTVSS

VH5

DVQLVQSGAEVKKPGASVKVSCKASGYTFTTRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWG
QGTTVTVSS

VH7

DVQLVQSGAEVKKPGASVKVSCKASGYTFTTRYTMHWVRQAPGQGLEWIGYINPSR
GYTNYNQKFKDRVTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWG
QGTTVTVSS

Fig. 2 A (cont.)

VL1

DIQMTQSPSSLASVGDRVTITCRASQSVSYMNWYQQKPGKAPKRWIYDT
SKVASGVPARFSGSGGTDYSLTINSLEAEDAATYYCQQWSSNPLTFGGG
TKVEIK

VL2

DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDT
SKVASGVPARFSGSGGTDYSLTINSLEAEDAATYYCQQWSSNPLTFGGG
TKVEIK

VL3

DIVLTQSPATLSLSPGERATLTCRASSVSYMNWYQQKPGKAPKRWIYDT
SKVASGVPARFSGSGGTDYSLTINSLEAEDAATYYCQQWSSNPLTFGGG
TKVEIK

Fig. 2 B

VH2

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACCTGGGGCCTCAGTGAAGGTGTCCTGC
AAGGCTTCTGGCTACACCGCTACTAGGTACACGATGCATGGTAAAGCAGGCACCTGGACAGGGT
CTGGAATGGATTGGATACATTAACTCCTAGCCGTGGTTATACTAATTACGCACAGAAAGTTGCAGGGC
CGCGTCACAATGACTACAGACACTTCCACCAGCACAGCCTACATGGAACCTGAGCAGCCTGCGTTCT
GAGGACACTGCAACCTATTACTGTGCAAGATATTATGATGATCATTAATGCTTGAATACTGAGGCG
CAAGGCCACCACGGTCACCGTCTCCTCA

VH3

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACCTGGGGCCTCAGTGAAGGTGTCCTGC
AAGGCTTCTGGCTACACCGCTACTAGGTACACGATGCATGGTAAAGCAGGCACCTGGACAGGGT
CTGGAATGGATTGGATACATTAACTCCTAGCCGTGGTTATACTAATTACGCACAGAAAGTTGCAGGGC
CGCGTCACAATGACTACAGACACTTCCACCAGCACAGCCTACCTGCAAAATGAACAGCCTGAAAACT
GAGGACACTGCAGTCTATTACTGTGCAAGATATTATGATGATCATTAATGCTTGAATACTGAGGCG
CAAGGCCACCACGGTCACCGTCTCCTCA

VH5

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACCTGGGGCCTCAGTGAAGGTGTCCTGC
AAGGCTTCTGGCTACACCGCTTACTAGGTACACGATGCATGGTAAAGCAGGCACCTGGACAGGGT
CTGGAATGGATTGGATACATTAACTCCTAGCCGTGGTTATACTAATTACGCACAGCCTGCAAGGGC
CGCTTCACAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAACCTGAGCAGCCTGCGTTCT
GAGGACACTGCAACCTATTACTGTGCAAGATATTATGATGATCATTAATGCTTGAATACTGAGGCG
CAAGGCCACCACGGTCACCGTCTCCTCA

Fig. 2 B (cont.)

VH7

GACGTCCAAC TGGTGCAGTCAGGGGCTGAAGTGAAAAACCTGGGGCCCTCAGTGAAGGTGTCTGC
AAGGCTTCTGGCTACACCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCTGGACAGGGT
CTGGAATGGATTGGATACATTAAATCCTAGCCGTGGTTACTAATTACAATCAGAAAGTTCAAGGAC
CGCGTCACAATCACTACAGACAAATCCACGACAGCCCTACATGGAACTGAGCAGCCCTGCGTTCT
GAGGACACTGCAGTCTATTACTGTGCAAGATATTATGATGATCATTAATGCTTGACTACTGGGGC
CAAGGCACCAAGTCACCGTCTCTCTCA

Fig. 2 B (cont.)

VL1

GACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCATCTGTCTGGGGACCGTGTACCATCACC
TGCAGAGCCAGTCAAAGTGTAAAGTTACATGAAGTGTACCAAGAGAGCCGGCAAGGCACCCCAA
AGATGGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCT
GGACCGACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA
CAGTGGAGTAGTAACCCGCTCACGTTCCGTGGCGGGACCAAGGTGGAGATCAAA

VL2

GACATTGTACTGACCCAGTCTCCAGCAAATCTGTCTGTCTCTCAGGGAGCGTGCCACCCCTGAGC
TGCAGAGCCAGTCAAAGTGTAAAGTTACATGAAGTGTACCAAGAGAGCCGGCAAGGCACCCCAA
AGATGGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCT
GGACCGACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA
CAGTGGAGTAGTAACCCGCTCACGTTCCGTGGCGGGACCAAGGTGGAGATCAAA

VL3

GACATTGTACTGACCCAGTCTCCAGCAAATCTGTCTGTCTCTCAGGGAGCGTGCCACCCCTGACC
TGCAGAGCCAGTCAAAGTGTAAAGTTACATGAAGTGTACCAAGAGAGCCGGCAAGGCACCCCAA
AGATGGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCT
GGACCGACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA
CAGTGGAGTAGTAACCCGCTCACGTTCCGTGGCGGGACCAAGGTGGAGATCAAA

Fig. 2 C

vH CDR1

Wt anti-CD3

VH2, 3

VH5, 7

GYTFTRYTMH

GYTATRYTMH

GYTFTRYTMH

vH CDR2

WT anti-CD3,

VH7

VH5

VH2, 3

YINPSRGYTNYNQKFCD

YINPSRGYTNYADSVKG

YINPSRGYTNYAQKLQG

vH CDR3

WT anti-CD3,

VH2, 3, 5, 7

YYDDHYCLDY

vK CDR1

WT anti-CD3,

VL3

VL1, 2

RASSSVSYMN

RASQSVSYMN

vK CDR2

WT anti-CD3,

VL1, 2, 3

DTSKVAS

vK CDR3

WT anti-CD3,

VL1, 2, 3

QQWSSNPLT

Fig. 2 D

vH CDR1

WT anti-CD3 GGCTACACCTTTACTAGGTACACGATG
CAC

VH2,3 GGCTACACCGCTACTAGGTACACGATG
CAC

VH5,7 GGCTACACCTTTACTAGGTACACGATG
CAC

vH CDR2

WT anti-CD3,
VH7 TACATTAATCCTAGCCGTGGTTATACT
AATTACAATCAGAAGTTCAAGGAC

VH5 TACATTAATCCTAGCCGTGGTTATACT
AATTACGCAGACAGCGTCAAGGGC

VH2,3 TACATTAATCCTAGCCGTGGTTATACT
AATTACGCACAGAAGTTGCAGGGC

VH CDR3

WT anti-CD3,
VH2, 3,
VH5, 7 TATTATGATGATCATTACTGCCTT
GACTAC

Fig. 2 D (cont.)

vK CDR1WT anti-CD3,
VL3AGAGCCAGTTCAAGTGTAAGTTACATG
AAC

VL1, 2

AGAGCCAGTCAAAGTGTAAGTTACATG
AAC**vK CDR2**WT anti-CD3,
VL1-3

ACACATCCAAAGTGGCTTCT

VK CDR3WT anti-CD3,
VL1-3

CAACAGTGGAGTAGTAACCCGCTCACG

Figure 3**A) anti-CD3 (VH2/VL1)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAAAGTGGAGGTTCAAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCACCATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) anti-CD3 (VH2/VL1)

DVQLVQSGAEVKKPGASVKVSKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNIAQKLQGRVTMTTDTSTSTAYME
LSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIQMTQSPSSLSASVGDRVITICRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARESGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 3**C) anti-CD3 (VH2/VL2)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAA-
AACCTGGGGCCTCAGTGAAGGTGTCCTG-
CAAGGCTTCTGGCTACACCGCTACTAGGTACACGATG-
CACTGGGTAAGGCAGGCACCTGGACAGGGTCTGGAATGGAT
TGGATACATTAATCCTAGCCGTGGTTATACTAATTACGCA-
CAGAAGTTGCAGGGCCGCGTCACAATGACTACAGA-
CACTTCCACCAGCACAGCCTACATGGAAGTGAAG-
CAGCCTGCGTTCTGAGGACACTGCAACCTATTACTGTGCAA
GATATTATGATGATCATTACTGCCTTGACTACTGGGGC-
CAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTAC-
TAGTACTGGTTCTGGTGGAAAGTGGAGGTTTCAGGTGGAGCA-
GACGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCT
GTCTCCAGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGT-
CAAAGTGTAAGTTACATGAACTGGTACCAGCA-
GAAGCCGGGCAAGGCACCCAAAAGATGGATTTATGACA-
CATCCAAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGC
AGTGGGTCTGGGACCGACTACTCTCTCACAATCAA-
CAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA-
CAGTGGAGTAGTAACCCGCTCACGTTCCGGTGGCGGGAC-
CAAGGTGGAGATCAAA

D) anti-CD3 (VH2/VL2)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVR-
QAPGQGLEWIGYINPSRGYTN-
AQKLQGRVTMTTDTSTSTAYMELSSLRSEDATYYCA-
RYYDDHYCLDYWGQGTTVTVSSGEGTSTGSGGSGGSGGADD
IVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPG-
KAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAE-
DAATYYCQQWSSNPLTFGGGTKVEIK

Figure 3**E) anti-CD3 (VH2/VL3)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAA-
AACCTGGGGCCTCAGTGAAGGTGTCCTG-
CAAGGCTTCTGGCTACACCGCTACTAGGTACACGATG-
CACTGGGTAAGGCAGGCACCTGGACAGGGTCTGGAATGGAT
TGGATACATTAATCCTAGCCGTGGTTATACTAATTACGCA-
CAGAAAGTTGCAGGGCCGCGTCACAATGACTACAGA-
CACTTCCACCAGCACAGCCTACATGGAAGTGAAG-
CAGCCTGCGTTCTGAGGACACTGCAACCTATTACTGTGCAA
GATATTATGATGATCATTACTGCCTTGACTACTGGGGC-
CAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTAC-
TAGTACTGGTTCTGGTGGAAAGTGGAGGTTTCAGGTGGAGCA-
GACGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCT
GTCTCCAGGGGAGCGTGCCACCCTGACCTGCAGAGC-
CAGTTCAAGTGTAAGTTACATGAACTGGTACCAGCA-
GAAGCCGGGCAAGGCACCCAAAAGATGGATTTATGACA-
CATCCAAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGC
AGTGGGTCTGGGACCGACTACTCTCTCACAATCAA-
CAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA-
CAGTGGAGTAGTAACCCGCTCACGTTTCGGTGGCGGGAC-
CAAGGTGGAGATCAAA

F) anti-CD3 (VH2/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVR-
QAPGQGLEWIGYINPSRGYTN-
AQKLQGRVTMTTDTSTSTAYMELSSLRSEDATYYCA-
RYYDDHYCLDYWGQGTITVTVSSGEGTSTGSGGSGGSGGADD
IVLTQSPATLSLSPGERATLTCRASSSVSYMNWYQQKPG-
KAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAE-
DAATYYCQQWSSNPLTFGGGTKVEIK

Figure 4**A) anti-CD3 (VH3/VL1)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACCTGCAA
ATGAACAGCCTGAAAACCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAGGTGGAGGTTTCAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCACCATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) anti-CD3 (VH3/VL1)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVR-
QAPGQGLEWIGYINPSRGYTN-
AQKLQGRVTMTTDTSTSTAYLQMNSLKTEDTAVYYCARYYDD-
HYCLDYWGQGTTVTVSSGEGTSTGSGGSGGSGGADDIQMTQSP
SSLSASVGRVTITCRASQSVSYMNWYQQKPG-
KAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAE-
DAATYYCQQWSSNPLTFGGGTKVEIK

Figure 4**C) anti-CD3 (VH3/VL2)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCGCTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCACAGAAGTTGCAGGGCCGCGTCA
CAATGACTACAGACACTTCCACCAGCACAGCCTACCTGCAA
ATGAACAGCCTGAAAACCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAGGTGGAGGTTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

D) anti-CD3 (VH3/VL2)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYAQKLQGRVTMTTDTSTSTAYLQ
MNSLKTEDTAVYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLSCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGGTKVEIK

Figure 4**E) anti-CD3 (VH3/VL3)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAA-
AACCTGGGGCCTCAGTGAAGGTGTCCTG-
CAAGGCTTCTGGCTACACCGCTACTAGGTACACGATG-
CACTGGGTAAGGCAGGCACCTGGACAGGGTCTGGAATGGAT
TGGATACATTAATCCTAGCCGTGGTTATACTAATTACGCA-
CAGAAGTTGCAGGGCCGCGTCACAATGACTACAGA-
CACTTCCACCAGCACAGCCTACCTGCAAATGAACAGCCT-
GAAAACCTGAGGACACTGCAGTCTATTACTGTGCAAGATATT
ATGATGATCATTACTGCCTTGACTACTGGGGCCAAGGCAC-
CACGGTCACCGTCTCCTCAGGCGAAGGTACTAG-
TACTGGTTCTGGTGGAAAGTGGAGGTTCAAGGTGGAGCAGAC-
GACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGTC
TCCAGGGGAGCGTGCCACCCTGACCTGCAGAGCCAGTT-
CAAGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGG-
CAAGGCACCCAAAAGATGGATTTATGACACATCCA-
AAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGG
TCTGGGACCGACTACTCTCTCACAATCAACAGCTTG-
GAGGCTGAAGATGCTGCCACTTATTACTGCCAACAGTG-
GAGTAGTAACCCGCTCACGTTCCGGTGGCGGGACCAAGGTG-
GAGATCAAA

F) anti-CD3 (VH3/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTATRYTMHWVR-
QAPGQGLEWIGYINPSRGYTNV-
AQKLQGRVTMTTDTSTSTAYLQMNSLKTEDTAVYYCA-
RYYDDHYCLDYWGQGTITVTVSSGEGTSTGSGGSGGSGGADD
IVLTQSPATLSLSPGERATLTCSRASSSVSYMNWYQQKPG-
KAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAE-
DAATYYCQQWSSNPLTFGGGTKVEIK

Figure 5**A) CD3 (VH5/VL1)**

GACGTCCAAC TGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCAGACAGCGTCAAGGGCCGCTTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAGTGGAGGTTTCAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCAACATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) CD3 (VH5/VL1)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYME
LSSLRSED TATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIQMTQSPSSLSASVGDRVITICRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 5**C) anti-CD3 (VH5/VL2)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACGCAGACAGCGTCAAGGGCCGCTTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAACCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAGTGGAGGTTTCAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

D) anti-CD3 (VH5/VL2)

DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAP
GQGLEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYME
LSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSGEGT
STGSGGSGGSGGADDIVLTQSPATLSLSPGERATLSCRASQ
SVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGT
DYSLTINSLEAEDAATYYCQQWSSNPLTFGGGTKVEIK

Figure 5**E) anti-CD3 (VH5/VL3)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAA-
AACCTGGGGCCTCAGTGAAGGTGTCCTG-
CAAGGCTTCTGGCTACACCTTTACTAGGTACACGATG-
CACTGGGTAAGGCAGGCACCTGGACAGGGTCTGGAATGGAT
TGGATACATTAATCCTAGCCGTGGTTATACTAATTACG-
CAGACAGCGTCAAGGGCCGCTTCACAATCACTACAGACA-
AATCCACCAGCACAGCCTACATGGAAGTGAAG-
CAGCCTGCGTTCTGAGGACACTGCAACCTATTACTGTGCAA
GATATTATGATGATCATTACTGCCTTGACTACTGGGGC-
CAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTAC-
TAGTACTGGTTCTGGTGGAAAGTGGAGGTTTCAGGTGGAG-
CAGACGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCT
CTGTCTCCAGGGGAGCGTGCCACCCTGACCTGCAGAGC-
CAGTTCAAGTGTAAGTTACATGAACTGGTACCAGCA-
GAAGCCGGGCAAGGCACCCAAAAGATGGATTTATGACA-
CATCCAAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGC
AGTGGGTCTGGGACCGACTACTCTCTCACAATCAA-
CAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGC-
CAACAGTGGAGTAGTAACCCGCTCACGTTTCGGTGGCGG-
GACCAAGGTGGAGATCAAA

F) anti-CD3 (VH5/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVR-
QAPGQGLEWIGYINPSRGYTN-
ADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCA-
RYYDDHYCLDYWGQGTTVTVSSGEGTSTGSGGSGGSGGADD
IVLTQSPATLSLSPGERATLTCRASSSVSYMNWYQQKPG-
KAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAE-
DAATYYCQQWSSNPLTFGGGTKVEIK

Figure 6**A) anti-CD3 (VH7/VL1)**

GACGTCCAAC TGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACAATCAGAAGTTCAAGGACCGCGTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCACTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAGTGGAGGTTCAAGGTGGAGCAGA
CGACATTCAGATGACCCAGTCTCCATCTAGCCTGTCTGCAT
CTGTCGGGGACCGTGTCACCATCACCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

B) anti-CD3 (VH7/VL1)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVR-
QAPGQGLEWIGYINPSRGYT-
NYNQKFKDRVITITDKSTSTAYMELSSLRSED TAVYYCA-
RYYDDHYCLDYWGQGTTVTVSSGEGTSTGSGGSGGSGGADD
IQMTQSPSSLSASVGRVTITCRASQSVSYMNWYQQKPG-
KAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAE-
DAATYYCQQWSSNPLTFGGGTKVEIK

Figure 6**C) anti-CD3 (VH7/VL2)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAAAACC
TGGGGCCTCAGTGAAGGTGTCCTGCAAGGCTTCTGGCTACA
CCTTTACTAGGTACACGATGCACTGGGTAAGGCAGGCACCT
GGACAGGGTCTGGAATGGATTGGATACATTAATCCTAGCCG
TGGTTATACTAATTACAATCAGAAGTTCAAGGACCGCGTCA
CAATCACTACAGACAAATCCACCAGCACAGCCTACATGGAA
CTGAGCAGCCTGCGTTCTGAGGACACTGCAGTCTATTACTG
TGCAAGATATTATGATGATCATTACTGCCTTGACTACTGGG
GCCAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTACT
AGTACTGGTTCTGGTGGAGTGGAGGTTCAAGGTGGAGCAGA
CGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCTGT
CTCCAGGGGAGCGTGCCACCCTGAGCTGCAGAGCCAGTCAA
AGTGTAAGTTACATGAACTGGTACCAGCAGAAGCCGGGCAA
GGCACCCAAAAGATGGATTTATGACACATCCAAAGTGGCTT
CTGGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACC
GACTACTCTCTCACAATCAACAGCTTGGAGGCTGAAGATGC
TGCCACTTATTACTGCCAACAGTGGAGTAGTAACCCGCTCA
CGTTCGGTGGCGGGACCAAGGTGGAGATCAAA

D) anti-CD3 (VH7/VL2)

DVQLVQSGAEVKKPGASVKV SCKASGYTFTRYTMHWVR-
QAPGQGLEWIGYINPSRGYT-
NYNQKFKDRVITITDKSTSTAYMELSSLRSED TAVYYCA-
RYYDDHYCLDYWGQGTTVT VSSGEGTSTGSGGSGGSGGADD
IVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPG-
KAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAE-
DAATYYCQQWSSNPLTFGGGTKVEIK

Figure 6**E) anti-CD3 (VH7/VL3)**

GACGTCCAACCTGGTGCAGTCAGGGGCTGAAGTGAAAA-
AACCTGGGGCCTCAGTGAAGGTGTCCTG-
CAAGGCTTCTGGCTACACCTTTACTAGGTACACGATG-
CACTGGGTAAGGCAGGCACCTGGACAGGGTCTGGAATGGAT
TGGATACATTAATCCTAGCCGTGGTTATACTAATTACAAT-
CAGAAGTTCAAGGACCGCGTCACAATCACTACAGACA-
AATCCACCAGCACAGCCTACATGGAAGTGAAG-
CAGCCTGCGTTCTGAGGACACTGCAGTCTATTACTGTGCAA
GATATTATGATGATCATTACTGCCTTGACTACTGGGGC-
CAAGGCACCACGGTCACCGTCTCCTCAGGCGAAGGTAC-
TAGTACTGGTTCTGGTGGAAAGTGGAGGTTCAAGGTGGAGCA-
GACGACATTGTACTGACCCAGTCTCCAGCAACTCTGTCTCT
GTCTCCAGGGGAGCGTGCCACCCTGACCTGCAGAGC-
CAGTTCAAGTGTAAGTTACATGAACTGGTACCAGCA-
GAAGCCGGGCAAGGCACCCAAAAGATGGATTTATGACA-
CATCCAAAGTGGCTTCTGGAGTCCCTGCTCGCTTCAGTGGC
AGTGGGTCTGGGACCGACTACTCTCTCACAATCAA-
CAGCTTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAA-
CAGTGGAGTAGTAACCCGCTCACGTTCCGGTGGCGGGAC-
CAAGGTGGAGATCAAA

F) anti-CD3 (VH7/VL3)

DVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWVR-
QAPGQGLEWIGYINPSRGYT-
NYNQKFKDRVITITDKSTSTAYMELSSLRSEDVAVYYCA-
RYYDDHYCLDYWGQGTITVTVSSGEGTSTGSGGSGGSGGADD
IVLTQSPATLSLSPGERATLTCRASSSVSYMNWYQQKPG-
KAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAE-
DAATYYCQQWSSNPLTFGGGTKVEIK

Figure 7A

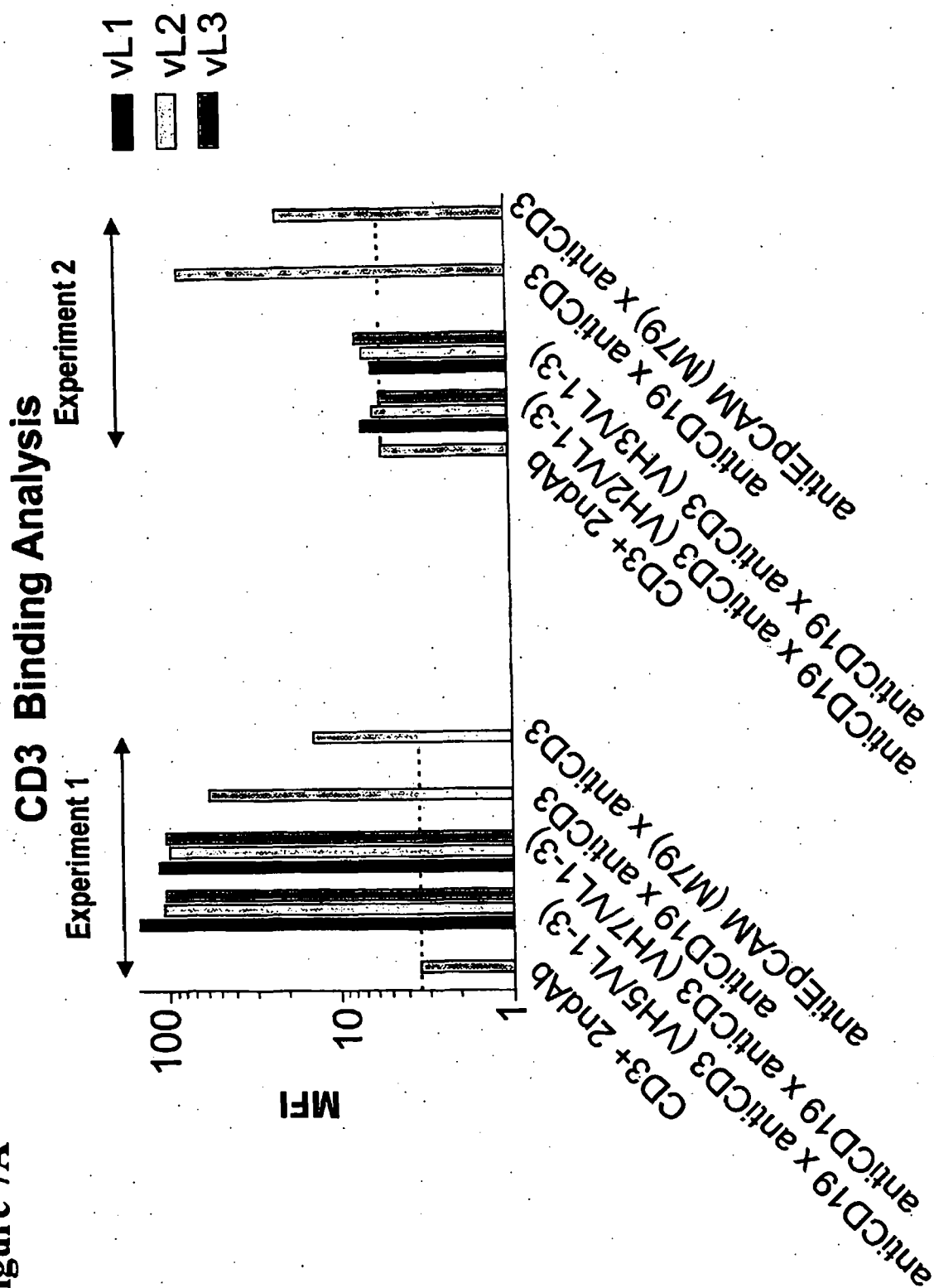


Figure 7B

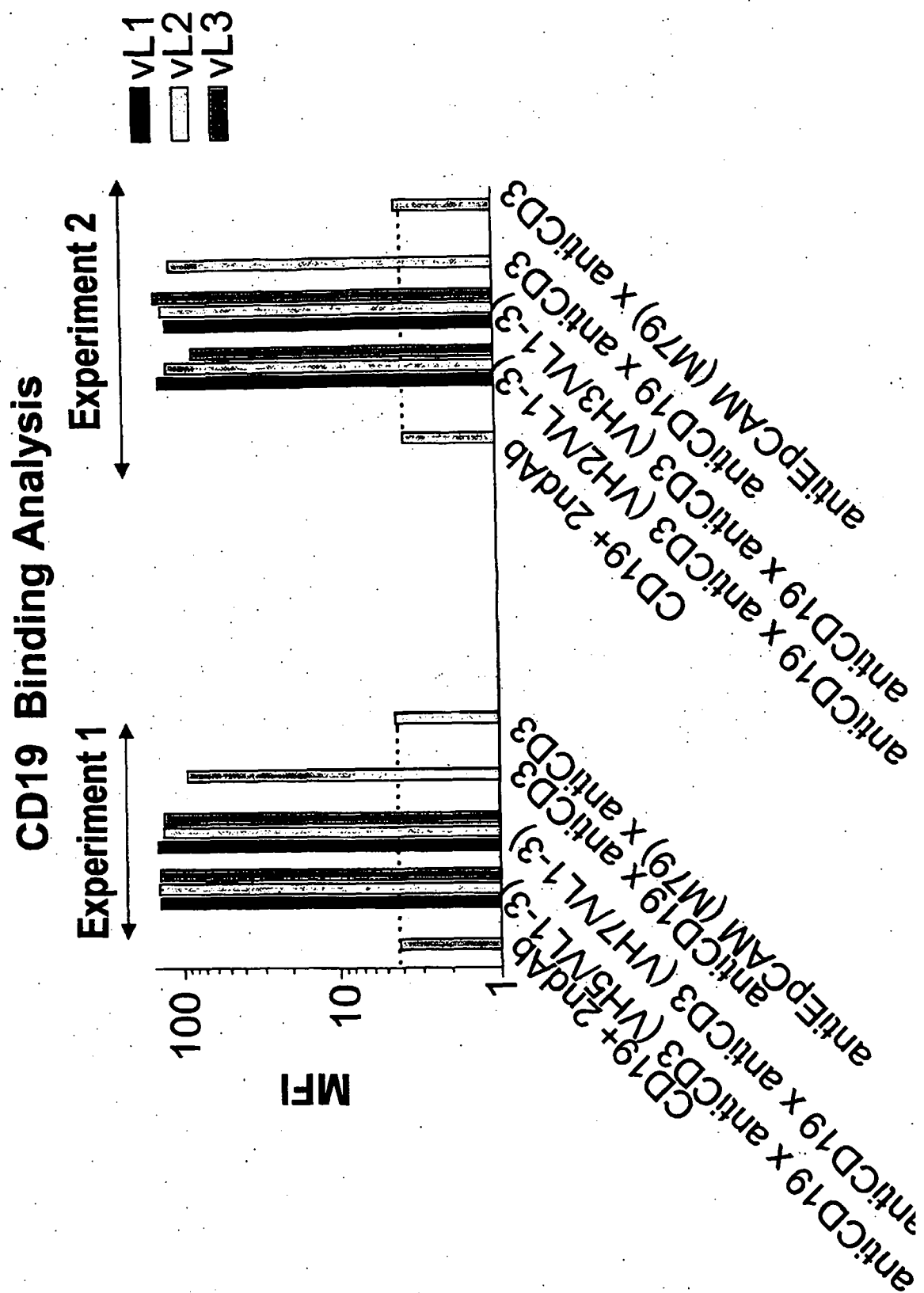


Figure 8

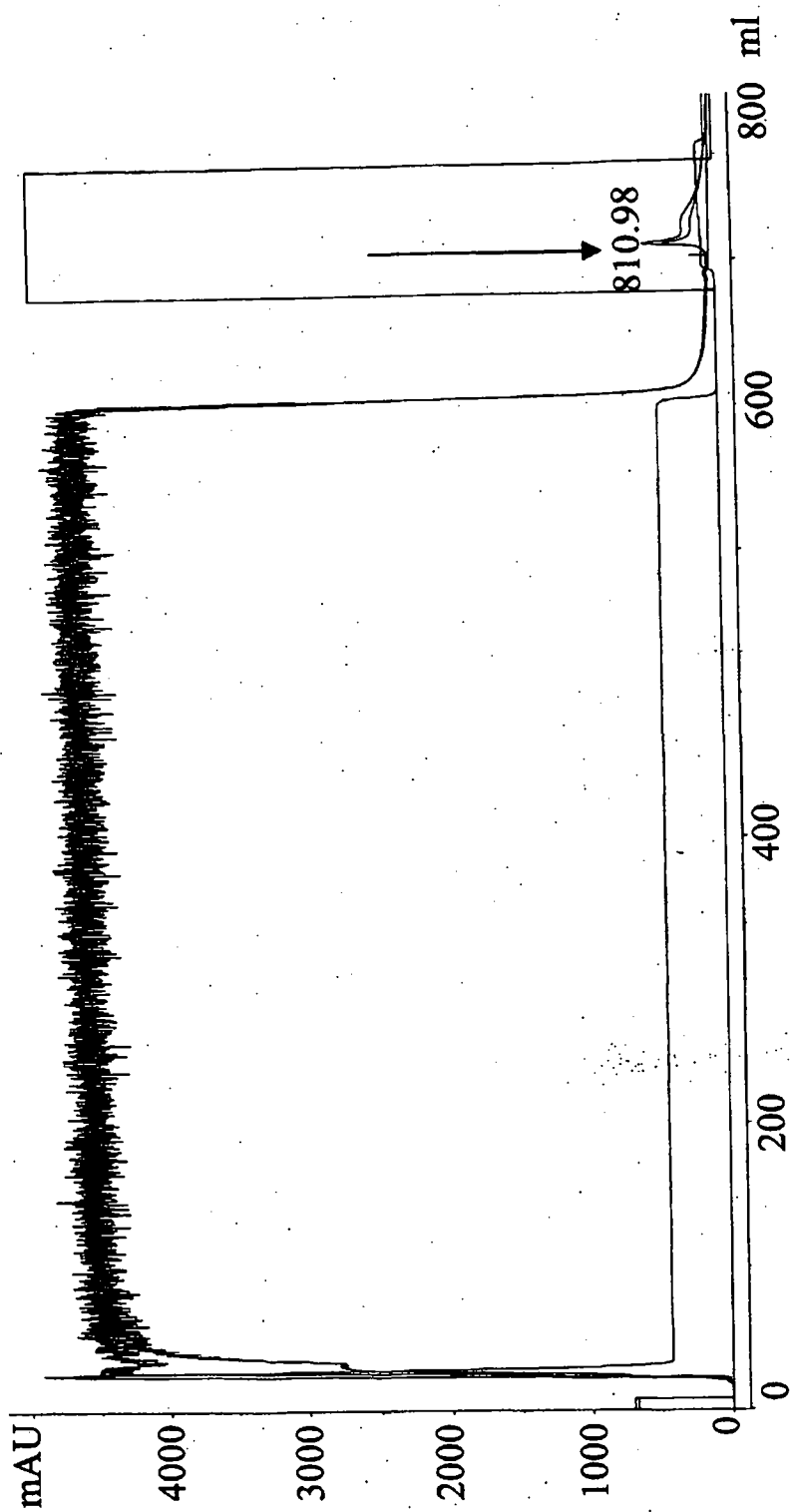


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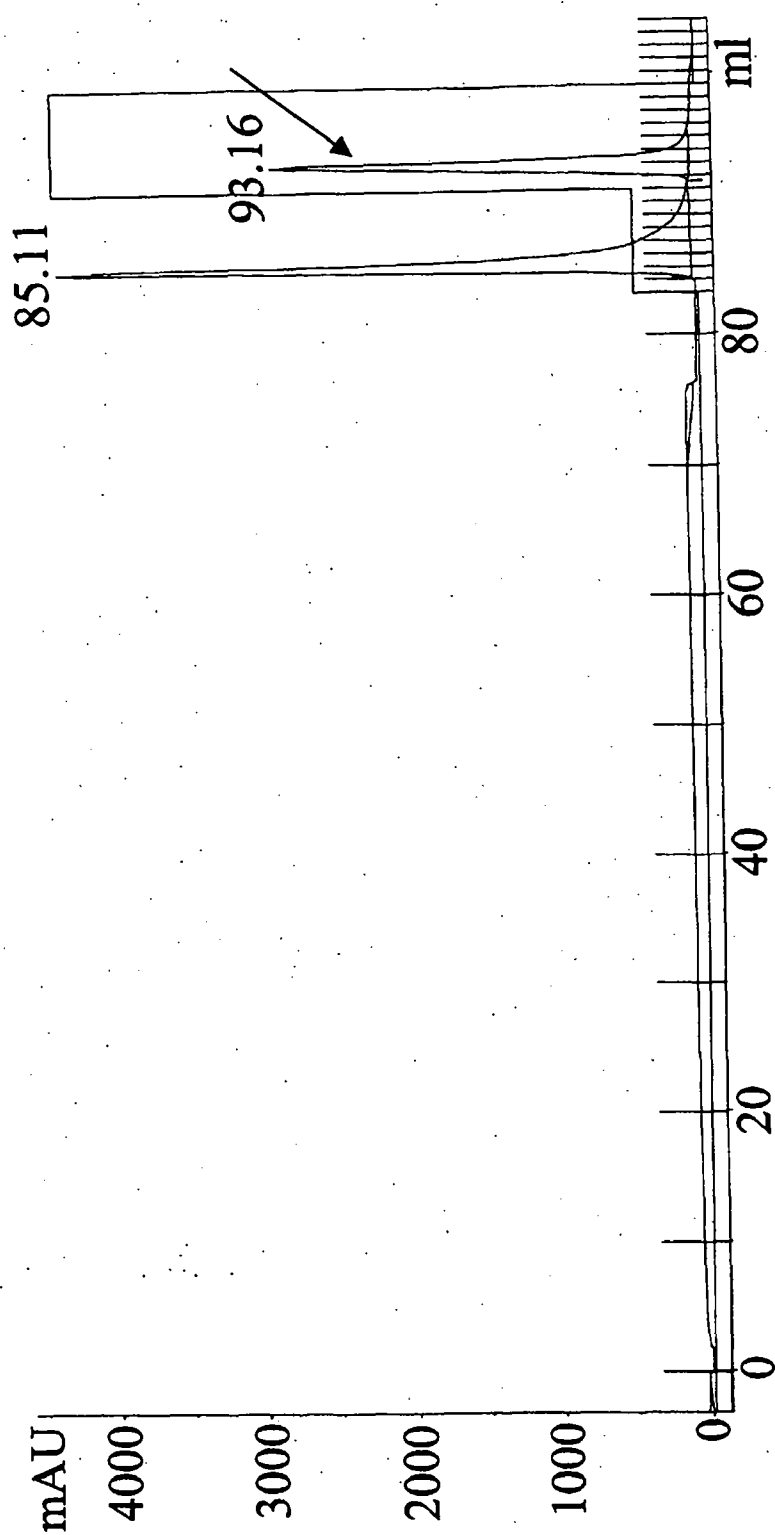


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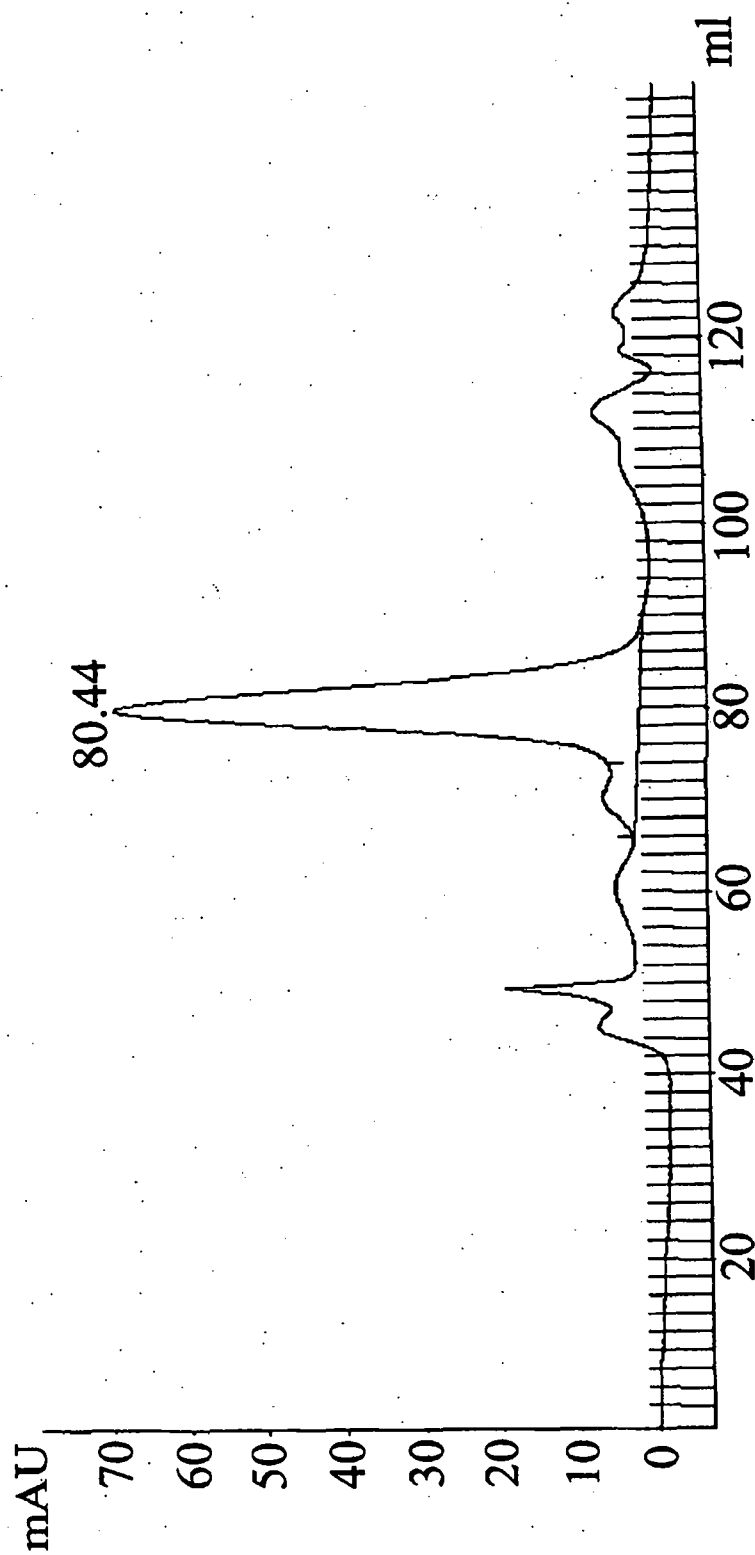


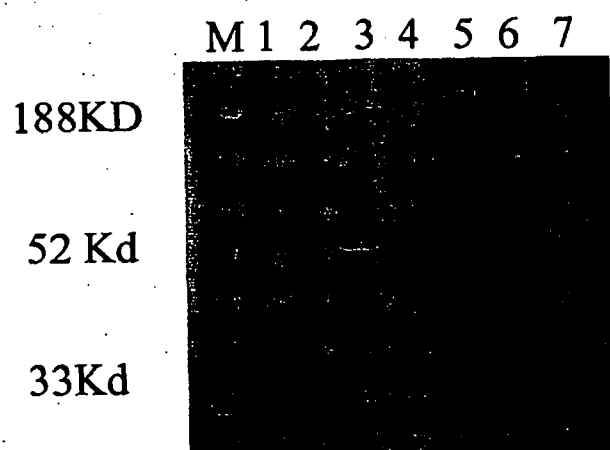
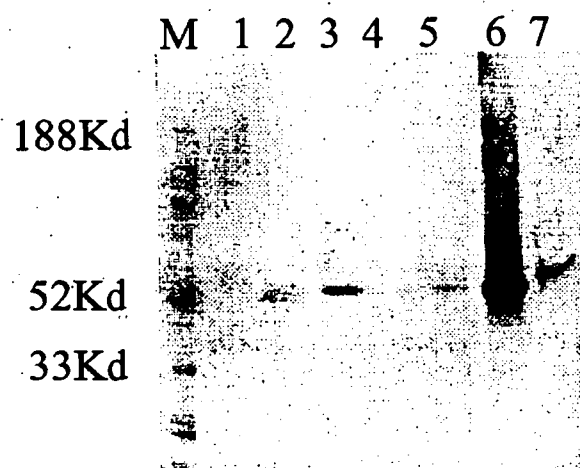
Figure 11**A)****B)**

Figure 12A

Binding on CD3

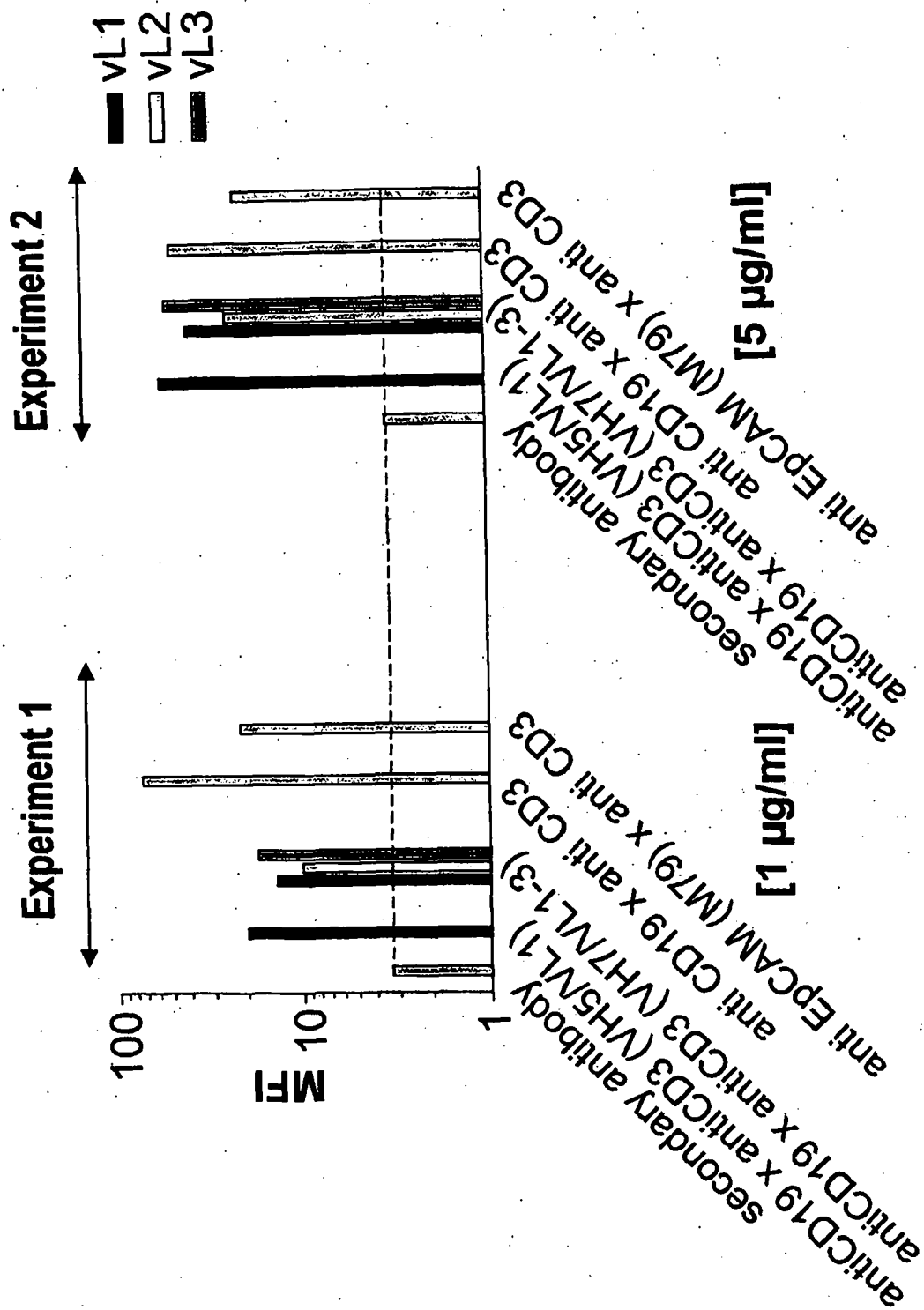


Figure 12B

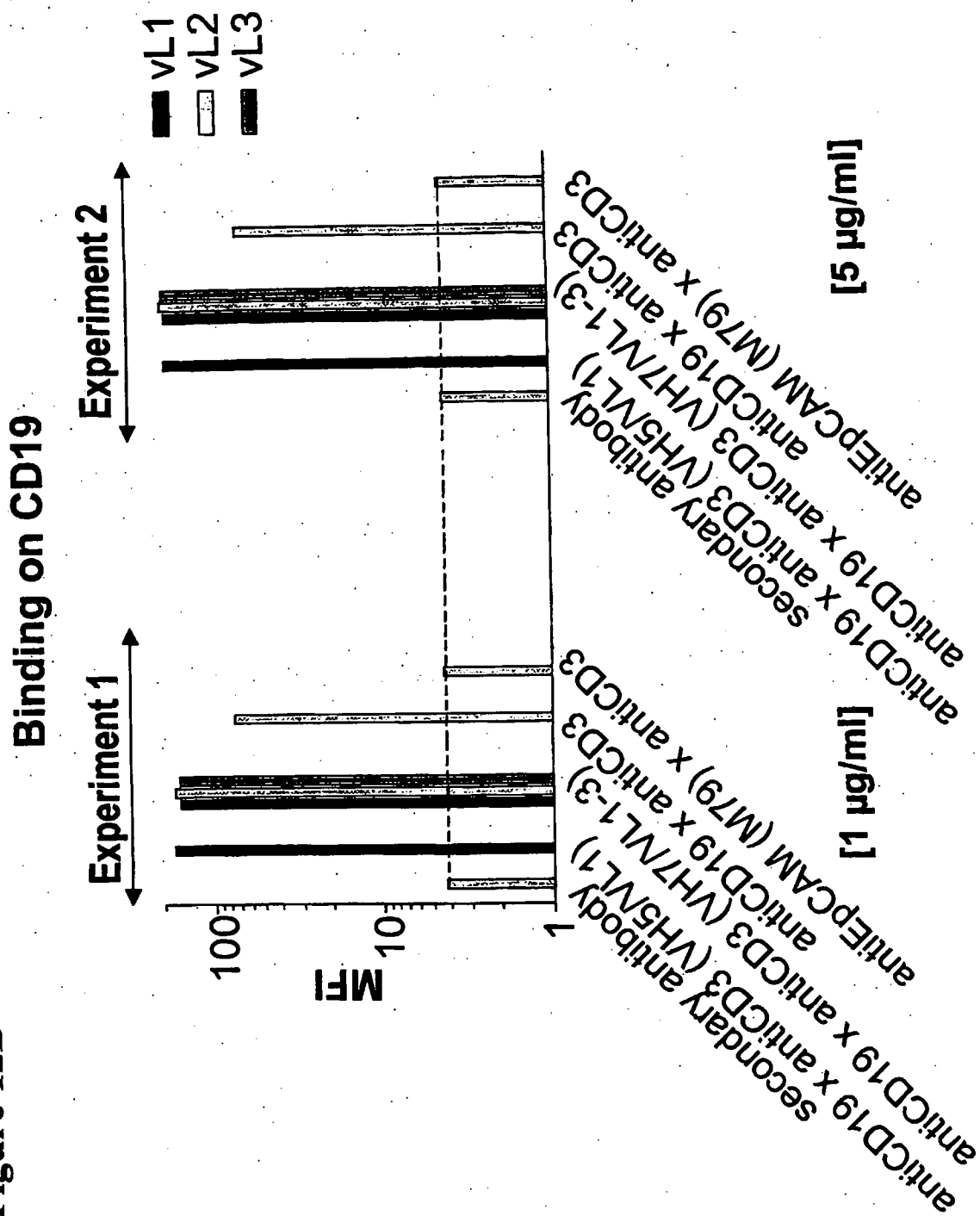


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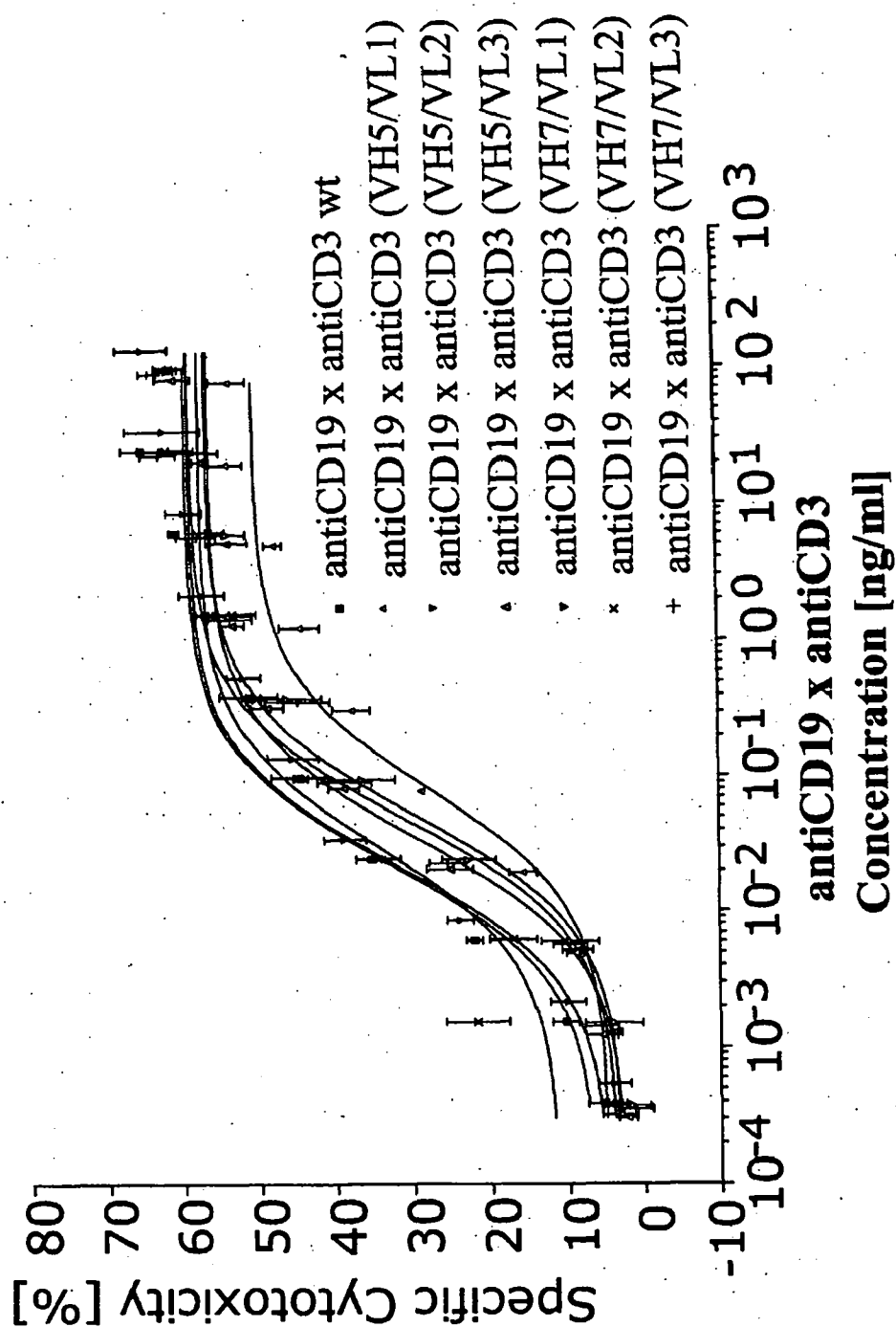


Figure 14

	FR1	CDR1	FR2	CDR2
nondeimmunized				
anti-CD3	DIKLOQSGAELARPGASVKMSCKTSGYTFETRYTMHWVKQRPQGQGLEWIGYINPSRGYTNYNQKFKD			
anti-CD3 VH5	DVQLVQSGAEVKKPGASVKVSKKASGYTFETRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSVKG			
anti-CD3 VH7	DVQLVQSGAEVKKPGASVKVSKKASGYTFETRYTMHWVRQAPGQGLEWIGYINPSRGYTNYNQKFKD			
anti-CD3 VH2	DVQLVQSGAEVKKPGASVKVSKKASGYTATRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAQKLQG			
anti-CD3 VH3	DVQLVQSGAEVKKPGASVKVSKKASGYTATRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAQKLQG			

	FR3	CDR3	FR4
nondeimmunized			
anti-CD3	KATLTIDKSSSTAYMQLSSLTSEDSAVYYCARYDDHYCLDYWGQGTTLTVSS		
anti-CD3 VH5	RFTHITIDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTTLTVSS		
anti-CD3 VH7	RVTHITIDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTTLTVSS		
anti-CD3 VH2	RVTHMTTDTSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTTLTVSS		
anti-CD3 VH3	RVTHMTTDTSTSTAYLQMNLSLKTEDAVYYCARYDDHYCLDYWGQGTTLTVSS		

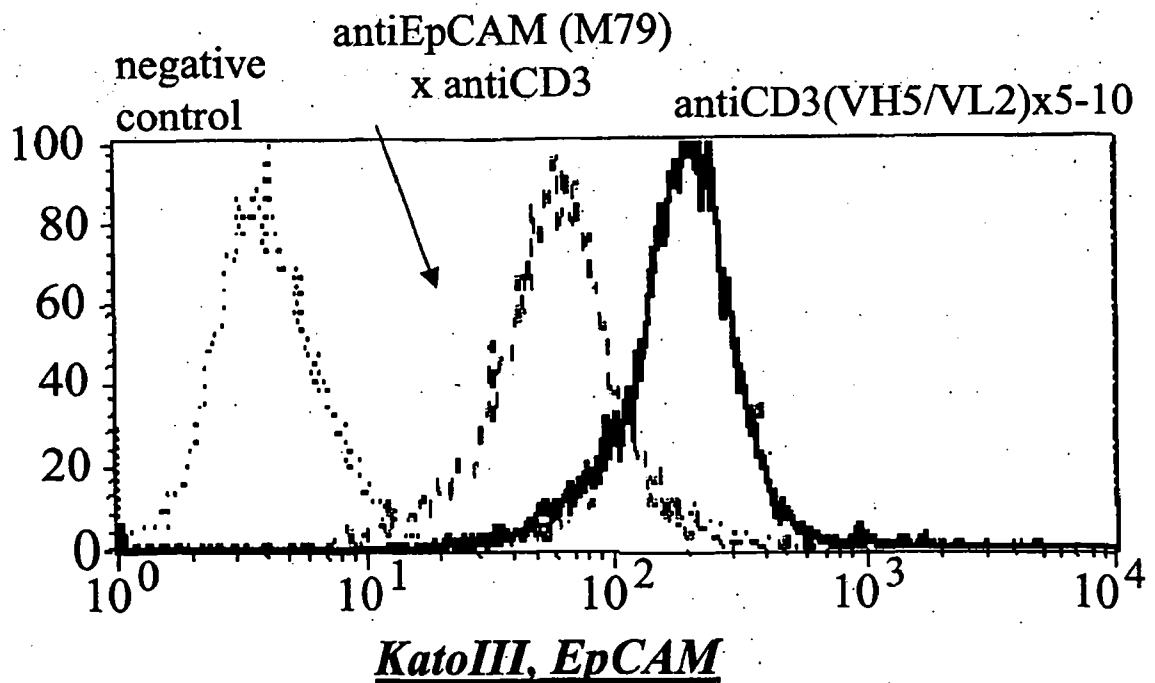
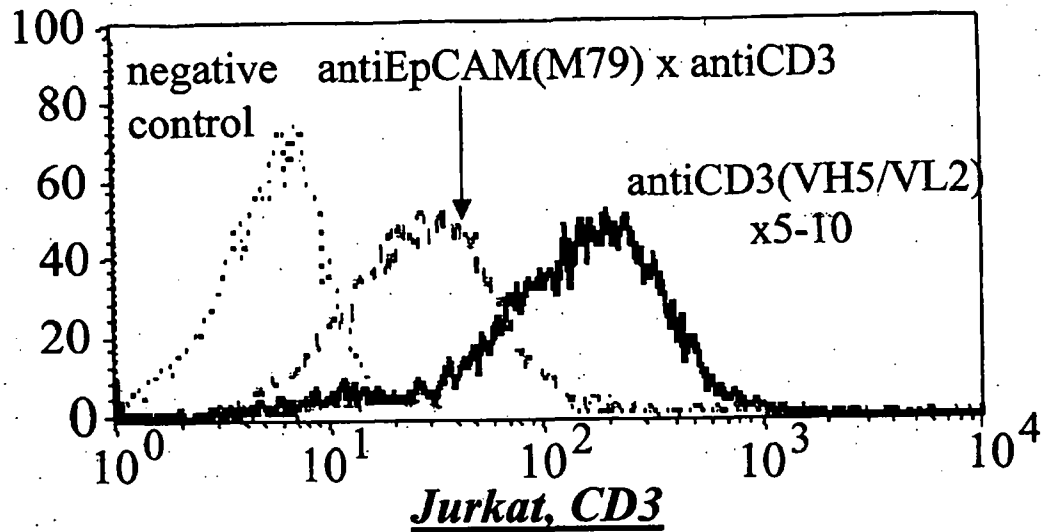
Figure 15 A**antiCD3(VH5/VL2) x 5-10 (SEQ ID NO: 37)**

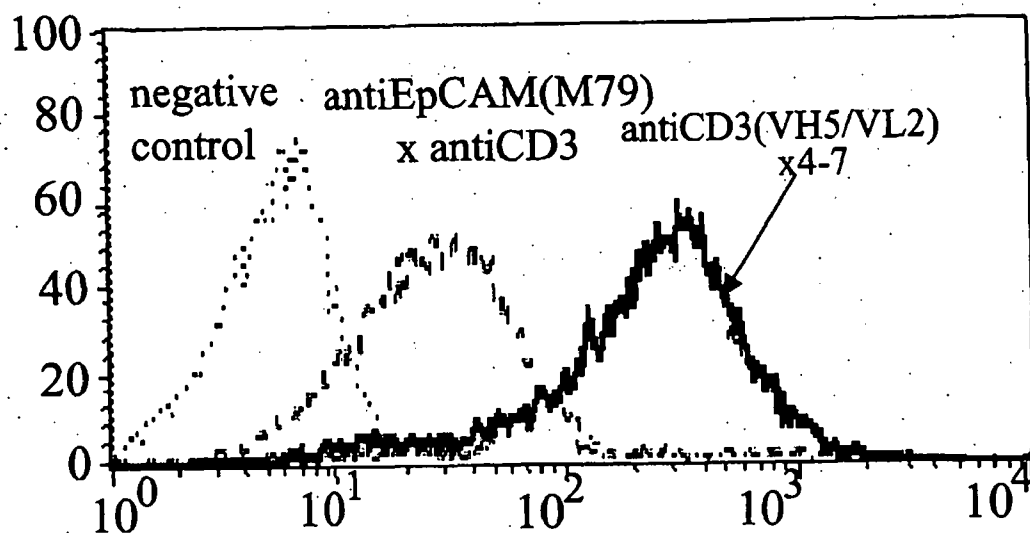
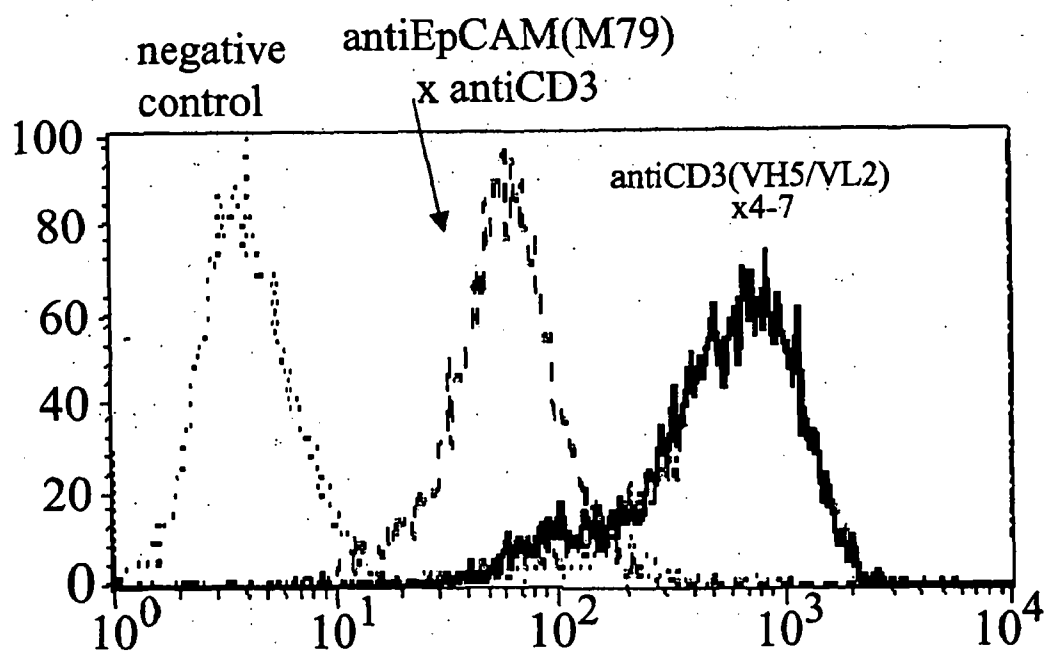
Figure 15B**antiCD3(VH5/VL2) x 4-7 (SEQ ID NO:33)****Jurkat, CD3****KatoIII, EpCAM**

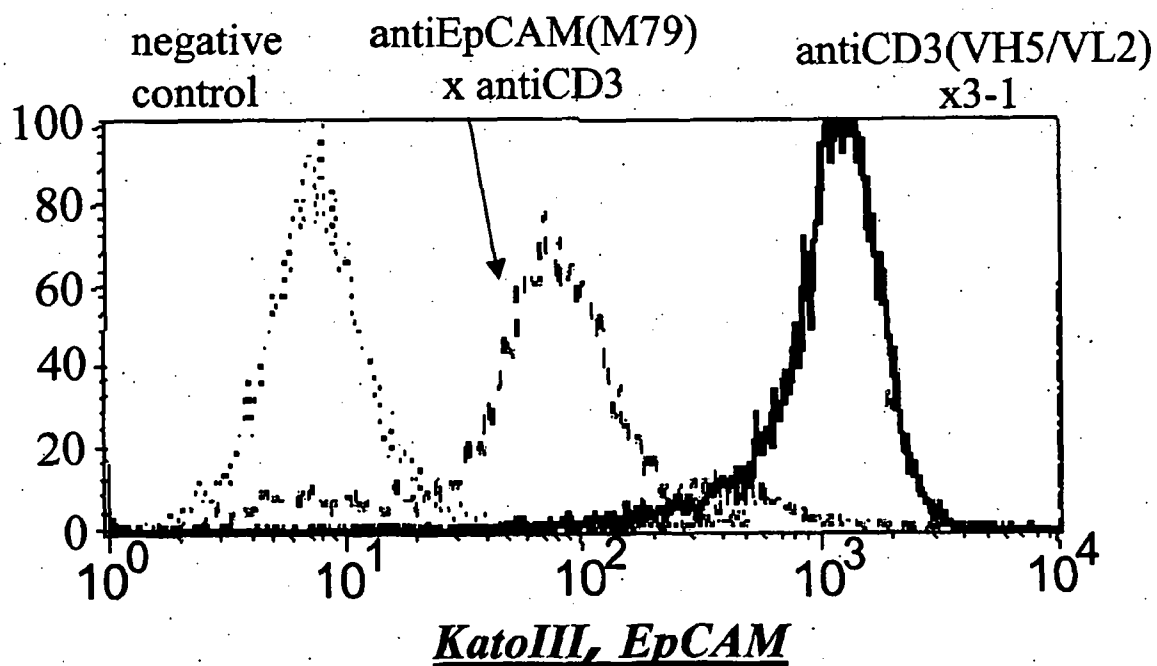
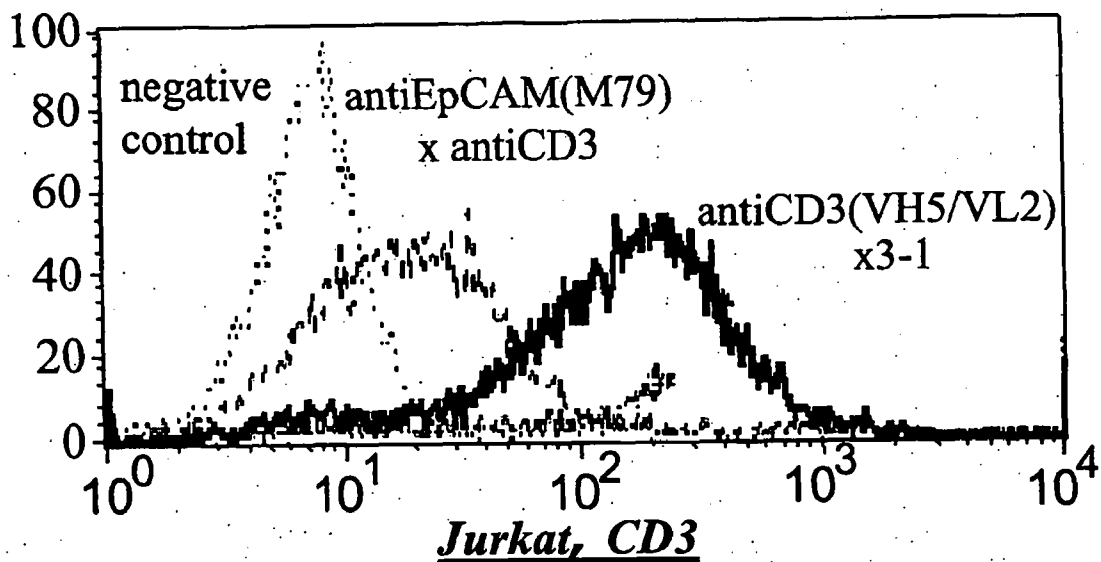
Figure 15C**antiCD3(VH5/VL2) x 3-1 (SEQ ID NO:31)**

Figure 15 D

**antiCD3(VH5/VL2) x 4-7 VL-VH
(SEQ ID NO: 35)**

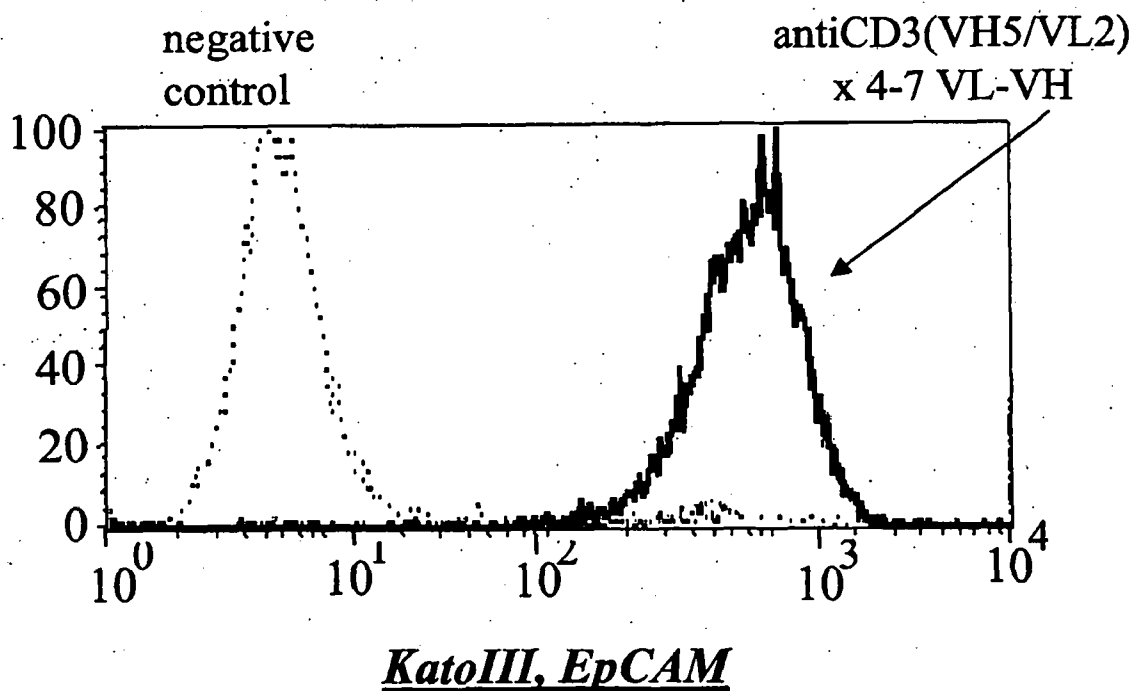
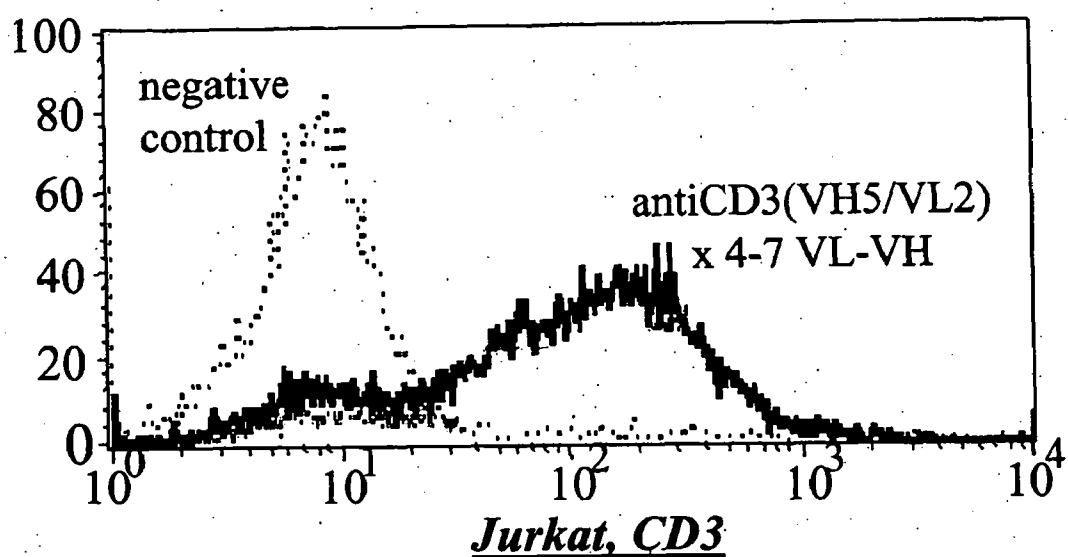


Figure 15 E

antiCD3(VH5/VL2) x 5-10 VL-VH
(SEQ ID NO:39)

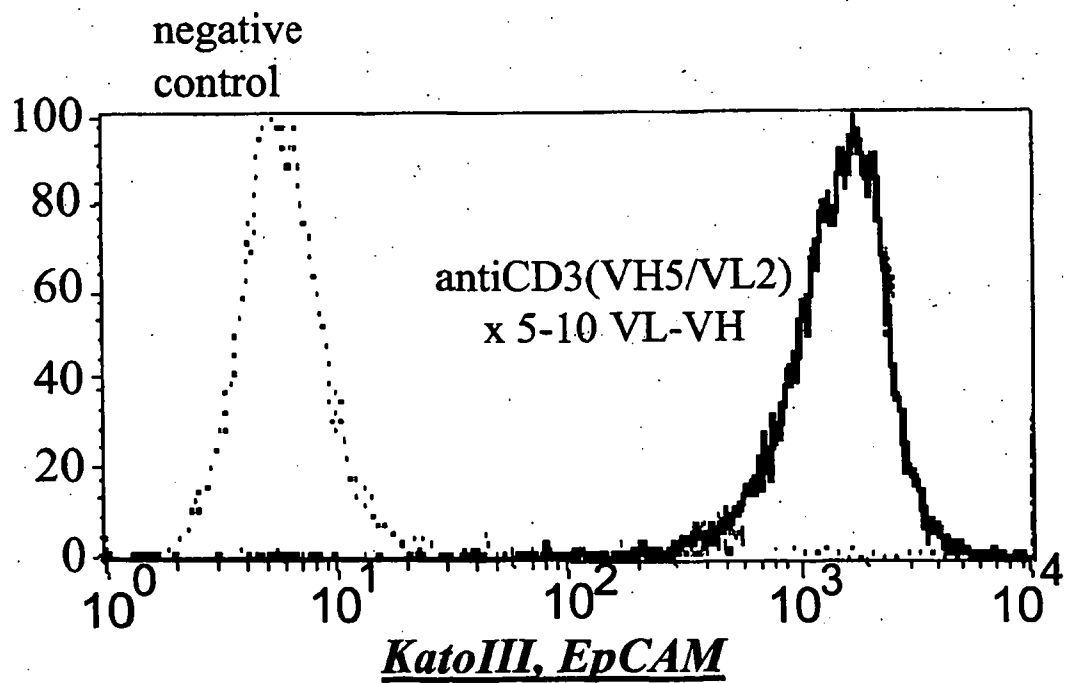
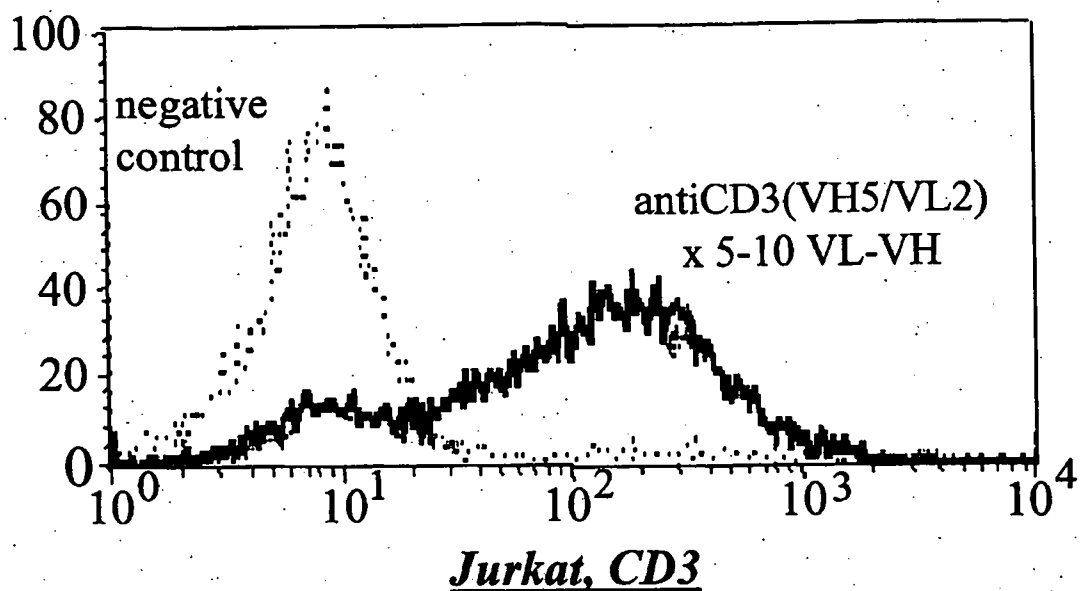
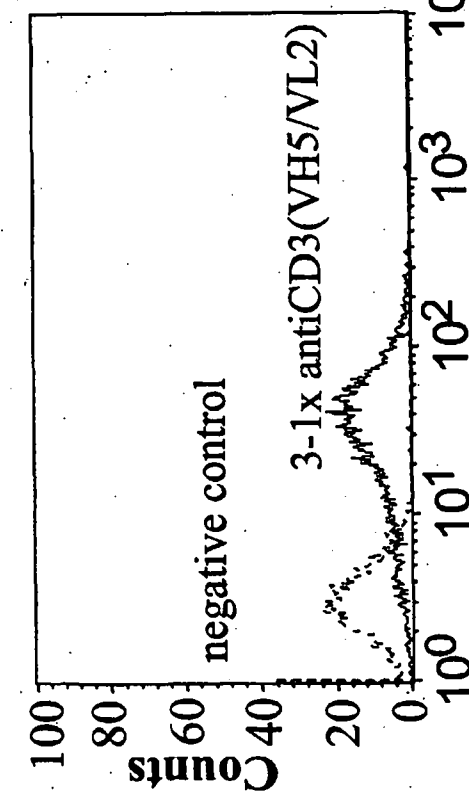
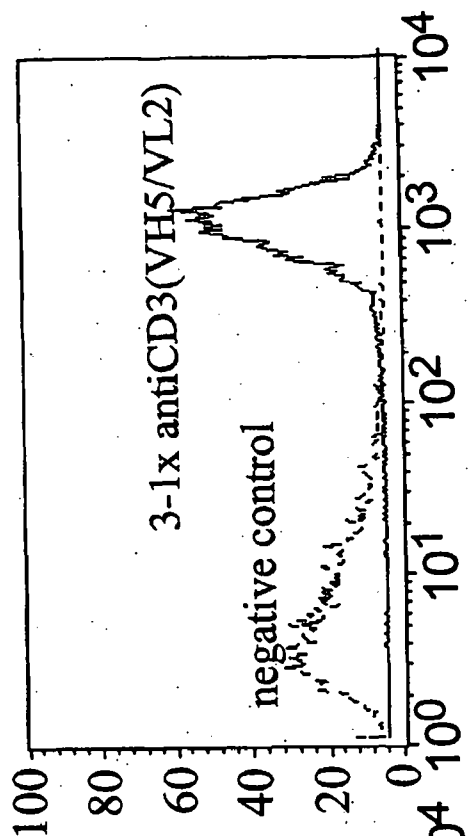


Figure 16 A

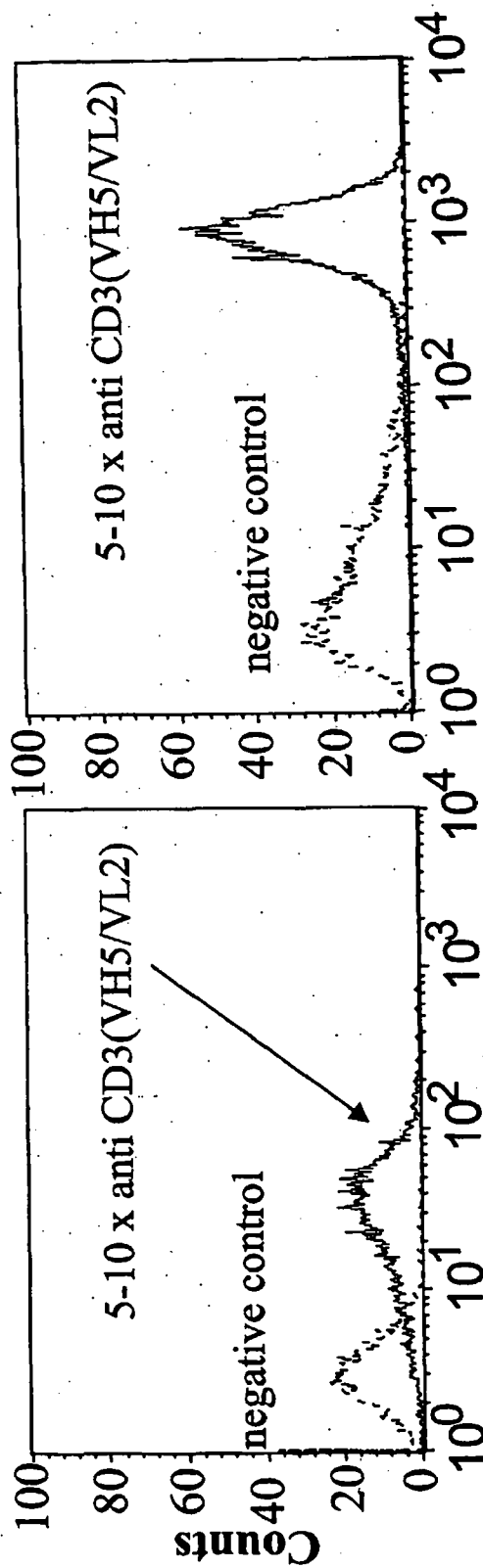
CD3 Binding (Jurkat cells)



EpCAM Binding (Kato cells)



3-1 x
antiCD3(VH5/VL2)
(SEQ ID NO: 49)

Figure 16 B**EpCAM Binding (Kato cells)****CD3 Binding (Jurkat cells)**

5-10 x antiCD3(VH5/VL2)

(SEQ ID NO:63)

Figure 17

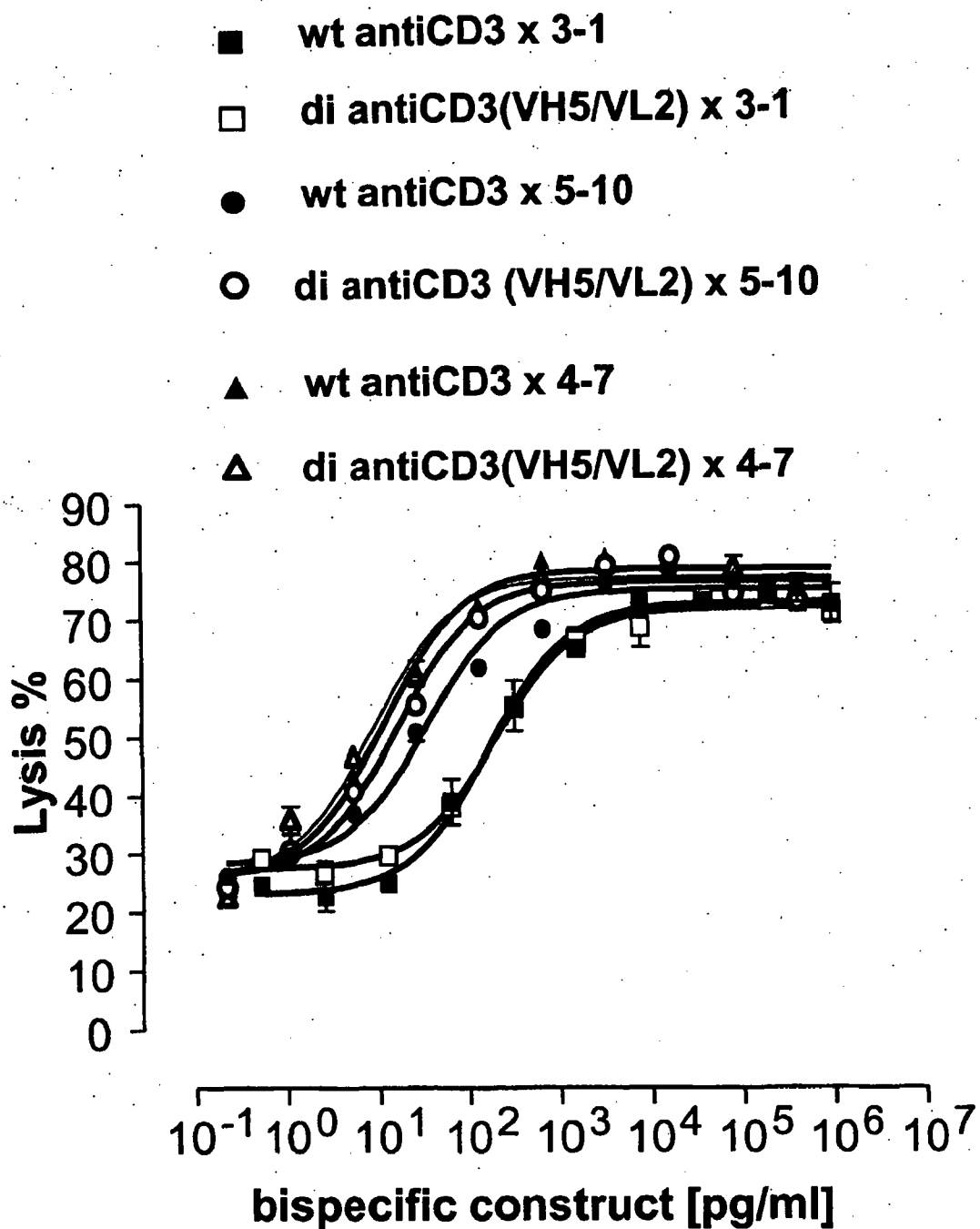
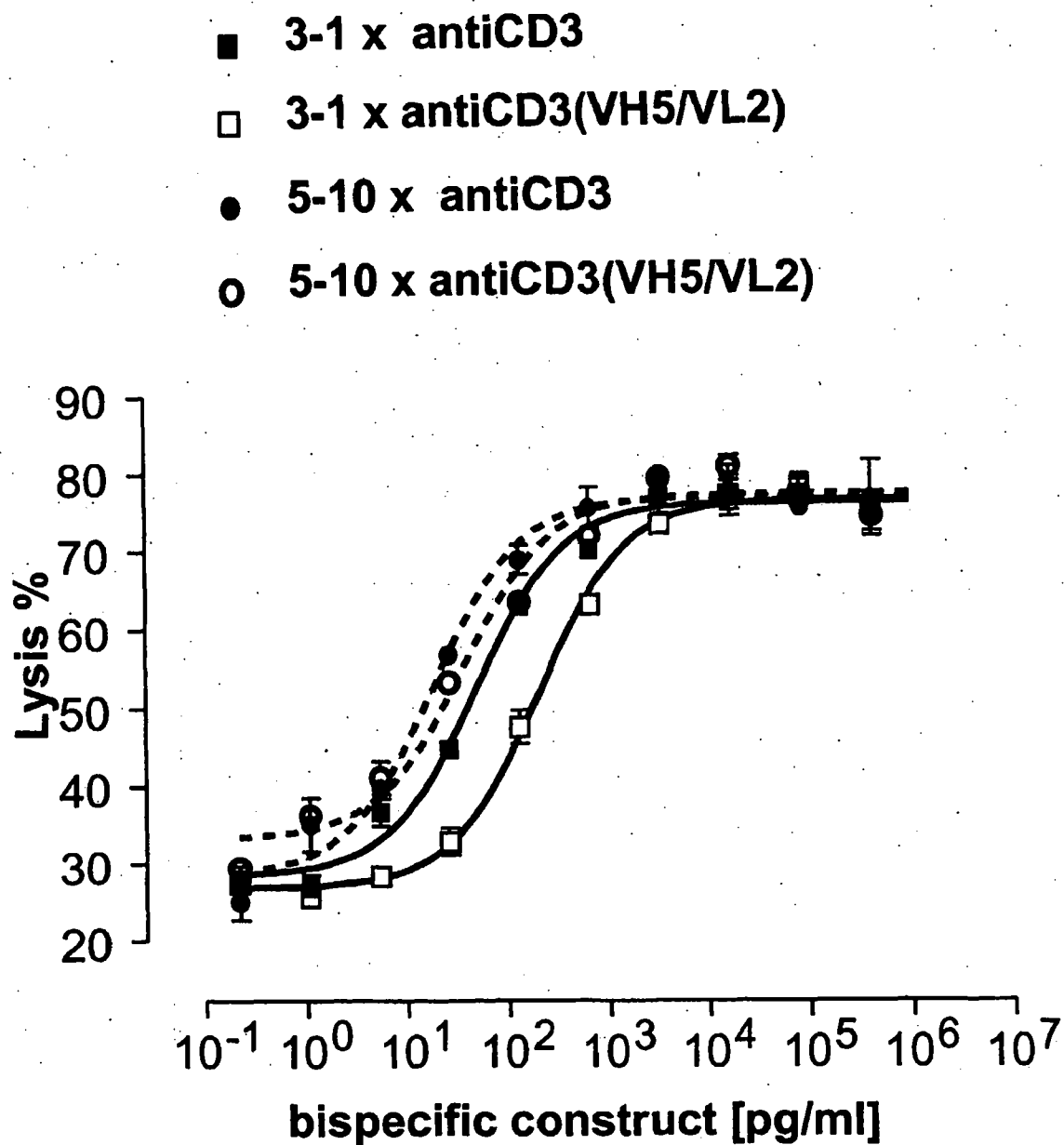


Figure 18

SEQUENCE LISTING

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 <130> G 2728 PCT
 <160> 409
 <170> PatentIn version 3.1

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 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 aatcagaagt tcaaggacaa ggccacattg actacagaca aatcctccag cacagcctac 240
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 gatgatcatt actgccttga ctactggggc caaggcacca ctctcacagt ctctcagtc 360
 gaaggtggaa gtggagggtc tgggtggaagt ggagggttcag gtggagtoga cgacattcag 420
 ctgacccagt ctccagcaat catgtctgca tctccagggg agaaggtcac catgacctgc 480
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 gagctgaaa 729

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 <213> artificial sequence

<220>
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Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile	35	40	45
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe	50	55	60
Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr	65	70	75
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys	85	90	95
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly	100	105	110
Thr Thr Leu Thr Val Ser Ser Val Glu Gly Gly Ser Gly Gly Ser Gly	115	120	125
Gly Ser Gly Gly Ser Gly Gly Val Asp Asp Ile Gln Leu Thr Gln Ser	130	135	140
Pro Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys	145	150	155
Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Ser	165	170	175
Gly Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser	180	185	190
Gly Val Pro Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser	195	200	205
Leu Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys	210	215	220
Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu	225	230	235
			240

Glu Leu Lys

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 <213> artificial sequence

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 <223> deimmunized linker

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Ala Asp

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 <212> DNA
 <213> artificial sequence

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 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
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 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
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<212> PRT
<213> artificial sequence

<220>
<223> VH2/VL1

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

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

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

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 cctggacagg gtctggaatg gattggatac attaatecta gccgtgggta tactaattac 180
 gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac 240
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 gaaggtaacta gtactgggtc tgggtgaagt ggaggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac totgtctctg tctccagggg agcgtgccac cctgagctgc 480
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 aaaagatgga tttatgacac atccaaagtg gcttctggag tcctgtctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
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Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

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

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

<210> 8
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 <212> DNA
 <213> artificial sequence

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 aaaagatgga tttatgacac atccaaagtg gcttctggag tccttgctcg cttcagtggc 600
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 gagatcaaa 729

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 <212> PRT
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 <223> VH2VL3

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

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

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

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<212> DNA
 <213> artificial sequence

<220>

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 gaagg tacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattcag 420
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 <212> PRT
 <213> artificial sequence

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<223> VH3/VL1

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
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Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

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

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

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<220>

<223> VH3/VL2

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60


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agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

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

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

<210> 14
 <211> 729
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH3/VL3

<400> 14
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg ottctggcta caccgctact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaataccta gccgtgggta tactaattac 180
 gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac 240
 ctgcaaatga acagcctgaa aactgaggac actgcagtct attactgtgc aagatattat 300

gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaaggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
 agagccagtt caagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
 gagatcaaa 729

<210> 15
 <211> 243
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH3/VL3

<400> 15

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

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

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 16
<211> 729
<212> DNA
<213> artificial sequence

<220>
<223> VH5/VL1

<400> 16
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaataccta gccgtgggta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctccctcaggc 360
gaagggtacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtgaa ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540

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aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc    600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc    660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg    720
gagatcaaaa                                         729

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<210> 17
<211> 243
<212> PRT
<213> artificial sequence

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<220>
<223> VH5/VL1

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```

<400> 17

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Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1              5              10              15

```

```

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20              25              30

```

```

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35              40              45

```

```

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50              55              60

```

```

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65              70              75              80

```

```

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85              90              95

```

```

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100             105             110

```

```

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115             120             125

```

```

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130             135             140

```

```

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145             150             155             160

```

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

<210> 18
 <211> 729
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH5/VL2

<400> 18
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcaactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaagggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtgag ttacatgaac tggtagccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcgggtggcg gaccaaggtg 720
 gagatcaaa 729

<210> 19
 <211> 243
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH5/VL2

<400> 19

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 20
<211> 729
<212> DNA
<213> artificial sequence

<220>
<223> VH5/VL3

<400> 20
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
gaaggtaacta gtactgggtc tgggtggaagt ggagggtcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
agagccagtt caagtgtgta ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcgggtggcg gaccaagggtg 720
gagatcaaa 729

<210> 21
<211> 243
<212> PRT
<213> artificial sequence

<220>

<223> VH5/VL3

<400> 21

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys

<210> 22
 <211> 729
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH7/VL1

<400> 22
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcaactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaattcta gccgtgggta tactaattac 180
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaaggctacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattcag 420
 atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
 agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tcctgtctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgtcacgt tcggtggcgg gaccaaggtg 720
 gagatcaaa 729

<210> 23
 <211> 243
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH7/VL1

<400> 23

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30
 Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60
 Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140
 Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160
 Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys

<210> 24
 <211> 729
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH7/VL2

<400> 24
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaaggtaacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
 ctgaccacgt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtgaa ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaa 729

<210> 25
 <211> 243
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH7/VL2

<400> 25

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 26
<211> 729
<212> DNA
<213> artificial sequence

<220>
<223> VH7/VL3

<400> 26
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaaggtacta gtactgggtc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
 agagccagtt caagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaa 729

<210> 27
 <211> 243
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH7/VL3

<400> 27

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Glu Ile Lys

<400> 28
cctcagacag tggttcaaag

20

<210>	29
<211>	18
<212>	DNA

<213> artificial sequence

<220>

<223> Sequencing primer

<400> 29

agccgccacg tgggcctc

18

<210> 30

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 3-1 VHVL

<400> 30

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcttgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac	180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc	360
gaagggtacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattgta	420
ctgacccagt ctccagcaac totgtctctg tctccagggg agcgtgccac cctgagctgc	480
agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg	720
gagatcaaat ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag	780
ctggtgaaac ctggggcctc agtgaagata tcttgcaagg cttctggata cgccttcact	840
aactactggc taggttgggt aaagcagagg cctggacatg gacttgagtg gattggagat	900
cttttccttg gaagtggtaa tactcactac aatgagaggt tcaggggcaa agccacactg	960
actgcagaca aatcctcgag cacagccttt atgcagctca gtagcctgac atctgaggac	1020
tctgctgtct atttctgtgc aagattgagg aactgggacg aggctatgga ctactggggc	1080
caagggacca cggtcaccgt ctctcagggt ggtggtggtt ctggcggcgg cggctccggt	1140
ggtggtggtt ctgagctcgt catgaccag tctccatctt atcttctgtc atctcctgga	1200
gaaaccatta ctattaattg cagggcaagt aagagcatta gcaaatattt agcctggtat	1260

caagagaaac ctgggaaaac taataagctt cttatctact ctggatccac ttgcaatct 1320
 ggaattccat caaggttcag tggcagtga tctggtacag atttactct caccatcagt 1380
 agcctggagc ctgaagattt tgcaatgtat tactgtcaac agcataatga atatccgtac 1440
 acgttcggag gggggaccaa gcttgagatc aaa 1473

<210> 31
 <211> 491
 <212> PRT
 <213> artificial sequence
 <220>
 <223> anti-CD3 VH5/VL2 x 3-1 VHVL
 <400> 31

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255

Ser Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Ile Ser Cys
 260 265 270

Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
 275 280 285

Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp Leu Phe Pro Gly
 290 295 300

Ser Gly Asn Thr His Tyr Asn Glu Arg Phe Arg Gly Lys Ala Thr Leu
 305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Phe Met Gln Leu Ser Ser Leu
 325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
 340 345 350

Asp Glu Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 355 360 365

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 370 375 380

Glu Leu Val Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly
 385 390 395 400

Glu Thr Ile Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Tyr
 405 410 415

Leu Ala Trp Tyr Gln Glu Lys Pro Gly Lys Thr Asn Lys Leu Leu Ile
 420 425 430

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ser Arg Phe Ser Gly
 435 440 445

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 450 455 460

Glu Asp Phe Ala Met Tyr Tyr Cys Gln Gln His Asn Glu Tyr Pro Tyr
 465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 485 490

<210> 32

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 4-7 VHVL

<400> 32

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cctggacagg gtctggaatg gattggatac attaataccta gccgtgggta tactaattac	180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc	360
gaaggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta	420
ctgaccagtc ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc	480
agagccagtc aaagtgtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tcctgtctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcgggtggcg gaccaaggtg	720

gagatcaaat ccggagggtgg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
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 aactatggtt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag 900
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 gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1440
 tgctctcaaa gtacacatgt tccgtacacg ttccggagggg ggaccaagct tgagatcaaa 1500

<210> 33
 <211> 500
 <212> PRT
 <213> artificial sequence

<220>
 <223> anti-CD3 VH5/VL2 x 4-7 VHVL

<400> 33

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
 260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
 275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
 290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu

325 330 335
 Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
 340 345 350
 Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
 355 360 365
 Val Thr Val Ser Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380
 Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
 385 390 395 400
 Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
 405 410 415
 Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
 420 425 430
 Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
 435 440 445
 Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 450 455 460
 Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
 465 470 475 480
 Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
 485 490 495
 Leu Glu Ile Lys
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<210> 34

<211> 1500

<212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 4-7 VLVH

<400> 34

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cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggg 360
gaaggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgtcacgt tcggtggcgg gaccaagggtg 720
gagatcaa at cggagggtg tggatccgag ctctgatga ccagactcc actctccctg 780
cctgtcagtc ttggagatca agcctccatc tcttgcatat ctatgcagag cctgttacac 840
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ctgatctaca aagtttccaa ccgattttct ggggtcccag acaggttcag tggcagtggg 960
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gtccctgagt ggattggaga ggtttatcct agaattggta atgcttacta caatgagaag 1320
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cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat 1440
actaactacg actggtactt cgatgtctgg ggccaaggga ccacggtcac cgtctcctca 1500

<210> 35
<211> 500
<212> PRT
<213> artificial sequence

<220>
<223> anti-CD3 VH5/VL2 x 4-7 VLVH

<400> 35

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

1	5	10	15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr	20	25	30
Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile	35	40	45
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val	50	55	60
Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr	65	70	75
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys	85	90	95
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly	100	105	110
Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly	115	120	125
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser	130	135	140
Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys	145	150	155
Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro	165	170	175
Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser	180	185	190
Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser	195	200	205
Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys	210	215	220
Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val	225	230	235
			240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
 245 250 255

Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
 260 265 270

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
 275 280 285

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
 290 295 300

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
 305 310 315 320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
 325 330 335

Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
 340 345 350

Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
 355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 370 375 380

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 420 425 430

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 485 490 495

Thr Val Ser Ser
 500

<210> 36
 <211> 1491
 <212> DNA
 <213> artificial sequence

<220>
 <223> anti-CD3 VH5/VL2 x 5-10 VHVL

<400> 36
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 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaaggtaacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggtga agatgctgcc 660
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 aactactggc taggttgggt aaagcagagg cctggacatg gacttgagtg gattggagat 900
 attttcctg gaagtggtaa tatccactac aatgagaagt tcaagggcaa agccacactg 960
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 caagggacca cggtcaccgt ctctcagggt ggtggtggtt ctggcggcgg cggctccggt 1140
 ggtggtggtt ctgagctcgt gatgacacag tctccatcct ccctgactgt gacagcagga 1200
 gagaagggtca ctatgagctg caagtccagt cagagtctgt taaacagtgg aaatcaaaag 1260

aactacttga cctggtacca gcagaaacca gggcagcctc cttaaactgtt gatctactgg 1320
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 ttcaactctca ccatcagcag tgtgcaggct gaagacctgg cagtttatta ctgtcagaat 1440
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<210> 37
 <211> 497
 <212> PRT
 <213> artificial sequence

<220>
 <223> anti-CD3 VH5/VL2 x 5-10 VHVL

<400> 37

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255

Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Ile Ser Cys
 260 265 270

Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
 275 280 285

Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp Ile Phe Pro Gly
 290 295 300

Ser Gly Asn Ile His Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu
 325 330 335

Thr Phe Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
 340 345 350

Asp Glu Pro Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 355 360 365

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 370 375 380

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 385 390 395 400

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 405 410 415

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 420 425 430

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 435 440 445

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 450 455 460

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 465 470 475 480

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 485 490 495

Lys

<210> 38
 <211> 1491
 <212> DNA
 <213> artificial sequence

<220>
 <223> anti-CD3 VH5/VL2 x 5-10 VLVH

<400> 38
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 cctggacagg gtctggaatg gattggatac attaataccta gccgtgggta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcacctg ctctcaggc 360
 gaaggctacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtaag ttacatgaac tggtagcagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600

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agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
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gagatcaaat ccggagggtg tggatccgag ctctgatga cacagtctcc atcctccctg 780
actgtgacag caggagagaa ggtcactatg agctgcaagt ccagtcagag tctgttaaac 840
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ctgttgatct actgggcata cactagggaa tctggggctc ctgatcgctt cacaggcagt 960
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aagttcaagg gcaaagccac actgactgca gacaaatctt cgagcacagc ctatatgcag 1380
ctcagtagcc tgacatttga ggactctgct gtctatttct gtgcaagact gaggaactgg 1440
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<210> 39

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH5/VL2 x 5-10 VLVH

<400> 39

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Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10          15

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20           25           30

```

```

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35           40           45

```

```

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50           55           60

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```

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65           70           75           80

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Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser
245 250 255

Pro Ser Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys
260 265 270

Lys Ser Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu
275 280 285

Thr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
290 295 300

Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser

305 310 315 320
 Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu
 325 330 335
 Asp Leu Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr
 340 345 350
 Phe Gly Ala Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly
 355 360 365
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 370 375 380
 Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Ile Ser Cys
 385 390 395 400
 Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
 405 410 415
 Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp Ile Phe Pro Gly
 420 425 430
 Ser Gly Asn Ile His Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 435 440 445
 Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu
 450 455 460
 Thr Phe Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
 465 470 475 480
 Asp Glu Pro Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 485 490 495

Ser

<210> 40
 <211> 35
 <212> DNA
 <213> artificial sequence

 <220>
 <223> DI anti-CD3 K52VHBSrGI

<400> 40
aggtgtacac tccgacgtcc aactggtgca gtcag 35

<210> 41
<211> 30
<212> DNA
<213> artificial sequence

<220>
<223> DI anti-CD3 52VLBspEI

<400> 41
aatccggatt tgatctccac cttggtcccg 30

<210> 42
<211> 51
<212> DNA
<213> artificial sequence

<220>
<223> 4-7 VH GS15 FOR

<400> 42
ggcggcgggcg gctccggtgg tgggtgttct gaggtgcagc tgctcgagca g 51

<210> 43
<211> 53
<212> DNA
<213> artificial sequence

<220>
<223> 4-7 VH SalI REV

<400> 43
ttttaagtgc acctaagtat gatgatgatg atgtgaggag acggtgaccg tgg 53

<210> 44
<211> 49
<212> DNA
<213> artificial sequence

<220>
<223> 510VLBspEI

<400> 44
ctgaaatccg gaggtggtgg atccgagctc gtgatgacac agtctccat 49

<210> 45
<211> 53
<212> DNA
<213> artificial sequence

<220>
<223> 510VLGS15REV

<400> 45
ggagccgccc cccccagaac caccaccacc ttgatctca agcttggtcc cag 53

<210> 46
<211> 49
<212> DNA
<213> artificial sequence

<220>
<223> 510VHGS15

<400> 46
ggcggcggcg gctccggtgg tgggtggtct gaggtgcagc tgctcgagc 49

<210> 47
<211> 53
<212> DNA
<213> artificial sequence

<220>
<223> 510VHSA1REV

<400> 47
ttttaagtcg acctaatgat gatgatgatg atgtgaggag acggtgaccg tgg 53

<210> 48
<211> 1518
<212> DNA
<213> artificial sequence

<220>
<223> 3-1(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 48
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt aactccgag 60
ctcgtcatga cccagtctcc atcttatctt gctgcatctc ctggagaaac cattactatt 120
aattgcaggg caagtaagag cattagcaaa tathtagcct ggtatcaaga gaaacctggg 180
aaaactaata agcttcttat ctactctgga tccactttgc aatctggaat tccatcaagg 240
ttcagtggca gtggatctgg tacagatttc actctcacca tcagtagcct ggagcctgaa 300
gattttgcaa tgtattactg tcaacagcat aatgaatata cgtacacgtt cggagggggg 360
accaagcttg agatcaaagg tgggtggtgg tctggcggcg gcggctccgg tgggtggtgg 420
tctgaggtgc agctgctcga gcagtctgga gctgagctgg tgaaacctgg ggcctcagt 480
aagatatcct gcaaggcttc tggatacgcc ttcactaact actggctagg ttgggtaaag 540
cagaggcctg gacatggact tgagtggatt ggagatcttt tccctggaag tggtataact 600
cactacaatg agaggttcag gggcaaagcc aactgactg cagacaaatc ctcgagcaca 660

gcctttatgc agctcagtag cctgacatct gaggactctg ctgtctatct ctgtgcaaga 720
 ttgaggaact gggacgaggc tatggactac tggggccaag ggaccacggt caccgtctcc 780
 tccggaggtg gtggctccga cgtccaactg gtgcagtcag gggctgaagt gaaaaaacct 840
 ggggcctcag tgaaggtgtc ctgcaaggct tctggctaca cctttactag gtacacgatg 900
 cactgggtaa ggcaggcacc tggacagggt ctggaatgga ttggatacat taatcctagc 960
 cgtgggtata ctaattacgc agacagcgtc aagggccgct tcacaatcac tacagacaaa 1020
 tccaccagca cagcctacat ggaactgagc agcctgcgtt ctgaggacac tgcaacctat 1080
 tactgtgcaa gatattatga tgatcattac tgccttgact actggggcca aggcaccacg 1140
 gtcaccgtct cctcaggcga aggtactagt actggttctg gaggttcagg tggagcagac 1200
 gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 1260
 ctgagctgca gagccagtca aagtgtagt tacatgaact ggtaccagca gaagccgggc 1320
 aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctgcg 1380
 ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 1440
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 1500
 accaaggtgg agatcaaa 1518

<210> 49
 <211> 506
 <212> PRT
 <213> artificial sequence

<220>
 <223> 3-1(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 49

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Glu Leu Val Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala
 20 25 30

Ser Pro Gly Glu Thr Ile Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile
 35 40 45

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

Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ser Arg

65		70		75		80
Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser						
		85		90		95
Leu Glu Pro Glu Asp Phe Ala Met Tyr Tyr Cys Gln Gln His Asn Glu						
		100		105		110
Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly						
		115		120		125
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln						
		130		135		140
Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val						
		145		150		155
Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu						
		165		170		175
Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly Asp						
		180		185		190
Leu Phe Pro Gly Ser Gly Asn Thr His Tyr Asn Glu Arg Phe Arg Gly						
		195		200		205
Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Phe Met Gln						
		210		215		220
Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg						
		225		230		235
Leu Arg Asn Trp Asp Glu Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr						
		245		250		255
Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln						
		260		265		270
Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys						
		275		280		285
Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg						
		290		295		300

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
 305 310 315 320

Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
 325 330 335

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
 340 345 350

Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
 355 360 365

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 370 375 380

Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ala Asp
 385 390 395 400

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 405 410 415

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 420 425 430

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 435 440 445

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 450 455 460

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 465 470 475 480

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 485 490 495

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 500 505

<210> 50
 <211> 60
 <212> DNA
 <213> artificial sequence

<220>
 <223> Me83

<400> 50
ggttctggcg gcggcggctc cgggtggtgt ggttctgagg tgcagctgct cgacagtctg 60

<210> 51
<211> 41
<212> DNA
<213> artificial sequence

<220>
<223> Me84

<400> 51
gtgctccgga ggagacggtg accgtggtcc cttggcccca g 41

<210> 52
<211> 53
<212> DNA
<213> artificial sequence

<220>
<223> Me90

<400> 52
ccggagccgc cgccgccaga accaccacca cctttgatct caagcttggt ccc 53

<210> 53
<211> 52
<212> DNA
<213> artificial sequence

<220>
<223> Me91a

<400> 53
ggattgtaca ctccgagctc gtcattgccc agtctccatc ttatcttgct gc 52

<210> 54
<211> 1560
<212> DNA
<213> artificial sequence

<220>
<223> 3-5(VL-VH)xanti-CD3 (VH(5)-VL(2))

<400> 54
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt aactccgcg 60
cgcgagctcg tgatgaccca gactccactc tccctgcctg tcagtcttgg agatcaagcc 120
tccatctctt gcagatctag tcagagcctt gtacacagta atggaaacac ctatttacat 180
tggtacctgc agaagccagg ccagtctcca aagctcctga tctacaaagt ttccaaccga 240
ttttctgggg tcccagacag gttcagtggc agtggatcag ggacagattt cacactcaag 300

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atcagcagag tggaggctga ggatctggga gtttatttct gctctcaaag tacacatgtt 360
ccgtacacgt tcggaggggg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 420
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 480
gtaaggcctg ggacttcagt gaagctgtcc tgcaaggctt ctggctacac cttcacaagc 540
tatggtttaa gctgggtgaa gcagagaact ggacagggcc ttgagtggat tggagaggtt 600
tattcctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 660
gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacatc tgaggactct 720
gcggtctatt tctgtgcaag acggggatcc tacggtagta actacgactg gtacttcgat 780
gtctggggcc aagggaccac ggtcacctgc tctccggag gtggtggctc cgacgtccaa 840
ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtcctgcaag 900
gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 960
ggtctggaat ggattggata cattaatcct agccgtgggt atactaatta cgcagacagc 1020
gtcaagggcc gttcacaat cactacagac aaatccacca gcacagccta catggaactg 1080
agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1140
tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctcagg cgaaggtaact 1200
agtactgggt ctggtggaag tggaggttca ggtggagcag acgacattgt actgaccag 1260
tctccagcaa ctctgtctct gtctccaggg gagcgtgcc aacctgagctg cagagccagt 1320
caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg 1380
atztatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 1440
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1500
tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1560

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<210> 55
 <211> 520
 <212> PRT
 <213> artificial sequence

<220>
 <223> 3-5(VL-VH)xanti-CD3 (VH(5)-VL(2))

<400> 55

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Ala Arg Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu

Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Gly Ser Asn Tyr Asp
245 250 255

Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 260 265 270

Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val
 275 280 285

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
 290 295 300

Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Gln
 305 310 315 320

Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn
 325 330 335

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser
 340 345 350

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
 355 360 365

Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp
 370 375 380

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr
 385 390 395 400

Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile
 405 410 415

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
 420 425 430

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
 435 440 445

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 450 455 460

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 465 470 475 480

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 485 490 495

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 500 505 510

Gly Gly Thr Lys Val Glu Ile Lys
 515 520

<210> 56
 <211> 40
 <212> DNA
 <213> artificial sequence

<220>
 <223> Me81

<400> 56
 ggatgcgcgc gagctcgtga tgaccacagac tccactctcc 40

<210> 57
 <211> 1545
 <212> DNA
 <213> artificial sequence

<220>
 <223> 4-1 (VL-VH)xanti-CD3 (VH(5)-VL(2)).

<400> 57
 atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt aactccgag 60
 ctctgtgatga cacagtctcc atcctccctg agtgtgtcag caggagagaa ggtcactatg 120
 agctgcaagt ccagtcagag tctgttaaac agtggaatc aaaagaacta cttggcctgg 180
 taccagcaga aaccagggca gcctcctaaa ctgttgatct acggggcacc cactagggaa 240
 tctgggggtcc ctgatcgctt cacaggcagt ggatctggaa cagatttcac tctcaccatc 300
 agcagtgtgc aggctgaaga cctggcagtt tattactgtc agaatgatta tagttatccg 360
 tacacgttcg gaggggggac caagcttgag atcaaaggtg gtggtggttc tggcggcggc 420
 ggctccggtg gtggtggttc tgaggtgcag ctgctcgagc agtctggagc tgagctggta 480
 aggcctggga cttcagtga gatatcctgc aaggcttctg gatacgctt cactaactac 540
 tggctaggtt ggggttaagca gaggcctgga catggacttg aatgggttgg agatattttc 600
 cctggaagtg gtaatgctca ctacaatgag aagttcaagg gcaaagccac actgactgca 660
 gacaagtcct cgtacacagc ctatatgcag ctcatagacc tgacatctga ggactctgct 720
 gtctatttct gtgcaagatt gcggaactgg gacgaggcta tggactactg gggccaaggg 780
 accacggtca ccgtctctc cgagggtggt ggctccgacg tccaactggt gcagtcaggg 840
 gctgaagtga aaaaacctg ggcctcagtg aaggtgtcct gcaaggcttc tggctacacc 900

ttactaggt acacgatgca ctgggtaagg caggcacctg gacagggctt ggaatggatt 960
 ggatacatta atcctagccg tgggtatact aattacgcag acagcgtcaa gggccgcttc 1020
 acaatcacta cagacaaatc caccagcaca gcctacatgg aactgagcag cctgcgttct 1080
 gaggacactg caacctatta ctgtgcaaga tattatgatg atcattactg ccttgactac 1140
 tggggccaag gcaccacggt caccgtctcc tcaggcgaag gtactagtagc tgggtctggt 1200
 ggaagtggag gttcaggtgg agcagacgac attgtactga cccagtctcc agcaactctg 1260
 tctctgtctc caggggagcg tgccaccctg agctgcagag ccagtcaaag tgtaagttac 1320
 atgaactggt accagcagaa gccgggcaag gcacccaaaa gatggattta tgacacatcc 1380
 aaagtggctt ctggagtccc tgctcgcttc agtggcagtg ggtctgggac cgactactct 1440
 ctcacaatca acagcttgga ggctgaagat gctgccactt attactgcca acagtggagt 1500
 agtaaccgcg tcacgttcgg tggcgggacc aaggtggaga tcaaa 1545

<210> ...58

<211> 515

<212> PRT

<213> artificial sequence

<220>

<223> 4-1(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 58

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val
 20 25 30

Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu
 35 40 45

Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys
 50 55 60

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Gly Ala Ser Thr Arg Glu
 65 70 75 80

Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe
 85 90 95

Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr

100	105	110
Cys Gln Asn Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys		
115	120	125
Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly		
130	135	140
Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val		
145	150	155
Arg Pro Gly Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala		
	165	170
Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly		
	180	185
Leu Glu Trp Val Gly Asp Ile Phe Pro Gly Ser Gly Asn Ala His Tyr		
	195	200
Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser		
	210	215
Tyr Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala		
225	230	235
Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp Asp Glu Ala Met Asp Tyr		
	245	250
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser		
	260	265
Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala		
	275	280
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr		
	290	300
Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile		
305	310	315
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val		
	325	330
		335

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 340 345 350

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 355 360 365

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 370 375 380

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 385 390 395 400

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 405 410 415

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 420 425 430

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 435 440 445

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 450 455 460

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 465 470 475 480

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 485 490 495

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 500 505 510

Glu Ile Lys
 515

<210> 59
 <211> 44
 <212> DNA
 <213> artificial sequence

<220>
 <223> Me92a

<400> 59
 ggattgtaca ctccgagctc gtgatgacac agtctccatc ctcc

<210> 60
<211> 1560
<212> DNA
<213> artificial sequence

<220>

<223> 4-7 (VL-VH) xanti-CD3 (VH(5)-VL(2))

<400> 60

atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgcg	60
cgcgagctcg tgatgaccca gactccactc tccctgcctg tcagtcttgg agatcaagcc	120
tccatctctt gcagatctag tcagagcctt gtacacagta atggaaacac ctattttacat	180
tggtacctgc agaagccagg ccagtctcca aagctcctga tctacaaagt ttccaaccga	240
ttttctgggg tcccagacag gttcagtggc agtggatcag ggacagattt cacactcaag	300
atcagcagag tggaggctga ggatctggga gtttatttct gctctcaaag tacacatgtt	360
ccgtacacgt tcggaggggg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc	420
ggcggtctcc gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg	480
gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcacaac	540
tatggtttaa gctgggtgaa gcagaggcct ggacaggctc ttgagtggat tggagagggt	600
tatcctagaa ttgtaaatgc ttactacaat gagaagttca agggcaaggc cacactgact	660
gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacctc tgaggactct	720
gcggtctatt tctgtgcaag acggggatcc tacgatacta actacgactg gtacttcgat	780
gtctggggcc aaggggaccac ggtcaccgtc tctccggag gtggtggctc cgacgtccaa	840
ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaagggt gtctgcaag	900
gcttctggct acacctttac taggtacacg atgcaactggg taaggcaggc acctggacag	960
ggtctggaat ggattggata cattaatcct agccgtgggt atactaatta cgcagacagc	1020
gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg	1080
agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat	1140
tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctcagg cgaagggtact	1200
agtactgggt ctggtggaag tggagggttca ggtggagcag acgacattgt actgaccag	1260
tctccagcaa ctctgtctct gtctccaggg gagcgtgcc aacctgagctg cagagccagt	1320
caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg	1380
atztatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct	1440
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac	1500

tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1560

<210> 61

<211> 520

<212> PRT

<213> artificial sequence

<220>

<223> 4-7.(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 61

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Ala Arg Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu
20 25 30

Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln
35 40 45

Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln
50 55 60

Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg
65 70 75 80

Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
85 90 95

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr
100 105 110

Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr
115 120 125

Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu
145 150 155 160

Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr
165 170 175

Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg Pro Gly Gln

180	185	190
Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly Asn Ala Tyr		
195	200	205
Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser		
210	215	220
Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser		
225	230	235
Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr Asn Tyr Asp		
245	250	255
Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser		
260	265	270
Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val		
275	280	285
Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr		
290	295	300
Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Gln		
305	310	315
Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn		
325	330	335
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser		
340	345	350
Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr		
355	360	365
Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp		
370	375	380
Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr		
385	390	395
Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile		
405	410	415

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
 420 425 430

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
 435 440 445

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 450 455 460

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 465 470 475 480

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 485 490 495

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 500 505 510

Gly Gly Thr Lys Val Glu Ile Lys
 515 520

<210> 62
 <211> 1545
 <212> DNA
 <213> artificial sequence

<220>
 <223> 5-10 (VL-VH)xanti-CD3 (VH(5)-VL(2))

<400> 62
 atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgag 60
 ctcgtgatga cacagtctcc atcctccctg actgtgacag caggagagaa ggtcactatg 120
 agctgcaagt ccagtcagag tctgttaaac agtggaatc aaaagaacta cttgacctgg 180
 taccagcaga aaccagggca gcctcctaaa ctgttgatct actgggcac cactagggaa 240
 tctgggggtcc ctgatcgctt cacaggcagt ggatctggaa cagatttcac tctcaccatc 300
 agcagtgtgc aggtgaaga cctggcagtt tattactgtc agaatgatta tagttatccg 360
 ctcacgttcg gtgctgggac caagcttgag atcaaagggtg gtggtgggtc tggcggcggc 420
 ggctccggtg gtggtgggtc tgaggtgcag ctgctcgagc agtctggagc tgagctggta 480
 aggcctggga cttcagtga gatacctgc aaggcttctg gatacgcctt cactaactac 540
 tggctaggtt gggtaaagca gaggcctgga catggacttg agtggattgg agatattttc 600
 cctggaagtg gtaatatcca ctacaatgag aagttcaagg gcaaagccac actgactgca 660

gacaaatctt cgagcacagc ctatatgcag ctccagtagcc tgacatttga ggactctgct 720
 gtctatttct gtgcaagact gaggaactgg gacgagccta tggactactg gggccaaggg 780
 accacggtca ccgtctcctc cggaggtggg ggctccgacg tccaactggg gcagtcaggg 840
 gctgaagtga aaaaacctgg ggctcagtg aaggtgtcct gcaaggcttc tggctacacc 900
 ttctactagg acacgatgca ctgggtaagg caggcacctg gacaggggtct ggaatggatt 960
 ggatacatta atcctagccg tggttatact aattacgcag acagcgtcaa gggccgcttc 1020
 acaatcacta cagacaaatc caccagcaca gcctacatgg aactgagcag cctgcgttct 1080
 gaggacactg caacctatta ctgtgcaaga tattatgatg atcattactg ccttgactac 1140
 tggggccaag gcaccacggt caccgtctcc tcaggcgaag gtactagtagc tggttctggg 1200
 ggaagtggag gttcaggtgg agcagacgac attgtactga ccagtcctcc agcaactctg 1260
 tctctgtctc caggggagcg tgccaccctg agctgcagag ccagtcaaag tgtaagttac 1320
 atgaactggg accagcagaa gccgggcaag gcacccaaaa gatggattta tgacacatcc 1380
 aaagtggctt ctggagtccc tgctcgcttc agtggcagtg ggtctgggac cgactactct 1440
 ctcacaatca acagcttgga ggctgaagat gctgccactt attactgcca acagtggagt 1500
 agtaacccgc tcacgttcgg tggcgggacc aaggtggaga tcaaa 1545

<210> 63
 <211> 515
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10(VL-VH)xanti-CD3(VH(5)-VL(2))

<400> 63

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val
 20 25 30

Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu
 35 40 45

Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys
 50 55 60

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu
 65 70 75 80

Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe
 85 90 95
 Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr
 100 105 110
 Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys
 115 120 125
 Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 130 135 140
 Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val
 145 150 155 160
 Arg Pro Gly Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala
 165 170 175
 Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly
 180 185 190
 Leu Glu Trp Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr
 195 200 205
 Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser
 210 215 220
 Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala
 225 230 235 240
 Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr
 245 250 255
 Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
 260 265 270
 Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 275 280 285
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 290 295 300
 Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile

305 310 315 320
 Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 325 330 335
 Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 340 345 350
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 355 360 365
 Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 370 375 380
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 385 390 395 400
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 405 410 415
 Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 420 425 430
 Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 435 440 445
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 450 455 460
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 465 470 475 480
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 485 490 495
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 500 505 510
 Glu Ile Lys
 515

<210> 64
 <211> 1500
 <212> DNA
 <213> artificial sequence

<220>

<223> VH5/VL2x3-5

<400> 64

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg	60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca	120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggtta tactaattac	180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac	240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat	300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc	360
gaaggtaacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattgta	420
ctgaccagtc ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc	480
agagccagtc aaagtgtgaa ttacatgaac tgggtaccagc agaagccggg caaggcaccc	540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc	600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc	660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg	720
gagatcaaat ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag	780
ctggtaaggc ctgggaactc agtgaagctg tcctgcaagg cttctggcta caccttcaca	840
agctatggtt taagctgggt gaagcagaga actggacagg gccttgagtg gattggagag	900
gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg	960
actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac atctgaggac	1020
tctgcggtct atttctgtgc aagacgggga tcctacggta gtaactacga ctggtacttc	1080
gatgtctggg gccaaaggac cacggtcacc gtctcctcag gtggtgggtg ttctggcggc	1140
ggcggctccg gtggtgggtg ttctgagctc gtgatgaccc agactccact ctccctgcct	1200
gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt	1260
aatggaaaca cctattttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg	1320
atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca	1380
gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agttttatttc	1440
tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa	1500

<210> 65

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5/VL2x3-5

<400> 65

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255

Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Leu Ser Cys
 260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Gly Leu Ser Trp Val Lys
 275 280 285

Gln Arg Thr Gly Gln Gly Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
 290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
 325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
 340 345 350

Gly Ser Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
 385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
 405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
 420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
 435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
 465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
 485 490 495

Leu Glu Ile Lys
 500

<210> 66
 <211> 1491
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH5/VL2x4-1

<400> 66
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaattcta gccgtgggta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaagg tacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtgaa ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcgggtggcg gaccaaggtg 720
 gagatcaa at ccggaggtgg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
 ctggtaaggc ctgggacttc agtgaagata tcctgcaagg cttctggata cgccttcact 840
 aactactggc taggttgggt taagcagagg cctggacatg gacttgaatg ggttggagat 900
 attttccctg gaagtggtaa tgctcactac aatgagaagt tcaagggcaa agccacactg 960
 actgcagaca agtcctcgta cacagcctat atgcagctca gtagcctgac atctgaggac 1020

tctgctgtct atttctgtgc aagattgctg aactgggacg aggctatgga ctactggggc 1080
 caagggacca cggtcaccgt ctctcaggt ggtggtggtt ctggcggcgg cggctccggt 1140
 ggtggtggtt ctgagctcgt gatgacacag tctccatcct ccctgagtgt gtcagcagga 1200
 gagaagggtca ctatgagctg caagtccagt cagagtctgt taaacagtgg aaatcaaaag 1260
 aactacttgg cctggtacca gcagaaacca gggcagcctc ctaaactgtt gatctacggg 1320
 gcatccacta gggaatctgg ggtccctgat cgcttcacag gcagtggatc tggaacagat 1380
 ttcactctca ccatcagcag tgtgcaggct gaagacctgg cagtttatta ctgtcagaat 1440
 gattatagtt atccgtacac gttcggaggg gggaccaagc ttgagatcaa a 1491

<210> 67
 <211> 497
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH5/VL2x4-1

<400> 67

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255

Ser Gly Ala Glu Leu Val Arg Pro Gly Thr Ser Val Lys Ile Ser Cys
 260 265 270

Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Trp Leu Gly Trp Val Lys
 275 280 285

Gln Arg Pro Gly His Gly Leu Glu Trp Val Gly Asp Ile Phe Pro Gly
 290 295 300

Ser Gly Asn Ala His Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 305 310 315 320

Thr Ala Asp Lys Ser Ser Tyr Thr Ala Tyr Met Gln Leu Ser Ser Leu
 325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Trp
 340 345 350

Asp Glu Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 355 360 365

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 370 375 380

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ala Gly
 385 390 395 400

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 405 410 415

Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
 420 425 430

Pro Pro Lys Leu Leu Ile Tyr Gly Ala Ser Thr Arg Glu Ser Gly Val
 435 440 445

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 450 455 460

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 465 470 475 480

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
 485 490 495

Lys

<210> 68
 <211> 18
 <212> PRT
 <213> artificial sequence

<220>
 <223> non-deimmunized linker sequence

<400> 68

Val Glu Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
 1 5 10 15

Val Asp

<210> 69
 <211> 357
 <212> DNA

<213> artificial sequence

<220>

<223> anti-CD3 VH2

<400> 69

```

gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctgggggcctc agtgaagggt      60
tcttgcaagg cttctggcta caccgctact aggtacacga tgcactgggt aaggcaggca      120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac      180
gcacagaagt tgcagggccg cgtcacaatg actacagaca cttccaccag cacagcctac      240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat      300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctca      357

```

<210> 70

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> anti-CD3 VH2

<400> 70

```

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10           15

```

```

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
20           25           30

```

```

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35           40           45

```

```

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

```

```

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65           70           75           80

```

```

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85           90           95

```

```

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100          105          110

```

```

Thr Thr Val Thr Val Ser Ser
115

```

<210> 71
 <211> 357
 <212> DNA
 <213> artificial sequence

<220>
 <223> anti-CD3 VH3

<400> 71
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta caccgctact aggtacacga tgcaactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 gcacagaagt tgcagggccg cgtcacaaatg actacagaca cttccaccag cacagcctac 240
 ctgcaaatga acagcctgaa aactgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctca 357

<210> 72
 <211> 119
 <212> PRT
 <213> artificial sequence

<220>
 <223> anti-CD3 VH3

<400> 72

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

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

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly

100

105

110

Thr Thr Val Thr Val Ser Ser
115

<210> 73
<211> 357
<212> DNA
<213> artificial sequence

<220>
<223> anti-CD3 VH5

<400> 73
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
gcagacacgg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcacctg ctctca 357

<210> 74
<211> 119
<212> PRT
<213> artificial sequence

<220>
<223> anti-CD3 VH5

<400> 74

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Thr Thr Val Thr Val Ser Ser
115

<220>
<223> anti-CD3 VH7

[illegible]

<220>
<223> anti-CD3 VH7

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 77
<211> 318
<212> DNA
<213> artificial sequence

<220>
<223> anti-CD3 VL1

<400> 77
gacattcaga tgaccacagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc 60
atcacctgca gagccagtc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt cctgtctgcg 180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
gatgctgccca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
accaaggtgg agatcaaa 318

<210> 78
<211> 106
<212> PRT
<213> artificial sequence

<220>
<223> anti-CD3 VL1

<400> 78

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 79
 <211> 318
 <212> DNA
 <213> artificial sequence

<220>
 <223> anti-CD3 VL2

<400> 79
 gacattgtac tgaccagtc tocagcaact ctgtctctgt ctccagggga gcgtgccacc 60
 ctgagctgca gagccagtca aagtgtagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccga aaagatgat ttatgacaca tccaaagtgg cttctggagt cctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
 accaaggtgg agatcaaa 318

<210> 80
 <211> 106
 <212> PRT
 <213> artificial sequence

<220>
 <223> anti-CD3 VL2

<400> 80

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr

35

40

45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 81
 <211> 318
 <212> DNA
 <213> artificial sequence

<220>
 <223> anti-CD3 VL3

<400> 81
 gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60
 ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccaca aaagatggat ttatgacaca tccaaagtgg cttctggagt cctgtctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa 240
 gatgtgcca ottattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
 accaagggtgg agatcaaa 318

<210> 82
 <211> 106
 <212> PRT
 <213> artificial sequence

<220>
 <223> anti-CD3 VL3

<400> 82

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 83
 <211> 30
 <212> DNA
 <213> artificial sequence

<220>
 <223> vH CDR1 anti-CD3 wt

<400> 83
 ggctacacct ttactagta cacgatgcac

30

<210> 84
 <211> 10
 <212> PRT
 <213> artificial sequence

<220>
 <223> vH CDR1 anti-CD3 wt

<400> 84

Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
 1 5 10

<210> 85
 <211> 30
 <212> DNA
 <213> artificial sequence

<220>
 <223> vH CDR1 VH2,3

<400> 85
 ggctacaccg ctactagta cacgatgcac

30

<210> 86

<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> vH CDR1 VH2,3

<400> 86

Gly Tyr Thr Ala Thr Arg Tyr Thr Met His
1 5 10

<210> 87
<211> 30
<212> DNA
<213> artificial sequence

<220>
<223> vH CDR1 VH5,7

<400> 87
ggctacacct ttactaggta cacgatgcac

30

<210> 88
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> vH CDR1 VH5,7

<400> 88

Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
1 5 10

<210> 89
<211> 51
<212> DNA
<213> artificial sequence

<220>
<223> vH CDR2 wt anti-CD3 VH7

<400> 89
tacattaatc ctagecgtgg ttatactaata tacaatcaga agttcaagga c

51

<210> 90
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> vH CDR2 wt anti-CD3 VH7

<400> 90

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 91
<211> 51
<212> DNA
<213> artificial sequence

<220>
<223> vH CDR2 VH5

<400> 91
tacattaatc ctagccgtgg ttatactaatac tacgcagaca gcgtcaaggg c 51

<210> 92
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> vH CDR2 VH5

<400> 92

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 93
<211> 51
<212> DNA
<213> artificial sequence

<220>
<223> vH CDR2 VH2,3

<400> 93
tacattaatc ctagccgtgg ttatactaatac tacgcacaga agttgcaggg c 51

<210> 94
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> vH CDR2 VH2,3

<400> 94

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> 95

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vH CDR3 wt anti-CD3 VH2,3,5,7

<400> 95

tattatgatg atcattactg ccttgactac

30

<210> 96

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vH CDR3 wt anti-CD3 VH2,3,5,7

<400> 96

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr
1 5 10

<210> 97

<211> 30

<212> DNA

<213> artificial sequence

<220>

<223> vK CDR1 wt anti-CD3 VL3

<400> 97

agagccagtt caagtgtaag ttacatgaac

30

<210> 98

<211> 10

<212> PRT

<213> artificial sequence

<220>

<223> vK CDR1 wt anti-CD3 VL3

<400> 98

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn
1 5 10

<210> 99
<211> 30
<212> DNA
<213> artificial sequence

<220>
<223> vK CDR1 VL 1,2

<400> 99
agagccagtc aaagtgtgaag ttacatgaac

30

<210> 100
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> vK CDR1 VL 1,2

<400> 100

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
1 5 10

<210> 101
<211> 21
<212> DNA
<213> artificial sequence

<220>
<223> vK CDR2 wt anti-CD3 VL1-3

<400> 101
gacacatcca aagtggcttc t

21

<210> 102
<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> vK CDR2 wt anti-CD3 VL1-3

<400> 102

Asp Thr Ser Lys Val Ala Ser
1 5

<210> 103
<211> 27
<212> DNA

<213> artificial sequence

<220>

<223> vK CDR3 wt anti-CD3 VL1-3

<400> 103

caacagtgga gtagtaaccc gctcacg

27

<210> 104

<211> 9

<212> PRT

<213> artificial sequence

<220>

<223> vK CDR3 wt anti-CD3 VL1-3

<400> 104

Gln Gln Trp Ser Ser Asn Pro Leu Thr

1

5

<210> 105

<211> 357

<212> DNA

<213> artificial sequence

<220>

<223> vH anti-CD3 with the mutations of cys->ser

<400> 105

gatatcaaac tgcagcagtc aggggctgaa ctggcaagac ctggggcctc agtgaagatg 60

tcctgcaaga cttctggcta cacctttact aggtacacga tgcaactgggt aaaacagagg 120

cctggacagg gtctggaatg gattggatac attaattcta gccgtgggta tactaattac 180

aatcagaagt tcaaggacaa ggccacattg actacagaca aatcctccag cacagcctac 240

atgcaactga gcagcctgac atctgaggac tctgcagtct attactgtgc aagatattat 300

gatgatcatt actcccttga ctactggggc caaggcacca ctctcacagt ctctca 357

<210> 106

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> vH anti-CD3 with the mutations of cys ->ser

<400> 106

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala

1

5

10

15

Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Leu Thr Val Ser Ser
 115

<210> 107
 <211> 30
 <212> DNA
 <213> artificial sequence

<220>
 <223> vH CDR3 anti-CD3 with the mutation cys-> ser

<400> 107
 tattatgatg atcattactc ccttgactac

30

<210> 108
 <211> 10
 <212> PRT
 <213> artificial sequence

<220>
 <223> vH CDR3 anti-CD3 with the mutation cys-> ser

<400> 108

Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr
 1 5 10

<210> 109
 <211> 357
 <212> DNA
 <213> artificial sequence

<220>

<223> wild type anti-CD3 VH

<400> 109

gatatacaaac tgcagcagtc aggggctgaa ctggcaagac ctggggcctc agtgaagatg 60
tcttgcaaga cttctggcta cacctttact aggtacacga tgcactgggt aaaacagagg 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
aatcagaagt tcaaggacaa ggccacattg actacagaca aatcctccag cacagcctac 240
atgcaactga gcagcctgac atctgaggac tctgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca ctctcacagt ctctca 357

<210> 110

<211> 119

<212> PRT

<213> artificial sequence

<220>

<223> wild type anti-CD3 VH

<400> 110

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Leu Thr Val Ser Ser
115

<210> 111
 <211> 318
 <212> DNA
 <213> artificial sequence

<220>
 <223> wild type anti-CD3 VK

<400> 111
 gacattcagc tgaccagtc tccagcaatc atgtctgcat ctccaggga gaaggtcacc 60
 atgacctgca gagccagttc aagtgtagt tacatgaact ggtaccagca gaagtcaggc 120
 acctccccc aaagatggat ttatgacaca tccaaagtgg cttctggagt cccttatcgc 180
 ttcagtggca gtgggtctgg gacctcatc tctctcaca tcagcagcat ggaggtgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtgctggg 300
 accaagctgg agctgaaa 318

<210> 112
 <211> 106
 <212> PRT
 <213> artificial sequence

<220>
 <223> wild type anti-CD3 VK

<400> 112

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Tyr Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
 100 105

<210> 113
<211> 372
<212> DNA
<213> artificial sequence

<220>
<223> CD19 VH

<400> 113
caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggcccaagg gaccacggtc 360
accgtctcct cc 372

<210> 114
<211> 124
<212> PRT
<213> artificial sequence

<220>
<223> CD19 VH

<400> 114

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> 115
 <211> 333
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD19 VL

<400> 115
 gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
 atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactgggtac 120
 caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
 gggatcccac ccaggttttag tggcagtggg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggaccaa gctcgagatc aaa 333

<210> 116
 <211> 111
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19 VL

<400> 116

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 117
<211> 47
<212> DNA
<213> artificial sequence

<220>
<223> 4-7 VL BspEI FOR

<400> 117
ctgaaatccg gaggtggtgg atccgagctc gtgatgaccc agactcc

47

<210> 118
<211> 52
<212> DNA
<213> artificial sequence

<220>
<223> 4-7 VL GS15 REV

<400> 118
ggagccgccg ccgccagaac caccaccacc tttgatctca agcttggtcc cc

52

<210> 119
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> CDRH3 M1 mutant

<400> 119

His Tyr Asp Asp His Tyr Cys Leu Asp Tyr
1 5 10

<210> 120
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> CDRH3 M4 mutant

<400> 120

Tyr Ser Asp Asp His Tyr Cys Leu Asp Tyr
1 5 10

<210> 121
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> CDRH3 M7 mutant

<400> 121

Tyr Tyr Asp Ala His Tyr Cys Leu Asp Tyr
1 5 10

<210> 122
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> CDRH3 M9 mutant

<400> 122

Tyr Tyr Asp Asp Gln Tyr Cys Leu Asp Tyr
1 5 10

<210> 123
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> CDRH3 M10 mutant

<400> 123

Tyr Tyr Asp Asp Pro Tyr Cys Leu Asp Tyr
1 5 10

<210> 124
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> CDRH3 M11 mutant

<400> 124

Tyr Phe Asn Asp His Tyr Cys Leu Asp Tyr
1 5 10

<210> 125

<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> CDRH3 M13 mutant

<400> 125

Tyr Tyr Asn Asp Gln Tyr Cys Leu Asp Tyr
1 5 10

<210> 126
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> CDRH3 M20 mutant

<400> 126

Tyr His Asp Asp Pro Tyr Cys Leu Asp Tyr
1 5 10

<210> 127
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> CDRH3 M76 mutant

<400> 127

Tyr Tyr Asp Asp Asn Tyr Cys Leu Asp Tyr
1 5 10

<210> 128
<211> 354
<212> DNA
<213> artificial sequence

<220>
<223> CCR5 Heavy chain

<400> 128

cagctggagc agtctggacc tgaactgaag aagcctggag agacagtcac gatctcctgc 60
aaggcttctg ggtatacctt cacgaagttc ggaatgaact gggatgaagca ggctccagga 120
aagggtttta agtggtatggg ctggatacac acctccactg gagagccaac atattctgat 180
gacttcaagg gacggtttgc cttctctttg gaaacgtctg ccagcactgc ctatttgcgg 240
atcaacaacc tcaaaaatga ggacatggct aaatacttct gtgccagagg tggtccttac 300

gtaaggggtg ctttggaacta ctgggggtcaa ggaacctcag tcaccgtctc ctcc 354

<210> 129
 <211> 118
 <212> PRT
 <213> artificial sequence

<220>
 <223> CCR5 Heavy chain

<400> 129

Gln Leu Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val
 1 5 10 15

Thr Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met
 20 25 30

Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp
 35 40 45

Ile His Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly
 50 55 60

Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg
 65 70 75 80

Ile Asn Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg
 85 90 95

Gly Gly Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr
 100 105 110

Ser Val Thr Val Ser Ser
 115

<210> 130
 <211> 333
 <212> DNA
 <213> artificial sequence

<220>
 <223> CCR5 Light chain

<400> 130
 gacattatcc tgatccaatc tccaccttct ttggtgtgt ctctaggga gagggccacc 60

atctcctgca gaaccagcga aaatgttgac ggatacggca ttagttttat aaactggtac 120

caacagaagc caggacagcc acccaaactc ctcattctatg ctgcatccca ccaaggatcc 180
 ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240
 cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg 300
 acgttcggtg gaggcaccaa gctggaaatc aaa 333

<210> 131
 <211> 111
 <212> PRT
 <213> artificial sequence

<220>
 <223> CCR5 Light chain

<400> 131

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
 20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
 65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
 85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 132
 <211> 360
 <212> DNA
 <213> artificial sequence

<220>
 <223> EpCAM5-10 heavy chain

<400> 132
 gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggctgggac ttcagtgaag 60
 atatcctgca aggccttctg atacgccttc actaactact ggctaggttg ggtaaagcag 120

aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
 tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240
 tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
 aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctctca 360

<210> 133
 <211> 120
 <212> PRT
 <213> artificial sequence

<220>
 <223> EpCAM5-10 heavy chain

<400> 133

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> 134
 <211> 339
 <212> DNA
 <213> artificial sequence

<220>
 <223> EpCAM5-10 light chain

<400> 134
 gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggctact 60
 atgagctgca agtccagtc gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
 tggtagcagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
 gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
 atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
 ccgctcacgt tccgtgctgg gaccaagctt gagatcaaa 339

<210> 135
 <211> 113
 <212> PRT
 <213> artificial sequence

<220>
 <223> EpCAM 5-10 light chain

<400> 135

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys

<210> 136
 <211> 360

<212> DNA

<213> artificial sequence

<220>

<223> EpCAM 3-1 VH

<400> 136

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gaggtgcagc tgctcgagca gtctggagct gagctggtga aacctggggc ctcaagtgaag   60
atatacctgca aggccttctgg atacgccttc actaactact ggctagggttg ggtaaagcag   120
aggcctggac atggacttga gtggattgga gatcttttcc ctggaagtgg taatactcac   180
tacaatgaga ggttcagggg caaagccaca ctgactgcag acaaatcctc gagcacagcc   240
tttatgcagc tcagtagcct gacatctgag gactctgctg tctatttctg tgcaagattg   300
aggaactggg acgaggctat ggactactgg ggccaaggga ccacggtcac cgtctctctca   360

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<210> 137

<211> 120

<212> PRT

<213> artificial sequence

<220>

<223> EpCAM 3-1 VH

<400> 137

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Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Lys Pro Gly
1           5           10           15

```

```

Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
          20           25           30

```

```

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35           40           45

```

```

Ile Gly Asp Leu Phe Pro Gly Ser Gly Asn Thr His Tyr Asn Glu Arg
50           55           60

```

```

Phe Arg Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65           70           75           80

```

```

Phe Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
85           90           95

```

```

Cys Ala Arg Leu Arg Asn Trp Asp Glu Ala Met Asp Tyr Trp Gly Gln
100           105           110

```

```

Gly Thr Thr Val Thr Val Ser Ser

```

115

120

<210> 138
 <211> 321
 <212> DNA
 <213> artificial sequence

<220>
 <223> EpCAM 3-1 VL

<400> 138
 gagctcgta tgaccagtc tccatcttat cttgctgcat ctccctggaga aaccattact 60
 attaattgca gggcaagtaa gagcattagc aaatatttag cctggatatca agagaaacct 120
 gggaaaacta ataagcttct tatctactct ggatccactt tgcaatctgg aattccatca 180
 aggttcagtg gcagtggatc tggtagatc ttcactctca ccatcagtag cctggagcct 240
 gaagattttg caatgtatta ctgtcaacag cataatgaat atccgtacac gttcggaggg 300
 gggaccaagc ttgagatcaa a 321

<210> 139
 <211> 107
 <212> PRT
 <213> artificial sequence

<220>
 <223> EpCAM 3-1 VL

<400> 139

Glu Leu Val Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly
 1 5 10 15

Glu Thr Ile Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Tyr
 20 25 30

Leu Ala Trp Tyr Gln Glu Lys Pro Gly Lys Thr Asn Lys Leu Leu Ile
 35 40 45

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

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

Glu Asp Phe Ala Met Tyr Tyr Cys Gln Gln His Asn Glu Tyr Pro Tyr
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 140
<211> 372
<212> DNA
<213> artificial sequence

<220>
<223> EpCAM 3-5 VH

<400> 140
gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggctggggac ttcagtgaag 60
ctgtcctgca aggcttcttg ctacaccttc acaagctatg gtttaagctg ggtgaagcag 120
agaactggac agggccttga gtggattgga gaggtttatc ctagaattgg taatgcttac 180
tacaatgaga agttcaaggg caaggccaca ctgactgcag acaaactctc cagcacagcg 240
tccatggagc tccgcagcct gacatctgag gactctgcgg tctatttctg tgcaagacgg 300
ggatcctacg gtagtaacta cgactgggtac ttgatgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 141
<211> 124
<212> PRT
<213> artificial sequence

<220>
<223> EpCAM 3-5 VH

<400> 141

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

Thr Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser
20 25 30

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

Ile Gly Glu Val Tyr Pro Arg Ile Gly Asn Ala Tyr Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Ser Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe

85

90

95

Cys Ala Arg Arg Gly Ser Tyr Gly Ser Asn Tyr Asp Trp Tyr Phe Asp
 100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> 142
 <211> 336
 <212> DNA
 <213> artificial sequence

<220>
 <223> EpCAM 3-5 VL

<400> 142
 gagctcgtga tgaccagac tccactctcc ctgctgtca gtcttgaga tcaagcctcc 60
 atctcttgca gatctagtca gagccttgta cacagtaatg gaaacaccta tttacattgg 120
 tacctgcaga agccaggcca gtctccaaag ctctgatct acaaagtttc caaccgattt 180
 tctgggggtcc cagacaggtt cagtggcagt ggatcaggga cagatttcac actcaagatc 240
 agcagagtgg aggctgagga tctgggagtt tatttctgct ctcaaagtac acatgttccg 300
 tacacgttcg gaggggggac caagcttgag atcaaa 336

<210> 143
 <211> 112
 <212> PRT
 <213> artificial sequence

<220>
 <223> EpCAM 3-5 VL

<400> 143

Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
 1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
 20 25 30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 144
<211> 360
<212> DNA
<213> artificial sequence

<220>
<223> EpCAM 4-1 VH

<400> 144
gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
atatcctgca aggcttctgg atacgccttc actaactact ggctagggtg ggttaagcag 120
aggcctggac atggacttga atgggttga gatattttcc ctggaagtgg taatgctcac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaagtcctc gtacacagcc 240
tatatgcagc tcagtagcct gacatctgag gactctgctg tctatttctg tgcaagattg 300
cggaactggg acgaggctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360

<210> 145
<211> 120
<212> PRT
<213> artificial sequence

<220>
<223> EpCAM 4-1 VH

<400> 145

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Val Gly Asp Ile Phe Pro Gly Ser Gly Asn Ala His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Tyr Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 146
<211> 339
<212> DNA
<213> artificial sequence

<220>
<223> EpCAM 4-1 VL

<400> 146
gagctcgtga tgacacagtc tccatcctcc ctgagtgtgt cagcaggaga gaaggtcact 60
atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttggcc 120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctacggggc atccactagg 180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
ccgtacacgt tcggaggggg gaccaagctt gagatcaaa 339

<210> 147
<211> 113
<212> PRT
<213> artificial sequence

<220>
<223> EpCAM 4-1 VL

<400> 147

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Gly Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
 100 105 110

Lys

<210> 148
 <211> 372
 <212> DNA
 <213> artificial sequence

<220>
 <223> EpCAM 4-7 VH

<400> 148
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 ctgtcctgca aggtctctgg ctacaccttc acaaactatg gtttaagctg ggtgaagcag 120
 aggccctggac aggtccttga gtggattgga gaggtttatc ctagaattgg taatgcttac 180
 tacaatgaga agttcaaggg caaggccaca ctgactgcag acaaactctc cagcacagcg 240
 tccatggagc tccgcagcct gacctctgag gactctgagg tctatttctg tgcaagacgg 300
 ggatcctacg atactaacta cgactggtac ttcgatgtct ggggccaagg gaccacggtc 360
 accgtctcct ca 372

<210> 149
 <211> 124
 <212> PRT
 <213> artificial sequence

<220>
 <223> EpCAM 4-7 VH

<400> 149

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

Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn
20 25 30

Tyr Gly Leu Ser Trp Val Lys Gln Arg Pro Gly Gln Val Leu Glu Trp
35 40 45

Ile Gly Glu Val Tyr Pro Arg Ile Gly Asn Ala Tyr Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Ser Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Arg Gly Ser Tyr Asp Thr Asn Tyr Asp Trp Tyr Phe Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 150
<211> 336
<212> DNA
<213> artificial sequence

<220>
<223> EpCAM 4-7 VL

<400> 150
gagctcgtga tgaccagac tccactctcc ctgcctgtca gtcttggaga tcaagcctcc 60
atctcttgca gatctagtca gagccttgta cacagtaatg gaaacaccta ttacattgg 120
tacctgcaga agccaggcca gtctccaaag ctctgatct acaaagtttc caaccgattt 180
tctgggggtcc cagacaggtt cagtggcagt ggatcaggga cagatttcac actcaagatc 240
agcagagtgg aggctgagga tctgggagtt tatttctgct ctcaaagtac acatgttccg 300
tacacgttcg gaggggggac caagcttgag atcaaa 336

<210> 151
<211> 112
<212> PRT
<213> artificial sequence

<220>
<223> EpCAM 4-7 VL

<400> 151

Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 152

<211> 25

<212> PRT

<213> artificial sequence

<220>

<223> VH5 Framework 1

<400> 152

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> 153

<211> 25

<212> PRT

<213> artificial sequence

<220>

<223> VH7 Framework 1

<400> 153

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> 154
<211> 25
<212> PRT
<213> artificial sequence

<220>
<223> VH2 Framework 1

<400> 154

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> 155
<211> 25
<212> PRT
<213> artificial sequence

<220>
<223> VH3 Framework 1

<400> 155

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> 156
<211> 15
<212> PRT
<213> artificial sequence

<220>
<223> VH5 Framework 2

<400> 156

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
1 5 10 15

<210> 157
<211> 15

<212> PRT
<213> artificial sequence

<220>
<223> VH7 Framework 2

<400> 157

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
1 5 10 15

<210> 158
<211> 22
<212> PRT
<213> artificial sequence

<220>
<223> VH2 Framework 2

<400> 158

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
1 5 10 15

Asn Pro Ser Arg Gly Tyr
20

<210> 159
<211> 22
<212> PRT
<213> artificial sequence

<220>
<223> VH3 Framework 2

<400> 159

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
1 5 10 15

Asn Pro Ser Arg Gly Tyr
20

<210> 160
<211> 32
<212> PRT
<213> artificial sequence

<220>
<223> VH5 Framework 3

<400> 160

Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu

1 5 10 15
Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
 20 25 30

<210> 161
<211> 32
<212> PRT
<213> artificial sequence

<220>
<223> VH7 Framework 3

<400> 161

Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
 20 25 30

<210> 162
<211> 32
<212> PRT
<213> artificial sequence

<220>
<223> VH2 Framework 3

<400> 162

Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
 20 25 30

<210> 163
<211> 32
<212> PRT
<213> artificial sequence

<220>
<223> VH3 Framework 3

<400> 163

Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Leu Gln
1 5 10 15

Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
 20 25 30

<210> 164
<211> 11
<212> PRT
<213> artificial sequence

<220>
<223> VH5 Framework 4

<400> 164

Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 165
<211> 11
<212> PRT
<213> artificial sequence

<220>
<223> VH7 Framework 4

<400> 165

Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 166
<211> 11
<212> PRT
<213> artificial sequence

<220>
<223> VH2 Framework 4

<400> 166

Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 167
<211> 11
<212> PRT
<213> artificial sequence

<220>
<223> VH3 Framework 4

<400> 167

Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 168

<211> 15
 <212> PRT
 <213> artificial sequence

<220>
 <223> Standard linker

<400> 168

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1 5 10 15

<210> 169
 <211> 366
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD20VH

<400> 169
 caggtgcaac tgcggcagcc tggggctgag ctggtgaagc ctggggcctc agtgaagatg 60
 tcctgcaagg cttctggcta cacatttacc agttacaata tgcactgggt aaagcagaca 120
 cctggacagg gcctggaatg gattggagct atttatccag gaaatgggtga tacttcctac 180
 aatcagaagt tcaaaggcaa ggccacattg actgcagaca aatcctccag cacagcctac 240
 atgcagctca gcagtctgac atctgaggac tctgcgggtct attactgtgc aagatcgcac 300
 tacggtagta actacgtaga ctactttgac tactggggcc aaggcacact agtcacagtc 360
 tcgaca 366

<210> 170
 <211> 122
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD20VH

<400> 170

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

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
 20 25 30

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Thr
 115 120

<210> 171
 <211> 318
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD20VL

<400> 171
 caaattgttc tctccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca 60
 atgacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga 120
 tctctcccca aacctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gacctcttac tctctcaca tcagcagagt ggaggctgaa 240
 gatgctgccca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300
 acaaaggtgg aaataaaa 318

<210> 172
 <211> 106
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD20VL

<400> 172

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 173
 <211> 15
 <212> DNA
 <213> artificial sequence

<220>
 <223> GGGGS linker

<400> 173
 ggaggtggtg gatcc

15

<210> 174
 <211> 5
 <212> PRT
 <213> artificial sequence

<220>
 <223> GGGGS linker

<400> 174

Gly Gly Gly Gly Ser
 1 5

<210> 175
 <211> 18
 <212> DNA
 <213> artificial sequence

<220>
 <223> SGGGS linker

<400> 175
 tccggaggtg gtggatcc

18

<210> 176
<211> 6
<212> PRT
<213> artificial sequence

<220>
<223> SGGGGS linker

<400> 176

Ser Gly Gly Gly Gly Ser
1 5

<210> 177
<211> 1527
<212> DNA
<213> artificial sequence

<220>
<223> antiCD19xantiCD3 VH2VL1

<400> 177
gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttatth gaactggtac 120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatcaa tctagtttct 180
gggatccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagtgc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggtg ggccgttatt actatgctat ggactactgg 720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactgggtg 780
cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840
ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acaggggtctg 900
gaatggattg gatacattaa tcctagccgt ggttatacta attacgcaca gaagttgcag 960
ggccgcgtca caatgactac agacacttcc accagcacag cctacatgga actgagcagc 1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc 1080

cttgactact ggggcccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
 ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttcagatgac ccagtctcca 1200
 tctagcctgt ctgcatctgt cggggaccgt gtcaccatca cctgcagagc cagtcaaagt 1260
 gtaagttaca tgaactggtg ccagcagaag ccgggcaagg caccctaaaag atggatttat 1320
 gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtgg gtctgggacc 1380
 gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440
 cagtggagta gtaaccgct cacgttcggt ggcggggacca aggtggagat caaacatcat 1500
 caccatcatc attagagatc tgtcgac 1527

<210> 178

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL1

<400> 178

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
 275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
 305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met
 325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
 340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro
385 390 395 400

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 179
<211> 1527
<212> DNA
<213> artificial sequence

<220>
<223> antiCD19xantiCD3 VH2VL2

<400> 179
gatatccagc tgaccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccagggttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttcttg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420


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gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg      480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga      540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa      600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat      660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg      720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactgggtg      780
cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct      840
ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg      900
gaatggattg gatacattaa tcctagccgt gggtatacta attacgcaca gaagttgcag      960
ggccgcgtca caatgactac agacacttcc accagcacag cctacatgga actgagcagc     1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc     1080
cttgactact ggggccaaagg caccacggtc accgtctcct caggcgaagg tactagtact     1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca     1200
gcaactctgt ctctgtctcc aggggagcgt gccaccctga gctgcagagc cagtcaaagt     1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg caccctaaaag atggatttat     1320
gacacatcca aagtggcttc tggagtcctt gctcgttcca gtggcagtgg gtctgggacc     1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa     1440
cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat     1500
caccatcatc attagagatc tgtcgac                                     1527

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<210> 180

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL2

<400> 180

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Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1           5           10           15

```

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

```

```

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro

```

35 40 45
 Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80
 Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95
 Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125
 Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140
 Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160
 Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175
 Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190
 Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205
 Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220
 Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240
 Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255
 Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
 275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
 305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met
 325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
 340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
 385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
 405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 181
<211> 1527
<212> DNA
<213> artificial sequence

<220>
<223> antiCD19xantiCD3 VH2VL3

<400> 181
gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
atctcctgca aggccagcca aagtgttgat tatgatgggtg atagttattt gaactgggtac 120
caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggttttag tggcagtggg tctgggacag acttcacct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcgggtg gagggacca gctcgagatc aaaggtgggtg gtggttctgg cggcggcggc 360
tccggtgggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
ggccaaggga ccacggtcac cgtctctctc ggaggtgggtg gctccgacgt ccaactgggtg 780
cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840
ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900
gaatggattg gatacattaa tcctagccgt ggttatacta attacgaca gaagttgcag 960
ggccgcgtca caatgactac agacacttcc accagcacag cctacatgga actgagcagc 1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc 1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
ggttctgggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca 1200
gcaactctgt ctctgtctcc aggggagcgt gccaccctga cctgcagagc cagttcaagt 1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg caccctaaag atggatttat 1320
gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380
gactactctc tcacaatcaa cagcttgag gctgaagatg ctgccactta ttactgcaa 1440
cagtgagta gtaaccgct cacgttcggt ggccggacca aggtggagat caaacatcat 1500

caccatcatc attagagatc tgtcgac

1527

<210> 182

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH2VL3

<400> 182

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly

180	185	190
Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln		
195	200	205
Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg		
210	215	220
Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp		
225	230	235
Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp		
245	250	255
Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser		
260	265	270
Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr		
275	280	285
Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly		
290	295	300
Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln		
305	310	315
Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met		
325	330	335
Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala		
340	345	350
Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr		
355	360	365
Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly		
370	375	380
Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro		
385	390	395
Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg		
405	410	415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 183
 <211> 1527
 <212> DNA
 <213> artificial sequence

<220>
 <223> antiCD19xantiCD3 VH3VL1

<400> 183
 gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
 atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
 caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
 gggatcccac ccaggttttag tggcagtggtg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
 tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
 gggctcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
 aactgggtga agcagaggcc tggacagggt cttgagtga ttggacagat ttggcctgga 540
 gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
 tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcgggtctat 660
 ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
 ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg 780

cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840
 ggctacaccg ctactaggtta cacgatgcac tgggtaaggc aggcacctgg acaggggtctg 900
 gaatggattg gatacattaa tcctagccgt gggtatacta attacgcaca gaagttgcag 960
 ggccgcgtca caatgactac agacacttcc accagcacag cctacctgca aatgaacagc 1020
 ctgaaaactg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc 1080
 cttgactact ggggcccaagg caccacggtc accgtctcct caggogaagg tactagtact 1140
 gggtctgggtg gaagtggagg ttcaggtgga gcagacgaca ttcagatgac ccagtctcca 1200
 tctagcctgt ctgcatctgt cggggaccgt gtcaccatca cctgcagagc cagtcaaagt 1260
 gtaagttaca tgaactggta ccagcagaag cggggcaagg cacccaaaag atggatttat 1320
 gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtggt gtctgggacc 1380
 gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440
 cagtgagta gtaaccgct cacgttcggt ggccgggacca aggtggagat caaacatcat 1500
 caccatcatc attagagatc tgtcgac 1527

<210> 184
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> antiCD19xantiCD3 VH3VL1

<400> 184

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
 275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
 305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Leu

[illegible]

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<210> 185
<211> 1527
<212> DNA
<213> artificial sequence
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<220>
<223> antiCD19xantiCD3 VH3VL2
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<400> 185
gatatccagc tgaccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
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caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaacaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggtg ggccgttatt actatgctat ggactactgg 720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg 780
cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840
ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900
gaatggattg gatacattaa tcctagccgt ggttatacta attacgcaca gaagttgcag 960
ggccgcgtca caatgactac agacacttcc accagcacag cctacctgca aatgaacagc 1020
ctgaaaactg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc 1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca 1200
gcaactctgt ctctgtctcc aggggagcgt gccaccctga gctgcagagc cagtcaaagt 1260
gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320
gacacatcca aagtggcttc tggagtccct gctcgcttca gtggcagtgg gtctgggacc 1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgcaa 1440
cagtgagta gtaaccoget cacgttcggt ggcgggacca aggtggagat caaacatcat 1500
caccatcatc attagagatc tgtcgac 1527

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<210> 186

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH3VL2

<400> 186

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15
 Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30
 Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45
 Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80
 Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95
 Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125
 Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140
 Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160
 Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175
 Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190
 Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205
 Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220
 Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Leu
325 330 335

Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln

465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 187
 <211> 1527
 <212> DNA
 <213> artificial sequence

<220>
 <223> antiCD19xantiCD3 VH3VL3

<400> 187
 gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
 atctcctgca aggccagcca aagtgttgat tatgatgggtg atagttattt gaactggtac 120
 caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
 gggatcccac ccaggttttag tggcagtggg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggaccaa gctcgagatc aaagggtggtg gtggttcttg cggcggcggc 360
 tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
 gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
 aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
 gatggtgata ctaactacaa tggaaagttc aagggtaaag ccaactctgac tgcagacgaa 600
 tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
 ttctgtgcaa gaaggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
 ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg 780
 cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840
 ggctacaccg ctactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900
 gaatggattg gatacattaa tcctagccgt gggtatacta attacgcaca gaagttgcag 960
 ggccgcgtca caatgactac agacacttcc accagcacag cctacctgca aatgaacagc 1020
 ctgaaaactg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc 1080
 cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
 ggttctggtg gaagtggagg ttcagggtga gcagacgaca ttgtactgac ccagtctcca 1200

gcaactctgt ctctgtctcc aggggagcgt gccaccctga cctgcagagc cagttcaagt 1260
 gtaagttaca tgaactggta ccagcagaag cggggcaagg caccctaaaag atggatttat 1320
 gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtgg gtctgggacc 1380
 gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440
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 caccatcatc attagagatc tgtcgac 1527

<210> 188
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> antiCD19xantiCD3 VH3VL3

<400> 188

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Ala Thr Arg Tyr Thr
 275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Gln Lys Leu Gln
 305 310 315 320

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Leu
 325 330 335

Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Ala
 340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg
405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 189
<211> 1527
<212> DNA
<213> artificial sequence

<220>
<223> antiCD19xantiCD3 VH5VL1

<400> 189
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caacagattc caggacagcc acccaaactc ctcatctatg atgcatcaa tctagtttct 180
gggatccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttcttg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480

aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
ggccaaggga ccacggtcac cgtctcctcc ggagggtggtg gctccgacgt ccaactggtg 780
cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggttct 840
ggctacacct ttactaggta cacgatgcac tgggtaaggc aggcacctgg acagggctctg 900
gaatggattg gatacattaa tcctagccgt gggtatacta attacgcaga cagcgtcaag 960
ggccgcttca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc 1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc 1080
cttgactact ggggccaaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttcagatgac ccagtctcca 1200
tctagcctgt ctgcatctgt cggggaccgt gtcaccatca cctgcagagc cagtcaaagt 1260
gtaagttaca tgaactggtg ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320
gacacatcca aagtggcttc tggagtcctt gctcgttcca gtggcagtgg gtctgggacc 1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgcaa 1440
cagtggagta gtaaccgct cacgttcggt ggccgggacca aggtggagat caaacatcat 1500
caccatcatc attagagatc tgtcgac 1527

<210> 190

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL1

<400> 190

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
 275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys
305 310 315 320

Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro
385 390 395 400

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
485 490 495

Ile Lys

<210> 191
<211> 1527

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL2

<400> 191

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caacagattc caggacagcc accaaaactc ctcatctatg atgcatcaa tctagtttct	180
gggatccac ccaggtttag tggcagtggtg tctgggacag acttcaccct caacatccat	240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg	300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc	360
tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct	420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg	480
aactgggtga agcagaggcc tggacagggt cttgagtga ttggacagat ttggcctgga	540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa	600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat	660
ttctgtgcaa gacgggagac tacgacggtg ggccgttatt actatgctat ggactactgg	720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg	780
cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct	840
ggctacacct ttactaggta cacgatgcac tgggtaaggc aggcacctgg acagggctctg	900
gaatggattg gatacatata tcctagccgt ggttatacta attacgcaga cagcgtcaag	960
ggccgcttca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc	1020
ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc	1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact	1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca	1200
gcaactctgt ctctgtctcc aggggagcgt gccaccctga gctgcagagc cagtcaaagt	1260
gtaagttaca tgaactggtg ccagcagaag ccgggcaagg caccctaaaag atggatttat	1320
gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtg gtctgggacc	1380
gactactctc tcacaatcaa cagcttgag gctgaagatg ctgccactta ttactgcaa	1440
cagtgagta gtaacctgct cacgttcggt ggccgggacca aggtggagat caaacatcat	1500
caccatcatc attagagatc tgctgac	1527

<210> 192
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> antiCD19xantiCD3 VH5VL2

<400> 192

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
 275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys
 305 310 315 320

Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
 325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
 340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
 385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
 405 410 415

Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 193
 <211> 1527
 <212> DNA
 <213> artificial sequence

<220>
 <223> antiCD19xantiCD3 VH5VL3

<400> 193
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 atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
 caacagattc caggacagcc accaaaactc ctcatctatg atgcatccaa tctagtttct 180
 gggatcccac ccaggttttag tggcagtggg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttcttg cggcggcggc 360
 tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
 gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
 aactgggtga agcagaggcc tggacagggt cttgagtga ttggacagat ttggcctgga 540
 gatggtgata ctaactacaa tggaaagttc aagggtaaag ccaactctgac tgcagacgaa 600
 tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
 ttctgtgcaa gacgggagac tacgacggtg ggccgttatt actatgctat ggactactgg 720
 ggccaaggga ccacggtcac cgtctctctc ggaggtggtg gctccgacgt ccaactggtg 780
 cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caaggcttct 840
 ggctacacct ttactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900

gaatggattg gatacattaa tcctagccgt gggtatacta attacgcaga cagcgtcaag 960
 ggccgcttca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc 1020
 ctgcgttctg aggacactgc aacctattac tgtgcaagat attatgatga tcattactgc 1080
 cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
 gggtctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca 1200
 gcaactctgt ctctgtctcc aggggagcgt gccaccctga cctgcagagc cagttcaagt 1260
 gtaagttaca tgaactggtg ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320
 gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtgg gtctgggacc 1380
 gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440
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 caccatcatc attagagatc tgtcgac 1527

<210> 194

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH5VL3

<400> 194

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly

100	105	110
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val		
115	120	125
Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val		
130	135	140
Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met		
145	150	155
Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln		
165	170	175
Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly		
180	185	190
Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln		
195	200	205
Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg		
210	215	220
Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp		
225	230	235
Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp		
245	250	255
Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser		
260	265	270
Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr		
275	280	285
Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly		
290	295	300
Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys		
305	310	315
Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met		
325	330	335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
 340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
 385 390 395 400

Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg
 405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430

Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460

Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495

Ile Lys

<210> 195
 <211> 1527
 <212> DNA
 <213> artificial sequence

<220>
 <223> antiCD19xantiCD3 VH7VL1

<400> 195
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 atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
 caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180

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gggatccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
ttctgtgcaa gacgggagac tacgacggtg ggcggttatt actatgctat ggactactgg 720
ggccaagggg ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg 780
cagtcagggg ctgaagtga aaaacctggg gcctcagtga aggtgtcctg caagccttct 840
ggctacacct ttactaggtg cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900
gaatggattg gatacatcaa tcctagccgt ggttatacta attacaatca gaagttcaag 960
gaccgcgtca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc 1020
ctgcgttctg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc 1080
cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttcagatgac ccagtctcca 1200
tctagcctgt ctgcatctgt cggggaccgt gtcaccatca cctgcagagc cagtcaaagt 1260
gtaagttaca tgaactggtg ccagcagaag ccgggcaagg caccctaaaag atggatttat 1320
gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtgg gtctgggacc 1380
gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgcaa 1440
cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500
caccatcatc attagagatc tgtcgac 1527

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<210> 196

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL1

<400> 196

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Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1           5           10           15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp

245	250	255
Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser		
260	265	270
Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr		
275	280	285
Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly		
290	295	300
Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys		
305	310	315
Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met		
325	330	335
Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala		
340	345	350
Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr		
355	360	365
Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly		
370	375	380
Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro		
385	390	395
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg		
405	410	415
Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly		
420	425	430
Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly		
435	440	445
Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu		
450	455	460
Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln		
465	470	475
		480

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<210> 197
<211> 1527
<212> DNA
<213> artificial sequence
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<400>	197					
gatatccagc	tgaccacagtc	tccagcttct	tgggtgtgt	ctctagggca	gagggccacc	60
atctcctgca	aggccagcca	aagtgtgat	tatgatggtg	atagttattt	gaactggtac	120
caacagattc	caggacagcc	acccaaactc	ctcatctatg	atgcattcaa	tctagtttct	180
gggatcccac	ccaggtttag	tggcagtggg	tctgggacag	acttcacct	caacatccat	240
cctgtggaga	aggtggatgc	tgcaacctat	cactgtcagc	aaagtactga	ggatccgtgg	300
acgttcggtg	gagggacca	gctcgagatc	aaaggtggtg	gtggttctgg	cggcggcggc	360
tccggtggtg	gtggttctca	ggtgcagctg	cagcagtctg	gggtgagct	ggtgaggcct	420
gggtcctcag	tgaagatttc	ctgcaaggct	tctggctatg	cattcagtag	ctactggatg	480
aactgggtga	agcagaggcc	tggacaggg	cttgagtgga	ttggacagat	ttggcctgga	540
gatggtgata	ctaactaca	tggaaagttc	aagggtaaag	ccactctgac	tgcagacgaa	600
tcctccagca	cagcctacat	gcaactcagc	agcctagcat	ctgaggactc	tgcggtctat	660
ttctgtgcaa	gacgggagac	tacgacggta	ggccgttatt	actatgctat	ggactactgg	720
ggccaaggga	ccacggtcac	cgtctctctc	ggaggtggtg	gctccgacgt	ccaactggtg	780
cagtcagggg	ctgaagtga	aaaacctggg	gcctcagtga	aggtgtctctg	caaggcttct	840
ggctacacct	ttactaggta	cacgatgcac	tgggtaaagg	aggcacctgg	acagggtctg	900
gaatggattg	gatacattaa	tcctagccgt	ggttatacta	attacaatca	gaagtccaag	960
gaccgctca	caatcactac	agacaaatcc	accagcacag	cctacatgga	actgagcagc	1020
ctgcgttctg	aggacactgc	agtctattac	tgtgcaagat	attatgatga	tcattactgc	1080
cttgactact	ggggccaagg	caccacggtc	accgtctct	caggcgaagg	tactagtact	1140
ggttctggtg	gaagtggagg	ttcaggtgga	gcagacgaca	ttgtactgac	ccagtctcca	1200
gcaactctgt	ctctgtctcc	aggggagcgt	gccacctga	gctgcagagc	cagtcaaagt	1260

gtaagttaca tgaactggta ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320
 gacacatcca aagtggcttc tggagtcctt gctcgcttca gtggcagtgg gtctgggacc 1380
 gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgccaa 1440
 cagtggagta gtaacccgct cacgttcggt ggcgggacca aggtggagat caaacatcat 1500
 caccatcatc attagagatc tgtcgac 1527

<210> 198
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> antiCD19xantiCD3 VH7VL2

<400> 198

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
 260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
 275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
 290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
 305 310 315 320

Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
 325 330 335

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
 340 345 350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380

Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro

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<210> 199
<211> 1527
<212> DNA
<213> artificial sequence
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<220>
<223> antiCD19xantiCD3 VH7VL3

<400> 199						
gatatccagc	tgaccagtc	tccagcttct	ttggctgtgt	ctctagggca	gagggccacc	60
atctcctgca	aggccagcca	aagtgttgat	tatgatggtg	atagttattt	gaactggtac	120
caacagattc	caggacagcc	acccaaactc	ctcatctatg	atgcatccaa	tctagtttct	180
gggatcccac	ccaggtttag	tggcagtggg	tctgggacag	acttcaccct	caacatccat	240
cctgtggaga	aggtggatgc	tgcaacctat	cactgtcagc	aaagtactga	ggatccgtgg	300
acgttcggtg	gagggaccaa	gctcgagatc	aaagggtggtg	gtggttctgg	cggcggcggc	360
tccggtggtg	gtggttctca	ggtgcagctg	cagcagtcctg	gggctgagct	ggtgaggcct	420
gggtcctcag	tgaagatttc	ctgcaaggct	tctggctatg	cattcagtag	ctactggatg	480
aactgggtga	agcagaggcc	tggacagggc	cttgagtgga	ttggacagat	ttggcctgga	540
gatggtgata	ctaactacaa	tggaaagttc	aagggtaaag	ccactctgac	tgcagacgaa	600

tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
 ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
 ggccaagggg ccacggtcac cgtctcctcc ggaggtggtg gctccgacgt ccaactggtg 780
 cagtcagggg ctgaagtga aaaaacctggg gcctcagtga aggtgtcctg caaggcttct 840
 ggctacacct ttactaggta cacgatgcac tgggtaaggc aggcacctgg acagggtctg 900
 gaatggattg gatacattaa tcctagccgt gggtatacta attacaatca gaagttcaag 960
 gaccgcgtca caatcactac agacaaatcc accagcacag cctacatgga actgagcagc 1020
 ctgcgttctg aggacactgc agtctattac tgtgcaagat attatgatga tcattactgc 1080
 cttgactact ggggccaagg caccacggtc accgtctcct caggcgaagg tactagtact 1140
 ggttctggtg gaagtggagg ttcaggtgga gcagacgaca ttgtactgac ccagtctcca 1200
 gcaactctgt ctctgtctcc aggggagcgt gccaccctga cctgcagagc cagttcaagt 1260
 gtaagttaca tgaactggtg ccagcagaag ccgggcaagg cacccaaaag atggatttat 1320
 gacacatcca aagtggcttc tggagtcctt gctcgttca gtggcagtggt gtctgggacc 1380
 gactactctc tcacaatcaa cagcttggag gctgaagatg ctgccactta ttactgcca 1440
 cagtgagta gtaaccgct cacgttcggt ggccggacca aggtggagat caaacatcat 1500
 caccatcatc attagagatc tgtcgac 1527

<210> 200

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> antiCD19xantiCD3 VH7VL3

<400> 200

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
275 280 285

Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
290 295 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
 305 310 315 320
 Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met
 325 330 335
 Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
 340 345 350
 Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365
 Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly
 370 375 380
 Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro
 385 390 395 400
 Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg
 405 410 415
 Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 420 425 430
 Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445
 Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu
 450 455 460
 Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480
 Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
 485 490 495
 Ile Lys

<210> 201
 <211> 45
 <212> DNA
 <213> artificial sequence

<220>

<223> standard linker

<400> 201

ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttct

45

<210> 202

<211> 54

<212> DNA

<213> artificial sequence

<220>

<223> deimmunized linker

<400> 202

ggcgaaggta ctagtactgg ttctggtgga agtggagggt caggtggagc agac

54

<210> 203

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> antiCD19xantiCD3

<400> 203

gatatccagc tgaccagtc tccagcttct ttggtgtgt ctctagggca gagggccacc	60
atctcctgca aggccagcca aagtgtgat tatgatggtg atagtatttt gaactggtac	120
caacagattc caggacagcc acccaaactc ctcattctatg atgcatccaa tctagtttct	180
gggatcccac ccaggttttag tggcagtggg tctgggacag acttcaccct caacatccat	240
cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg	300
acgttcggtg gagggaccaa gctcgagatc aaagggtggtg gtggttctgg cggcggcggc	360
tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct	420
gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg	480
aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga	540
gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa	600
tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat	660
ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg	720
ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gatccgatat caaactgcag	780
cagtcagggg ctgaactggc aagacctggg gcctcagtga agatgtcctg caagacttct	840
ggctacacct ttactaggta cacgatgcac tgggtaaaac agaggcctgg acagggtctg	900
gaatggattg gatacatcaa tcctagccgt ggttatacta attacaatca gaagttcaag	960

gacaaggcca cattgactac agacaaatcc tccagcacag cctacatgca actgagcagc 1020
 ctgacatctg aggactctgc agtctattac tgtgcaagat attatgatga tcattactgc 1080
 cttgactact ggggccaaagg caccactctc acagtctcct cagtcgaagg tggaagtgga 1140
 ggttctggtg gaagtggagg ttcaggtgga gtcgacgaca ttcagctgac ccagtctcca 1200
 gcaatcatgt ctgcatctcc aggggagaag gtcacatga cctgcagagc cagttcaagt 1260
 gtaagttaca tgaactggta ccagcagaag tcaggcacct cccccaaaag atggatttat 1320
 gacacatcca aagtggcttc tggagtcctt tatcgcttca gtggcagtggt gtctgggacc 1380
 tcatactctc tcacaatcag cagcatggag gctgaagatg ctgccactta ttactgccaa 1440
 cagtggagta gtaacccgct cacgttcggt gctggggacca agctggagct gaaa 1494

<210> 204
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> antiCD19xantiCD3

<400> 204

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gln Val

115		120		125
Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val				
130		135		140
Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met				
145		150		155
				160
Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln				
	165		170	175
Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly				
	180		185	190
Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln				
	195		200	205
Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg				
	210		215	220
Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp				
	225		230	235
				240
Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp				
	245		250	255
Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser				
	260		265	270
Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr Thr				
	275		280	285
Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly				
	290		295	300
Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys				
	305		310	315
				320
Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr Met				
	325		330	335
Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala				
	340		345	350

Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
 355 360 365

Thr Leu Thr Val Ser Ser Val Glu Gly Gly Ser Gly Gly Ser Gly Gly
 370 375 380

Ser Gly Gly Ser Gly Gly Val Asp Asp Ile Gln Leu Thr Gln Ser Pro
 385 390 395 400

Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg
 405 410 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Ser Gly
 420 425 430

Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
 435 440 445

Val Pro Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu
 450 455 460

Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
 465 470 475 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu
 485 490 495

Leu Lys

<210> 205

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH5VL1

<400> 205

gacattatcc tgatccaatc tccaccttct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca gaaccagcga aaatgttgac ggatacggca ttagttttat aaactggtac 120

caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc 180

gggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240

cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa gggtccgtgg 300

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acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag 420
acagtacga tctcctgcaa ggcttctggg tataccttca cgaagttcgg aatgaactgg 480
gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga 540
gagccaacat attctgatga cttcaaggga cggtttgcct tctctttgga aacgtctgcc 600
agcactgcct atttgcgga caacaacctc aaaaatgagg acatggctaa atacttctgt 660
gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc 720
accgtctcct cgggaggtg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg 780
aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg 840
tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt 900
aatcctagcc gtggttatac taattacgca gacagcgtca agggccgctt cacaatcact 960
acagacaaat ccaccagcac agcctacatg gaactgagca gcctgcgttc tgaggacact 1020
gcaacctatt actgtgcaag atattatgat gatcattact gccttgacta ctggggccaa 1080
ggcaccacgg tcaccgtctc ctcaggcgaa ggtactagta ctggttctgg tggaagtgga 1140
ggttcaggtg gagcagacga cattcagatg acccagtctc catctagcct gtctgcatct 1200
gtcggggacc gtgtcaccat cacctgcaga gccagtcaaa gtgtaagtta catgaactgg 1260
taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct 1320
tctggagtcc ctgctcgctt cagtggcagt gggctctggga ccgactactc tctcacaatc 1380
aacagcttgg aggtgaaga tgctgccact tattactgcc aacagtggag tagtaaccgg 1440
ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

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<210> 206
 <211> 492
 <212> PRT
 <213> artificial sequence

<220>
 <223> CCR5xanti-CD3 VH5VL1

<400> 206

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
 20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
 65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
 85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
 115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
 145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
 165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
 180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
 195 200 205

Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
 210 215 220

Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
 225 230 235 240

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
 245 250 255

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
275 280 285

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
290 295 300

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
305 310 315 320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
325 330 335

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
340 345 350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
355 360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
385 390 395 400

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser
405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 207

<211> 1476

<212> DNA
<213> artificial sequence

<220>
<223> CCR5xanti-CD3 VH5VL2

<400> 207
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caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc 180
ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240
cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg 300
acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttctgg cggcggcggc 360
tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag 420
acagtcaaga tctcctgcaa ggcttctggg tataccttca cgaagtccg aatgaactgg 480
gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga 540
gagccaacat attctgatga cttcaaggga cggtttgctt tctctttgga aacgtctgcc 600
agcaactgct atttgcggat caacaacctc aaaaatgagg acatggctaa atacttctgt 660
gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc 720
accgtctcct cgggaggtgg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg 780
aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg 840
tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt 900
aatcctagcc gtggttatac taattacgca gacagcgtca agggccgctt cacaatcact 960
acagacaaat ccaccagcac agcctacatg gaactgagca gcctgcgttc tgaggacact 1020
gcaacctatt actgtgcaag atattatgat gatcattact gccttgacta ctggggccaa 1080
ggcaccacgg tcaccgtctc ctccaggcga ggtactagta ctggttctgg tggaagtgga 1140
ggttcaggtg gagcagacga cattgtactg acccagtctc cagcaactct gtctctgtct 1200
ccaggggagc gtgccaccct gagctgcaga gccagtcaaa gtgtaagtta catgaactgg 1260
taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct 1320
tctggagtcc ctgctcgctt cagtggcagt gggctctgga ccgactactc tctcacaatc 1380
aacagcttgg aggtgaaga tgctgccact tattactgcc aacagtggag tagtaaccgc 1440
ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

<210> 208

<211> 492
 <212> PRT
 <213> artificial sequence

<220>
 <223> CCR5xanti-CD3 VH5VL2

<400> 208

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
 20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
 65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
 85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
 115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
 145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
 165 170 175

Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
 180 185 190

Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
 195 200 205

Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
210 215 220

Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
225 230 235 240

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
245 250 255

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
275 280 285

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
290 295 300

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
305 310 315 320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
325 330 335

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
340 345 350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
355 360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
385 390 395 400

Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser
405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser

435 440 445
 Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
 450 455 460
 Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
 465 470 475 480
 Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490

<210> 209
 <211> 1476
 <212> DNA
 <213> artificial sequence

<220>
 <223> CCR5xanti-CD3 VH5VL3

<400> 209
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 atctcctgca gaaccagcga aaatgttgac ggatacggca ttagttttat aaactggtac 120
 caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatcca ccaaggatcc 180
 ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240
 cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg 300
 acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttctgg cggcggcggc 360
 tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag 420
 acagtacga tctcctgcaa ggcttctggg tataccttca cgaagttcgg aatgaactgg 480
 gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga 540
 gagccaacat attctgatga cttcaaggga cggtttgcct tctctttgga aacgtctgcc 600
 agcactgcct atttgcgat caacaacctc aaaaatgagg acatggctaa atacttctgt 660
 gccagagggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc 720
 accgtctcct ccggaggtgg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg 780
 aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg 840
 tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt 900
 aatcctagcc gtggttatac taattacgca gacagcgtca agggccgctt cacaatcact 960
 acagacaaat ccaccagcac agcctacatg gaactgagca gcctgcgttc tgaggacact 1020
 gcaacctatt actgtgcaag atattatgat gatcattact gccttgacta ctggggccaa 1080


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ggcaccacgg tcaccgtctc ctcaggcgaa ggtactagta ctggttctgg tggaagtgga 1140
ggttcaggtg gagcagacga cattgtactg acccagtctc cagcaactct gtctctgtct 1200
ccaggggagc gtgccaccct gacctgcaga gccagttcaa gtgtaagtta catgaactgg 1260
taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct 1320
tctggagtcc ctgctcgctt cagtggcagt gggctctggga ccgactactc tctcacaatc 1380
aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaacccg 1440
ctcacgttcg gtggcgggac caaggtggag atcaaaa 1476

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<210> 210
<211> 492
<212> PRT
<213> artificial sequence

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<220>
<223> CCR5xanti-CD3 VH5VL3

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<400> 210

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```

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
1.          5          10          15

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Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
          20          25          30

```

```

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
          35          40          45

```

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Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
          50          55          60

```

```

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
65          70          75          80

```

```

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
          85          90          95

```

```

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
          100          105          110

```

```

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
          115          120          125

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Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile

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130	135	140
Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp		
145	150	155 160
Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His		
	165	170 175
Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe		
	180	185 190
Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn		
	195	200 205
Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly		
	210	215 220
Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val		
	225	230 235 240
Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser		
	245	250 255
Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys		
	260	265 270
Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln		
	275	280 285
Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg		
	290	295 300
Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr		
	305	310 315 320
Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg		
	325	330 335
Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His		
	340	345 350
Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser		
	355	360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
385 390 395 400

Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser
405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 211

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL1

<400> 211

gacattatcc tgatccaatc tccaccttct ttggctgtgt ctctagggca gagggccacc 60

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caacagaagc caggacagcc acccaaactc ctcctctatg ctgcatccca ccaaggatcc 180

ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240

cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa gggtccgtgg 300

acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttcttg cggcggcggc 360

tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag 420

acagtcacga tctcctgcaa ggcttctggg tataccttca cgaagttcgg aatgaactgg 480

gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga 540

gagccaacat attctgatga cttcaaggga cggtttgcct tctctttgga aacgtctgcc 600
 agcactgcct atttgcgat caacaacctc aaaaatgagg acatggctaa ataacttctgt 660
 gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc 720
 accgtctcct cgggaggtgg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg 780
 aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg 840
 tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt 900
 aatcctagcc gtggttatac taattacaat cagaagttca aggaccgct cacaatcact 960
 acagacaaat ccaccagcac agcctacatg gaactgagca gcctgcgttc tgaggacact 1020
 gcagtctatt actgtgcaag atattatgat gatcattact gccttgacta ctggggccaa 1080
 ggcaccacgg tcaccgtctc ctcaggcgaa ggtactagta ctggttctgg tggaagtggg 1140
 ggttcaggtg gagcagacga cattcagatg acccagtctc catctagcct gtctgcatct 1200
 gtcggggacc gtgtcaccat cacctgcaga gccagtcaa gtgtaagtta catgaactgg 1260
 taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct 1320
 tctggagtcc ctgctcgctt cagtggcagt gggctctggg ccgactactc tctcacaatc 1380
 aacagcttgg aggtgaaga tgetgccact tattactgcc aacagtggag tagtaaccgg 1440
 ctacacgttcg gtggcgggac caaggtggag atcaaa 1476

<210> 212
 <211> 492
 <212> PRT
 <213> artificial sequence

<220>
 <223> CCR5xanti-CD3 VH7VL1

<400> 212

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
 20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
 65 70 75 80
 Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
 85 90 95
 Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
 115 120 125
 Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
 130 135 140
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
 145 150 155 160
 Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
 165 170 175
 Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
 180 185 190
 Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
 195 200 205
 Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
 210 215 220
 Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
 225 230 235 240
 Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
 245 250 255
 Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 260 265 270
 Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
 275 280 285
 Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
 290 295 300

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
305 310 315 320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
325 330 335

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
340 345 350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
355 360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
385 390 395 400

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser
405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 213

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL2

<400> 213

gacattatcc tgatccaatc tccaccttct ttggctgtgt ctctagggca gagggccacc

60

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caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc 180
ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat 240
cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg 300
acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttcttg cggcggcggc 360
tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag 420
acagtcacga tctcctgcaa ggcttctggg tataccttca cgaagtccgg aatgaactgg 480
gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga 540
gagccaacat attctgatga cttcaaggga cggtttgctt tctctttgga aacgtctgcc 600
agcactgcct atttgcggt caacaacctc aaaaatgagg acatggctaa atacttctgt 660
gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc 720
accgtctcct ccggaggttg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg 780
aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg 840
tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt 900
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ccaggggagc gtgccaccct gagctgcaga gccagtcaa gtgtaagtta catgaactgg 1260
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tctggagtcc ctgctcgctt cagtggcagt gggctctggga ccgactactc tctcacaatc 1380
aacagcttgg aggtgaaga tgctgccact tattactgcc aacagtggag tagtaaccg 1440
ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

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<210> 214
<211> 492
<212> PRT
<213> artificial sequence

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<220>
<223> CCR5xanti-CD3 VH7VL2
<400> 214

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Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
 1 5 10 15
 Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
 20 25 30
 Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45
 Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
 65 70 75 80
 Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
 85 90 95
 Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
 115 120 125
 Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
 130 135 140
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
 145 150 155 160
 Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His
 165 170 175
 Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe
 180 185 190
 Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn
 195 200 205
 Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly
 210 215 220
 Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
 225 230 235 240

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser
245 250 255

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
275 280 285

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
290 295 300

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
305 310 315 320

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
325 330 335

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
340 345 350

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
355 360 365

Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly
370 375 380

Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
385 390 395 400

Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser
405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro

465

470

475

480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490

<210> 215

<211> 1476

<212> DNA

<213> artificial sequence

<220>

<223> CCR5xanti-CD3 VH7VL3

<400> 215

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caacagaagc caggacagcc acccaaactc ctcatctatg ctgcatccca ccaaggatcc      180
ggggtccctg ccagatttag tggcagtggg tctgggacag acttcagcct caacatccat      240
cctttggagg aggatgatac tgcaatgtat ttctgtcacc aaagtaagaa ggttccgtgg      300
acgttcggtg gaggcaccaa gctggaaatc aaaggtggtg gtggttcttg cggcggcggc      360
tccggtggtg gtggttctca gctggagcag tctggacctg aactgaagaa gcctggagag      420
acagtcacga tctcctgcaa ggcttctggg tataccttca cgaagtccg aatgaactgg      480
gtgaagcagg ctccaggaaa gggtttaaag tggatgggct ggatacacac ctccactgga      540
gagccaacat attctgatga cttcaaggga cggtttgct tctctttgga aacgtctgcc      600
agcactgcct atttgcggat caacaacctc aaaaatgagg acatggctaa atacttctgt      660
gccagaggtg gtccttacgt aaggggtgct ttggactact ggggtcaagg aacctcagtc      720
accgtctcct ccggaggtgg tggatccgac gtccaactgg tgcagtcagg ggctgaagtg      780
aaaaaacctg gggcctcagt gaaggtgtcc tgcaaggctt ctggctacac ctttactagg      840
tacacgatgc actgggtaag gcaggcacct ggacagggtc tggaatggat tggatacatt      900
aatcctagcc gtggttatac taattacaat cagaagttca aggaccgct cacaatcact      960
acagacaaat ccaccagcac agcctacatg gaactgagca gcctgcgttc tgaggacact     1020
gcagtctatt actgtgcaag atattatgat gatcattact gccttgacta ctggggccaa     1080
ggcaccacgg tcaccgtctc ctcaggcgaa ggtactagta ctggttcttg tggaagtgga     1140
ggttcaggtg gagcagacga cattgtactg acccagctc cagcaactct gtctctgtct     1200
ccaggggagc gtgccaccct gacctgcaga gccagttcaa gtgtaagtta catgaactgg     1260
taccagcaga agccgggcaa ggcacccaaa agatggattt atgacacatc caaagtggct     1320

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tctggagtc ctcgtcgctt cagtggcagt gggctctggga ccgactactc tctcacaatc 1380
 aacagcttgg aggctgaaga tgctgccact tattactgcc aacagtggag tagtaaccgc 1440
 ctcacgttcg gtggcgggac caaggtggag atcaaa 1476

<210> 216
 <211> 492
 <212> PRT
 <213> artificial sequence

<220>
 <223> CCR5xanti-CD3 VH7VL3

<400> 216

Asp Ile Ile Leu Ile Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Thr Ser Glu Asn Val Asp Gly Tyr
 20 25 30

Gly Ile Ser Phe Ile Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser His Gln Gly Ser Gly Val Pro Ala
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Leu Asn Ile His
 65 70 75 80

Pro Leu Glu Glu Asp Asp Thr Ala Met Tyr Phe Cys His Gln Ser Lys
 85 90 95

Lys Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Leu
 115 120 125

Glu Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu Thr Val Thr Ile
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Lys Phe Gly Met Asn Trp
 145 150 155 160

Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met Gly Trp Ile His

165	170	175
Thr Ser Thr Gly Glu Pro Thr Tyr Ser Asp Asp Phe Lys Gly Arg Phe		
180	185	190
Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr Leu Arg Ile Asn		
195	200	205
Asn Leu Lys Asn Glu Asp Met Ala Lys Tyr Phe Cys Ala Arg Gly Gly		
210	215	220
Pro Tyr Val Arg Gly Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val		
225	230	235
Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser		
245	250	255
Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys		
260	265	270
Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln		
275	280	285
Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg		
290	295	300
Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr		
305	310	315
Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg		
325	330	335
Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His		
340	345	350
Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser		
355	360	365
Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly		
370	375	380
Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser		
385	390	395
		400

Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser
405 410 415

Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp
420 425 430

Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser
435 440 445

Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu
450 455 460

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
465 470 475 480

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 217

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL1

<400> 217

caaattgttc tctccagtc tccagcaatc cttctgcat ctccagggga gaaggtcaca	60
atgacttgca gggccagctc aagtttaagt ttcattgcaact ggtaccagca gaagccagga	120
tcctccccc aacctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gacctcttac tctctcaca tccagcagagt ggaggctgaa	240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cgggtgctggg	300
acaaaggtgg aaataaaagg tgggtggtgt tctggcgggc gcggtccgg tgggtggtgt	360
tctcaggtgc aactgaggca gctggggct gagctggtga agcctggggc ctcaagtgaag	420
atgtcctgca aggtctctgg ctacacattt accagttaca atatgcactg ggtaaagcag	480
acacctggac agggcctgga atggattgga gctatttata caggaaatgg tgatacttcc	540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc	600
tacatgcagc tcagcagttc gacatctgag gactctgcgg tctattactg tgcaagatcg	660
cactacggtg gtaactacgt agactacttt gactactggg gccaaaggcac actagtcaca	720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaag	780

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aaacctgggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtac      840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat      900
cctagccgtg gttatactaa ttacgcagac agcgtcaagg gccgcttcac aatcactaca      960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca     1020
acctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc     1080
accacgggtc ccgctctctc aggcgaaggt actagtactg gttctggtgg aagtggaggt     1140
tcagggtggag cagacgacat tcagatgacc cagtctccat ctagcctgtc tgcctctgtc     1200
ggggaccgtg tcaccatcac ctgcagagcc agtcaaagtg taagttacat gaactggtac     1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct     1320
ggagtccttg ctgccttcag tggcagtggg tctgggaccg actactctct cacaatcaac     1380
agcttggagg ctgaagatgc tgccacttat tactgccaac agtggagtag taaccgctc     1440
acgttcggtg gcgggaccaa ggtggagatc aaa                                1473

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<210> 218
<211> 491
<212> PRT
<213> artificial sequence

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<220>
<223> CD20xanti-CD3 VH5VL1

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<400> 218

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```

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1           5           10          15

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```

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
          20          25          30

```

```

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
          35          40          45

```

```

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
          50          55          60

```

```

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65          70          75          80

```

```

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
          85          90          95

```

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
 100 105 110
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
 115 120 125
 Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
 130 135 140
 Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
 145 150 155 160
 Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
 165 170 175
 Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
 180 185 190
 Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
 195 200 205
 Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
 210 215 220
 Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
 225 230 235 240
 Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
 245 250 255
 Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
 260 265 270
 Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
 275 280 285
 Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
 290 295 300
 Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr
 305 310 315 320
 Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
 325 330 335

Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
 340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
 355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
 370 375 380

Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
 385 390 395 400

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr
 405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
 420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
 435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
 450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
 465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490

<210> 219

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH5VL2

<400> 219

caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca 60

atgacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga 120

tcctcccca aaccctggat ttatgccaca tccaacctgg cttctggagt cctgtctcgc 180

ttcagtgga gtgggtctgg gacctcttac tctctcaca tcagcagagt ggaggctgaa 240

gatgctgcca cttatttctg ccatcagtg agtagtaacc cgctcacgtt cggtgctggg 300


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acaaaggtgg aaataaaagg tgggtggtgg tctggcggcg gcggctccgg tggtggtggt 360
tctcaggtgc aactgcggca gcctggggct gagctggtga agcctggggc ctcagtgaag 420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag 480
acacctggac agggcctgga atggattgga gctatttacc caggaaatgg tgatacttcc 540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaaccctc cagcacagcc 600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg 660
cactacggta gtaactacgt agactacttt gactactggg gccaaaggcac actagtcaca 720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaag 780
aaacctgggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtac 840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat 900
cctagccgtg gttatactaa ttacgcagac agcgtcaagg gccgcttcac aatcactaca 960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca 1020
acctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc 1080
accacggtca ccgtctctc aggcgaaggc actagtactg gttctggtgg aagtggaggt 1140
tcaggtggag cagacgacat tgtactgacc cagtctccag caactctgtc tctgtctcca 1200
ggggagcgtg ccacctgag ctgcagagcc agtcaaagtg taagttacat gaactggtac 1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct 1320
ggagtccctg ctgccttcag tggcagtggg tctgggaccg actactctct cacaatcaac 1380
agcttgaggc ctgaagatgc tgccacttat tactgccaac agtggagtag taaccgctc 1440
acgttcggtg gcgggaccaa ggtggagatc aaa 1473

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<210> 220
<211> 491
<212> PRT
<213> artificial sequence

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<220>
<223> CD20xanti-CD3 VH5VL2

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<400> 220

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```

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1           5           10          15

```

```

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
20          25          30

```

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
 115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
 130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
 145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
 165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
 180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
 195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
 210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
 225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
 245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
 260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
290 295 300

Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr
305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
325 330 335

Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
370 375 380

Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
385 390 395 400

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr
405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 221

<211> 1473
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD20xanti-CD3 VH5VL3

<400> 221
 caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca 60
 atgacttgca gggccagctc aagtttaagt ttcatgcaact ggtaccagca gaagccagga 120
 tcctccccc aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtcttg gacctcttac tctctcacia tcagcagagt ggaggctgaa 240
 gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300
 acaaagggtg aaataaaagg tgggtggtgt tctggcggcg gcggtccgg tgggtggtgt 360
 tctcaggtgc aactgcggca gcctggggct gagctggtga agcctggggc ctcaagtgaag 420
 atgtcctgca aggtctcttg ctacacattt accagttaca atatgcaact ggtaaagcag 480
 acacctggac agggcctgga atggattgga gctatttata caggaaatgg tgatacttcc 540
 tacaatcaga agttcaaagg caagccaca ttgactgcag acaaatcctc cagcacagcc 600
 tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg 660
 cactacggta gtaactacgt agactacttt gactactggg gccaaaggac actagtcaca 720
 gtctcgacag gaggtggttg atccgacgtc caactggtgc agtcaggggc tgaagtgaag 780
 aaactctggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtac 840
 acgatgcaact gggtaaggca ggcacctgga cagggtcttg aatggattgg atacattaat 900
 cctagccgtg gttatactaa ttacgcagac agcgtcaagg gccgcttcac aatcactaca 960
 gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca 1020
 acctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc 1080
 accacgggtc ccgtctctc aggcgaaggt actagtactg gttctggttg aagtggaggt 1140
 tcaggtggag cagacgacat tgtactgacc cagtctccag caactctgtc tctgtctcca 1200
 ggggagcgtg ccacctgac ctgcagagcc agttcaagt taagttacat gaactggtac 1260
 cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct 1320
 ggagtccctg ctgcttcag tggcagtggg tctgggaccg actactctct cacaatcaac 1380
 agcttgagg ctgaagatgc tgccaattat tactgccaac agtggagtag taaccgctc 1440
 acgttcggtg gcgggaccaa ggtggagatc aaa 1473

<210> 222
 <211> 491
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD20xanti-CD3 VH5VL3

<400> 222

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
 115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
 130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
 145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
 165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
 180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr

195	200	205
Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser		
210	215	220
Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr		
225	230	235 240
Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly		
	245	250 255
Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala		
	260	265 270
Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala		
	275	280 285
Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly		
	290	295 300
Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr Thr		
305	310	315 320
Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser		
	325	330 335
Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr		
	340	345 350
Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly		
	355	360 365
Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala		
	370	375 380
Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro		
385	390	395 400
Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr		
	405	410 415
Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile		
	420	425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
 435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
 450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
 465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490

<210> 223
 <211> 1473
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD20xanti-CD3 VH7VL1

<400> 223
 caaattgttc tctccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca 60
 atgacttgca gggccagctc aagtttaagt ttcattgact ggtaccagca gaagccagga 120
 tcctccccc aacctggat ttatgccaca tccaacctgg cttctggagt cctgctcgc 180
 ttcagtggca gtgggtctgg gacctcttac tctctcaca tcagcagagt ggaggctgaa 240
 gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cgggtgctggg 300
 acaaaggtgg aaataaaagg tgggtggtgt tctggcggcg gcggctccgg tgggtggtgt 360
 tctcaggtgc aactgoggca gcctggggct gagctggtga agcctggggc ctcagtgaag 420
 atgtctgca aggttctg ctacacattt accagttaca atatgactg ggtaaagcag 480
 acacctggac agggcctgga atggattgga gctatttata caggaaatgg tgatacttcc 540
 tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc 600
 tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg 660
 cactacggtg gtaactacgt agactacttt gactactggg gccaaaggac actagtcaca 720
 gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaag 780
 aaacctgggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtac 840
 acgatgact gggttaaggca ggcacctgga cagggtctgg aatggattgg atacattaat 900
 cctagccgtg gttatactaa ttacaatcag aagttcaagg accgcgtcac aatcactaca 960
 gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca 1020

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gtctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc 1080
accacgggtca ccgtctcctc aggcgaaggt actagtactg gttctgggtg aagtggaggt 1140
tcaggtggag cagacgacat tcagatgacc cagtctccat ctgcctgtc tgcattgtc 1200
ggggaccgtg tcaccatcac ctgcagagcc agtcaaagtg taagttacat gaactggtac 1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct 1320
ggagtccctg ctgccttcag tggcagtggg tctgggaccg actactctct cacaatcaac 1380
agcttgaggg ctgaagatgc tgccacttat tactgccaac agtggagtag taaccgctc 1440
acgttcggtg gcgggaccaa ggtggagatc aaa 1473

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<210> 224
<211> 491
<212> PRT
<213> artificial sequence

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<220>
<223> CD20xanti-CD3 VH7VL1

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<400> 224

```

```

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1           5           10           15

```

```

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
          20           25           30

```

```

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
          35           40           45

```

```

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50           55           60

```

```

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65           70           75           80

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Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
          85           90           95

```

```

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
          100           105           110

```

```

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
          115           120           125

```


Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
290 295 300

Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Thr
305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
325 330 335

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
370 375 380

Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
385 390 395 400

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr
405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 225
<211> 1473
<212> DNA
<213> artificial sequence

<220>
<223> CD20xanti-CD3 VH7VL2

<400> 225
caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca 60
atgacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga 120
tcctccccc aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gacctcttac tctctcacia tcagcagagt ggaggctgaa 240
gatgctgcc cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300
acaaaggtgg aaataaaagg tgggtggtgt tctggcggcg gcggctccgg tgggtggtgt 360
tctcaggtgc aactgaggca gcctggggct gagctggtga agcctggggc ctcaagtgaag 420
atgtcctgca aggttctctg ctacacattt accagttaca atatgcactg ggtaaagcag 480
acacctggac agggcctgga atggattgga gctatttatc caggaaatgg tgatacttcc 540

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tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatcctc cagcacagcc 600
tacatgcagc tcagcagtct gacatctgag gactctgcgg tctattactg tgcaagatcg 660
cactacggta gtaactacgt agactacttt gactactggg gccaaaggcac actagtcaca 720
gtctcgacag gaggtggtgg atccgacgtc caactggtgc agtcaggggc tgaagtgaag 780
aaacctgggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtag 840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat 900
cctagccgtg gttatactaa ttacaatcag aagttcaagg accgcgtcac aatcactaca 960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca 1020
gtctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc 1080
accacggtca cegtctctc aggcgaagg actagtactg gttctggtgg aagtggaggt 1140
tcaggtggag cagacgacat tgtactgacc cagtctccag caactctgtc tctgtctcca 1200
ggggagcgtg ccacctgag ctgcagagcc agtcaaagt taagttacat gaactggtac 1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct 1320
ggagtccctg ctgccttcag tggcagtggg tctgggaccg actactctct cacaatcaac 1380
agcttgagg ctgaagatgc tgccacttat tactgccaac agtggagtag taaccgctc 1440
acgttcggtg gcgggaccaa ggtggagatc aaa 1473

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<210> 226
<211> 491
<212> PRT
<213> artificial sequence

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<220>
<223> CD20xanti-CD3 VH7VL2
<400> 226

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```

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1           5           10          15

```

```

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
20           25           30

```

```

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35           40           45

```

```

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50           55           60

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Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
 115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
 130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
 145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
 165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
 180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
 195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
 210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
 225 230 235 240

Val Ser Thr Gly Gly Gly Gly Ser Asp Val Gln Leu Val Gln Ser Gly
 245 250 255

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
 260 265 270

Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala
 275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly
 290 295 300

Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Thr
305 310 315 320

Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
325 330 335

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His Tyr
340 345 350

Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
355 360 365

Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala
370 375 380

Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
385 390 395 400

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr
405 410 415

Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile
420 425 430

Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
435 440 445

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala
450 455 460

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 227

<211> 1473

<212> DNA

<213> artificial sequence

<220>

<223> CD20xanti-CD3 VH7VL3

<400> 227

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caaattgttc tctcccagtc tccagcaatc ctttctgcat ctccagggga gaaggtcaca      60
atgacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga      120
tcctccccc aaccctggat ttatgccaca tccaacctgg cttctggagt ccctgctcgc      180
ttcagtggca gtgggtctgg gacctcttac tctctcacia tcagcagagt ggaggctgaa      240
gatgctgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg      300
acaaagggtg aaataaaagg tgggtgggtg tctggcggcg gcggctccgg tgggtgggtg      360
tctcaggtag aactgcggca gcctggggct gagctgggtg agcctggggc ctcaagtgaag      420
atgtcctgca aggcttctgg ctacacattt accagttaca atatgcactg ggtaaagcag      480
acacctggac agggcctgga atggattgga gctatttata caggaaatgg tgatacttcc      540
tacaatcaga agttcaaagg caaggccaca ttgactgcag acaaatoctc cagcacagcc      600
tacatgcagc tcagcagctc gacatctgag gactctgcgg tctattactg tgcaagatcg      660
cactacggta gtaactacgt agactacttt gactactggg gccaaaggcac actagtcaca      720
gtctcgacag gaggtgggtg atccgacgtc caactgggtg agtcaggggc tgaagtgaag      780
aaacctgggg cctcagtga ggtgtcctgc aaggcttctg gctacacctt tactaggtac      840
acgatgcact gggtaaggca ggcacctgga cagggtctgg aatggattgg atacattaat      900
cctagccgtg gttatactaa ttacaatcag aagttcaagg accgcgtcac aatcactaca      960
gacaaatcca ccagcacagc ctacatggaa ctgagcagcc tgcgttctga ggacactgca     1020
gtctattact gtgcaagata ttatgatgat cattactgcc ttgactactg gggccaaggc     1080
accacggtea ccgtctctc aggcgaaggc actagtactg gttctgggtg aagtggaggt     1140
tcagggtggag cagacgacat tgtactgacc cagtctccag caactctgtc tctgtctcca     1200
ggggagcgtg ccacctgac ctgcagagcc agttcaagtg taagttacat gaactggtac     1260
cagcagaagc cgggcaaggc acccaaaaga tggatttatg acacatccaa agtggcttct     1320
ggagtccctg ctcgcttcag tggcagtggg tctgggaccg actactctct cacaatcaac     1380
agcttggagg ctgaagatgc tgccacttat tactgccaac agtggagtag taaccgctc     1440
acgttcggtg gcgggaccaa ggtggagatc aaa                                     1473

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<210> 228
 <211> 491
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD20xanti-CD3 VH7VL3

<400> 228

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Arg Gln Pro
 115 120 125

Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
 130 135 140

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln
 145 150 155 160

Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
 165 170 175

Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr
 180 185 190

Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr
 195 200 205

Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser His Tyr Gly Ser
 210 215 220

Asn Tyr Val Asp Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr

225		230		235		240
Val Ser Thr Gly	Gly Gly Gly Ser Asp	Val Gln Leu Val	Gln Ser Gly			
	245	250	255			
Ala Glu Val Lys	Lys Pro Gly Ala Ser Val	Lys Val Ser	Cys Lys Ala			
	260	265	270			
Ser Gly Tyr Thr	Phe Thr Arg Tyr Thr Met	His Trp Val	Arg Gln Ala			
	275	280	285			
Pro Gly Gln Gly	Leu Glu Trp Ile Gly Tyr	Ile Asn Pro	Ser Arg Gly			
	290	295	300			
Tyr Thr Asn Tyr	Asn Gln Lys Phe Lys Asp	Arg Val Thr	Ile Thr Thr			
	305	310	315			320
Asp Lys Ser Thr	Ser Thr Ala Tyr Met	Glu Leu Ser	Ser Leu Arg Ser			
	325	330	335			
Glu Asp Thr Ala	Val Tyr Tyr Cys Ala Arg	Tyr Tyr Asp	Asp His Tyr			
	340	345	350			
Cys Leu Asp Tyr	Trp Gly Gln Gly Thr Thr	Val Thr Val	Ser Ser Gly			
	355	360	365			
Glu Gly Thr Ser	Thr Gly Ser Gly Gly Ser	Gly Gly Ser	Gly Gly Ala			
	370	375	380			
Asp Asp Ile Val	Leu Thr Gln Ser Pro Ala	Thr Leu Ser	Leu Ser Pro			
	385	390	395			400
Gly Glu Arg Ala	Thr Leu Thr Cys Arg Ala	Ser Ser Ser	Val Ser Tyr			
	405	410	415			
Met Asn Trp Tyr	Gln Gln Lys Pro Gly Lys	Ala Pro Lys	Arg Trp Ile			
	420	425	430			
Tyr Asp Thr Ser	Lys Val Ala Ser Gly Val	Pro Ala Arg	Phe Ser Gly			
	435	440	445			
Ser Gly Ser Gly	Thr Asp Tyr Ser Leu	Thr Ile Asn	Ser Leu Glu Ala			
	450	455	460			

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu
465 470 475 480

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490

<210> 229

<211> 25

<212> PRT

<213> artificial sequence

<220>

<223> non-deimmunized anti-CD3 Framework 1

<400> 229

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Thr Ser
20 25

<210> 230

<211> 15

<212> PRT

<213> artificial sequence

<220>

<223> non-deimmunized anti-CD3 Framework 2

<400> 230

Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
1 5 10 15

<210> 231

<211> 32

<212> PRT

<213> artificial sequence

<220>

<223> non-deimmunized anti-CD3 Framework 3

<400> 231

Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln
1 5 10 15

Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> 232

<211> 11
<212> PRT
<213> artificial sequence

<220>
<223> non-deimmunized anti-CD3 Framework 4
<400> 232

Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser
1 5 10

<210> 233
<211> 6
<212> PRT
<213> artificial sequence

<220>
<223> Sequence motif
<400> 233

Ala Ser Gly Tyr Thr Phe
1 5

<210> 234
<211> 4
<212> PRT
<213> artificial sequence

<220>
<223> Sequence motif
<400> 234

Met Glu Leu Ser
1

<210> 235
<211> 5
<212> PRT
<213> artificial sequence

<220>
<223> Sequence motif
<400> 235

Ile Thr Thr Asp Lys
1 5

<210> 236
<211> 1488
<212> DNA
<213> artificial sequence

<220>

<223> 5-10xVH5VL1 LHHL

<400> 236

gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggctact	60
atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc	120
tgggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg	180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc	240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat	300
ccgctcacgt tccgtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc	360
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg	420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac	480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt	540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact	600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct	660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa	720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acgtccaact ggtgcagtca	780
ggggctgaag tgaaaaaacc tggggcctca gtgaagggtg cctgcaaggc ttctggctac	840
acctttacta ggtacacgat gcactgggta aggcaggcac ctggacaggg tctggaatgg	900
attggataca ttaatcctag ccgtggttat actaattacg cagacagcgt caagggccgc	960
ttcacaatca ctacagacaa atccaccagc acagcctaca tggaactgag cagcctgcgt	1020
tctgaggaca ctgcaacctt ttactgtgca agatattatg atgacatta ctgccttgac	1080
tactggggcc aaggcaccac ggtcacctgc tctcaggcg aaggtagtag tactggttct	1140
ggtggaagtg gaggttcagg tggagcagac gacattcaga tgaccagtc tccatctagc	1200
ctgtctgcat ctgtcgggga ccgtgtcacc atcacctgca gagccagtca aagtgttaagt	1260
tacatgaact ggtaccagca gaagccgggc aaggcaccga aaagatggat ttatgacaca	1320
tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac	1380
tctctcacia tcaacagctt ggaggctgaa gatgctgcc cttattactg ccaacagtgg	1440
agtagtaacc cgctcacgtt cggtaggggg accaaggtgg agatcaaa	1488

<210> 237

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVH5VL1 LHHL

<400> 237

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
 245 250 255

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
 260 265 270

Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
 275 280 285

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
 290 295 300

Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg
 305 310 315 320

Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
 325 330 335

Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr
 340 345 350

Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
 370 375 380

Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
 385 390 395 400

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
 405 410 415

Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
 420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
 435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490 495

<210> 238
<211> 1491
<212> DNA
<213> artificial sequence

<220>
<223> 5-10xVH5VL1 HLHL

<400> 238
gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggctgggac ttcagtgaag 60
atatcctgca aggttctctg atacgccttc actaactact ggctaggttg ggtaaagcag 120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaactctc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggtcc ggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcaactatgag ctgcaagtcc 480
agtcagagtc tgtaaacag tggaaatcaa aagaactact tgacctggtg ccagcagaaa 540
ccagggcagc ctccataaact gttgatctac tgggcatcca ctagggaatc tggggtcctt 600
gatocttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag 780
tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgtcctgcaa ggcttctggc 840
tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa 900
tggattggat acattaatcc tagccgtggt tatactaatt acgcagacag cgtcaagggc 960
cgcttcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020
cgttctgagg aactgcaac ctattactgt gcaagatatt atgatgatca ttactgcctt 1080
gactactggg gccaaaggcac cacggtcacc gtctcctcag gcgaaggtac tagtactggt 1140

tctggtggaa gtggaggttc aggtggagca gacgacattc agatgaccca gtctccatct 1200
 agcctgtctg catctgtcgg ggaccgtgtc accatcacct gcagagccag tcaaagtgtg 1260
 agttacatga actggtacca gcagaagccg ggcaaggcac ccaaaagatg gatttatgac 1320
 acatccaaag tggcttctgg agtcctgtct cgcttcagtg gcagtgggtc tgggaccgac 1380
 tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440
 tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a 1491

<210> 239
 <211> 497
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10xVH5VL1 HLHL

<400> 239

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly
305 310 315 320

Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
340 345 350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser
385 390 395 400

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
405 410 415

Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
485 490 495

Lys

<210> 240
<211> 1488
<212> DNA
<213> artificial sequence

<220>
<223> 5-10xVL1VH5 LHLH

<400> 240
gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggctcact 60
atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcgcc 360
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagctctg agctgagctg 420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480

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tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattcagat gacccagtct 780
ccatctagcc tgtctgcatc tgtcggggac cgtgtcacca tcacctgcag agccagtcaa 840
agtgtaaagt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 900
tatgacacat ccaaagtggc ttctggagtc cctgctcgtc tcagtggcag tgggtctggg 960
accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1020
caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaagtgga gatcaaaggc 1080
gaaggtaacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacgtccaa 1140
ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtcctgcaag 1200
gcttctggct acacctttac taggtacacg atgcaactgg taaggcaggc acctggacag 1260
ggtctggaat ggattggata cattaatcct agccgtgggt atactaatta cgagacagc 1320
gtcaagggcc gcttcacaat cactacagac aaatccaacca gcacagccta catggaactg 1380
agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1440
tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

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<210> 241
 <211> 496
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10xVL1VH5 LHLH

<400> 241

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
245 250 255

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
260 265 270

Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr
275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser

[illegible]

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<210> 242
<211> 1491
<212> DNA
<213> artificial sequence
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<220>
<223> 5-10xVL1VH5 HLLH

<400> 242
gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcttgggac ttcagtgaag 60
atatcctgca aggcttctgg atacgccttc actaactact ggctagggtg ggtaaagcag 120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaactctc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
aggaaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggtcc gggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgtaaacag tggaaatcaa aagaactact tgacctggtg ccagcagaaa 540
ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattca gatgaccag 780
tctccatcta gcctgtctgc atctgtoggg gaccgtgtca ccatcacctg cagagccagt 840
caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg 900
atztatgaca catccaaagt ggcttctgga gtccctgctc gtttcagtgg cagtgggtct 960
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1020
tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1080
ggcgaaggta ctagtactgg ttctggtgga agtggagggt cagggtggagc agacgacgtc 1140
caactggtgc agtcaggggc tgaagtgaaa aaacctgggg cctcagtga ggtgtcctgc 1200
aaggcttctg gctacacctt tactaggtac acgatgcact gggttaaggca ggcacctgga 1260
cagggctctg aatggattgg atacattaat cctagccgtg gttatactaa ttacgcagac 1320
agcgtcaagg gccgcttcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380
ctgagcagcc tgcgttctga ggacactgca acctattact gtgcaagata ttatgatgat 1440
cattactgcc ttgactactg gggccaaggc accacgggtc ccgtctcctc a 1491

<210> 243
<211> 497
<212> PRT
<213> artificial sequence

<220>
<223> 5-10xVL1VH5 HLLH

<400> 243

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
245 250 255

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
260 265 270

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
370 375 380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
385 390 395 400

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
405 410 415

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
420 425 430

Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
435 440 445

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
450 455 460

Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
 465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 485 490 495

Ser

<210> 244
 <211> 1491
 <212> DNA
 <213> artificial sequence

<220>
 <223> 5-10xVH5VL2 HLHL

<400> 244
 gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggctgggac ttcagtgaag 60
 atatcctgca aggtctctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120
 aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
 tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240
 tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
 aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
 ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
 cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
 agtcagagtc tgtaaacag tggaaatcaa aagaactact tgacctggtt ccagcagaaa 540
 ccagggcagc ctccctaaact gttgatctac tgggcatcca ctagggaatc tggggtcctt 600
 gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
 gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct caggttcggt 720
 gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag 780
 tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgtcctgcaa ggcttctggc 840
 tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa 900
 tggattggat acattaatcc tagccgtggt tataactaatt acgcagacag cgtcaagggc 960
 cgcttcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020
 cgttctgagg aactgcaac ctattactgt gcaagatatt atgatgatca ttactgcctt 1080
 gactactggg gccaaaggcac caggttcacc gtctcctcag gcgaaggtag tagtactggt 1140

tctgggtggaa gtggagggttc aggtggagca gacgacattg tactgaccca gtctccagca 1200
 actctgtctc tgtctccagg ggagcgtgcc accctgagct gcagagccag tcaaagtgtg 1260
 agttacatga actggtacca gcagaagccg ggcaaggcac ccaaaagatg gatttatgac 1320
 acatccaaag tggcttctgg agtccttgct cgcttcagtg gcagtgggtc tgggaccgac 1380
 tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440
 tggagtagta acccgctcac gttcgggtggc gggaccaagg tggagatcaa a 1491

<210> 245
 <211> 497
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10xVH5VL2 HLHL

<400> 245

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly
305 310 315 320

Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
340 345 350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala
385 390 395 400

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
405 410 415

Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
485 490 495

Lys

<210> 246
<211> 1488
<212> DNA
<213> artificial sequence

<220>
<223> 5-10xVL2VH5 LHLH

<400> 246
gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggctact 60
atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagctctg agctgagctg 420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480

tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540
 ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600
 gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660
 gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
 gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattgtact gacccagtct 780
 ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgagctgcag agccagtcaa 840
 agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 900
 tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 960
 accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1020
 caacagtggg gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaaggc 1080
 gaaggtaacta gtactggttc tgggtggaagt ggaggttcag gtggagcaga cgacgtccaa 1140
 ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtcctgcaag 1200
 gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 1260
 ggtctggaat ggattggata cattaatcct agccgtggtt atactaatta cgcagacagc 1320
 gtcaaggggc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
 agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1440
 tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 247
 <211> 496
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10xVL2VH5 LHLH

<400> 247

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val
245 250 255

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
260 265 270

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr
275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser

290	295	300
Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly		
305	310	315 320
Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala		
	325	330 335
Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly		
	340	345 350
Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly		
	355	360 365
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser		
	370	375 380
Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys		
	385	390 395 400
Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln		
	405	410 415
Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg		
	420	425 430
Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr		
	435	440 445
Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg		
	450	455 460
Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His		
	465	470 475 480
Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser		
	485	490 495

<210> 248
 <211> 1491
 <212> DNA
 <213> artificial sequence
 <220>
 <223> 5-10xVL2VH5 HLLH

<400> 248
gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggctgggac ttcagtgaag 60
atatcctgca aggccttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaattctc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctcctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgt cactgtcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattgt actgaccag 780
tctccagcaa ctctgtctct gtctccaggg gagcgtgcc aacctgagctg cagagccagt 840
caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaagatgg 900
atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 960
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1020
tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1080
ggcgaaggta ctagtactgg ttctggtgga agtggagggt cagggtggagc agacgacgtc 1140
caactggtgc agtcaggggc tgaagtga aaacctgggg cctcagtga ggtgtcctgc 1200
aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga 1260
cagggtctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacgcagac 1320
agcgtcaagg gccgcttcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380
ctgagcagcc tgcgttctga ggacactgca acctattact gtgcaagata ttatgatgat 1440
cattactgcc ttgactactg gggccaaggc accacgggtc ccgtctctc a 1491

<210> 249

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10xVL2VH5 HLLH

<400> 249

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
245 250 255

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
260 265 270

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
370 375 380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
385 390 395 400

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
405 410 415

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
420 425 430

Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
435 440 445

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
450 455 460

Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
485 490 495

Ser

<210> 250
<211> 1488
<212> DNA
<213> artificial sequence

<220>
<223> 5-10 VH5VL3 LHHL

<400> 250
gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact 60
atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
tgggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cactactgact 600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acgtccaact ggtgcagtca 780
ggggctgaag tgaaaaaacc tggggcctca gtgaagggtg cctgcaaggc ttctggctac 840
acctttacta ggtacacgat gcactgggta aggcaggcac ctggacaggg tctggaatgg 900
attggataca ttaatcctag ccgtggttat actaattacg cagacagcgt caagggccgc 960
ttcacaatca ctacagacaa atccaccagc acagcctaca tggaactgag cagcctgcgt 1020
tctgaggaca ctgcaacctt ttactgtgca agatattatg atgatcatta ctgccttgac 1080
tactggggcc aaggcaccac ggtcaccgtc tctcaggcg aaggtagtag tactggttct 1140

ggtggaagtg gaggttcagg tggagcagac gacattgtac tgacccagtc tccagcaact 1200
 ctgtctctgt ctccagggga gcgtgccacc ctgacctgca gagccagttc aagtgttaagt 1260
 tacatgaact ggtaccagca gaagccgggc aaggcaccga aaagatggat ttatgacaca 1320
 tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380
 tctctcacia tcaacagctt ggaggctgaa gatgctgcca cttattactg ccaacagtgg 1440
 agtagtaacc cgctcacgtt cggtggcggg accaaggtgg agatcaaa 1488

<210> 251
 <211> 496
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10VH5VL3 LHHL

<400> 251

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
245 250 255

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
260 265 270

Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
275 280 285

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
290 295 300

Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg
305 310 315 320

Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
325 330 335

Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr
340 345 350

Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr
385 390 395 400

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser
405 410 415

Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
485 490 495

<210> 252

<211> 1491

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VH5VL3 HLHL

<400> 252

gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggctgggac ttcagtgaag	60
atatcctgca aggttctg atagccttc actaactact ggctaggttg ggtaaagcag	120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac	180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaattctc gagcacagcc	240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg	300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca	360
ggtggtggtg gttctggcgg cggcggtccc ggtggtggtg gttctgagct cgtgatgaca	420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc	480
agtcagagtc tgttaaagcag tggaaatcaa aagaactact tgacctggtg ccagcagaaa	540
ccagggcagc ctctctaaact gttgatctac tgggcatcca ctagggaatc tggggtcct	600

gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag 780
tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgtcctgcaa ggcttctggc 840
tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa 900
tggattggat acattaatcc tagccgtggt tatactaatt acgcagacag cgtcaagggc 960
cgcttcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020
cgttctgagg aactgcaac ctattactgt gcaagatatt atgatgatca ttactgcctt 1080
gactactggg gccaaaggcac cacggtcacc gtctcctcag gcgaaggtag tagtactggt 1140
tctggtggaa gtggaggttc aggtggagca gacgacattg tactgaccca gtctccagca 1200
actctgtctc tgtctccagg ggagcgtgcc accctgacct gcagagccag ttcaagtgt 1260
agttacatga actggtacca gcagaagccg ggcaaggcac caaaagatg gatttatgac 1320
acatccaaag tggcttctgg agtccttctg cgcttcagtg gcagtgggtc tgggaccgac 1380
tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440
tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a 1491

<210> 253
<211> 497
<212> PRT
<213> artificial sequence

<220>
<223> 5-10VH5VL3 HLHL

<400> 253

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 85 90 95
 Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 110
 Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125
 Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140
 Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160
 Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175
 Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190
 Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205
 Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220
 Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240
 Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
 245 250 255
 Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
 260 265 270
 Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
 275 280 285
 His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
 290 295 300
 Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly

305 310 315 320
 Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
 325 330 335
 Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
 340 345 350
 Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365
 Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
 370 375 380
 Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala
 385 390 395 400
 Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala
 405 410 415
 Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
 420 425 430
 Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
 435 440 445
 Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
 450 455 460
 Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
 465 470 475 480
 Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
 485 490 495

Lys

<210> 254
 <211> 1488
 <212> DNA
 <213> artificial sequence
 <220>
 <223> 5-10VL3VH5 LHLH

<400> 254
gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact 60
atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
tgggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtgggtgttg ttctggcggc 360
ggcggctccg gtgggtgttg ttctgaggtg cagctgctcg agcagctctg agctgagctg 420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cactctgact 600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattgtact gaccagctct 780
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgacctgcag agccagttca 840
agtgtgaagt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 900
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 960
accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1020
caacagtgga gtagtaaccc gtcacgctt ggtggcggga ccaaggtgga gatcaaaggc 1080
gaaggtacta gtactggctc tgggtggaagt ggaggttcag gtggagcaga cgacgtccaa 1140
ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtcctgcaag 1200
gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 1260
ggtctggaat ggattggata cattaatcct agccgtggtt atactaatta cgcagacagc 1320
gtcaagggcc gcttcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
agcagcctgc gttctgagga cactgcaacc tattactgtg caagatatta tgatgatcat 1440
tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

<210> 255

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10VL3VH5 LHLH

<400> 255

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val
 245 250 255

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
 260 265 270

Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr
 275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
 290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
 325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
 340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
 355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
 370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
 405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
 420 425 430

Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Thr
 435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
 450 455 460

Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
 465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 485 490 495

<210> 256
 <211> 1491
 <212> DNA
 <213> artificial sequence

<220>
 <223> 5-10VL3VH5 HLLH

<400> 256
 gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
 atatcctgca aggcttcttg atacgccttc actaactact ggctaggttg ggtaaagcag 120
 aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
 tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaattctc gagcacagcc 240
 tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
 aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
 ggtggtggtg gttctggcgg cggcggtccc ggtggtggtg gttctgagct cgtgatgaca 420
 cagtctccat cctccctgac tgtgacagca ggagagaagg tcaactatgag ctgcaagtcc 480
 agtcagagtc tgtaaacag tggaaatcaa aagaactact tgacctggtg ccagcagaaa 540
 ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tggggtcctt 600
 gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
 gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
 gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattgt actgaccag 780
 tctccagcaa ctctgtctct gtctccaggg gagegtgcc aactgacctg cagagccagt 840
 tcaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaagatgg 900
 atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 960
 gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1020
 tgccaacagt ggagtagtaa cccgctcagc ttcggtggcg ggaccaaggt ggagatcaaa 1080
 ggccaaggta ctagtactgg ttctggtgga agtggaggtt caggtggagc agacgacgtc 1140
 caactggtgc agtcaggggc tgaagtgaaa aaacctgggg cctcagtga ggtgtcctgc 1200
 aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga 1260

cagggctctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacgcagac 1320
 agcgtcaagg gcgcgttcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380
 ctgagcagcc tgcgtttotga ggacactgca acctattact gtgcaagata ttatgatgat 1440
 cattactgcc ttgactactg gggccaaggc accacgggtca ccgtctcctc a 1491

<210> 257
 <211> 497
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10VL3VH5 HLLH

<400> 257

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
 245 250 255

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
 260 265 270

Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp
 275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
 355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
 370 375 380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
 385 390 395 400

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
 405 410 415

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
 420 425 430

Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
 435 440 445

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
 450 455 460

Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
 465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 485 490 495

Ser

<210> 258

<211> 1488

<212> DNA

<213> artificial sequence

<220>

<223> 5-10VH7VL1 LHHL

<400> 258

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atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc	120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg	180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc	240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat	300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc	360
ggcggtccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg	420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac	480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt	540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact	600

gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acgtccaact ggtgcagtca 780
ggggctgaag tgaaaaaacc tggggcctca gtgaagggtgt cctgcaaggc ttctggctac 840
acctttacta ggtacacgat gcactgggta aggcaggcac ctggacaggg tctggaatgg 900
attggataca ttaatcctag cctgtggttat actaattaca atcagaagtt caaggaccgc 960
gtcacaatca ctacagacaa atccaccagc acagcctaca tggaactgag cagcctgcgt 1020
tctgaggaca ctgcagtcta ttactgtgca agatattatg atgatcatta ctgccttgac 1080
tactggggcc aaggcaccac ggtcacgcgc tcctcaggcg aaggtactag tactggttct 1140
ggtggaagtg gaggttcagg tggagcagac gacattcaga tgaccagtc tccatctagc 1200
ctgtctgcat ctgtcgggga ccgtgtcacc atcacctgca gagccagtca aagtgttaagt 1260
tacaatgaact ggtaccagca gaagccgggc aaggcaccca aaagatggat ttatgacaca 1320
tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380
tctctcacia tcaacagctt ggaggctgaa gatgctgcca cttattactg ccaacagtgg 1440
agtagtaacc cgctcacgtt cggtggcggg accaaggtgg agatcaaa 1488

<210> 259
<211> 496
<212> PRT
<213> artificial sequence

<220>
<223> 5-10VH7VL1 LHHL

<400> 259

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
 245 250 255

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
 260 265 270

Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
 275 280 285

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
 290 295 300

Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg

305 310 315 320
 Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
 325 330 335
 Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr
 340 345 350
 Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365
 Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
 370 375 380
 Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
 385 390 395 400
 Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
 405 410 415
 Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
 420 425 430
 Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
 435 440 445
 Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
 450 455 460
 Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
 465 470 475 480
 Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490 495

<210> 260
 <211> 1491
 <212> DNA
 <213> artificial sequence

<220>
 <223> 5-10VH7VL1 HLHL

<400> 260
 gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggctgggac ttcagtgaag 60
 atatcctgca aggccttctg atacgccttc actaactact ggctaggttg ggtaaagcag 120

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aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaattctc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
ccagggcagc ctcctaaact gttgatctac tgggcatcca ctagggaatc tggggtccct 600
gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag 780
tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgcctgcaa ggcttctggc 840
tacaccttta ctaggtaacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa 900
tggattggat acattaatcc tagccgtggt tatactaatt acaatcagaa gttcaaggac 960
cgcgtcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020
cgttctgagg aactgcagt ctattactgt gcaagatatt atgatgatca ttactgcctt 1080
gactactggg gccaaaggcac cacggtcacc gtctcctcag gcgaaggtag tagtactggt 1140
tctggtggaa gtggagggtc aggtggagca gacgacattc agatgaccca gtctccatct 1200
agcctgtctg catctgtcgg ggaccgtgtc accatcacct gcagagccag tcaaagtgtg 1260
agttacatga actggtacca gcagaagccg ggcaaggcac caaaaagatg gatttatgac 1320
acatccaaag tggcttctgg agtccctgct cgcttcagtg gcagtgggtc tgggaccgac 1380
tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440
tggagtagta acccgctcac gttcggtggc gggaccaagg tggagatcaa a 1491

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<210> 261
 <211> 497
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10VH7VL1 HLHL

<400> 261

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
 245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
 260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
 275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
 290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp
 305 310 315 320

Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
 325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
 340 345 350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
 370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser Pro Ser
 385 390 395 400

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
 405 410 415

Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
 420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
 435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
 450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
 465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
 485 490 495

Lys

<210> 262
 <211> 1488
 <212> DNA
 <213> artificial sequence

<220>
 <223> 5-10VL1VH7 LHLH

<400> 262
 gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact 60
 atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
 tgggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
 gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
 atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
 ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360
 ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420
 gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480
 tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540
 ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600
 gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660
 gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
 gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattcagat gacccagtct 780
 ccatctagcc tgtctgcac tgctggggac cgtgtcacca tcacctgcag agccagtcaa 840
 agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 900
 tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 960
 accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1020
 caacagtgga gtagtaacct gctcacgttc ggtggcggga ccaaggtgga gatcaaaggc 1080
 gaaggtacta gtactggttc tgggtgaagt ggaggttcag gtggagcaga cgacgtccaa 1140
 ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtctgcaag 1200
 gcttctggct acacctttac taggtacacg atgcactggg taaggcagc acctggacag 1260

ggtctggaat ggattggata cattaatcct agccgtggtt atactaatta caatcagaag 1320
 ttcaaggacc gcgtcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
 agcagcctgc gttctgagga cactgcagtc tattactgtg caagatatta tgatgatcat 1440
 tactgccttg actactgggg ccaaggcacc acggtcaccg tctctca 1488

<210> 263
 <211> 496
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10VL1VH7 LHLH

<400> 263

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
 245 250 255

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
 260 265 270

Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr
 275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
 290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
 325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
 340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
 355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
 370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
 405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
 420 425 430

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
 435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
 450 455 460

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
 465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 485 490 495

<210> 264
 <211> 1491
 <212> DNA
 <213> artificial sequence

<220>
 <223> 5-10VL1VH7 HLLH

<400> 264
 gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
 atatcctgca aggcttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120
 aggctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
 tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaatcttc gagcacagcc 240
 tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
 aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
 ggtggtggtg gttctggcgg cggcggtcc ggtggtggtg gttctgagct cgtgatgaca 420
 cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
 agtcagagtc tggttaaagcagg tggaaatcaa aagaactact tgacctggtg ccagcagaaa 540
 ccagggcagc ctctctaaact gttgatctac tgggcatcca ctagggaatc tggggctcct 600
 gatcgcttca caggcagtggt atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
 gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720

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gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattca gatgacccag      780
tctccatcta gcctgtctgc atctgtcggg gaccgtgtca ccatcacctg cagagccagt      840
caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg      900
atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct      960
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac     1020
tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa     1080
ggcgaaggta ctagtactgg ttctggtgga agtggagggt cagggtggagc agacgacgctc     1140
caactggtgc agtcaggggc tgaagtga aaacctgggg cctcagtga ggtgtcctgc      1200
aaggcttctg gctacacctt tactaggtac acgatgcact gggttaaggca ggcacctgga     1260
cagggtctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacaatcag     1320
aagttcaagg accgcgtcac aatcactaca gacaaatcca ccagcacagc ctacatggaa     1380
ctgagcagcc tgcgttctga ggacactgca gtctattact gtgcaagata ttatgatgat     1440
cattactgcc ttgactactg ggccaaggc accacgggtc ccgtctctc a                  1491

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<210> 265
 <211> 497
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10VL1VH7 HLLH

<400> 265

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
 245 250 255

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
 260 265 270

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
 275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala

325 330 335
 Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 340 345 350
 Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
 355 360 365
 Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
 370 375 380
 Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
 385 390 395 400
 Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
 405 410 415
 Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
 420 425 430
 Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile
 435 440 445
 Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
 450 455 460
 Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
 465 470 475 480
 His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 485 490 495

Ser

<210> 266
 <211> 1488
 <212> DNA
 <213> artificial sequence

<220>
 <223> 5-10/VH7VL2 LHHL

<400> 266
 gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact 60
 atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120

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tggtagcagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
ccgctcacgt tgggtgctgg gaccaagctt gagatcaaag gtgggtggtg ttctggcggc 360
ggcggtccg gtgggtggtg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttactaac 480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acgtccaact ggtgcagtca 780
ggggctgaag tgaaaaaacc tggggcctca gtgaagggtg cctgcaaggc ttctggctac 840
acctttacta ggtacacgat gcactgggta aggcaggcac ctggacaggg tctggaatgg 900
attggataca ttaatcctag ccgtggttat actaattaca atcagaagtt caaggaccgc 960
gtcacaatca ctacagacaa atccaccagc acagcctaca tggaactgag cagcctgcgt 1020
tctgaggaca ctgcagtcta ttactgtgca agatattatg atgattatta ctgccttgac 1080
tactggggcc aaggcaccac ggtcacgcgc tctcaggcg aaggtagtag tactggttct 1140
ggtggaagtg gaggttcagg tggagcagac gacattgtac tgaccagtc tccagcaact 1200
ctgtctctgt ctccagggga gcgtgccacc ctgagctgca gagccagtc aagtgttaagt 1260
tacatgaact ggtaccagca gaagccgggc aaggcaccca aaagatggat ttatgacaca 1320
tccaaagtgg cttctggagt ccctgctcgc ttcaagtggc gtgggtctgg gaccgactac 1380
tctctcacia tcaacagctt ggaggtgaa gatgctgcca cttattactg ccaacagtgg 1440
agtagtaacc cgctcacgtt cggtggcggg accaagggtg agatcaaa 1488

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<210> 267
<211> 496
<212> PRT
<213> artificial sequence

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<220>
<223> 5-10/VH7VL2 LHL

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<400> 267

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Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly

1 5 10 15
 Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30
 Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45
 Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60
 Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80
 Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95
 Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110
 Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125
 Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140
 Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 145 150 155 160
 Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 165 170 175
 Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 180 185 190
 Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 195 200 205
 Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220
 Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
245 250 255

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
260 265 270

Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
275 280 285

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
290 295 300

Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg
305 310 315 320

Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
325 330 335

Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr
340 345 350

Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
370 375 380

Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr
385 390 395 400

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser
405 410 415

Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490 495

<210> 268
 <211> 1491
 <212> DNA
 <213> artificial sequence

<220>
 <223> 5-10/VH7VL2 HLHL

<400> 268
 gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
 atatcctgca aggcttcttg atacgccttc actaactact ggctaggttg ggtaaagcag 120
 aggcctggac atggacttga gtggattgga gataftttcc ctggaagtgg taatatccac 180
 tacaatgaga agttcaaggg caaagccaça ctgactgcag acaaatcttc gagcacagcc 240
 tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
 aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
 ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
 cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
 agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggtg ccagcagaaa 540
 ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tggggtcctc 600
 gatcgcttca caggcagtgg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
 gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct caggttcggt 720
 gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag 780
 tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgtcctgcaa ggcttctggc 840
 tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa 900
 tggattggat acattaatcc tagccgtggt tatactaatt acaatcagaa gttcaaggac 960
 cgcgtcacaa tcactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020
 cgttctgagg acactgcagt ctattactgt gcaagatatt atgatgatca ttactgcctt 1080
 gactactggg gccaaaggcac cacggtcacc gtctcctcag gcgaaggtag tagtactggt 1140
 tctggtggaa gtggaggttc aggtggagca gacgacattg tactgaccca gtctccagca 1200
 actctgtctc tgtctccagg ggagcgtgcc accctgagct gcagagccag tcaaagtgtg 1260
 agttacatga actggtacca gcagaagccg ggcaaggcac ccaaaagatg gatttatgac 1320
 acatccaaag tggcttcttg agtccctgct cgcttcagtg gcagtgggtc tgggaccgac 1380

tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440

tggagtagta acccgctcac gttcgggtggc gggaccaagg tggagatcaa a 1491

<210> 269

<211> 497

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VH7VL2 HLHL

<400> 269

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
 245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
 260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
 275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
 290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp
 305 310 315 320

Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
 325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
 340 345 350

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser
 370 375 380

Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala
 385 390 395 400

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
 405 410 415

Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys
 420 425 430

Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val
 435 440 445

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr
 450 455 460

Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln
 465 470 475 480

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
 485 490 495

Lys

<210> 270
 <211> 1488
 <212> DNA
 <213> artificial sequence

<220>
 <223> 5-10/VL2VH7 LHLH

<400> 270
 gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggtcact 60
 atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
 tgggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
 gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
 atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
 ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc 360
 ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg 420
 gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480
 tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540
 ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600
 gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660
 gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720

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gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattgtact gaccagttct 780
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgagctgcag agccagtcaa 840
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 900
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 960
accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1020
caacagtgga gtagtaaccc gtcacgttc ggtggcgga ccaaggtgga gatcaaaggc 1080
gaaggtacta gtactggttc tgggtgaagt ggaggttcag gtggagcaga cgacgtccaa 1140
ctggtgcagt caggggctga agtgaaaaa cctggggcct cagtgaaggt gtcctgcaag 1200
gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag 1260
ggtctggaat ggattggata cattaatcct agcogtgggt atactaatta caatcagaag 1320
ttcaaggacc gcgtcacaat cactacagac aaatccacca gcacagccta catggaactg 1380
agcagcctgc gttctgagga cactgcagtc tattactgtg caagatatta tgatgatcat 1440
tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca 1488

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<210> 271
 <211> 496
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10/VL2VH7 LHLH

<400> 271

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val
 245 250 255

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
 260 265 270

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr
 275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
 290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala

325 330 335
 Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
 340 345 350
 Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
 355 360 365
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
 370 375 380
 Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 385 390 395 400
 Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
 405 410 415
 Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
 420 425 430
 Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
 435 440 445
 Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
 450 455 460
 Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
 465 470 475 480
 Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 485 490 495

<210> 272
 <211> 1491
 <212> DNA
 <213> artificial sequence

<220>
 <223> 5-10/VL2VH7 HLLH

<400> 272
 gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggcctgggac ttcagtgaag 60
 atatcctgca aggccttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120
 aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
 tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaattcttc gagcacagcc 240

tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
 aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
 ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
 cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
 agtcagagtc tgttaaacag tggaaatcaa aagaactact tgacctggtg ccagcagaaa 540
 ccagggcagc ctccctaaact gttgatctac tgggcatcca ctagggaatc tggggctcct 600
 gatcgcttca caggcagtgg atctggaaca gatttcactc tcacatcag cagtgtgcag 660
 gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
 gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattgt actgaccag 780
 tctccagcaa ctctgtctct gtctccaggg gagcgtgcc aacctgagctg cagagccagt 840
 caaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaaagatgg 900
 atttatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 960
 gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1020
 tgccaacagt ggagtagtaa cccgctcacg ttcggtggcg ggaccaaggt ggagatcaaa 1080
 ggcgaaggta ctagtactgg ttctggtgga agtggagggt caggtggagc agacgacgac 1140
 caactggtgc agtcaggggc tgaagtga aaacctgggg cctcagtga ggtgtcctgc 1200
 aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga 1260
 cagggtctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacaatcag 1320
 aagttcaagg accgcgtcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380
 ctgagcagcc tgcgttctga ggacactgca gtctattact gtgcaagata ttatgatgat 1440
 cattactgcc ttgactactg gggccaaggc accacgggtc ccgtctcctc a 1491

<210> 273
 <211> 497
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10/VL2VH7 HLLH

<400> 273

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn

20	25	30
Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp		
35	40	45
Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys		
50	55	60
Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala		
65	70	75
Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe		
85	90	95
Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln		
100	105	110
Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly		
115	120	125
Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser		
130	135	140
Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser		
145	150	155
Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp		
165	170	175
Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala		
180	185	190
Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser		
195	200	205
Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu		
210	215	220
Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly		
225	230	235
Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile		
245	250	255

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
 260 265 270

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp
 275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
 355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
 370 375 380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
 385 390 395 400

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
 405 410 415

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
 420 425 430

Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile
 435 440 445

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
 450 455 460

Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
 465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 485 490 495

Ser

<210> 274
<211> 1488
<212> DNA
<213> artificial sequence

<220>
<223> 5-10/VH7VL3 LHHL

<400> 274
gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggctcact 60
atgagctgca agtccagtcga gagtctgtta aacagtggaa atcaaaagaa ctacttgacc 120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg 180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc 240
atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat 300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtgggtgggtg ttctggcggc 360
ggcggtcccg gtgggtgggtg ttctgaggtg cagctgctcg agcagctctg agctgagctg 420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac 480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt 540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact 600
gcagacaaat cttcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct 660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa 720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acgtccaact ggtgcagtca 780
ggggctgaag tgaaaaaacc tggggcctca gtgaagggtg cctgcaaggc ttctggctac 840
acctttacta ggtacacgat gcactgggta aggcaggcac ctggacaggg tctggaatgg 900
attggatata ttaatcctag ccgtggttat actaattaca atcagaagtt caaggaccgc 960
gtcacaaatca ctacagacaa atccaccagc acagcctaca tggaactgag cagcctgcgt 1020
tctgaggaca ctgcagtcta ttactgtgca agatattatg atgatcatta ctgccttgac 1080
tactggggcc aaggcaccac ggtcacctgc tctcaggcg aaggtagtag tactggttct 1140
ggtggaagtg gaggttcagg tggagcagac gacattgtac tgaccagtc tccagcaact 1200
ctgtctctgt ctccagggga gcgtgccacc ctgacctgca gagccagttc aagtgttaagt 1260
tacatgaact ggtaccagca gaagccgggc aaggcaccca aaagatggat ttatgacaca 1320
tccaaagtgg cttctggagt ccctgctcgc ttcagtggca gtgggtctgg gaccgactac 1380

tctctcaciaa tcaacagctt ggaggctgaa gatgctgccca cttattactg ccaacagtgg 1440
 agtagtaacc cgctcacgtt cggtggcggg accaaggtgg agatcaaa 1488

<210> 275
 <211> 496
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10/VH7VL3 LHHL

<400> 275

Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
 85 90 95

Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
 100 105 110

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly
 130 135 140

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 145 150 155 160

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 165 170 175

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 180 185 190

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 195 200 205

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 210 215 220

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 225 230 235 240

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Val Gln
 245 250 255

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
 260 265 270

Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
 275 280 285

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile
 290 295 300

Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg
 305 310 315 320

Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu
 325 330 335

Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr
 340 345 350

Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly Gly Ser Gly
 370 375 380

Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser Pro Ala Thr
 385 390 395 400

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser
 405 410 415

Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
 420 425 430

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly Val Pro
 435 440 445

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
 450 455 460

Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
 465 470 475 480

Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 485 490 495

<210> 276
 <211> 1491
 <212> DNA
 <213> artificial sequence

<220>
 <223> 5-10/VH7VL3 HLHL

<400> 276
 gaggtgcagc tgctcgagca gtctggagct gagctggtaa ggctgggac ttcagtgaag 60
 atatcctgca aggccttctgg atacgccttc actaactact ggctaggttg ggtaaagcag 120
 aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
 tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaattcttc gagcacagcc 240
 tatatgcagc tcagtagcct gacatttgag gactctgctg tctattttctg tgcaagactg 300
 aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
 ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
 cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
 agtcagagtc tggttaaagcagg tggaaatcaa aagaactact tgacctggta ccagcagaaa 540
 ccagggcagc ctctctaaact gttgatctac tgggcatcca ctagggaatc tggggtcctt 600
 gatcgcttca caggcagtggt atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
 gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
 gctgggacca agcttgagat caaatccgga ggtggtggat ccgacgtcca actggtgcag 780
 tcaggggctg aagtgaaaaa acctggggcc tcagtgaagg tgcctgcaa ggcttctggc 840

tacaccttta ctaggtacac gatgcactgg gtaaggcagg cacctggaca gggctctggaa 900
 tggattggat acattaatcc tagccgtgggt tataactaatt acaatcagaa gttcaaggac 960
 cgcgtcacaa tcaactacaga caaatccacc agcacagcct acatggaact gagcagcctg 1020
 cgttctgagg acaactgcagt ctattactgt gcaagatatt atgatgatca ttactgcctt 1080
 gactactggg gccaaaggcac cacggtcacc gtctcctcag gcgaaggta tagtactggg 1140
 tctgggtggaa gtggagggtc aggtggagca gacgacattg tactgacca gtctccagca 1200
 actctgtctc tgtctccagg ggagcgtgcc accctgacct gcagagccag ttcaagtgt 1260
 agttacatga actggtacca gcagaagccg ggcaaggcac caaaagatg gatttatgac 1320
 acatccaaag tggcttctgg agtccctgct cgcttcagtg gcagtgggtc tgggaccgac 1380
 tactctctca caatcaacag cttggaggct gaagatgctg ccacttatta ctgccaacag 1440
 tggagtagta acccgctcac gtccggtggc gggaccaagg tggagatcaa a 1491

<210> 277
 <211> 497
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10/VH7VL3 HLHL

<400> 277

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Val
245 250 255

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
260 265 270

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met
275 280 285

His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr
290 295 300

Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp
305 310 315 320

Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
325 330 335

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg

Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
485 490 495

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<400> 278
gagctcgtga tgacacagtc tccatcctcc ctgactgtga cagcaggaga gaaggctact      60
atgagctgca agtccagtca gagtctgtta aacagtggaa atcaaaagaa ctacttgacc      120
tggtaccagc agaaaccagg gcagcctcct aaactgttga tctactgggc atccactagg      180
gaatctgggg tccctgatcg cttcacaggc agtggatctg gaacagattt cactctcacc      240
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atcagcagtg tgcaggctga agacctggca gtttattact gtcagaatga ttatagttat   300
ccgctcacgt tcggtgctgg gaccaagctt gagatcaaag gtggtggtgg ttctggcggc   360
ggcggctccg gtggtggtgg ttctgaggtg cagctgctcg agcagtctgg agctgagctg   420
gtaaggcctg ggacttcagt gaagatatcc tgcaaggctt ctggatacgc cttcactaac   480
tactggctag gttgggtaaa gcagaggcct ggacatggac ttgagtggat tggagatatt   540
ttccctggaa gtggtaatat ccactacaat gagaagttca agggcaaagc cacactgact   600
gcagacaaat ctcgagcac agcctatatg cagctcagta gcctgacatt tgaggactct   660
gctgtctatt tctgtgcaag actgaggaac tgggacgagc ctatggacta ctggggccaa   720
gggaccacgg tcaccgtctc ctccggaggt ggtggatccg acattgtact gaccagctct   780
ccagcaacte tgtctctgtc tccaggggag cgtgccaccc tgacctgcag agccagttca   840
agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt   900
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg   960
accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc  1020
caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaaggc  1080
gaaggtacta gtactggttc tgggtggaagt ggaggttcag gtggagcaga cgacgtccaa  1140
ctggtgcagt caggggctga agtgaaaaaa cctggggcct cagtgaaggt gtctgcaag  1200
gcttctggct acacctttac taggtacacg atgcactggg taaggcaggc acctggacag  1260
ggtctggaat ggattggata cattaatcct agccgtggtt atactaatta caatcagaag  1320
ttcaaggacc gcgtcacaat cactacagac aaatccacca gcacagccta catggaactg  1380
agcagcctgc gttctgagga cactgcagtc tattactgtg caagatatta tgatgatcat  1440
tactgccttg actactgggg ccaaggcacc acggtcaccg tctcctca   1488

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<210> 279

<211> 496

<212> PRT

<213> artificial sequence

<220>

<223> 5-10/VL3VH7 LHLH

<400> 279

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Glu Leu Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly
1           5           10          15

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Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser

```

20	25	30	
Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln			
35	40	45	
Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val			
50	55	60	
Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr			
65	70	75	80
Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn			
85	90	95	
Asp Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile			
100	105	110	
Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser			
115	120	125	
Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Leu Val Arg Pro Gly			
130	135	140	
Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn			
145	150	155	160
Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp			
165	170	175	
Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys			
180	185	190	
Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala			
195	200	205	
Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe			
210	215	220	
Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln			
225	230	235	240
Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val			
245	250	255	

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
 260 265 270

Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr
 275 280 285

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
 290 295 300

Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320

Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala
 325 330 335

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly
 340 345 350

Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser Gly
 355 360 365

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln Ser
 370 375 380

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
 385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
 405 410 415

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
 420 425 430

Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr
 435 440 445

Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
 450 455 460

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp His
 465 470 475 480

Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 485 490 495

<210> 280
<211> 1491
<212> DNA
<213> artificial sequence

<220>
<223> 5-10/VL3VH7 HLLH

<400> 280
gagggtgcagc tgctcgagca gtctggagct gagctggtaa ggctgggac ttcagtgaag 60
atatcctgca aggcttcttg atacgccttc actaactact ggctaggttg ggtaaagcag 120
aggcctggac atggacttga gtggattgga gatattttcc ctggaagtgg taatatccac 180
tacaatgaga agttcaaggg caaagccaca ctgactgcag acaaattctc gagcacagcc 240
tatatgcagc tcagtagcct gacatttgag gactctgctg tctatttctg tgcaagactg 300
aggaactggg acgagcctat ggactactgg ggccaaggga ccacggtcac cgtctcctca 360
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgagct cgtgatgaca 420
cagtctccat cctccctgac tgtgacagca ggagagaagg tcactatgag ctgcaagtcc 480
agtcagagtc tgtaaacag tggaaatcaa aagaactact tgacctggtg ccagcagaaa 540
ccagggcagc ctctaaact gttgatctac tgggcatcca ctagggaatc tggggctcct 600
gatcgttca caggcagtg atctggaaca gatttcactc tcaccatcag cagtgtgcag 660
gctgaagacc tggcagttta ttactgtcag aatgattata gttatccgct cacgttcggt 720
gctgggacca agcttgagat caaatccgga ggtggtggat ccgacattgt actgaccag 780
tctccagcaa ctctgtctct gtctccaggg gagcgtgcc aacctgacctg cagagccagt 840
tcaagtgtaa gttacatgaa ctggtaccag cagaagccgg gcaaggcacc caaagatgg 900
atztatgaca catccaaagt ggcttctgga gtccctgctc gcttcagtgg cagtgggtct 960
gggaccgact actctctcac aatcaacagc ttggaggctg aagatgctgc cacttattac 1020
tgccaacagt ggagtagtaa cccgctcagc ttcggtggcg ggaccaaggt ggagatcaaa 1080
ggcgaaggta ctagtactgg ttctggtgga agtggagggt caggtggagc agacgacgtc 1140
caactggtgc agtcaggggc tgaagtga aaacctgggg cctcagtga ggtgtcctgc 1200
aaggcttctg gctacacctt tactaggtac acgatgcact gggtaaggca ggcacctgga 1260
cagggtctgg aatggattgg atacattaat cctagccgtg gttatactaa ttacaatcag 1320
aagttcaagg accgcgtcac aatcactaca gacaaatcca ccagcacagc ctacatggaa 1380
ctgagcagcc tgcgttctga ggacactgca gtctattact gtgcaagata ttatgatgat 1440
cattactgcc ttgactactg gggccaaggc accacggtca ccgtctctc a 1491

<210> 281
 <211> 497
 <212> PRT
 <213> artificial sequence

<220>
 <223> 5-10/VL3VH7 HLLH

<400> 281

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

Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn
 20 25 30

Tyr Trp Leu Gly Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp
 35 40 45

Ile Gly Asp Ile Phe Pro Gly Ser Gly Asn Ile His Tyr Asn Glu Lys
 50 55 60

Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala
 65 70 75 80

Tyr Met Gln Leu Ser Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe
 85 90 95

Cys Ala Arg Leu Arg Asn Trp Asp Glu Pro Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Ser Pro Ser
 130 135 140

Ser Leu Thr Val Thr Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser
 145 150 155 160

Ser Gln Ser Leu Leu Asn Ser Gly Asn Gln Lys Asn Tyr Leu Thr Trp
 165 170 175

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala
 180 185 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
 195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu
 210 215 220

Ala Val Tyr Tyr Cys Gln Asn Asp Tyr Ser Tyr Pro Leu Thr Phe Gly
 225 230 235 240

Ala Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile
 245 250 255

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
 260 265 270

Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp
 275 280 285

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr
 290 295 300

Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
 325 330 335

Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly Ser
 355 360 365

Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val Gln
 370 375 380

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
 385 390 395 400

Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg
 405 410 415

Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser
 420 425 430

Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile
 435 440 445

Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu
 450 455 460

Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp Asp
 465 470 475 480

His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
 485 490 495

Ser

<210> 282
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL1/VH5x4-7 LHHL

<400> 282
 gacattcaga tgaccagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc 60
 atcacctgca gagccagtca aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgtctgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggtgaa 240
 gatgtgcca cttattactg ccaacagtgg agtagtaacc cgtcacgtt cgggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtaaac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctgga tggattggat acattaatcc tagccgtggt 540
 tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcaactacaga caaatccacc 600
 agcacagcct acatggaact gagcagcctg cgcttctgagg aactgcaac ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc 720
 gtctcctccg gaggtggtgg atccgaggtg cagctgctcg agcagctctg agctgagctg 780
 gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcacaac 840

tatggttttaa gctgggtgaa gcagaggcct ggacagggtcc ttgagtggat tggagagggt 900
 taccctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 960
 gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacctc tgaggactct 1020
 gcggtctatt tctgtgcaag acgggggatcc tacgatacta actacgactg gtacttogat 1080
 gtctggggcc aagggaccac ggtcaccgtc tctcagggtg gtggtgggtc tggcggcggc 1140
 ggctccggtg gtggtgggtc tgagctcgtg atgaccaga ctccactctc cctgcctgtc 1200
 agtcttgag atcaagcctc catctcttgc agatctagtc agagccttgt acacagtaat 1260
 ggaaacacct atttacattg gtacctgcag aagccaggcc agtctccaaa gctcctgac 1320
 tacaaagttt ccaaccgatt ttctggggtc ccagacaggt tcagtggcag tggatcaggg 1380
 acagatttca cactcaagat cagcagagtg gaggtgagg atctgggagt ttatttctgc 1440
 tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa 1497

<210> 283
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL1/VH5x4-7 LHHL

<400> 283

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 275 280 285

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp

340

345

350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
 385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
 405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
 420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
 435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
 465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 284
 <211> 1500
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH5/VL1x4-7 HLHL

<400> 284
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 gcagacagcg tcaagggcgcg cttcacaatc actacagaca aatccaccag cacagcctac 240

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atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctccctcagge 360
gaaggtacta gtactgggtc tgggtgaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtgaa ttacatgaac tggtagcagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgtctgc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
gagatcaaat ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
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gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg 960
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gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 1260
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<210> 285
<211> 500
<212> PRT
<213> artificial sequence

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<220>
<223> VH5/VL1x4-7 HLHL

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<400> 285

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Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10          15

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr

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20	25	30
Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile		
35	40	45
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val		
50	55	60
Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr		
65	70	75
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys		
85	90	95
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly		
100	105	110
Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly		
115	120	125
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser		
130	135	140
Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys		
145	150	155
Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro		
165	170	175
Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser		
180	185	190
Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser		
195	200	205
Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys		
210	215	220
Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val		
225	230	235
Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln		
245	250	255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
 260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
 275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
 290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
 325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
 340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
 385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
 405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
 420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
 435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
 465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
 485 490 495

Leu Glu Ile Lys
500

<210> 286
<211> 1497
<212> DNA
<213> artificial sequence

<220>
<223> VL1/VH5x4-7 LHLH

<400> 286
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aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggagggttca 360
gggtggagcag acgacgtcca actgggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtaaac gatgcaactgg 480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtgggt 540
tatactaatt acgcagacag cgtcaagggc cgcttcacia tcaactacaga caaatccacc 600
agcagagcct acatggaact gagcagcctg cgcttctgagg aactgcaac ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac caggttcacc 720
gtctcctccg gaggtgggtg atccgagctc gtgatgaccc agactccact ctccctgcct 780
gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 840
aatggaaaca cctattttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 900
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tctggctaca ccttcacaaa ctatggttta agctgggtga agcagaggcc tggacaggctc 1260
cttgagtgga ttggagaggt ttatcctaga attggtaatg ctactacaa tgagaagttc 1320
aagggaagg ccacactgac tgcagacaaa tctccagca cagcgtccat ggagctccgc 1380

agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact 1440

aactacgact ggtacttcga tgtctggggc caagggacca cggtcaccgt ctctctca 1497

<210> 287

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL1/VH5x4-7 LHLH

<400> 287

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
 245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
 260 265 270

Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
 275 280 285

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
 290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
 325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
 370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
 385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
 405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
 420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
 450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
 465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 288
 <211> 1500
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH5/VL1x4-7 HLLH

<400> 288
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 tcctgcaagg cttctggcta cacctttact aggtacacga tgcaactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatacta gccgtgggta tactaattac 180
 gcagacagcg tcaagggcgc cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaaggacta gtactgggtc tgggtgaagt ggaggttcag gtggagcaga cgacattcag 420
 atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
 agagccagtc aaagtgtaag ttacatgaac tggtagcagc agaagccggg caaggcacc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 atttattact gccaacagtg gagtagtaac ccgctcacgt tcgggtggcgg gaccaaggtg 720

gagatcaaat ccggagggtg tggatccgag ctctgatga cccagactcc actctccctg 780
 cctgtcagtc ttggagatca agcctccatc tcttgcatat ctatgcagag ccttgtagac 840
 agtaatggaa acacctatctt acattggtac ctgcagaagc caggccagtc tccaaagctc 900
 ctgatctaca aagttttccaa ccgattttct ggggtcccag acaggttcag tggcagtggg 960
 tcagggacag atttcacact caagatcagc agagtggagg ctgaggatct gggagtttat 1020
 ttctgctctc aaagtacaca tgttccgtac acgttcggag gggggaccaa gcttgagatc 1080
 aaaggtggtg gtggttcttg cggcggcggc tccggtggtg gtggttctga ggtgcagctg 1140
 ctcgagcagt ctggagctga gctggcgagg cctggggctt cagtgaagct gtcttgcaag 1200
 gcttctggct acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag 1260
 gtcttgagt ggattggaga ggtttatcct agaattggtg atgcttacta caatgagaag 1320
 ttcaaggga aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc 1380
 cgcagcctga cctctgagga ctctgcgtc tatttctgtg caagacgggg atcctacgat 1440
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<210> 289
 <211> 500
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH5/VL1x4-7 HLLH
 <400> 289

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140
 Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160
 Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
 245 250 255
 Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
 260 265 270
 Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
 275 280 285
 Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
 290 295 300
 Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
 305 310 315 320
 Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp

325 330 335
 Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
 340 345 350
 Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
 355 360 365
 Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 370 375 380
 Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 385 390 395 400
 Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 405 410 415
 Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 420 425 430
 Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 435 440 445
 Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 450 455 460
 Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 465 470 475 480
 Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 485 490 495
 Thr Val Ser Ser
 500

<210> 290
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL2/VH5x4-7 LHHL

<400> 290
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 ctgagctgca gagccagtca aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120

aaggcaccce aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaiaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtaaac gatgcactgg 480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggg 540
tatactaatt acgcagacag cgtcaagggc cgcttcacia tctactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgctctgagg aactgcaac ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc 720
gtctcctccg gaggtgggtg atccgaggtg cagctgctcg agcagtctgg agctgagctg 780
gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctaac cttcaciaaa 840
tatggtttaa gctgggtgaa gcagaggcct ggacaggtcc ttgagtggat tggagaggtt 900
tatactagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 960
gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacctc tgaggactct 1020
gcggtctatt tctgtgcaag acggggatcc tacgatacta actacgactg gtacttcgat 1080
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taciaaagttt ccaaccgatt ttctggggtc ccagacaggt tcagtggcag tggatcaggg 1380
acagatttca cactcaagat cagcagagtg gaggtgagg atctgggagt ttatttctgc 1440
tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa 1497

<210> 291
<211> 499
<212> PRT
<213> artificial sequence

<220>
<223> VL2/VH5x4-7 LHHL

<400> 291

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly

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Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met	20	25	30
Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr	35	40	45
Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser	50	55	60
Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu	65	70	75
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr	85	90	95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr	100	105	110
Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu	115	120	125
Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val	130	135	140
Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp	145	150	155
Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn	165	170	175
Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe	180	185	190
Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser	195	200	205
Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr	210	215	220
Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr	225	230	235
			240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 275 280 285

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
 385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
 405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
 420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
 435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
 465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 292
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL2/VH5x4-7 LHLH

<400> 292
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 aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttccagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacacctta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctgga tggattggat acattaatcc tagccgtggt 540
 tatactaatt acgcagacag cgtcaagggc cgcttcacaa tctactacaga caaatccacc 600
 agcacagcct acatggaact gagcagcctg cgcttctgagg aactgcaac ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac cacggtcacc 720
 gtctctcccg gaggtgggtg atccgagctc gtgatgaccc agactccact ctccctgcct 780
 gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 840
 aatggaacaa cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 900
 atctacaaag ttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 960
 gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1020
 tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1080
 ggtgggtggtg gttctggcgg cggcggtcc ggtgggtggtg gttctgaggt gcagctgctc 1140
 gagcagtctg gagctgagct ggcgaggcct ggggcttcag tgaagctgtc ctgcaaggct 1200
 tctggctaca ccttcacaaa ctatggttta agctgggtga agcagaggcc tggacaggtc 1260

cttgagtgga ttggagaggt ttatcctaga attggtaatg cttactacaa tgagaagttc 1320
 aagggaagg ccacactgac tgcagacaaa tcctccagca cagcgtccat ggagctccgc 1380
 agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact 1440
 aactacgact ggtacttcga tgtctggggc caagggacca cggtcaccgt ctcctca 1497

<210> 293
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL2/VH5x4-7 LHLH

<400> 293

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
260 265 270

Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
275 280 285

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
 405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
 420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
 450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
 465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 294
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL3VH5x4-7 LHHL

<400> 294
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 aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt cctgtctcgc 180
 ttcagtggca gtgggtcttg gaccgactac tctctcaca tcaacagctt ggaggctgaa 240
 gatgctgcc cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggg 540
 tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcaactacaga caaatccacc 600

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gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc 720
gtctcctccg gaggtggtgg atccgaggtg cagctgctcg agcagtctgg agctgagctg 780
gcgaggcctg gggttcagt gaagctgtcc tgcaaggctt ctggctacac cttcacaac 840
tatggtttaa gctgggtgaa gcagaggcct ggacaggctc ttgagtggat tggagaggtt 900
tattctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 960
gcagacaaat cctccagcac agcgtccatg gagctccgca gctgacctc tgaggactct 1020
gcggtctatt tctgtgcaag acggggatcc tacgatacta actacgactg gtacttcgat 1080
gtctggggcc aagggaccac ggtcaccgtc tctcaggtg gtggtggttc tggcggcggc 1140
ggctccggtg gtggtggttc tgagctctg atgaccaga ctccactctc cctgcctgtc 1200
agtcttgag atcaagcctc catctcttgc agatctagtc agagccttgt acacagtaat 1260
ggaaacacct atttacattg gtacctgcag aagccaggcc agtctccaaa gctcctgac 1320
tacaaagttt ccaaccgatt ttctggggtc ccagacaggt tcagtggcag tggatcaggg 1380
acagatttca cactcaagat cagcagagtg gaggtgagg atctgggagt ttatttctgc 1440
tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa 1497

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<210> 295
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL3/VH5x4-7 LHHL

<400> 295

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr

305 310 315 320
 Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 325 330 335
 Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 340 345 350
 Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 355 360 365
 Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380
 Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
 385 390 395 400
 Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
 405 410 415
 Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
 420 425 430
 Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
 435 440 445
 Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460
 Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
 465 470 475 480
 Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495
 Glu Ile Lys

<210> 296
 <211> 1503
 <212> DNA
 <213> artificial sequence

 <220>
 <223> VH5VL3x4-7 HLHL

<400> 296
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tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtaacta gtactgggtc tgggtgaagt ggagggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
agagccagtt caagtgtgta ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
gagatcaaat ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
ctggcgaggc ctggggcttc agtgaagctg tcctgcaagg cttctggcta caccttcaca 840
aactatggtt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag 900
gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg 960
actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac ctctgaggac 1020
tctgcggtct atttctgtgc aagacgggga tcctacgata ctaactacga ctggtacttc 1080
gatgtctggg gccaaaggac cacggtcacc gtctcctcag gtggtgggtg ttctggcggc 1140
ggcggctccg gtggtgggtg ttctgagctc gtgatgacct agactccact ctccctgcct 1200
gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 1260
aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 1320
atctacaaag tttccaaccg attttctggg gtcccagaca gggtcagtgg cagtggatca 1380
gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1440
tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1500
cat 1503

<210> 297

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH5VL3x4-7 HLHL

<400> 297

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
 260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
 275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
 290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
 325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
 340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
 385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
 405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
 420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
 435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe

450

455

460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
 465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
 485 490 495

Leu Glu Ile Lys
 500

<210> 298
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL3VH5x4-7 LHLH

<400> 298
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 ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccaca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
 accaagggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
 tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600
 agcacagcct acatggaact gagcagcctg cgttctgagg aactgcaac ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac cagggtcacc 720
 gtctcctccg gaggtgggtg atccgagctc gtgatgacct agactccact ctccctgcct 780
 gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 840
 aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 900
 atctacaaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 960
 gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agttttattc 1020
 tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1080

ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgaggt gcagctgctc 1140
 gagcagtctg gagctgagct ggcgaggcct ggggcttcag tgaagctgtc ctgcaaggct 1200
 tctggctaca ccttcacaaa ctatggttta agctgggtga agcagaggcc tggacaggtc 1260
 cttgagtgga ttggagaggt ttatcctaga attggtaatg cttactacaa tgagaagttc 1320
 aagggcaagg ccacactgac tgcagacaaa tcctccagca cagcgtccat ggagctccgc 1380
 agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact 1440
 aactacgact ggtacttcga tgtctggggc caagggacca cggtcacctg ctctca 1497

<210> 299
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL3/VH5x4-7 LHLH

<400> 299

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
 370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
 385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
 405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
 420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
 450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
 465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 300
 <211> 1500
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH5VL3x4-7 HLLH

<400> 300
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 tcttgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaataccta gccgtgggta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
 gaagggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta 420

ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
agagccagtt caagtgtatg ttacatgaac tggatccagc agaagccggg caaggcacc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatccgag ctctgtatga ccagactcc actctccctg 780
cctgtcagtc ttggagatca agcctccatc tcttgagat ctatgcagag cctgttacac 840
agtaatggaa acacctattt acattggtac ctgcagaagc caggccagtc tccaaagctc 900
ctgatctaca aagtttccaa ccgattttct ggggtcccag acaggttcag tggcagtgga 960
tcaggacag atttcacact caagatcagc agagtggagg ctgaggatct gggagtttat 1020
ttctgctctc aaagtacaca tgttccgtac acgttcggag gggggaccaa gcttgagatc 1080
aaaggtggtg gtggttctgg cggcggcggc tccggtggtg gtggttctga ggtgcagctg 1140
ctcgagcagt ctggagctga gctggcgagg cctggggctt cagtgaagct gtctgcaag 1200
gcttctggct acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag 1260
gtccttgagt ggattggaga ggtttatcct agaattggta atgcttacta caatgagaag 1320
ttcaagggca aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc 1380
cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat 1440
actaactacg actggtactt cgatgtctgg ggccaaggga ccacggtcac cgtctcctca 1500

<210> 301
<211> 500
<212> PRT
<213> artificial sequence

<220>
<223> VH5VL3x4-7 HLLH

<400> 301

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
245 250 255

Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
260 265 270

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
275 280 285

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
 290 295 300

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
 305 310 315 320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
 325 330 335

Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
 340 345 350

Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
 355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 370 375 380

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 420 425 430

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 485 490 495

Thr Val Ser Ser
 500

<210> 302
 <211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> VL1VH7x4-7 LHHL

<400> 302

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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc      180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggtgaa      240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg      300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca      360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc      420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg      480
gtaaggcagg cacctggaca gggctctgga tggattggat acattaatcc tagccgtggg      540
tatactaatt acaatcagaa gttcaaggac cgcgtcacia tctactacaga caaatccacc      600
agcacagcct acatggaact gagcagcctg cgctctgagg aactgcagt ctattactgt      660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc      720
gtctcctccg gaggtgggtg atccgaggtg cagctgctcg agcagtctgg agctgagctg      780
gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcaciaaac      840
tatggtttaa gctgggtgaa gcagaggcct ggacaggctc ttgagtggat tggagaggtt      900
tactctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cactactgact      960
gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacctc tgaggactct     1020
gcggtctatt tctgtgcaag acggggatcc tacgatacta actacgactg gtacttcgat     1080
gtctggggcc aagggaaccac ggtcaccgtc tcctcaggtg gtggtggttc tggcggcggc     1140
ggctccggtg gtggtggttc tgagctcgtg atgaccaga ctccactctc cctgcctgtc     1200
agtcttgag atcaagcctc catctcttgc agatctagtc agagccttgt acacagtaat     1260
ggaaacacct atttacattg gtacctgcag aagccaggcc agtctccaaa gctcctgatc     1320
taciaaagttt ccaaccgatt ttctggggtc ccagacaggt tcagtggcag tggatcaggg     1380
acagatttca cactcaagat cagcagagtg gaggtgagg atctgggagt ttatttctgc     1440
tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa      1497
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<210> 303

<211> 499
<212> PRT
<213> artificial sequence

<220>
<223> VL1VH7x4-7 LHHL

<400> 303

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 275 280 285

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
 385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
 405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
 420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser

435 440 445
 Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460
 Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
 465 470 475 480
 Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495
 Glu Ile Lys

<210> 304
 <211> 1500
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH7-VL1x4-7 HLHL

<400> 304
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaattcta gccgtgggta tactaattac 180
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaaggtaacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattcag 420
 atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
 agagccagtc aaagtgtaag ttacatgaac tggatccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccttgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgtcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaatt cgggaggtgg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
 ctggcgaggc ctggggcctc agtgaagctg tcctgcaagg cttctggcta caccttcaca 840
 aactatggtt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag 900
 gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg 960

actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac ctctgaggac 1020
 tctgcggtct atttctgtgc aagaaggga tcctacgata ctaactacga ctggtacttc 1080
 gatgtctggg gccaaaggac cacggtcacc gtctcctcag gtggtggtgg ttctggcggc 1140
 ggcggtccg gtggtggtgg ttctgagctc gtgatgacc agactccact ctccctgcct 1200
 gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 1260
 aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 1320
 atctacaaag tttccaaccg atttctggg gtccagaca ggttcagtgg cagtggatca 1380
 gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1440
 tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1500

<210> 305
 <211> 500
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH7-VL1x4-7 HLHL

<400> 305

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly

115	120	125
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser		
130	135	140
Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys		
145	150	155
Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro		
	165	170
Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser		
	180	185
Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser		
	195	200
Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys		
	210	215
Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val		
	225	230
Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln		
	245	250
Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys		
	260	265
Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys		
	275	280
Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg		
	290	295
Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu		
	305	310
Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu		
	325	330
Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr		
	340	345
		350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
 385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
 405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
 420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
 435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
 465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
 485 490 495

Leu Glu Ile Lys
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<210> 306
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL1-VH7x4-7 LHLH

<400> 306
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 aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt cctgtctgcg 180
 ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa 240
 gatgctgccca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300

accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca 360
 ggtggagcag acgaagtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
 tatactaatt acaatcagaa gttcaaggac cgcgtcaca tctactacaga caaatccacc 600
 agcacagcct acatggaact gagcagcctg cgttctgagg aactgcagt ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc 720
 gtctcctcgg gaggtggtgg atccgagctc gtgatgacct agactccact ctccctgcct 780
 gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 840
 aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctectg 900
 atctacaaag tttccaaccg attttctggg gtccagaca ggttcagtgg cagtggatca 960
 gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1020
 tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1080
 ggtggtggtg gttctggcgg cggcggtcc ggtggtggtg gttctgaggt gcagctgctc 1140
 gagcagtctg gagctgagct ggcgaggcct ggggcttcag tgaagctgtc ctgcaaggct 1200
 tctggctaca ccttcacaaa ctatggttta agctgggtga agcagaggcc tggacaggtc 1260
 cttgagtgga ttggagaggt ttatcctaga attggtaatg cttactacaa tgagaagttc 1320
 aagggcaagg ccacactgac tgcagacaaa tccctcagca cagcgtccat ggagctccgc 1380
 agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact 1440
 aactacgact ggtacttcca tgtctggggc caagggacca cggtcaccgt ctccctca 1497

<210> 307

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VL1-VH7x4-7 LHLH

<400> 307

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
 245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
 260 265 270

Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
 275 280 285

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
 290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
 325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
 370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
 385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
 405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
 420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
 450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
 465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 308
<211> 1500
<212> DNA
<213> artificial sequence

<220>
<223> VH7-VL1x4-7 HLLH

<400> 308
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
tcttgcaagg cttctgggta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatecta gccgtgggta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
gaagg tacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattcag 420
atgaccagtc ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtgaa ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
gagatcaaat ccggaggtgg tggatccgag ctctgatga cccagactcc actctccctg 780
cctgtcagtc ttggagatca agcctccatc tottgagat ctagtcagag cctgttacac 840
agtaatggaa acacctatct acattggtac ctgcagaagc caggccagtc tccaaagctc 900
ctgatctaca aagtttccaa ccgattttct ggggtcccag acaggttcag tggcagtgga 960
tcagggacag atttcacact caagatcagc agagtggagg ctgaggatct gggagtttat 1020
ttctgctctc aaagtacaca tggtccgtac acgttcggag gggggaccaa gcttgagatc 1080
aaaggtggtg gtggttcttg cggcggcggc tccggtggtg gtggttctga ggtgcagctg 1140
ctcgagcagt ctggagctga gctggcgagg cctggggcct cagtgaagct gtcctgcaag 1200
gcttctggct acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag 1260
gtccttgagt ggattggaga ggtttatcct agaattggta atgcttacta caatgagaag 1320
ttcaagggca aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc 1380
cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat 1440

actaactacg actggtactt cgatgtctgg ggccaaggga ccacgggtcac cgtctcctca 1500

<210> 309
 <211> 500
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH7-VL1x4-7 HLLH

<400> 309

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
245 250 255

Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
260 265 270

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
275 280 285

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
290 295 300

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
325 330 335

Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
340 345 350

Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
370 375 380

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile

420 425 430
 Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 435 440 445
 Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 450 455 460
 Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 465 470 475 480
 Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 485 490 495
 Thr Val Ser Ser
 500

<210> 310
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL2VH7x4-7 LHHL

<400> 310
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 ctgagctgca gagccagtca aagtgtagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggtgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca ggtctctgga tggattggat acattaatcc tagccgtggt 540
 tatactaatt acaatcagaa gttcaaggac cgcgtcaca tctactacaga caaatccacc 600
 agcacagcct acatggaact ggcagcctg cgttctgagg aactgcagt ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc 720
 gtctcctccg gaggtggtgg atccgaggtg cagctgctcg agcagtctgg agctgagctg 780
 gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcacaac 840

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tatggtttaa gctgggtgaa gcagaggcct ggacagggtcc ttgagtggat tggagagggt 900
tattcctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 960
gcagacaaat cctccagcac agcgtccatg gagtccgca gcctgacctc tgaggactct 1020
gcggtctatt tctgtgcaag acggggatcc tacgatacta actacgactg gtacttcgat 1080
gtctggggcc aaggggaccac ggtcacgcgc tcctcagggtg gtggtgggtc tggcggcggc 1140
ggctccggtg gtggtgggtc tgagctcgtg atgaccaga ctccactctc cctgcctgtc 1200
agtcttgag atcaagcctc catctcttgc agatctagtc agagccttgt acacagtaat 1260
ggaaacacct atttacattg gtacctgcag aagccaggcc agtctccaaa gctcctgac 1320
taciaaagttt ccaaccgatt ttctggggtc ccagacaggt tcagtggcag tggatcaggg 1380
acagatttca cactcaagat cagcagagtg gaggtgagg atctgggagt ttatttctgc 1440
tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa 1497

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<210> 311
<211> 499
<212> PRT
<213> artificial sequence

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<220>
<223> VL2VH7x4-7 LHHL

```

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<400> 311

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Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1           5           10           15

```

```

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20           25           30

```

```

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35           40           45

```

```

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50           55           60

```

```

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65           70           75           80

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Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85           90           95

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Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr

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100	105	110
Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu		
115	120	125
Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val		
130	135	140
Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp		
145	150	155
Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn		
165	170	175
Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val		
180	185	190
Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser		
195	200	205
Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr		
210	215	220
Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr		
225	230	235
Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser		
245	250	255
Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys		
260	265	270
Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln		
275	280	285
Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile		
290	295	300
Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr		
305	310	315
Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr		
325	330	335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
 385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
 405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
 420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
 435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
 465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 312
 <211> 1500
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH7VL2x4-7 HLHL

<400> 312
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatocta gccgtgggta tactaattac 180

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aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac      240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat      300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc      360
gaaggtacta gtactggttc tggtggaagt ggaggttcag gtggagcaga cgacattgta      420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc      480
agagccagtc aaagtgtaag ttacatgaac tggtagcagc agaagccggg caaggcaccc      540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc      600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc      660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg      720
gagatcaaat ccggaggtgg tggatccgag gtgcagctgc tcgagcagtc tggagctgag      780
ctggcgaggc ctggggcttc agtgaagctg tcctgcaagg cttctggcta caccttcaca      840
aactatggtt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag      900
gtttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg      960
actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac ctctgaggac     1020
tctgcggtct atttctgtgc aagacgggga tcctacgata ctaactacga ctggtacttc     1080
gatgtctggg gccaagggac cacggtcacc gtctcctcag gtggtggtgg ttctggcggc     1140
ggcggtccg gtggtggtgg ttctgagctc gtgatgacc agactccact ctccctgcct     1200
gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt     1260
aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg     1320
atctacaaag ttccaaccg attttctggg gtccagaca ggttcagtgg cagtggatca     1380
gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc     1440
tgctctcaaa gtacacatgt tccgtacacg ttoggagggg ggaccaagct tgagatcaaa     1500

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<210> 313
 <211> 500
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH7VL2x4-7 HLHL

<400> 313

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro
385 390 395 400

Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
405 410 415

Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
420 425 430

Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
435 440 445

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
450 455 460

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
465 470 475 480

Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
485 490 495

Leu Glu Ile Lys
500

<210> 314
<211> 1497
<212> DNA
<213> artificial sequence

<220>
<223> VL2VH7x4-7 LHLH

<400> 314
gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60
ctgagctgca gagccagtc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtctgcaa ggcttctggc tacaccttta ctaggtacac gatgcaactgg 480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggg 540
tatactaatt acaatcagaa gttcaaggac cgcgtcacia tcaactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgcttctgagg aactgcagt ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720
gtctcctccg gaggtgggtg atccgagctc gtgatgacct agactccact ctccctgcct 780
gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 840
aatggaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 900
atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 960
gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1020
tgctctcaaa gtacacatgt tccgtacacg ttcggagggg ggaccaagct tgagatcaaa 1080
ggtgggtggtg gttctggcgg cggcggctcc ggtgggtggtg gttctgaggt gcagctgctc 1140
gagcagtctg gagctgagct ggcgaggcct ggggcttcag tgaagctgtc ctgcaaggct 1200
tctggctaca ccttcacaaa ctatggttta agctgggtga agcagaggcc tggacagctc 1260
cttgagtgga ttggagaggt ttatcctaga attggtaatg cttactacaa tgagaagtgc 1320

aagggcaagg ccacactgac tgcagacaaa tcctccagca cagcgtccat ggagctccgc 1380
 agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact 1440
 aactacgact ggtacttcga tgtctggggc caagggacca cggtcaccgt ctctca 1497

<210> 315
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL2VH7x4-7 LHLH

<400> 315

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro
 245 250 255

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
 260 265 270

Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp
 275 280 285

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
 290 295 300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
 325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
 370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
 385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg

405 410 415
 Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
 420 425 430
 Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 435 440 445
 Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
 450 455 460
 Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
 465 470 475 480
 Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495
 Val Ser Ser

<210> 316
 <211> 1500
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH7VL2x4-7 HLLH

<400> 316
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatocta gccgtgggta tactaattac 180
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctccctcaggc 360
 gaaggtaact gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta 420
 ctgaccagtc ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtgta ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcgggtggcgg gaccaagggtg 720

gagatcaaat cgggaggtgg tggatccgag ctcgatgatga cccagactcc actctccctg 780
 cctgtcagtc ttggagatca agcctccatc tcttgcatat ctatgcagag ccttgatcac 840
 agtaatggaa acacctatct acattggtac ctgcagaagc caggccagtc tccaaagctc 900
 ctgatctaca aagtttccaa ccgattttct ggggtcccag acaggttcag tggcagtggg 960
 tcagggacag atttcacact caagatcagc agagtggagg ctgaggatct gggagtttat 1020
 ttctgctctc aaagtacaca tgtccgtac acgttcggag gggggaccaa gcttgagatc 1080
 aaaggtggtg gtggttctgg cggcgggcgc tccggtggtg gtggttctga ggtgcagctg 1140
 ctcgagcagt ctggagctga gctggcgagg cctggggctt cagtgaagct gtcctgcaag 1200
 gcttctggct acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag 1260
 gtccttgagt ggattggaga ggtttatcct agaattggtg atgcttacta caatgagaag 1320
 ttcaagggca aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc 1380
 cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat 1440
 actaactacg actggtactt cgatgtctgg ggccaaggga ccacgggtcac cgtctcctca 1500

<210> 317
 <211> 500
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH7VL2x4-7 HLLH

<400> 317

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

85	90	95
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly		
100	105	110
Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly		
115	120	125
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser		
130	135	140
Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys		
145	150	155
Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro		
165	170	175
Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser		
180	185	190
Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser		
195	200	205
Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys		
210	215	220
Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val		
225	230	235
Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr		
245	250	255
Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys		
260	265	270
Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His		
275	280	285
Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys		
290	295	300
Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly		
305	310	315
		320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
 325 330 335

Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
 340 345 350

Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
 355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 370 375 380

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 420 425 430

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 485 490 495

Thr Val Ser Ser
 500

<210> 318
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL3VH7x4-7 LHHL

<400> 318
 gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc

ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggagggtca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgtaaaa acctggggcc 420
tcagtgaagg tgctctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggctctgaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acaatcagaa gttcaaggac cgcgtcaca tcactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgctctgagg aactgcagt ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc 720
gtctcctccg gaggtggtgg atccgaggtg cagctgctcg agcagtctgg agctgagctg 780
gcgaggcctg gggcttcagt gaagctgtcc tgcaaggctt ctggctacac cttcaciaaac 840
tatggtttaa gctgggtgaa gcagaggcct ggacaggctc ttgagtggat tggagaggtt 900
tatcctagaa ttggtaatgc ttactacaat gagaagttca agggcaaggc cacactgact 960
gcagacaaat cctccagcac agcgtccatg gagctccgca gcctgacctc tgaggactct 1020
gcggtctatt tctgtgcaag acggggatcc tacgatacta actacgactg gtacttcgat 1080
gtctggggcc aagggaccac ggtcacctgc tctcaggtg gtggtggttc tggcggcggc 1140
ggctccggtg gtggtggttc tgagctcgtg atgaccaga ctccactctc cctgcctgtc 1200
agtcttgag atcaagcctc catctcttgc agatctagtc agagccttgt acacagtaat 1260
ggaaacacct atttacattg gtacctgcag aagccaggcc agtctccaaa gctcctgac 1320
tacaaagttt ccaaccgatt ttctggggtc ccagacaggt tcagtggcag tggatcaggg 1380
acagatttca cactcaagat cagcagagtg gaggctgagg atctgggagt ttatttctgc 1440
tctcaaagta cacatgttcc gtacacgttc ggagggggga ccaagcttga gatcaaa 1497

<210> 319
<211> 499
<212> PRT
<213> artificial sequence

<220>
<223> VL3VH7x4-7 LHHL
<400> 319

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
245 250 255

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
290 295 300

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
340 345 350

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
385 390 395 400

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
405 410 415

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
420 425 430

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
435 440 445

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
450 455 460

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
465 470 475 480

Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 320
 <211> 1500
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH7VL3x4-7 HLHL

<400> 320
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctccctcaggc 360
 gaagggtacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
 agagccagtt caagtgtgag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaat ccggagggtg tggatccgag gtgcagctgc tcgagcagtc tggagctgag 780
 ctggcgaggc ctggggcttc agtgaagctg tcctgcaagg cttctggcta caccttcaca 840
 aactatggtt taagctgggt gaagcagagg cctggacagg tccttgagtg gattggagag 900
 gttttatccta gaattggtaa tgcttactac aatgagaagt tcaagggcaa ggccacactg 960
 actgcagaca aatcctccag cacagcgtcc atggagctcc gcagcctgac ctctgaggac 1020
 tctgcggtct atttctgtgc aagacgggga tcctacgata ctaactacga ctggtacttc 1080
 gatgtctggg gccaaaggac cacggtcacc gtctcctcag gtggtgggtg ttctggcggc 1140
 ggcggtccg gtggtgggtg ttctgagctc gtgatgaccc agactccact ctccctgcct 1200

gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 1260
aatggaaaca cctatttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 1320
atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 1380
gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1440
tgctctcaaa gtacacatgt tccgtacacg ttccgagggg ggaccaagct tgagatcaaa 1500

<210> 321
<211> 500
<212> PRT
<213> artificial sequence

<220>
<223> VH7VL3x4-7 HLHL

<400> 321

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln
 245 250 255

Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys
 260 265 270

Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys
 275 280 285

Gln Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg
 290 295 300

Ile Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu
 305 310 315 320

Thr Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu
 325 330 335

Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr
 340 345 350

Asp Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro

385 390 395 400
 Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
 405 410 415
 Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys
 420 425 430
 Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe
 435 440 445
 Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 450 455 460
 Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe
 465 470 475 480
 Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys
 485 490 495
 Leu Glu Ile Lys
 500

<210> 322
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL3VH7x4-7 LHLH

<400> 322
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 ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
 gatgctgcca ottattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggagggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacacottta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
 tatactaatt acaatcagaa gttcaaggac cgcgtcacia tctactacaga caaatccacc 600

agcacagcct acatggaact gacgagcctg cgttctgagg aactgcagt ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac cacggtcacc 720
 gtctctcccg gaggtggtgg atccgagctc gtgatgaccc agactccact ctccctgcct 780
 gtcagtcttg gagatcaagc ctccatctct tgcagatcta gtcagagcct tgtacacagt 840
 aatggaaaca cctattttaca ttggtacctg cagaagccag gccagtctcc aaagctcctg 900
 atctacaaag tttccaaccg attttctggg gtcccagaca ggttcagtgg cagtggatca 960
 gggacagatt tcacactcaa gatcagcaga gtggaggctg aggatctggg agtttatttc 1020
 tgctctcaaa gtacacatgt tccgtacacg ttoggagggg ggaccaagct tgagatcaaa 1080
 ggtggtggtg gttctggcgg cggcggtccc ggtggtggtg gttctgaggt gcagctgctc 1140
 gagcagtctg gagctgagct ggcgaggcct ggggcttcag tgaagctgct ctgcaaggct 1200
 tctggctaca ccttcacaaa ctatggttta agctgggtga agcagaggcc tggacaggtc 1260
 cttgagtggg ttggagaggt ttatcctaga attggtaatg cttactacaa tgagaagttc 1320
 aagggcaagg ccacactgac tgcagacaaa tcctccagca cagcgtccat ggagctccgc 1380
 agcctgacct ctgaggactc tgcggtctat ttctgtgcaa gacggggatc ctacgatact 1440
 aactacgact ggtacttcga tgtctggggc caagggacca cggtcaccgt ctcctca 1497

<210> 323
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL3VH7x4-7 LHLH

<400> 323

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu

65	70	75	80
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr	85	90	95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr	100	105	110
Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu	115	120	125
Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val	130	135	140
Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp	145	150	155
Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn	165	170	175
Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val	180	185	190
Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser	195	200	205
Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr	210	215	220
Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr	225	230	235
Val Ser Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr Pro	245	250	255
Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg	260	265	270
Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp	275	280	285
Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val	290	295	300

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
 325 330 335

Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser Gly
 370 375 380

Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala
 385 390 395 400

Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln Arg
 405 410 415

Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile Gly
 420 425 430

Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 435 440 445

Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr Ser
 450 455 460

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp Thr
 465 470 475 480

Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 324
 <211> 1500
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH7VL3x4-7 HLLH

<400> 324
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaataccta gccgtgggta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaaggtracta gtactgggtc tggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
agagccagtt caagtgttaag ttacatgaac tggtagcagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcaagt tccgtggcgg gaccaagggtg 720
gagatcaaat ccggagggtg tggatccgag ctctgtgatga cccagactcc actctccctg 780
cctgtcagtc ttggagatca agcctccatc tcttgagat ctagtcagag ccttgtagac 840
agtaatggaa acacctatct acattggtac ctgcagaagc caggccagtc tccaaagctc 900
ctgatctaca aagtttccaa ccgattttct ggggtcccag acaggttcag tggcagtgga 960
tcagggacag atttcacact caagatcagc agagtggagg ctgaggatct gggagtttat 1020
ttctgctctc aaagtacaca tgttccgtac acgttcggag gggggaccaa gcttgagatc 1080
aaagggtggtg gtggttctg cggcggcggc tccggtggtg gtggttctga ggtgcagctg 1140
ctcgagcagt ctggagctga gctggcgagg cctggggcct cagtgaagct gtcctgcaag 1200
gcttctggtt acaccttcac aaactatggt ttaagctggg tgaagcagag gcctggacag 1260
gtccttgagt ggattggaga ggtttatcct agaattggtg atgcttacta caatgagaag 1320
ttcaaggga aggccacact gactgcagac aaatcctcca gcacagcgtc catggagctc 1380
cgcagcctga cctctgagga ctctgcggtc tatttctgtg caagacgggg atcctacgat 1440
actaactacg actggtactt cgatgtctgg ggccaaggga ccacggtcac cgtctcctca 1500

<210> 325

<211> 500

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL3x4-7 HLLH

<400> 325

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Leu Val Met Thr Gln Thr
 245 250 255

Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys
 260 265 270

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
 275 280 285

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys
 290 295 300

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
 305 310 315 320

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
 325 330 335

Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr His Val Pro Tyr Thr Phe
 340 345 350

Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
 355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Gln Ser
 370 375 380

Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys
 385 390 395 400

Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Leu Ser Trp Val Lys Gln
 405 410 415

Arg Pro Gly Gln Val Leu Glu Trp Ile Gly Glu Val Tyr Pro Arg Ile
 420 425 430

Gly Asn Ala Tyr Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
 435 440 445

Ala Asp Lys Ser Ser Ser Thr Ala Ser Met Glu Leu Arg Ser Leu Thr
 450 455 460

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Gly Ser Tyr Asp
 465 470 475 480

Thr Asn Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val
 485 490 495

Thr Val Ser Ser
 500

<210> 326
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL1VH5xCD19 LHHL

<400> 326
 gacattcaga tgaccagtc tccatctagc ctgtctgcat ctgtcgggga ccgtgtcacc 60
 atcacctgca gagccagtca aagtgtaatg tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggagggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaataa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
 tatactaatt acgcagacag cgtcaagggc cgcttcacaa tctactacaga caaatccacc 600
 agcacagcct acatggaact gagcagcctg cgcttctgagg aactgcaac ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac caccgtcacc 720
 gtctcctccg gaggtggtgg atcccagggtg cagctgcagc agtctggggc tgagctggtg 780
 aggctgggt cctcagtga gatttctgc aaggcttctg gctatgcatt cagtagctac 840
 tggatgaact gggatgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg 900
 cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca 960
 gacgaatcct ccagcacagc ctacatgcaa ctacgagcc tagcatctga ggactctgcg 1020
 gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac 1080

tactggggcc aagggaaccac ggtcacccgtc tcctccgggtg gtggtggttc tggcggcggc 1140
 gggtccgggtg gtggtggttc tgatatccag ctgaccagctt ctccagcttc tttggctgtg 1200
 tctctagggc agagggccac catctcctgc aaggccagcc aaagtgttga ttatgatggt 1260
 gatagttatt tgaactggta ccaacagatt ccaggacagc caccctaaact cctcatctat 1320
 gatgcatcca atctagtttc tgggatccca ccaggttta gtggcagtggt gtctgggaca 1380
 gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaaccta tcaactgtcag 1440
 caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa 1494

<210> 327
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL1VH5xCD19 LHHL

<400> 327

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
 245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
 260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
 275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
 290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
 325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
 340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly

370 375 380
 Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
 385 390 395 400
 Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
 405 410 415
 Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
 420 425 430
 Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
 435 440 445
 Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
 450 455 460
 Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
 465 470 475 480
 Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
 485 490 495
 Ile Lys

<210> 328
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH5VL1xCD19 HLHL

<400> 328
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcttgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcacctg ctcctcaggc 360
 gaaggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattcag 420
 atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480

agagccagtc aaagtgtaag ttacatgaac tggtagcagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcgggtggcgg gaccaaggtg 720
 gagatcaaat ccggaggtgg tggatccag gtgcagctgc agcagctctg ggctgagctg 780
 gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
 tactggatga actgggtgaa gcagaggcct ggacagggtc ttgagtggat tggacagatt 900
 tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact 960
 gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020
 gcggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080
 gactactggg gccaaaggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc 1140
 ggcggctccg gtggtggtgg ttctgatata cagctgaccc agtctccagc ttctttggt 1200
 gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 1260
 ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320
 tatgatgcat ccaatctagt ttctgggata ccaccaggt ttagtggcag tgggtctggg 1380
 acagacttca cctcaacat ccacctgtg gagaaggtgg atgctgcaac ctatcactgt 1440
 cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ocaagctcga gatcaaa 1497

<210> 329
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH5VL1xCD19 HLHL

<400> 329

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val

50 55 60
 Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95
 Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140
 Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160
 Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
 245 250 255
 Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
 260 265 270
 Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
 275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
 290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
 325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
 340 345 350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
 385 390 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
 405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
 420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
 435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
 465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 330

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL1VH5xCD19 LHLH

<400> 330

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atcacctgca gagccagtca aagtgttaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa	240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg	300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca	360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc	420
tcagtgaagg tgcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggg	540
tatactaatt acgcagacag cgtcaagggc cgcttcacia tcaactacaga caaatccacc	600
agcacagcct acatggaact gagcagcctg cgcttctgagg aactgcaac ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac caggttcacc	720
gtctcctcgc gaggtgggtg atccgatatc cagctgaccc agtctccagc ttctttgggt	780
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat	840
ggtgatagtt atttgaactg gtaccaacag attccaggac agccaccaa actcctcacc	900
tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg	960
acagacttca ccctcaacat ccatcctgtg gagaaggtgg atgtgcaac ctatcactgt	1020
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt	1080
ggtggtgggt ctggcgggcg cggtccgggt ggtggtgggt ctgaggtgca gctgcagcag	1140
tctggggctg agctggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc	1200
tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggctctgag	1260
tggattggac agatttggcc tggagatggt gatactaact acaatggaaa gttcaagggt	1320
aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta	1380
gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt	1440
tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc	1494

<210> 331

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL1VH5xCD19 LHLH

<400> 331

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
 245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
 260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
 275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
 290 295 300

Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320

Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
 325 330 335

Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
 340 345 350

Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
 355 360 365

Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
 370 375 380

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
 385 390 395 400

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
 405 410 415

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
 420 425 430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
 435 440 445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
 450 455 460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
 465 470 475 480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495

Ser Ser

<210> 332
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH5VL1xCD19 HLLH

<400> 332
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 cctggacagg gtctggaatg gattggatac attaataccta gccgtgggta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaaggacta gtactgggtc tgggtggaagt ggagggtcag gtggagcaga cgacattcag 420
 atgaccagtc ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
 agagccagtc aaagtgtgag ttacatgaac tggtagcagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgtcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaat ccggagggtg tggatccgat atccagctga cccagtctcc agcttctttg 780
 gctgtgtctc tagggcagag ggccaccatc tcctgcaagg ccagccaaag tgttgattat 840
 gatggtgata gttatttgaa ctggtaccaa cagattccag gacagccacc caaactctc 900
 atctatgatg catccaatct agtttctggg atcccacca ggtttagtgg cagtgggtct 960

gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac 1020
 tgtcagcaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa 1080
 ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctcaggt gcagctgcag 1140
 cagtctgggg ctgagctggt gaggcctggg tctcagtgga agatttcctg caaggcttct 1200
 ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggtctt 1260
 gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag 1320
 ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcage 1380
 ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc 1440
 cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctctcc 1497

<210> 333
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH5VL1xCD19 HLLH

<400> 333

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
 245 250 255

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

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
 275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
 290 295 300

Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
 325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly

355 360 365
 Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
 370 375 380
 Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
 385 390 395 400
 Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
 405 410 415
 Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
 420 425 430
 Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
 435 440 445
 Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
 450 455 460
 Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
 465 470 475 480
 Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 334
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL2/VH5xCD19 LHHL

<400> 334
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 aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
 gatgctgcc cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

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ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acgcagacag cgtcaagggc cgcttcacaa tcactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgttctgagg aactgcaac ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc 720
gtctcctccg gaggtggtgg atcccagggtg cagctgcagc agtctggggc tgagctggtg 780
aggcctgggt cctcagtga gatttctgc aaggcttctg gctatgcatt cagtagctac 840
tggatgaact gggatgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg 900
cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca 960
gacgaatcct ccagcacagc ctacatgcaa ctacagcagc tagcatctga ggactctgcg 1020
gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac 1080
tactggggcc aaggggaccac ggtcacccgc tcctccggtg gtggtggttc tggcggcggc 1140
ggctccggtg gtggtggttc tgatatccag ctgaccagc ctccagcttc tttggtgtg 1200
tctctagggc agaggggccac catctcctgc aaggccagcc aaagtgttga ttatgatggt 1260
gatagttatt tgaactggta ccaacagatt ccaggacagc caccctaaact cctcatctat 1320
gatgcatcca atctagtctc tgggatccca ccaggttta gtggcagtgg gtctgggaca 1380
gacttcaccc tcaacatcca tcctgtggag aagggtggat ctgcaacctc tactgtcag 1440
caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa 1494

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<210> 335
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL2/VH5xCD19 LHHL

<400> 335

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr

35	40	45
Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser		
50	55	60
Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu		
65	70	75
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr		
85	90	95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr		
100	105	110
Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu		
115	120	125
Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val		
130	135	140
Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp		
145	150	155
Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn		
165	170	175
Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe		
180	185	190
Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser		
195	200	205
Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr		
210	215	220
Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr		
225	230	235
Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly		
245	250	255
Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala		
260	265	270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
 275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
 290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
 325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
 340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
 385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
 405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
 420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
 435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
 450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
 465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
 485 490 495

Ile Lys

<210> 336
<211> 1497
<212> DNA
<213> artificial sequence

<220>
<223> VH5VL2xCD19 HLHL

<400> 336
gacgtccaac tggatgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
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cctggacagg gtctggaatg gattggatac attaatacta gccgtgggta tactaattac 180
gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcaggc 360
gaagggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtgaa ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
gagatcaaat ccggaggtgg tggatcccag gtgcagctgc agcagtctgg ggctgagctg 780
gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
tactggatga actgggtgaa gcagaggcct ggacagggtc ttgagtggat tggacagatt 900
tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact 960
gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020
gcggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080
gactactggg gccaaaggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc 1140
ggcggctccg gtggtggtgg ttctgatatc cagctgaccc agtctccagc ttctttggct 1200
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 1260
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320
tatgatgcat ccaatctagt ttctgggatc ccacccaggt ttagtggcag tgggtctggg 1380
acagacttca ccctcaacat ccatcctgtg gagaagggtg atgctgcaac ctatcactgt 1440
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

<210> 337
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH5VL2xCD19 HLHL

<400> 337

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
340 345 350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
385 390 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
 435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
 465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 338
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL2/VH5xCD19

<400> 338
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 aaggcaccoca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggtgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctgga tggattggat acattaatcc tagccgtggt 540
 tatactaatt acgcagacag cgtcaagggc cgcttcacaa tctactacaga caaatccacc 600
 agcacagcct acatggaact gagcagcctg cgttctgagg aactgcaac ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac cagggtcacc 720
 gtctcctccg gaggtggtgg atccgatata cagctgaccc agtctccagc ttctttggct 780
 gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840

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ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 900
tatgatgcat ccaatctagt ttctgggatc ccaccagggt ttagtggcag tgggtctggg 960
acagacttca ccctcaacat ccctcctgtg gagaagggtg atgctgcaac ctatcactgt 1020
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt 1080
ggtggtggtt ctggcggcgg cggtccgggt ggtggtggtt ctcagggtga gctgcagcag 1140
tctggggctg agctggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc 1200
tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca ggtctttgag 1260
tggattggac agatttggcc tggagatggt gatactaact acaatggaaa gttcaaggggt 1320
aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta 1380
gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440
tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

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<210> 339
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL2/VH5xCD19

<400> 339

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
 245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
 260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
 275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
 290 295 300

Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320

Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
 325 330 335

Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly

340 345 350
 Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
 355 360 365
 Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
 370 375 380
 Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
 385 390 395 400
 Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
 405 410 415
 Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
 420 425 430
 Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
 435 440 445
 Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
 450 455 460
 Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
 465 470 475 480
 Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495
 Ser Ser

<210> 340
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH5VL2xCD19 HLLH

<400> 340
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 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240


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atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctccctcaggc 360
gaaggtacta gtactggttc tggtggaagt ggagggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgttaag ttacatgaac tggtagcagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaaggtg 720
gagatcaaat ccggaggtgg tggatccgat atccagctga ccagctctcc agcttctttg 780
gctgtgtctc tagggcagag ggccaccatc tcctgcaagg ccagccaaag tgttgattat 840
gatggtgata gttatttgaa ctggtaccaa cagattccag gacagccacc caaactctc 900
atctatgatg catccaatct agtttctggg atcccacca ggtttagtgg cagtgggtct 960
gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac 1020
tgtcagcaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa 1080
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctcaggt gcagctgcag 1140
cagtctgggg ctgagctggt gaggcctggg tcctcagtga agatttctg caaggcttct 1200
ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggctct 1260
gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag 1320
ggtaaagcca ctctgactgc agacgaatcc tocagcacag cctacatgca actcagcagc 1380
ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc 1440
cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctctctcc 1497

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<210> 341
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH5VL2xCD19 HLLH

<400> 341

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr

20 25 30
 Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95
 Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125
 Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140
 Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160
 Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205
 Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240
 Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
 245 250 255

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

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
 275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
 290 295 300

Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
 325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
 370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
 385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
 405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
 420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
 435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
 450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
 465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 342
<211> 1494
<212> DNA
<213> artificial sequence

<220>
<223> VL3VH5xCD19 LHHL

<400> 342
gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60
ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt cctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac totctcacia tcaacagctt ggaggctgaa 240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acgcagacag cgtcaagggc cgcttcacia tctactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgctctgagg aactgcaac ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac cacggtcacc 720
gtctcctccg gaggtggtgg atcccagggtg cagctgcagc agtctggggc tgagctggtg 780
aggcctgggt cctcagtga gatttctctg aaggcttctg gctatgcatt cagtagctac 840
tggatgaact gggatgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg 900
cctggagatg gtgatactaa ctacaatgga aagttaagg gtaaagccac tctgactgca 960
gacgaatcct ccagcacagc ctacatgcaa ctacagagcc tagcatctga ggactctgcg 1020
gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac 1080
tactggggcc aagggaccac ggtcacgctc tctccgggtg gtgggtggtc tggcggcggc 1140
ggctccgggt gtgggtggtc tgatatccag ctgaccagct ctccagcttc tttggctgtg 1200
tctctagggc agaggggccac catctcctgc aaggccagcc aaagtgttga ttatgatggt 1260
gatagttatt tgaactggta ccaacagatt ccaggacagc caccctaaact cctcatctat 1320
gatgcatcca atctagtttc tgggatccca ccaggttta gtggcagtggt gtctgggaca 1380

gacttcaccc tcaacatcca tctgtggag aaggtggatg ctgcaaccta tcaactgtcag 1440
 caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa 1494

<210> 343
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL3VH5xCD19 LHHL

<400> 343

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
 245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
 260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
 275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
 290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
 325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
 340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
 385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
 405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
 420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
 435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
 450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
 465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
 485 490 495

Ile Lys

<210> 344
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH5VL3xCD19 HLHL

<400> 344
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
 tcttgcaagg cttctggcta cacctttact aggtacacga tgcaactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaattcta gccgtgggta tactaattac 180
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaaggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
 agagccagtt caagtgtgaa ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tgggtggcgg gaccaaggtg 720

gagatcaaat ccggagggtgg tggatcccag gtgcagctgc agcagctctgg ggctgagctg 780
 gtgaggcctg ggctctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
 tactggatga actgggtgaa gcagaggcct ggacagggtc ttgagtggat tggacagatt 900
 tggcctggag atggtgatac taactacaat ggaaagtcca agggtaaagc cactctgact 960
 gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020
 gcggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080
 gactactggg gccaaaggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc 1140
 ggcggtccg gtggtggtgg ttctgatata cagctgaccc agtctccagc ttctttggct 1200
 gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 1260
 ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320
 tatgatgcat ccaatctagt ttctgggata ccaccaggt ttagtggcag tgggtctggg 1380
 acagacttca ccctcaacat ccctcctgtg gagaagggtg atgctgcaac ctatcactgt 1440
 cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

<210> 345
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH5VL3xCD19 HLHL

<400> 345

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
 245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
 275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
 290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala

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<400> 346
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ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
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aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
gatgctgccca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtgccggg 300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca 360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acgcagacag cgtcaagggc cgcttcacia tcactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgtctgagg aactgcaac ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac cacggtcacc 720
gtctcctccg gaggtggtgg atccgatatc cagctgaccc agtctccagc ttctttggct 780
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 900
tatgatgcat ccaatctagt ttctgggatc ccaccaggt ttagtggcag tgggtctggg 960
acagacttca cctcaacat ccatcctgtg gagaaggtgg atgtgcaac ctatcactgt 1020
cagcaaagta ctgaggatcc gtggacgttc ggtggagggg ccaagctcga gatcaaaggt 1080
ggtggtggtt ctggcggcgg cggctccggt ggtggtggtt ctcaggtgca gctgcagcag 1140
tctggggctg agctggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc 1200
tatgcattca gtagctactg gatgaactgg gtgaagcaga ggctggaca gggctctgag 1260
tggattggac agatttggtc tggagatggt gatactaact acaatggaaa gttcaagggt 1320
aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta 1380
gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440
tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

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<210> 347
<211> 498
<212> PRT
<213> artificial sequence

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<220>
<223> VL3VR5xCD19 LHLH

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<400> 347

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Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly

1	5	10	15
Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met	20	25	30
Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr	35	40	45
Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser	50	55	60
Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu	65	70	75
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr	85	90	95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr	100	105	110
Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu	115	120	125
Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val	130	135	140
Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp	145	150	155
Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn	165	170	175
Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe	180	185	190
Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser	195	200	205
Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr	210	215	220
Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr	225	230	235
			240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
 245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
 260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
 275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
 290 295 300

Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320

Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
 325 330 335

Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
 340 345 350

Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
 355 360 365

Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
 370 375 380

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
 385 390 395 400

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
 405 410 415

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
 420 425 430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
 435 440 445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
 450 455 460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
 465 470 475 480

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<210> 348
<211> 1497
<212> DNA
<213> artificial sequence
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<220>
<223> VH5VL3xCD19 HLLH

<400>	348						
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cctggacagg	gtctggaatg	gattggatac	attaatccta	gccgtggtta	tactaattac		180
gcagacagcg	tcaagggccg	cttcacaatc	actacagaca	aatccaccag	cacagcctac		240
atggaactga	gcagcctgcg	ttctgaggac	actgcaacct	attactgtgc	aagatattat		300
gatgatcatt	actgccttga	ctactggggc	caaggcacca	cggtcaccgt	ctcctcaggg		360
gaaggtacta	gtactggttc	tggtggaagt	ggaggttcag	gtggagcaga	cgacattgta		420
ctgacctcagt	ctccagcaac	tctgtctctg	tctccagggg	agcgtgccac	cctgacctgc		480
agagccagtt	caagtgtaag	ttacatgaac	tggtagcagc	agaagccggg	caaggcaccc		540
aaaagatgga	tttatgacac	atccaaagtg	gcttctggag	tccctgctcg	cttcagtggc		600
agtgggtctg	ggaccgacta	ctctctcaca	atcaacagct	tggaggetga	agatgctgcc		660
acttattact	gccaacagtg	gagtagtaac	ccgctcacgt	tcggtggcgg	gaccaagggtg		720
gagatcaaata	ccggagggtg	tggatccgat	atccagctga	cccagtctcc	agcttctttg		780
gctgtgtctc	tagggcagag	ggccaccatc	tcttgcaagg	ccagccaaag	tgttgattat		840
gatggtgata	gttatttgaa	ctgggtaccaa	cagattccag	gacagccacc	caaactcctc		900
atctatgatg	catccaatct	agtttctggg	atccccacca	ggtttagtgg	cagtgggtct		960
gggacagact	tcacctcaa	catccatcct	gtggagaagg	tggatgctgc	aacctatcac		1020
tgtcagcaaa	gtactgagga	tccgtggacg	ttcggtgagg	ggaccaagct	cgagatcaaa		1080
gggtggtggtg	gttctggcgg	cggcggctcc	gggtggtggtg	gttctcaggt	gcagctgcag		1140
cagtctgggg	ctgagctggt	gaggcctggg	tcctcagtga	agatttcctg	caaggcttct		1200
ggctatgcat	tcagtagcta	ctggatgaac	tgggtgaagc	agaggcctgg	acagggtctt		1260

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 ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc 1380
 ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc 1440
 cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctctcc 1497

<210> 349
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH5VL3xCD19 HLLH

<400> 349

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
 245 250 255

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

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
 275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
 290 295 300

Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
 325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
 370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
 385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
 405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
 420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
 435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
 450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
 465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 350
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL1VH7xCD19 LHHL

<400> 350
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 aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctgcg 180
 ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
 gatgtgccca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
 tatactaatt acaatcagaa gttcaaggac cgcgtcacia tctactacaga caaatccacc 600

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agcacagcct acatggaact gagcagcctg cgttctgagg acaactgcagt ctattactgt      660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggcac cacggtcacc      720
gtctcctccg gaggtggtgg atcccagggtg cagctgcagc agtctggggc tgagctggtg      780
aggcctgggt cctcagtga gatttcctgc aaggcttctg gctatgcatt cagtagctac      840
tggatgaact gggatgaagca gaggcctgga caggggtcttg agtggattgg acagatttgg      900
cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca      960
gacgaatcct ccagcacagc ctacatgcaa ctcagcagcc tagcatctga ggactctgcg     1020
gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac     1080
tactggggcc aagggaccac ggtcacgctc tctccgggtg gtggtggttc tggcggcgcc     1140
ggctccgggt gtggtggttc tgatatccag ctgacccagt ctccagcttc tttggctgtg     1200
tctctagggc agagggccac catctcctgc aaggccagcc aaagtgttga ttatgatggt     1260
gatagttatt tgaactggta ccaacagatt ccaggacagc caccctaaact cctcatctat     1320
gatgcatcca atctagtttc tgggatccca ccaggttta gtggcagtgg gtctgggaca     1380
gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaaccta tcaactgtcag     1440
caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa           1494

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<210> 351
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL1VH7xCD19 LHHL

<400> 351

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
 245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
 260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
 275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
 290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala

305 310 315 320
 Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
 325 330 335
 Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
 340 345 350
 Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365
 Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380
 Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
 385 390 395 400
 Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
 405 410 415
 Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
 420 425 430
 Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
 435 440 445
 Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
 450 455 460
 Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
 465 470 475 480
 Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
 485 490 495

Ile Lys

<210> 352
 <211> 1497
 <212> DNA
 <213> artificial sequence

 <220>
 <223> VH7VL1xCD19 HLHL

<400> 352
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cctggacagg gtctggaatg gattggatac attaataccta gccgtgggta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaaac actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
gaaggctacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480
agagccagtc aaagtgtgaa ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tgggtggcgg gaccaagggtg 720
gagatcaaat ccggagggtg tggatcccag gtgcagctgc agcagtctgg ggctgagctg 780
gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
tactggatga actgggtgaa gcagaggcct ggacagggtc ttgagtggat tggacagatt 900
tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact 960
gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020
gcgggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080
gactactggg gccaaaggac cacggtcacc gtctcctccg gtgggtgggtg ttctggcggc 1140
ggcggctccg gtgggtgggtg ttctgatata cagctgaccc agtctccagc ttctttggct 1200
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ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320
tatgatgcat ccaatctagt ttctgggata ccaccaggt ttagtggcag tgggtctggg 1380
acagacttca ccctcaacat ccactctgtg gagaagggtg atgctgcaac ctatcactgt 1440
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctoga gatcaaa 1497

<210> 353

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL1xCD19 HLHL

<400> 353

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
 130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
 245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
 275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
 290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
 325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
 340 345 350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
 385 390 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
 405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
 420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
 435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
 465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 354
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL1VH7xCD19 LHLH

<400> 354
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 aaggcaccca aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgtcacgctt cgggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaataa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcaactg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
 tatactaatt acaatcagaa gttcaaggac cgcgtcacaa tcaactacaga caaatccacc 600
 agcacagcct acatggaact gagcagcctg cgttctgagg aactgcagt ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac cacggtcacc 720
 gtctcctccg gaggtgggtg atccgatatc cagctgaccc agtctocagc ttctttggct 780
 gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840
 ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 900
 tatgatgcat ccaatctagt ttctgggatc ccaccaggt ttagtggcag tgggtctggg 960
 acagacttca ccctcaacat ccacctctgt gagaaggtgg atgctgcaac ctatcactgt 1020
 cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt 1080
 ggtggtgggt ctggcgggcg cggtccgggt ggtggtgggt ctgaggtgca gctgcagcag 1140

tctggggctg agctggtag gcttgggtcc tcagtgaaga tttcctgcaa ggcttctggc 1200
 tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggctcttgag 1260
 tggattggac agatttggcc tggagatggt gatactaact acaatggaaa gttcaagggt 1320
 aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta 1380
 gcatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440
 tattactatg ctatggacta ctggggccaa gggaccaagg tcaccgtctc ctcc 1494

<210> 355
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL1VH7xCD19 LHLH

<400> 355

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
290 295 300

Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
305 310 315 320

Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
325 330 335

Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
340 345 350

Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
355 360 365

Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
370 375 380

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
385 390 395 400

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
405 410 415

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
420 425 430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
435 440 445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
450 455 460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
465 470 475 480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 356
<211> 1497
<212> DNA
<213> artificial sequence

<220>
<223> VH7VL1xCD19 HLLH

<400> 356
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cctggacagg gtctggaatg gattggatac attaataccta gccgtgggta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
gaaggctacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattcag 420
atgacccagt ctccatctag cctgtctgca tctgtcgggg accgtgtcac catcacctgc 480

agagccagtc aaagtgttaag ttacatgaac tggtagcagc agaagccggg caaggcacc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaat ccggagggtg tggatccgat atccagctga cccagtctcc agcttctttg 780
 gctgtgtctc tagggcagag ggccaccatc tcctgcaagg ccagccaaag tgttgattat 840
 gatggtgata gttatttgaa ctggtaccaa cagattccag gacagccacc caaactcctc 900
 atctatgatg catccaatct agttctggg atcccaccca ggtttagtgg cagtgggtct 960
 gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac 1020
 tgtagcaaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa 1080
 ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctcaggt gcagctgcag 1140
 cagtctgggg ctgagctggt gaggcctggg tcctcagtga agatttcctg caaggcttct 1200
 ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggtctt 1260
 gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag 1320
 ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc 1380
 ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc 1440
 cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctctctcc 1497

<210> 357
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH7VL1xCD19 HLLH

<400> 357

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
245 250 255

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

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala

290 295 300
 Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

 Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
 325 330 335

 Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350

 Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

 Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
 370 375 380

 Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
 385 390 395 400

 Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
 405 410 415

 Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
 420 425 430

 Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
 435 440 445

 Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
 450 455 460

 Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
 465 470 475 480

 Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

 Val Ser Ser

<210> 358
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>

<223> VL2VH7xCD19 LHHL

<400> 358

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aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggctgaa	240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg	300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggaggttca	360
ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc	420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt	540
tatactaatt acaatcagaa gttcaaggac cgcgtcaca tcaactacaga caaatccacc	600
agcacagcct acatggaact gagcagcctg cgcttctgagg aactgcagt ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc	720
gtctcctccg gaggtggtgg atcccagggt cagctgcagc agtctggggc tgagctggtg	780
aggcctgggt cctcagtga gatttcctgc aaggcttctg gctatgcatt cagtagctac	840
tggatgaact gggatgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg	900
cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca	960
gacgaatcct ccagcacagc ctacatgcaa ctacagagcc tagcatctga ggactctgcg	1020
gtctattttc gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac	1080
tactggggcc aagggaccac ggtcaccgtc tcctccggtg gtggtggttc tggcggcggc	1140
ggctccggtg gtggtggttc tgatatccag ctgacccagt ctccagcttc ttggtctgtg	1200
tctctagggc agagggccac catctcctgc aaggccagcc aaagtgttga ttatgatggt	1260
gatagttatt tgaactggtg ccaacagatt ccaggacagc caccctaaact cctcatctat	1320
gatgcattcca atctagtttc tgggatccca cccaggttta gtggcagtgg gtctgggaca	1380
gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaacctc tcaactgtcag	1440
caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaa	1494

<210> 359

<211> 498

<212> PRT

<213> artificial sequence

<220>

<223> VL2VH7xCD19 LHHL

<400> 359

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
 245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
 260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
 275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
 290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
 305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
 325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
 340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
 385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
 405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
 420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
 435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
 450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
 465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
 485 490 495

Ile Lys

<210> 360
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH7VL2xCD19 HLHL

<400> 360
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 tcttgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaagggtacta gtactgggtc tgggtggaagt ggaggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac totgtctctg tctccagggg agcgtgccac cctgagctgc 480
 agagccagtc aaagtgtgaa ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
 gagatcaaat ccggagggtg tggatcccag gtgcagctgc agcagtctgg ggctgagctg 780
 gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
 tactggatga actgggtgaa gcagaggcct ggacagggtc ttgagtggat tggacagatt 900
 tggcctggag atggtgatac taactacaat ggaaagttca agggtaaagc cactctgact 960
 gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020

gcgggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080
gactactggg gccaaaggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc 1140
ggcggctccg gtggtggtgg ttctgatatc cagctgaccc agtctccagc ttctttggct 1200
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 1260
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320
tatgatgcat ccaatctagt ttctgggatc ccaccagggt ttagtggcag tgggtctggg 1380
acagacttca cctcaacat ccacctgtg gagaagggtg atgctgcaac ctatcactgt 1440
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

<210> 361
<211> 499
<212> PRT
<213> artificial sequence

<220>
<223> VH7VL2xCD19 HLHL

<400> 361

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
 245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys
 260 265 270

Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln
 275 280 285

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp
 290 295 300

Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
 305 310 315 320

Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala
 325 330 335

Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr
 340 345 350

Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr
 355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 370 375 380

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala
 385 390 395 400

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
 405 410 415

Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro
 420 425 430

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser
 435 440 445

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 450 455 460

Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys
 465 470 475 480

Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
 485 490 495

Glu Ile Lys

<210> 362
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL2VH7xCD19 LHLH

<400> 362
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 ctgagctgca gagccagtca aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcaca tcaacagctt ggaggtgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggaggttca 360

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ggtaggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaa acctggggcc 420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
tatactaatt acaatcagaa gttcaaggac cgcgtcacia tctactacaga caaatccacc 600
agcacagcct acatggaact gagcagcctg cgttctgagg acactgcagt ctattactgt 660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac cacggtcacc 720
gtctcctccg gaggtggtgg atccgatata cagctgacct agtctccage ttctttggct 780
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 840
ggtagatagt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 900
tatgatgcat ccaatctagt ttctgggata ccaccagggt ttagtggcag tgggtctggg 960
acagacttca ccctcaacat ccactctgtg gagaagggtg atgctgcaac ctatcactgt 1020
cagcaaagta ctgaggatcc gtggacgttc ggtggagggg ccaagctcga gatcaaaggt 1080
gggtggtggt ctggcggcgg cggtccgggt ggtggtggt ctcaggtgca gctgcagcag 1140
tctggggctg agctggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc 1200
tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcttgaca gggctctgag 1260
tggtattggac agatttgcc ttgagatggt gatactaact acaatggaaa gttcaagggt 1320
aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta 1380
gcatctgagg actctcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440
tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

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<210> 363
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL2VH7xCD19 LHLH

<400> 363

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
 245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
 260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr

275 280 285
 Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
 290 295 300
 Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320
 Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
 325 330 335
 Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
 340 345 350
 Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
 355 360 365
 Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
 370 375 380
 Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
 385 390 395 400
 Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
 405 410 415
 Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
 420 425 430
 Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
 435 440 445
 Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
 450 455 460
 Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
 465 470 475 480
 Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495
 Ser Ser

<210> 364
<211> 1497
<212> DNA
<213> artificial sequence

<220>
<223> VH7VL2xCD19 HLLH

<400> 364
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
tcttgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
cctggacagg gtctggaatg gattggatac attaatccta gccgtggta tactaattac 180
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
atggaactga gcagcctgcg tcttgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
gaaggtaacta gtactggttc tgggtgaagt ggagggtcag gtggagcaga cgacattgta 420
ctgaccagtc ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgagctgc 480
agagccagtc aaagtgtgaa ttacatgaac tggtagcagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tgggtggcgg gaccaagggtg 720
gagatcaaat ccggagggtg tggatccgat atccagctga cccagtctcc agcttctttg 780
gctgtgtctc tagggcagag ggccaccatc tcttgcaagg ccagccaaag tgttgattat 840
gatggtgata gttatttgaa ctggtacca cagattccag gacagccacc caaactctc 900
atctatgatg catccaatct agtttctggg atcccacca ggtttagtgg cagtgggtct 960
gggacagact tcacctcaa catccatcct gtggagaagg tggatgctgc aacctatcac 1020
tgtcagcaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa 1080
ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctcaggt gcagctgcag 1140
cagtctgggg ctgagctggt gaggcctggg tctcagtga agatttctg caaggcttct 1200
ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggtctt 1260
gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag 1320
ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc 1380
ctagcatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc 1440
cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctctcc 1497

<210> 365
<211> 499
<212> PRT
<213> artificial sequence

<220>
<223> VH7VL2xCD19 HLLH

<400> 365

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
 245 250 255

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

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
 275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
 290 295 300

Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
 305 310 315 320

Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
 325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
 370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
 385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
 405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
 420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
 435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
 450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
 465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 366
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> VL3VH7xCD19 LHHL

<400> 366
 gacattgtac tgaccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc 60
 ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc 120
 aaggcaccoca aaagatggat ttatgacaca tccaaagtgg cttctggagt cctgctcgc 180
 ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa 240
 gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggaggcggg 300
 accaaggtgg agatcaaagg cgaaggtact agtactggtt ctggtggaag tggagggtca 360
 ggtggagcag acgacgtcca actggtgcag tcaggggctg aagtgaaaaa acctggggcc 420
 tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg 480
 gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggt 540
 tatactaatt acaatcagaa gttcaaggac cgcgtcacia tcactacaga caaatccacc 600
 agcacagcct acatggaact gagcagcctg cggtctgagg aactgcagt ctattactgt 660
 gcaagatatt atgatgatca ttactgcctt gactactggg gccaaaggac cagggtcacc 720
 gtctcctccg gaggtgggtg atcccaggtg cagctgcagc agtctggggc tgagctggtg 780
 aggcctgggt cctcagtga gatttctgc aaggcttctg gctatgcatt cagtagctac 840
 tggatgaact gggatgaagca gaggcctgga cagggtcttg agtggattgg acagatttgg 900

```

cctggagatg gtgatactaa ctacaatgga aagttcaagg gtaaagccac tctgactgca    960
gacgaatcct ccagcacagc ctacatgcaa ctccagcagcc tagcatctga ggactctgcg    1020
gtctatttct gtgcaagacg ggagactacg acggtaggcc gttattacta tgctatggac    1080
tactggggcc aagggaccac ggtcaccgtc tcctccggtg gtggtggttc tggcggcggc    1140
ggctccggtg gtggtggttc tgatatccag ctgaccagctt ctcagcttc tttggctgtg    1200
tctctagggc agagggccac catctcctgc aaggccagcc aaagtgttga ttatgatggt    1260
gatagttatt tgaactggta ccaacagatt ccaggacagc caccctaaact cctcatctat    1320
gatgcatcca atctagtttc tgggatccca ccaggttta gtggcagtggt gtctgggaca    1380
gacttcaccc tcaacatcca tcctgtggag aaggtggatg ctgcaaccta tcaactgtcag    1440
caaagtactg aggatccgtg gacgttcggt ggagggacca agctcgagat caaaa        1494

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<210> 367
<211> 498
<212> PRT
<213> artificial sequence

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<220>
<223> VL3VH7xCD19 LHHL

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```

<400> 367

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Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1             5             10             15

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```

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20             25             30

```

```

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35             40             45

```

```

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50             55             60

```

```

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65             70             75             80

```

```

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85             90             95

```

```

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
100            105            110

```

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly
245 250 255

Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala
260 265 270

Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg
275 280 285

Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly
290 295 300

Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala
305 310 315 320

Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser
325 330 335

Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val
340 345 350

Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val
 355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 370 375 380

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
 385 390 395 400

Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
 405 410 415

Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly
 420 425 430

Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly
 435 440 445

Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
 450 455 460

Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln
 465 470 475 480

Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu
 485 490 495

Ile Lys

<210> 368
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH7VL3xCD19 HLHL

<400> 368
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 60
 tcttgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatocta gccgtgggta tactaattac 180
 aatcagaagt tcaaggaccg cgtcacaaac actacagaca aatccaccag cacagcctac 240

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atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctcagggc 360
gaaggtacta gtactgggtc tggtggaagt ggagggttcag gtggagcaga cgacattgta 420
ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
agagccagtt caagtgtaag ttacatgaac tggtagcagc agaagccggg caaggcaccc 540
aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
acttattact gccaacagtg gagtagtaac ccgctcacgt tcggtggcgg gaccaagggtg 720
gagatcaaat ccggagggtg tggatccag gtgcagctgc agcagtctgg ggctgagctg 780
gtgaggcctg ggtcctcagt gaagatttcc tgcaaggctt ctggctatgc attcagtagc 840
tactggatga actgggtgaa gcagaggcct ggacagggtc ttgagtggat tggacagatt 900
tggcctggag atggtgatac taactacaat ggaaagtcca agggtaaagc cactctgact 960
gcagacgaat cctccagcac agcctacatg caactcagca gcctagcatc tgaggactct 1020
gcggtctatt tctgtgcaag acgggagact acgacggtag gccgttatta ctatgctatg 1080
gactactggg gccaaaggac cacggtcacc gtctcctccg gtggtggtgg ttctggcggc 1140
ggcggctccg gtggtggtgg ttctgatatc cagctgaccc agtctccagc ttctttggct 1200
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat 1260
ggtgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc 1320
tatgatgcat ccaatctagt ttctgggatc ccaccaggt ttagtggcag tgggtctggg 1380
acagacttca cctcaacat ccctcctgtg gagaagggtg atgctgcaac ctatcactgt 1440
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaa 1497

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<210> 369
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> VH7VL3xCD19 HLHL

<400> 369

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
 115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser
 245 250 255

Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys

260	265	270
Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln		
275	280	285
Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp		
290	295	300
Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr		
305	310	315
Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala		
325	330	335
Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr		
340	345	350
Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr		
355	360	365
Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly		
370	375	380
Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala		
385	390	395
Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser		
405	410	415
Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro		
420	425	430
Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser		
435	440	445
Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr		
450	455	460
Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys		
465	470	475
Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu		
485	490	495

Glu Ile Lys

<210> 370

<211> 1494

<212> DNA

<213> artificial sequence

<220>

<223> VL3VH7xCD19 LHLH

<400> 370

gacattgtac tgacccagtc tccagcaact ctgtctctgt ctccagggga gcgtgccacc	60
ctgacctgca gagccagttc aagtgttaagt tacatgaact ggtaccagca gaagccgggc	120
aaggcaccga aaagatggat ttatgacaca tccaaagtgg cttctggagt ccctgctcgc	180
ttcagtggca gtgggtctgg gaccgactac tctctcacia tcaacagctt ggaggctgaa	240
gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cgggtggcggg	300
accaaggtgg agatcaaagg cgaaggtact agtactgggt ctggtggaag tggagggttca	360
gggtggagcag acgacgtcca actgggtgcag tcaggggctg aagtgaacaa acctggggcc	420
tcagtgaagg tgtcctgcaa ggcttctggc tacaccttta ctaggtacac gatgcactgg	480
gtaaggcagg cacctggaca gggctctggaa tggattggat acattaatcc tagccgtggg	540
tatactaatt acaatcagaa gttcaaggac cgcgtcacia tcaactacaga caaatccacc	600
agcacagcct acatggaact gagcagcctg cgctctgagg aactgcagt ctattactgt	660
gcaagatatt atgatgatca ttactgcctt gactactggg gccaaggcac cacggtcacc	720
gtctcctccg gaggtgggtg atccgatatc cagctgaccc agtctccagc ttctttgggt	780
gtgtctctag ggcagagggc caccatctcc tgcaaggcca gccaaagtgt tgattatgat	840
ggatgatagtt atttgaactg gtaccaacag attccaggac agccacccaa actcctcatc	900
tatgatgcat ccaatctagt ttctgggatc ccaccagggt ttagtggcag tgggtctggg	960
acagacttca ccctcaacat ccctcctgtg gagaagggtg atgctgcaac ctatcactgt	1020
cagcaaagta ctgaggatcc gtggacgttc ggtggaggga ccaagctcga gatcaaaggt	1080
gggtgggtggt ctggcgccgg cggctccggt ggtgggtggt ctcagggtgca gctgcagcag	1140
tctggggctg agctgggtgag gcctgggtcc tcagtgaaga tttcctgcaa ggcttctggc	1200
tatgcattca gtagctactg gatgaactgg gtgaagcaga ggcctggaca gggctctgag	1260
tggattggac agatttggtc tggagatggt gatactaact acaatggaaa gttcaagggt	1320
aaagccactc tgactgcaga cgaatcctcc agcacagcct acatgcaact cagcagccta	1380

gcacatctgagg actctgcggt ctatttctgt gcaagacggg agactacgac ggtaggccgt 1440
 tattactatg ctatggacta ctggggccaa gggaccacgg tcaccgtctc ctcc 1494

<210> 371
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> VL3VH7xCD19 LHLH

<400> 371

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 100 105 110

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 115 120 125

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 145 150 155 160

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 165 170 175

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 180 185 190

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 195 200 205

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 210 215 220

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 225 230 235 240

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
 245 250 255

Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Lys
 260 265 270

Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp Tyr
 275 280 285

Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
 290 295 300

Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly
 305 310 315 320

Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala Ala
 325 330 335

Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly Gly
 340 345 350

Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
 355 360 365

Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu
 370 375 380

Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser Gly
 385 390 395 400

Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly
 405 410 415

Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr
 420 425 430

Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu
 435 440 445

Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
 450 455 460

Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly Arg
 465 470 475 480

Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495

Ser Ser

<210> 372
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> VH7VL3xCD19 HLLH

<400> 372
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 60
 tcttgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 120
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 180
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 240
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 300
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctcaggc 360
 gaaggtaacta gtactgggtc tgggtggaagt ggagggttcag gtggagcaga cgacattgta 420
 ctgacccagt ctccagcaac tctgtctctg tctccagggg agcgtgccac cctgacctgc 480
 agagccagtt caagtgtgtaag ttacatgaac tgggtaccagc agaagccggg caaggcaccc 540
 aaaagatgga tttatgacac atccaaagtg gcttctggag tccctgctcg cttcagtggc 600
 agtgggtctg ggaccgacta ctctctcaca atcaacagct tggaggctga agatgctgcc 660
 acttattact gccaacagtg gagtagtaac ccgctcacgt tcgggtggcgg gaccaagggtg 720
 gagatcaaat ccggaggtgg tggatccgat atccagctga cccagtctcc agcttctttg 780

getgtgtctc tagggcagag ggccaccatc tcctgcaagg ccagccaaag tggtgattat 840
 gatggtgata gttatttgaa ctggtaccaa cagattccag gacagccacc caaactcctc 900
 atctatgatg catccaatct agtttctggg atcccaccca ggtttagtgg cagtgggtct 960
 gggacagact tcaccctcaa catccatcct gtggagaagg tggatgctgc aacctatcac 1020
 tgtcagcaaa gtactgagga tccgtggacg ttcggtggag ggaccaagct cgagatcaaa 1080
 ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctcaggt gcagctgcag 1140
 cagtctgggg ctgagctggt gaggcctggg tcctcagtga agatttcctg caaggcttct 1200
 ggctatgcat tcagtagcta ctggatgaac tgggtgaagc agaggcctgg acagggctct 1260
 gagtggattg gacagatttg gcctggagat ggtgatacta actacaatgg aaagttcaag 1320
 ggtaaagcca ctctgactgc agacgaatcc tccagcacag cctacatgca actcagcagc 1380
 ctacatctg aggactctgc ggtctatttc tgtgcaagac gggagactac gacggtaggc 1440
 cgttattact atgctatgga ctactggggc caagggacca cggtcaccgt ctctcc 1497

<210> 373

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> VH7VL3xCD19 HLLH

<400> 373

Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly
115 120 125

Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
145 150 155 160

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
195 200 205

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
245 250 255

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

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn Trp
275 280 285

Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala
290 295 300

Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser
305 310 315 320

Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val Asp Ala
325 330 335

Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr Phe Gly
 340 345 350

Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
 355 360 365

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Gln Ser Gly Ala
 370 375 380

Glu Leu Val Arg Pro Gly Ser Ser Val Lys Ile Ser Cys Lys Ala Ser
 385 390 395 400

Gly Tyr Ala Phe Ser Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
 405 410 415

Gly Gln Gly Leu Glu Trp Ile Gly Gln Ile Trp Pro Gly Asp Gly Asp
 420 425 430

Thr Asn Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp
 435 440 445

Glu Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Ala Ser Glu
 450 455 460

Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Glu Thr Thr Thr Val Gly
 465 470 475 480

Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 374
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD19xVH5/VL1 HLHL

<400> 374
 caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
 tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120

cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
 aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
 atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
 actacgacgg taggccgtta ttactatgct atggactact ggggccaaagg gaccacggtc 360
 accgtctcct ccggtggtgg tggttctggc ggcggcggtc ccggtggtgg tggttctgat 420
 atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
 tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
 cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
 atccccacca ggtttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
 gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
 ttcggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cgtccaactg 780
 gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaagggtgc ctgcaaggct 840
 tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900
 ctggaatgga ttggatacat taatcctagc cgtgggtata ctaattacgc agacagcgtc 960
 aagggccgct tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020
 agcctgcgtt ctgaggacac tgcaacctat tactgtgcaa gatattatga tgatcattac 1080
 tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt 1140
 aotggttctg gtggaagtgg aggttcaggt ggagcagacg acattcagat gaccagctc 1200
 ccatctagcc tgtctgcac tgtcggggac cgtgtcacca tcacctgcag agccagtcaa 1260
 agtgtaagtt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320
 tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380
 accgactact ctctcacaat caacagcttg gaggtgaaag atgctgccac ttattactgc 1440
 caacagtgga gtagtaacct gctcacgttc ggtggcgggg ccaaggtgga gatcaaa 1497

<210> 375
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVH5VL1 HLHL

<400> 375

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
 210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
 225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser

245	250	255
Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala		
260	265	270
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr		
275	280	285
Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile		
290	295	300
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val		
305	310	315
Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr		
325	330	335
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys		
340	345	350
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly		
355	360	365
Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly		
370	375	380
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser		
385	390	395
Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys		
405	410	415
Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro		
420	425	430
Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser		
435	440	445
Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser		
450	455	460
Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys		
465	470	475
		480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 485 490 495

Glu Ile Lys

<210> 376
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD19xVL1VH5 LHLH

<400> 376
 gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
 atctcctgca aggccagcca aagtgtgat tatgatggtg atagttattt gaactggtac 120
 caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
 gggatcccac ccaggttttag tggcagtggg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
 tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
 gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
 aactgggtga agcagaggcc tggacagggt cttgagtga ttggacagat ttggcctgga 540
 gatggtgata ctaactacaa tggaaagttc aagggtaaag cactctgac tgcagacgaa 600
 tctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
 ttctgtgcaa gacgggagac tacgacggtg ggcggttatt actatgctat ggactactgg 720
 ggccaaggga ccacggtcac cgtctctctc ggaggtggtg gatccgacat tcagatgacc 780
 cagtctccat ctagcctgtc tgcattctgtc ggggaaccgtg tcaccatcac ctgcagagcc 840
 agtcaaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga 900
 tggatttatg acacatccaa agtggcttct ggagtccttg ctgccttcag tggcagtggg 960
 tctgggaccg actactctct cacaatcaac agcttgaggg ctgaagatgc tgccacttat 1020
 tactgccaac agtggagtag taaccogctc acgttcggtg gcgggaccaa ggtggagatc 1080
 aaaggcgaag gtactagtac tggttctggt ggaagtggag gttcaggtgg agcagacgac 1140
 gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaaggtgtcc 1200
 tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260

ggacaggggtc tggaatggat tggatacatt aatcctagcc gtggttatac taattacgca 1320
 gacagcgtca agggccgctt cacaatcact acagacaaat ccaccagcac agcctacatg 1380
 gaactgagca gcctgcgttc tgaggacact gcaacctatt actgtgcaag atattatgat. 1440
 gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

<210> 377
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVL1VH5 LHLH

<400> 377

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
 260 265 270

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
 275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
 290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
 325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
 340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
 355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
 370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
 385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
 405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
 420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
 435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
 450 455 460

Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp
 465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495

Ser Ser

<210> 378

<211> 1497

<212> DNA

<213> artificial sequence

<220>

<223> CD19xVL1VH5 HLLH

<400> 378

caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt	60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg	120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac	180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac	240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag	300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc	360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat	420
atccagctga ccagtcctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc	480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa	540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg	600
atcccaccca ggttttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct	660

gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
 ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatecga cattcagatg 780
 acccagtctc catctagcct gtctgcatct gtcggggacc gtgtcaccat cacctgcaga 840
 gccagtcaaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
 agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960
 gggctctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact 1020
 tattactgcc aacagtggag tagtaaccog ctcacgttcg gtggcgggac caaggtggag 1080
 atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac 1140
 gacgtccaac tgggtcagtc aggggtgaa gtgaaaaaac ctggggcctc agtgaagggtg 1200
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 1260
 cctggacagg gtctggaatg gattggatac attaatccta gccgtgggta tactaattac 1320
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 1380
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 1440
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctcctca 1497

<210> 379

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVL1VH5 HLLH

<400> 379

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 380
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD19xVH5VL2 HLHL

<400> 380

cagggtgcagc tgcagcagtc tggggctgag ctgggtgaggc ctgggtcctc agtgaagatt 60
tcttgcaagg ottotggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggcccgtta ttactatgct atggactact ggggccaaagg gaccacggtc 360
accgtctcct ccggtgggtg tggttctggc ggcggcggtc ccggtgggtg tggttctgat 420
atccagctga ccagctctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcttgcaagg ccagccaaag tgttgattat gatgggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atccccacca ggtttagtgg cagtgggtct gggacagact tcacctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcgttgagg ggaccaagct cgagatcaaa tccggagggtg gtggatccga cgtccaactg 780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaagggtgc ctgcaaggct 840
tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900
ctggaatgga ttggatacat taatcctagc cgtgggttata ctaattacgc agacagcgtc 960
aagggccgct tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020
agcctgcgtt ctgaggacac tgcaacctat tactgtgcaa gatattatga tgatcattac 1080
tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt 1140
actggttctg gtggaagtgg aggttcaggt ggagcagacg acattgtact gaccagctct 1200
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgagctgcag agccagtcaa 1260
agtgtaaagt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380
accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1440
caacagtgga gtagtaacct gctcacgttc ggtggcgggg ccaaggtgga gatcaaa 1497

<210> 381
<211> 499
<212> PRT
<213> artificial sequence

<220>
<223> CD19xVH5VL2 HLHL

<400> 381

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
 210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr

225		230		235		240
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser						
	245			250		255
Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala						
	260		265			270
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr						
	275		280			285
Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile						
	290		295		300	
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val						
	305		310		315	320
Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr						
		325		330		335
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys						
		340		345		350
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly						
	355		360			365
Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly						
	370		375		380	
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser						
	385		390		395	400
Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys						
		405		410		415
Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro						
		420		425		430
Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser						
	435		440			445
Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser						
	450		455		460	

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 485 490 495

Glu Ile Lys

<210> 382
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD19xVL2VH5 LHLH

<400> 382
 gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
 atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
 caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180
 gggatccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttcttg cggcggcggc 360
 tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420
 gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
 aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
 gatggtgata ctaactacaa tggaaagttc aagggtaaag ccaactctgac tgcagacgaa 600
 tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
 ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
 ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gatccgacat tgtactgacc 780
 cagtctccag caactctgtc totgtctcca ggggagcgtg ccaccctgag ctgcagagcc 840
 agtcaaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga 900
 tggatttatg acacatccaa agtggcttct ggagtccttg ctcgcttcag tggcagtggg 960
 tctgggaccg actactctct cacaatcaac agcttggagg ctgaagatgc tgccaattat 1020
 tactgccaac agtggagtag taaccgcgtc acgttcggtg gcgggaccaa ggtggagatc 1080
 aaaggcgaag gtactagtac tggttctggt ggaagtggag gttcaggtgg agcagacgac 1140

gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaaggtgtcc 1200
 tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260
 ggacagggtc tggaatggat tggatacatt aatcctagcc gtggttatac taattacgca 1320
 gacagcgtca agggccgctt cacaatcact acagacaaat ccaccagcac agcctacatg 1380
 gaactgagca gcctgcgttc tgaggacact gcaacctatt actgtgcaag atattatgat 1440
 gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

<210> 383
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVL2VH5 LHLH

<400> 383

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
245 250 255

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
260 265 270

Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
450 455 460

Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp
465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 384
<211> 1497
<212> DNA
<213> artificial sequence

<220>
<223> CD19xVL2VH5 HLLH

<400> 384
caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact gggccaagg gaccacggtc 360
accgtctcct ccggtgggtg tggttctggc ggcggcggct ccggtgggtg tggttctgat 420
atccagctga ccagctctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540

cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
 atccccacca ggttttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
 gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
 ttcggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cattgtactg 780
 acccagtctc cagcaactct gtctctgtct ccaggggagc gtgccaccct gagctgcaga 840
 gccagtcaaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
 agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960
 gggctctggga ccgactactc tctcacaatc aacagcttgg aggtgaaga tgctgccact 1020
 tattactgcc aacagtggag tagtaaccgc ctcacgttcg gtggcgggac caaggtggag 1080
 atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac 1140
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 1200
 tcctgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 1260
 cctggacagg gtctggaatg gattggatac attaactcta gccgtgggta tactaattac 1320
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 1380
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 1440
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcacogt ctctca 1497

<210> 385
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVL2VH5 HLLH

<400> 385

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
260 265 270

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
290 295 300

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

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
 435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
 465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
 485 490 495

Val Ser Ser

<210> 386
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>

<223> CD19xVH5VL3 HLHL

<400> 386

caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggttagtggt cagtgggtct gggacagact tcaccctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcggtgagg ggaccaagct cgagatcaaa tccggagggtg gtggatccga cgtccaactg 780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaagggtgc ctgcaaggct 840
tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900
ctggaatgga ttggatacat taatcctagc cgtgggtata ctaattacgc agacagcgtc 960
aagggccgct tcacaatcac tacagacaaa tocaccagca cagcctacat ggaactgagc 1020
agcctgcgtt ctgaggacac tgcaacctat tactgtgcaa gatattatga tgatcattac 1080
tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt 1140
actggttctg gtggaagtgg aggttcaggt ggagcagacg acattgtact gaccagtcct 1200
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgacctgcag agccagttca 1260
agtgtaaagt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320
tatgacacat ccaaagtggc ttctggagtc cctgctcgtc tcagtggcag tgggtctggg 1380
accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1440
caacagtgga gtagtaaccc gtcacgttc ggtggcggga ccaaggtgga gatcaaa 1497

<210> 387

<211> 499

<212> PRT

<213> artificial sequence

<220>

<223> CD19xVH5VL3 HLHL

<400> 387

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val

210	215	220
Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr		
225	230	235 240
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser		
	245	250 255
Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala		
	260	265 270
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr		
	275	280 285
Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile		
	290	295 300
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val		
305	310	315 320
Lys Gly Arg Phe Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr		
	325	330 335
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys		
	340	345 350
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly		
	355	360 365
Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly		
	370	375 380
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser		
385	390	395 400
Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys		
	405	410 415
Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro		
	420	425 430
Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser		
	435	440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 485 490 495

Glu Ile Lys

<210> 388
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD19xVL3VH5 LHLH

<400> 388
 gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60
 atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
 caacagattc caggacagcc acccaaactc ctcattctatg atgcatccaa tctagtttct 180
 gggatcccac ccagggttag tggcagtggg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggaccaa gctcgagatc aaagggtggtg gtggttctgg cggcgcgggc 360
 tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
 gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
 aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
 gatggtgata ctaactacaa tggaaagttc aagggttaaag ccactctgac tgcagacgaa 600
 tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
 ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
 ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gatccgacat tgtactgacc 780
 cagtctccag caactctgtc tctgtctcca ggggagcgtg ccaccctgac ctgcagagcc 840
 agttcaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga 900
 tggatttatg acacatccaa agtggcttct ggagtccttg ctgccttcag tggcagtggg 960
 tctgggaccg actactctct cacaatcaac agcttggagg ctgaagatgc tgccacttat 1020

tactgccaac agtggagtag taaccgctc acgttcggtg gcgggaccaa ggtggagatc 1080
 aaaggcgaag gtactagtag tgggtctggt ggaagtggag gttcaggtgg agcagacgac 1140
 gtccaactgg tgcagtcagg ggctgaagtg aaaaaacctg gggctcagc gaaggtgtcc 1200
 tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260
 ggacagggtc tggaatggat tggatacatt aatcctagcc gtgggttatac taattacgca 1320
 gacagcgtca agggccgctt cacaatcact acagacaaat ccaccagcac agcctacatg 1380
 gaactgagca gcctgcgttc tgaggacact gcaacctatt actgtgcaag atattatgat 1440
 gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

<210> 389
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVL3VH5 LHLH

<400> 389

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
 260 265 270

Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn
 275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
 290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
 325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
 340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
 355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
450 455 460

Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr Asp
465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 390
<211> 1497
<212> DNA
<213> artificial sequence

<220>
<223> CD19xVL3VH5 HLLH

<400> 390
cagggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagt gattggacag atttggcctg gagatgggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420

atccagctga cccagctctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
 tcttgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
 cagattccag gacagccacc caaactcttc atctatgatg catccaatct agtttctggg 600
 atcccaccca ggttttagtgg cagtgggtct gggacagact tcacctcaa catccatcct 660
 gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
 ttcggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cattgtactg 780
 acccagtctc cagcaactct gtctctgtct ccaggggagc gtgccaccct gacctgcaga 840
 gccagttcaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
 agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960
 ggggtctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact 1020
 tattactgcc aacagtggag tagtaacccg ctcacgttcg gtggcgggac caaggtggag 1080
 atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac 1140
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg 1200
 tcttgcaagg cttctggcta cacctttact aggtacacga tgcactgggt aaggcaggca 1260
 cctggacagg gtctggaatg gattggatac attaactcta gccgtgggta tactaattac 1320
 gcagacagcg tcaagggccg cttcacaatc actacagaca aatccaccag cacagcctac 1380
 atggaactga gcagcctgcg ttctgaggac actgcaacct attactgtgc aagatattat 1440
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctca 1497

<210> 391
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVL3VH5 HLLH

<400> 391

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
 210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
 225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 260 265 270

Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
 275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
290 295 300

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

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Tyr Tyr
465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 392

<211> 1497
<212> DNA
<213> artificial sequence

<220>
<223> CD19xVH7VL1 HLHL

<400> 392
cagggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga ccagctctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcacctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcgtgagag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cgtccaactg 780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaagggtgc ctgcaaggct 840
tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900
ctggaatgga ttggatacat taatcctagc cgtgggtata ctaattacaa tcagaagtgc 960
aaggaccgcy tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020
agcctgcgtt ctgaggacac tgcagtctat tactgtgcaa gatattatga tgatcattac 1080
tgccttgact actggggcca aggcaccacg gtcacogtct cctcaggcga aggtactagt 1140
actggttctg gtggaagtgg aggttcaggt ggagcagacg acattcagat gacccagtct 1200
ccatctagcc tgtctgcac tgtcggggac cgtgtcacca tcacctgcag agccagtcaa 1260
agtgtgaagt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320
tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380
accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1440
caacagtgga gtagtaacct gtcacgttc ggtggcggga ccaagggtgga gatcaaa 1497

<210> 393
<211> 499
<212> PRT
<213> artificial sequence

<220>
<223> CD19xVH7VL1 HLHL

<400> 393

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser

195	200	205
Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val 210 215 220		
Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr 225 230 235 240		
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser 245 250 255		
Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 260 265 270		
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr 275 280 285		
Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile 290 295 300		
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe 305 310 315 320		
Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr 325 330 335		
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys 340 345 350		
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly 355 360 365		
Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly 370 375 380		
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Gln Met Thr Gln Ser 385 390 395 400		
Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys 405 410 415		
Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro 420 425 430		

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 485 490 495

Glu Ile Lys

<210> 394
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD19xVL1VH7 LHLH

<400> 394
 gatatccagc tgaccagtc tccagcttct ttggtgtgt ctctagggca gagggccacc 60
 atctcctgca aggcagcca aagtgtgat tatgatggtg atagttattt gaactggtac 120
 caacagattc caggacagcc acccaaactc ctcatctatg atgcatcaa tctagtttct 180
 gggatccac ccaggttag tggcagtggt tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360
 tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
 gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
 aactgggtga agcagaggcc tggacagggt cttgagtga ttggacagat ttggcctgga 540
 gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
 tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
 ttctgtgcaa gacgggagac tacgacggtg ggccgttatt actatgctat ggactactgg 720
 ggccaagggg ccacggtcac cgtctcctcc ggaggtggtg gatccgacat tcagatgacc 780
 cagtctccat ctagcctgtc tgcatctgtc ggggaccgtg tcaccatcac ctgcagagcc 840
 agtcaaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga 900

tggatttatg acacatccaa agtggcttct ggagtcctg ctgccttcag tggcagtggg 960
 tctgggaccg actactctct cacaatcaac agcttggagg ctgaagatgc tgccacttat 1020
 tactgccaac agtggagtag taaccgcctc acgttcggtg gcgggaccaa ggtggagatc 1080
 aaaggcgaag gtactagtag tggttctggt ggaagtggag gttcaggtgg agcagacgac 1140
 gtccaactgg tgcagtcagg ggtgaagtg aaaaaacctg gggcctcagt gaaggtgtcc 1200
 tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260
 ggacagggtc tggaatggat tggatacatt aatcctagcc gtggttatac taattacaat 1320
 cagaagttca aggaccgcgt cacaatcact acagacaaat ccaccagcac agcctacatg 1380
 gaactgagca gcctgcgttc tgaggacact gcagtctatt actgtgcaag atattatgat 1440
 gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

<210> 395
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVL1VH7 LHLH

<400> 395

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
 260 265 270

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
 275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
 290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
 325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
 340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr
435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
450 455 460

Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp
465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
485 490 495

Ser Ser

<210> 396
<211> 1497
<212> DNA
<213> artificial sequence

<220>
<223> CD19xVL1VH7 HLLH

<400> 396
caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
tcttgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300

actacgacgg taggccgtta ttactatgct atggactact ggggcccaagg gaccacggtc 360
 accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
 atccagctga ccagctctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
 tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
 cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
 atcccaccca ggttttagtgg cagtgggtct gggacagact tcaccctcaa catccatcct 660
 gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
 ttcggtggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cattcagatg 780
 acccagtctc catctagcct gtctgcatct gtcggggacc gtgtcaccat cacctgcaga 840
 gccagtcaaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
 agatggattt atgacacatc caaagtggct tctggagtcc ctgctcgctt cagtggcagt 960
 gggctctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact 1020
 tattactgcc aacagtggag tagtaacccg ctcacgttcg gtggcgggac caaggtggag 1080
 atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac 1140
 gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaagggtg 1200
 tcctgcaagg cttctggcta cacctttact aggtacacga tgactgggt aaggcaggca 1260
 cctggacagg gtctggaatg gattggatac attaactcta gccgtgggta tactaattac 1320
 aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac 1380
 atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat 1440
 gatgatcatt actgccttga ctactggggc caaggcacca cggtcacogt ctctca 1497

<210> 397
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVL1VH7 HLLH

<400> 397

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
 210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
 225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 260 265 270

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
290 295 300

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

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser

<210> 398
<211> 1497
<212> DNA
<213> artificial sequence

<220>
<223> CD19xVH7VL2 HLHL

<400> 398
caggtgcagc tgcagcagtc tgggctgag ctggtgaggc ctgggtcctc agtgaagatt 60
tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggcccaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat 420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactctc atctatgatg catccaatct agtttctggg 600
atccccacca ggtttagtgg cagtgggtct gggacagact tcacctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcggtgagg ggaccaagct cgagatcaaa tccggagggtg gtggatccga cgtccaactg 780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaagggtgc ctgcaaggct 840
tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900
ctggaatgga ttggatacat taatcctagc cgtgggtata ctaattacaa tcagaagtgc 960
aaggaccgag tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020
agcctgcgtt ctgaggacac tgcagtctat tactgtgcaa gatattatga tgatcattac 1080
tgccttgact actggggcca aggcaccacg gtcaccgtct cctcaggcga aggtactagt 1140
actggttctg gtggaagtgg aggttcaggt ggagcagacg acattgtact gaccagctct 1200
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgagctgcag agccagtcaa 1260
agtgtaaagt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320
tatgacacat ccaaagtggc ttctggagtc cctgctcgtc tcagtggcag tgggtctggg 1380
accgactact ctctcacaat caacagcttg gaggetgaag atgctgccac ttattactgc 1440

caacagtgga gtagtaaccc gtcacgttc ggtggcgga ccaaggtgga gatcaaa 1497

<210> 399
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVH7VL2 HLHL

<400> 399

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
 165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr

180	185	190
Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser		
195	200	205
Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val		
210	215	220
Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr		
225	230	235
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser		
245	250	255
Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala		
260	265	270
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr		
275	280	285
Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile		
290	295	300
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe		
305	310	315
Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr		
325	330	335
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys		
340	345	350
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly		
355	360	365
Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly		
370	375	380
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser		
385	390	395
Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys		
405	410	415

Arg Ala Ser Gln Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 420 425 430

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 485 490 495

Glu Ile Lys

<210> 400
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD19xVL2VH7 LHLH

<400> 400
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 caacagattc caggacagcc acccaaactc ctcattctatg atgcatccaa tctagtttct 180
 gggatcccac ccaggtttag tggcagtggtg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcgggtg gagggaccaa gctcgagatc aaaggtggtg gtggttcttg cggcggcggc 360
 tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
 gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
 aactgggtga agcagaggcc tggacagggt cttgagtga ttggacagat ttggcctgga 540
 gatggtgata ctaactacaa tggaaagttc aagggttaaag ccactctgac tgcagacgaa 600
 tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660
 ttctgtgcaa gacgggagac tacgacggtg ggcggttatt actatgctat ggactactgg 720
 ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gatccgacat tgtactgacc 780

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cagtctccag caactctgtc tctgtctcca ggggagcgtg ccaccctgag ctgcagagcc      840
agtcaaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga      900
tggatttatg acacatccaa agtggcttct ggagtccttg ctgccttcag tggcagtggg      960
tctgggaccg actactctct cacaatcaac agcttgaggg ctgaagatgc tgccacttat     1020
tactgccaac agtggagtag taacccgctc acgttcggtg gcgggaccaa ggtggagatc     1080
aaaggcgaag gtactagtag tggttctggt ggaagtggag gttcaggtgg agcagacgac     1140
gtccaactgg tgcaagtcagg ggctgaagtg aaaaaacctg gggcctcagt gaaggtgtcc     1200
tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct     1260
ggacagggtc tggaatggat tggatacatt aatcctagcc gtggttatac taattacaat     1320
cagaagttca aggaccgctg cacaatcact acagacaaat ccaccagcac agcctacatg     1380
gaactgagca gcctgcgttc tgaggacact gcagtctatt actgtgcaag atattatgat     1440
gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca           1494

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<210> 401
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVL2VH7 LHLH

<400> 401

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

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

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 65 70 75 80

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
 260 265 270

Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met Asn
 275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
 290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
 325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
 340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
 355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
 370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
 385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
 405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
 420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr
 435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
 450 455 460

Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp
 465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495

Ser Ser

<210> 402
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD19xVL2VH7 HLLH

<400> 402
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 tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
 cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac 180


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aatggaaagt tcaagggttaa agccactctg actgcagacg aatcctccag cacagcctac    240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag    300
actacgacgg taggccgtta ttactatgct atggactact ggggccaaagg gaccacggtc    360
accgtctcct ccggtggtgg tggttctggc ggcggcggct ccggtggtgg tggttctgat    420
atccagctga cccagtctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc    480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa    540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg    600
atcccaccca ggttttagtgg cagtgggtct gggacagact tcacctcaa catccatcct    660
gtggagaagg tggatgtgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg    720
ttcggtgagg ggaccaagct cgagatcaaa tccggaggtg gtggatccga cattgtactg    780
accagctctc cagcaactct gtctctgtct ccaggggagc gtgccaccct gagctgcaga    840
gccagtcaaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa    900
agatggattt atgacacatc caaagtggct totggagtcc ctgctcgctt cagtggcagt    960
gggtctggga ccgactactc tctcacaatc aacagcttgg aggctgaaga tgctgccact   1020
tattactgcc aacagtggag tagtaaccgc ctcacgttcg gtggcgggac caaggtggag   1080
atcaaaggcg aaggtactag tactggttct ggtggaagtg gaggttcagg tggagcagac   1140
gacgtccaac tgggtgcagtc aggggctgaa gtgaaaaaac ctggggcctc agtgaaggtg   1200
tcctgcaagg cttctggcta cacctttact aggtacacga tgactgggt aaggcaggca   1260
cctggacagg gtctggaatg gattggatac attaactcta gccgtgggta tactaattac   1320
aatcagaagt tcaaggaccg cgtcacaatc actacagaca aatccaccag cacagcctac   1380
atggaactga gcagcctgcg ttctgaggac actgcagtct attactgtgc aagatattat   1440
gatgatcatt actgccttga ctactggggc caaggcacca cggtcaccgt ctctca    1497

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<210> 403
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVL2VH7 HLLH

<400> 403

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
165 170 175

Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
180 185 190

Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val
210 215 220

Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 260 265 270

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr Met
 275 280 285

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
 290 295 300

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

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
 325 330 335

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
 340 345 350

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
 355 360 365

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
 370 375 380

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
 385 390 395 400

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
 405 410 415

Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
 420 425 430

Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
 435 440 445

Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
 450 455 460

Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr
 465 470 475 480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr

485

490

495

Val Ser Ser

<210> 404
<211> 1497
<212> DNA
<213> artificial sequence

<220>
<223> CD19xVH7VL3 HLHL

<400> 404
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tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg 120
cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaaagg gaccacggtc 360
accgtctcct ccggtggtgg tggttctggc ggccggcggt ccggtggtgg tggttctgat 420
atccagctga ccagctctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggttttagtgg cagtgggtct gggacagact tcacctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcgggtggag ggaccaagct cgagatcaaa tccggaggtg gtggatccga cgtccaactg 780
gtgcagtcag gggctgaagt gaaaaaacct ggggcctcag tgaagggtgc ctgcaaggct 840
tctggctaca cctttactag gtacacgatg cactgggtaa ggcaggcacc tggacagggt 900
ctggaatgga ttggatacat taatcctagc cgtgggtata ctaattacaa tcagaagtgc 960
aaggaccgag tcacaatcac tacagacaaa tccaccagca cagcctacat ggaactgagc 1020
agcctgcgtt ctgaggacac tgcagtctat tactgtgcaa gatattatga tgatcattac 1080
tgcttgact actggggcca aggcaccacg gtacccgtct cctcaggcga aggtactagt 1140
actggttctg gtggaagtgg aggttcaggt ggagcagacg acattgtact gaccagctct 1200
ccagcaactc tgtctctgtc tccaggggag cgtgccaccc tgacctgcag agccagttca 1260
agtgtgaagt acatgaactg gtaccagcag aagccgggca aggcacccaa aagatggatt 1320

tatgacacat ccaaagtggc ttctggagtc cctgctcgct tcagtggcag tgggtctggg 1380
 accgactact ctctcacaat caacagcttg gaggtgaag atgctgccac ttattactgc 1440
 caacagtgga gtagtaaccc gctcacgttc ggtggcggga ccaaggtgga gatcaaa 1497

<210> 405
 <211> 499
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVH7VL3 HLHL

<400> 405

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
 130 135 140

Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
 145 150 155 160

Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu

165	170	175
Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr		
180	185	190
Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro Arg Phe Ser Gly Ser		
195	200	205
Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu Lys Val		
210	215	220
Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr		
225	230	235
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser		
245	250	255
Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala		
260	265	270
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr		
275	280	285
Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile		
290	295	300
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe		
305	310	315
Lys Asp Arg Val Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr		
325	330	335
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys		
340	345	350
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly		
355	360	365
Thr Thr Val Thr Val Ser Ser Gly Glu Gly Thr Ser Thr Gly Ser Gly		
370	375	380
Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Ile Val Leu Thr Gln Ser		
385	390	395
		400

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Thr Cys
 405 410 415

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 420 425 430

Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser
 435 440 445

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser
 450 455 460

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
 465 470 475 480

Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
 485 490 495

Glu Ile Lys

<210> 406
 <211> 1494
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD19xVL3VH7 LHLH

<400> 406
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 atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120
 caacagattc caggacagcc acccaaactc ctcatctatg atgcatcaa tctagtttct 180
 gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240
 cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300
 acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttcttg cggcggcggc 360
 tccggtggtg gtggttctca ggtgcagctg cagcagctctg gggctgagct ggtgaggcct 420
 gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480
 aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540
 gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600
 tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660

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ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720
ggccaaggga ccacggtcac cgtctcctcc ggagggtggtg gatccgacat tgtactgacc 780
cagtctccag caactctgtc tctgtctcca ggggagcgtg ccaccctgac ctgcagagcc 840
agttcaagtg taagttacat gaactggtac cagcagaagc cgggcaaggc acccaaaaga 900
tggatttatg acacatccaa agtggcttct ggagtccctg ctcgcttcag tggcagtggg 960
tctgggaccg actactctct cacaatcaac agcttgaggg ctgaagatgc tgccacttat 1020
tactgccaac agtggagtag taaccgctc acgttcggtg gcgggaccaa ggtggagatc 1080
aaaggcgaag gtactagtag tggttctggt ggaagtggag gttcaggtgg agcagacgac 1140
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tgcaaggctt ctggctacac ctttactagg tacacgatgc actgggtaag gcaggcacct 1260
ggacagggtc tggaatggat tggatacatt aatcctagcc gtgggttatac taattacaat 1320
cagaagttca aggaccgct cacaatcact acagacaaat ccaccagcac agcctacatg 1380
gaactgagca gcctgcgttc tgaggacact gcagtctatt actgtgcaag atattatgat 1440
gatcattact gccttgacta ctggggccaa ggcaccacgg tcaccgtctc ctca 1494

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<210> 407
 <211> 498
 <212> PRT
 <213> artificial sequence

<220>
 <223> CD19xVL3VH7 LHLH

<400> 407

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Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1           5           10           15

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

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Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro
35           40           45

```

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Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50           55           60

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Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65           70           75           80

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Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
 85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
 115 120 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
 130 135 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
 145 150 155 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
 165 170 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
 180 185 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
 195 200 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 210 215 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
 245 250 255

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
 260 265 270

Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met Asn
 275 280 285

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
 290 295 300

Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 305 310 315 320

Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp
 325 330 335

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
 340 345 350

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr Gly
 355 360 365

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu Val
 370 375 380

Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser
 385 390 395 400

Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val
 405 410 415

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro
 420 425 430

Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr
 435 440 445

Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser
 450 455 460

Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Asp
 465 470 475 480

Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
 485 490 495

Ser Ser

<210> 408
 <211> 1497
 <212> DNA
 <213> artificial sequence

<220>
 <223> CD19xVL3VH7 HLLH

<400> 408
 caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt

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cctggacagg gtcttgagtg gattggacag atttggcctg gagatgggtga tactaactac 180
aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac 240
atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag 300
actacgacgg taggccgtta ttactatgct atggactact ggggccaaagg gaccacggtc 360
accgtctcct ccggtgggtg tggttctggc ggcgggcggt ccggtgggtg tggttctgat 420
atccagctga ccagctctcc agcttctttg gctgtgtctc tagggcagag ggccaccatc 480
tcctgcaagg ccagccaaag tgttgattat gatgggtgata gttatttgaa ctggtaccaa 540
cagattccag gacagccacc caaactcctc atctatgatg catccaatct agtttctggg 600
atcccaccca ggtttagtgg cagtgggtct gggacagact tcacctcaa catccatcct 660
gtggagaagg tggatgctgc aacctatcac tgtcagcaaa gtactgagga tccgtggacg 720
ttcgtgggag ggaccaagct cgagatcaaa tccggagggtg gtggatccga cattgtactg 780
accagctctc cagcaactct gtctctgtct ccaggggagc gtgccaccct gacctgcaga 840
gccagttcaa gtgtaagtta catgaactgg taccagcaga agccgggcaa ggcacccaaa 900
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Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
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Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
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Lys Gly Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr
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Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys
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Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
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Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
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Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
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Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile
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Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu
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Asn Trp Tyr Gln Gln Ile Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
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Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr Glu Asp Pro Trp Thr
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Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
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Glu Arg Ala Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
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Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
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Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
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Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Glu Gly Thr Ser Thr
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Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ala Asp Asp Val Gln Leu
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Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val
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Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp
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Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn
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Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys Asp Arg Val
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Thr Ile Thr Thr Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser
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Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr

465

470

475

480

Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
485 490 495

Val Ser Ser