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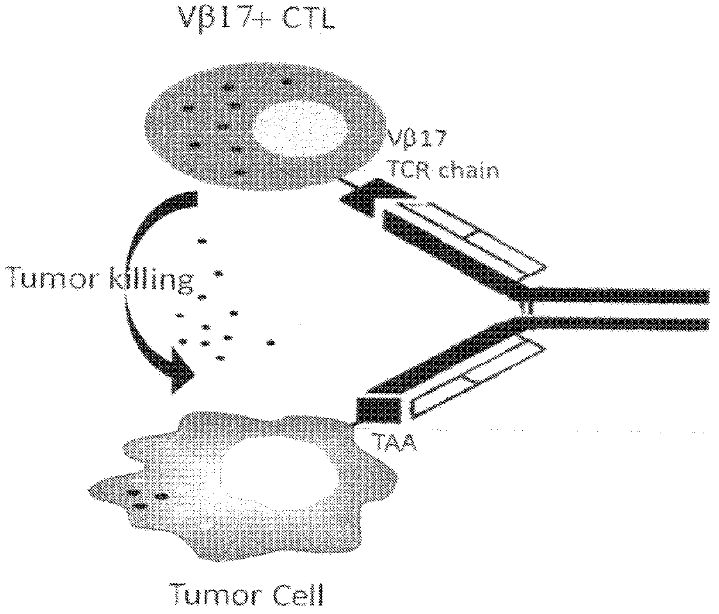

FIG. 1

(57) **Abstract:** The present disclosure relates to Vβ17 /CD123 bispecific antibodies. The antibodies are characterized by their CDRs sequences. Toxicity experiments are performed on Kasumi-3 cells (used to perform acute myeloblastic leukaemia pathologies)

[Continued on next page]

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ANTI-Vβ17/ANTI-CD123 BISPECIFIC ANTIBODIES

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 62/816,464, filed on March 11, 2019, the disclosure of which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

[0002] This invention relates to monoclonal anti-Vβ17/anti-CD123 bispecific antibodies, nucleic acids and expression vectors encoding the antibodies, recombinant cells containing the vectors, and compositions comprising the antibodies. Methods of making the antibodies, and methods of using the antibodies to kill cancer cells, are also provided.

REFERENCE TO SEQUENCE LISTING SUBMITTED ELECTRONICALLY

[0003] This application contains a sequence listing, which is submitted electronically via EFS-Web as an ASCII formatted sequence listing with a file name "PRD4012WOPCT Sequence Listing" and a creation date of March 11, 2020 and having a size of 85 kb. The sequence listing submitted via EFS-Web is part of the specification and is herein incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

[0004] Cytotoxic T cells (e.g., CD8+ T cells) can be utilized to directly kill cancer cells. Finding a way to direct cytotoxic T cells to a cancer cell could lead to the killing of such cells and an inhibition of cancer cell propagation. It has been demonstrated that cytotoxic T cells can be activated against cancer cells expressing cancer-associated antigens, by bring said cytotoxic T cells into close proximity to the cancer cells for an extended period of time using a bispecific antibody that binds both the cytotoxic T cell and the cancer cell. A variety of potential complications to this approach of killing cancer cells exist, such as selecting T cell and cancer cell antigens that mediate T cell activation, selecting parental antibodies that will have adequate affinity to mediate binding in the context of a bispecific antibody, and choosing a cancer cell antigen that will activate T cells to act specifically against cancer cells, rather than elicit nonspecific T cell activation. These complications are only compounded in the context of attempting to activate T cells to destroy cancer cells in an animal subject.

BRIEF SUMMARY OF THE INVENTION

[0005] Provided herein are bispecific antibodies capable of binding Vβ17, an antigen associated with T cells, and CD123, an antigen associated with cancer cells. Cytotoxic T cells express T cell receptors that consist of α- and β-chains, such as Vβ17. It is hypothesized that a bispecific antibody binding to Vβ17 and a cancer-associated antigen, such as CD123, may direct a cytotoxic T cell to an antigen-expressing cancer cell. Utilizing a bispecific antibody of this sort to recruit, or redirect, the cytotoxic T cell to an antigen-expressing cancer cell and could allow the T cell to kill the cancer cell.

[0006] In one general aspect, the present disclosure relates to isolated bispecific antibodies or antigen-binding fragments thereof that bind to Vβ17 and CD123.

[0007] Provided herein are isolated Vβ17 bispecific antibodies or antigen-binding fragments thereof. The isolated Vβ17 bispecific antibody or antigen-binding fragment thereof comprises:

a. a first heavy chain (HC1);
b. a second heavy chain (HC2);
c. a first light chain (LC1); and
d. a second light chain (LC2),

wherein HC1 is associated with LC1 and HC2 is associated with LC2, and wherein HC1 comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, respectively, and LC1 comprises a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6, respectively, to form a binding site for a first antigen, and wherein HC2 and LC2 form a binding site for a second antigen. In certain embodiments, the binding site for the first antigen binds to a Vβ17 on the surface of a CD8+ or CD4+ T cell. In certain embodiments, the binding site for the second antigen binds to a tumor antigen present on the surface of a cancer cell.

[0008] In certain embodiments, the binding of the bispecific antibody to Vβ17 present on the surface of the CD8+ or CD4+ T cell and the binding of the tumor antigen present on the surface of the cancer cells results in the killing of the cancer cell.

[0009] In certain embodiments, HC2 and LC2 bind to CD123.

[0010] In certain embodiments, the bispecific antibody or antigen-binding fragment thereof is an IgG isotype, such as IgG4.

[0011] In certain embodiments, the bispecific antibody or antigen-binding fragment thereof induces CD8+ or CD4+ T-cell dependent cytotoxicity of a cancer cell *in vitro* with an EC_{50} of less than about 0.2 pM.

[0012] Also provided are isolated anti-Vβ17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof. The anti-Vβ17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof comprise:

a. a first heavy chain (HC1);
b. a second heavy chain (HC2)
c. a first light chain (LC1); and
d. a second light chain (LC2),

wherein HC1 is associated with LC1 and HC2 is associated with LC2, and wherein HC1 comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, respectively, and LC1 comprises a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6, respectively, to form a binding site for a first antigen that specifically binds Vβ17, and wherein HC2 comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:34, SEQ ID NO:35, and SEQ ID NO:36, respectively, and LC2 comprises a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:37, SEQ ID NO:38, and SEQ ID NO:39, respectively, to form a biding site for a second antigen that specifically binds CD123. In certain embodiments, the HC1 comprises the amino acid sequence of SEQ ID NO:13 and LC1 comprises the amino acid sequence of SEQ ID NO:14, and the HC2 comprises the amino acid sequence of SEQ ID NO:15 and LC2 comprises the amino acid sequence of SEQ ID NO:16. In certain embodiments, the Vβ17 is on the surface of a CD8+ or CD4+ T cell. In certain embodiments, the CD123 is on the surface of a cancer cell. In certain embodiments, the bispecific antibody or antigen-binding fragment thereof induces CD8+ or CD4+ T-cell dependent cytotoxicity of a cancer cell in vitro with an EC50 of less than about 0.2 pM.

[0013] In certain embodiments, the anti-Vβ17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof are chimeric, partially humanized, or fully humanized.

[0014] Also provided are isolated humanized Vβ17 monoclonal antibodies or antigen-binding fragments thereof. The isolated humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof can comprise an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:28. In certain embodiments, the isolated humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof comprises an amino acid sequence of SEQ ID NO:28.

[0015] Also provided are isolated nucleic acids encoding the monoclonal antibodies or antigen-binding fragments thereof and the bispecific antibodies or antigen-binding fragments thereof disclosed herein.

[0016] Also provided are vectors comprising the isolated nucleic acids encoding the monoclonal antibodies or antigen-binding fragments thereof and the bispecific antibodies or antigen-binding fragments thereof disclosed herein.

[0017] Also provided are host cells comprising the vectors comprising the isolated nucleic acids disclosed herein.

[0018] Also provided are methods of directing a Vβ17-expressing CD8+ or CD4+ T cell to a cancer cell. The methods comprise contacting a Vβ17-expressing CD8+ or CD4+ T cell with a anti-Vβ17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof disclosed herein. Contacting the Vβ17-expressing CD8+ or CD4+ T cell with the anti-Vβ17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof can direct the Vβ17-expressing CD8+ or CD4+ T cell to a cancer cell.

[0019] Also provided are methods for inhibiting growth or proliferation of cancer cells. The methods comprise contacting the cancer cells with the bispecific antibodies disclosed herein. Contacting the cancer cells with the described antibodies can, for example, inhibit the growth or proliferation of the cancer cells, or promote T cell mediated killing of the cancer cells.

[0020] Also provided are methods of producing the bispecific antibodies or antigen-binding fragments thereof disclosed herein. The methods comprise culturing a cell comprising a nucleic acid encoding one heavy and light chain pair of the bispecific antibody under conditions to produce the heavy and light chains or an antigen-binding fragment thereof, and recovering the heavy and light chains of the bispecific antibody or an antigen-binding fragment thereof from the cell or culture. Following collection of heavy and light chains for both arms of the bispecific antibody, the heavy and light chain pairs are mixed in conditions suitable to allow for self-assembly, after which the self-assembled bispecific antibodies are collected.

[0021] Also provided are methods of producing compositions comprising the bispecific antibodies or antigen-binding fragments disclosed herein, such as buffered compositions or purified compositions and the like. For example, the methods may comprise combining the bispecific antibody or antigen-binding fragment thereof with a buffer acceptable that is acceptable for storage and use of the bispecific antibody.

[0022] Also provided are kits comprising bispecific antibodies or antigen-binding fragments thereof disclosed herein and packaging for the same.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] The foregoing summary, as well as the following detailed description of preferred embodiments of the present application, will be better understood when read in conjunction with the appended drawings. It should be understood, however, that the application is not limited to the precise embodiments shown in the drawings.

[0024] **FIG. 1** shows a schematic demonstrating the binding of an anti-Vβ17/anti-tumor antigen bispecific antibody to recruit T-cells to a cancer cell and to induce cancer cell death.

[0025] **FIGS. 2A-2B** shows that Vβ17+ CD8+ T cells exist in healthy subjects and upon culture with M1 peptide these cells can be expanded *in vitro*. **FIG. 2A** shows FACS histograms of gated peripheral blood mononuclear cells (PBMCs) for CD8+ T cells expressing Vβ17 (Vβ17+) on the cells surface from healthy subjects. **FIG. 2B** shows HLA sub-type of various donors and presence of percent Vβ17+ CD8+ T cells identified as day 0, and after *in vitro* expansion with M1 peptide for 14 days (Day 14).

[0026] **FIGS. 3** shows Vβ17+ CD8+ T cells have hallmarks of killer cytotoxic cells. Bar graph indicates expression of CD107a, CD69, Granzyme B (Gzb) and Interferon-γ (IFNγ) on gated PBMCs for CD8+ T cells expressing Vβ17 (Vβ17+) on the cell surface at day 0 (no M1) and at day 14 after stimulation with M1 peptide (+M1).

[0027] **FIG. 4** shows binding of VB11 [anti-Vβ17/anti-CD123] bispecific as well as VB13 [Vβ17 null control bispecific] antibodies to CD8+ T cells. Data presented from CD8+ T cells isolated from PBMCs from 3 different donors (D203517, HPU09381 and HPU08694). The table below each graph presents EC_{50} values for binding in nM.

[0028] **FIG. 5** shows binding of Vβ17 and CD123 bispecific (VB11) as well as Vβ17 null control bispecific (VB13) antibodies to AML cancer cell line. Data presented shows binding of bispecific antibodies to Kasumi3 AML cell line. The table below the graph presents EC_{50} values for binding in nM.

[0029] **FIG. 6** shows redirection of Vβ17+ T cells by bispecific antibodies that induce efficient killing of AML cancer cells. Data in the left graph shows killing of Kasumi3 cancer cells at an effector to target (E:T) ratio 0.5:1 and dose titration of bispecific antibodies. Data in the middle graph shows killing of Kasumi3 cancer cells at an E:T ratio 1:1 and dose titration of bispecific antibodies. Data in the right graph shows killing of Kasumi3 cancer cells at an E:T ratio 5:1 and dose titration of bispecific antibodies. The table below the graphs shows EC_{50} values calculated from the above graphs given in pM.

[0030] **FIGS. 7A-7B** show specific binding of an anti-Vβ17/anti-CD123 bispecific antibody (VB11) and a Vβ17 null bispecific antibody (VB13) to CD8+ T cells isolated from PBMCs. **FIG. 7A** shows FACS histograms of gated PBMCs for CD8+ T cells expressing Vβ17 (Vβ17+) on the cell surface from healthy subjects (left graph, Vβ17 non-depleted) and from PBMCs that were depleted of Vβ17+ T cells using negative selection (right graph, Vβ17 depleted). **FIG 7B** shows specific binding of an anti-Vβ17/anti-CD123 bispecific antibody (VB11) and a Vβ17 null bispecific antibody (VB13) to CD8+ T cells from **FIG 7A**. A dose response of bispecific antibodies is shown in the figure. The table below the graph shows EC_{50} values for binding calculated from the above graph given in nM.

[0031] **FIG. 8** shows specific recruitment of Vβ17 T cells by a Vβ17-bispecific antibody for killing of Kasumi3 cancer cells. Left figure shows killing of Kasumi3 AML cell line when effectors cells were isolated from PBMCs containing CD8+ T cells expressing Vβ17 (Vβ17+) on the cell surface (untouched CD8 T cells). Insert shows presence of 10.1% Vβ17+ CD8 T cells in the effector cell population. Right figure shows killing of Kasumi3 AML cell line when effector CD8+ T cells were isolated from PBMCs, but Vβ17+ T cells were depleted by negative selection. Insert shows presence of a minor population (0.086%) Vβ17+ CD8+ T cells in the effector cell population.

[0032] **FIGS. 9A-9B** show that there is no pan activation of T cells when using Vβ17 bispecific antibodies. **FIG. 9A** shows FACS plots of Vβ17+ and Vβ17- gated CD8+ T cells. When T cells were activated with Vβ17 bispecific antibody there was high level of upregulation of CD69 (62.5 %) on Vβ17+ as compared to Vβ17- CD8+ T cells (1.80%). **FIG. 9B** shows a bar graph for upregulation of CD69 on Vβ17+ and Vβ17- gated CD8+ T cells when activated using Vβ17 bispecific antibody.

[0033] **FIG. 10** shows that Vβ17+ T cells from HLA A2 negative donor are also effector killer cells and no pre-stimulation of Vβ17+ cell required. Efficient cytotoxicity mediated by Vβ17 bispecific antibody of Kasumi3 cancer cells is shown from PBMCs containing Vβ17+ T cells from HLA A2 negative donor (HPU 09381).

DETAILED DESCRIPTION OF THE INVENTION

[0034] Discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is for the purpose of providing context for the invention.

Such discussion is not an admission that any or all of these matters form part of the prior art with respect to any inventions disclosed or claimed.

[0035] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood to one of ordinary skill in the art to which this invention pertains. Otherwise, certain terms used herein have the meanings as set forth in the specification.

[0036] Unless otherwise stated, any numerical values, such as a concentration or a concentration range described herein, are to be understood as being modified in all instances by the term "about." Thus, a numerical value typically includes ± 10% of the recited value. For example, a concentration of 1 mg/mL includes 0.9 mg/mL to 1.1 mg/mL. Likewise, a concentration range of 1% to 10% (w/v) includes 0.9% (w/v) to 11% (w/v). As used herein, the use of a numerical range expressly includes all possible subranges, all individual numerical values within that range, including integers within such ranges and fractions of the values unless the context clearly indicates otherwise.

[0037] Unless otherwise indicated, the term "at least" preceding a series of elements is to be understood to refer to every element in the series. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the invention.

[0038] It must be noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference unless the context clearly dictates otherwise.

[0039] As used herein, the terms "comprises," "comprising," "includes," "including," "has," "having," "contains" or "containing," or any other variation thereof, will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers and are intended to be non-exclusive or open-ended. For example, a composition, a mixture, a process, a method, an article, or an apparatus that comprises a list of elements is not necessarily limited to only those elements but can include other elements not expressly listed or inherent to such composition, mixture, process, method, article, or apparatus. Further, unless expressly stated to the contrary, "or" refers to an inclusive or and not to an exclusive or. For example, a condition A or B is satisfied by any one of the following: A is true (or present) and B is false (or not present), A is false (or not present) and B is true (or present), and both A and B are true (or present).

[0040] As used herein, the conjunctive term "and/or" between multiple recited elements is understood as encompassing both individual and combined options. For instance, where two elements are conjoined by "and/or," a first option refers to the applicability of the first element without the second. A second option refers to the applicability of the second element without the first. A third option refers to the applicability of the first and second elements together. Any one of these options is understood to fall within the meaning, and therefore satisfy the requirement of the term "and/or" as used herein. Concurrent applicability of more than one of the options is also understood to fall within the meaning, and therefore satisfy the requirement of the term "and/or."

[0041] It should also be understood that the terms "about," "approximately," "generally," "substantially," and like terms, used herein when referring to a dimension or characteristic of a component of the preferred invention, indicate that the described dimension/characteristic is not a strict boundary or parameter and does not exclude minor variations therefrom that are functionally the same or similar, as would be understood by one having ordinary skill in the art. At a minimum, such references that include a numerical parameter would include variations that, using mathematical and industrial principles accepted in the art (e.g., rounding, measurement or other systematic errors, manufacturing tolerances, etc.), would not vary the least significant digit.

[0042] The terms "identical" or percent "identity," in the context of two or more nucleic acids or polypeptide sequences (*e.g.*, anti-Vβ17/anti-CD123 bispecific antibodies and polynucleotides that encode them, Vβ17 polypeptides and Vβ17 polynucleotides that encode them, CD123 polypeptides and CD123 polynucleotides that encode them), refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues or nucleotides that are the same, when compared and aligned for maximum correspondence, as measured using one of the following sequence comparison algorithms or by visual inspection.

[0043] For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are input into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. The sequence comparison algorithm then calculates the percent sequence identity for the test sequence(s) relative to the reference sequence, based on the designated program parameters.

[0044] Optimal alignment of sequences for comparison can be conducted, *e.g.*, by the local homology algorithm of Smith & Waterman, *Adv. Appl. Math.* 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, *J. Mol. Biol.* 48:443 (1970), by the search for similarity method of Pearson & Lipman, *Proc. Nat'l. Acad. Sci. USA* 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by visual inspection (*see generally*, *Current Protocols in Molecular Biology*, F.M. Ausubel *et al.*, eds., Current Protocols, a joint venture between Greene Publishing Associates, Inc. and John Wiley & Sons, Inc., (1995 Supplement) (Ausubel)).

[0045] Examples of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al.* (1990) *J. Mol. Biol.* 215: 403-410 and Altschul *et al.* (1997) *Nucleic Acids Res.* 25: 3389-3402, respectively. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al.*, *supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are then extended in both directions along each sequence for as far as the cumulative alignment score can be increased.

[0046] Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N= -4, and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength (W) of 3, an expectation (E) of 10, and the BLOSUM62 scoring matrix (*see* Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915 (1989)).

[0047] In addition to calculating percent sequence identity, the BLAST algorithm also performs a statistical analysis of the similarity between two sequences (*see, e.g.*, Karlin & Altschul, *Proc. Nat'l. Acad. Sci. USA* 90:5873-5787 (1993)). One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a nucleic acid is considered similar to a reference sequence if the smallest sum probability in a comparison of the test nucleic acid to the reference nucleic acid is less than about 0.1, more preferably less than about 0.01, and most preferably less than about 0.001.

[0048] A further indication that two nucleic acid sequences or polypeptides are substantially identical is that the polypeptide encoded by the first nucleic acid is immunologically cross reactive with the polypeptide encoded by the second nucleic acid, as described below. Thus, a polypeptide is typically substantially identical to a second polypeptide, for example, where the two peptides differ only by conservative substitutions. Another indication that two nucleic acid sequences are substantially identical is that the two molecules hybridize to each other under stringent conditions.

[0049] Antibodies

[0050] Described herein are isolated anti-Vβ17 bispecific antibodies or antigen-binding fragments thereof, nucleic acids and expression vectors encoding the antibodies, recombinant cells containing the vectors, and compositions comprising the antibodies. The invention additionally relates to isolated anti-Vβ17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof, nucleic acids and expression vectors encoding the antibodies, recombinant cells containing the vectors, and compositions comprising the bispecific antibodies. Methods of making the antibodies, and methods of using the antibodies to treat diseases, including cancer, are also provided. The antibodies disclosed herein possess one or more desirable functional properties, including but not limited to high-affinity binding to Vβ17 and/or CD123, high specificity to Vβ17 and/or CD123, and the ability to treat or prevent cancer when administered alone or in combination with other anti-cancer therapies.

[0051] As used herein, the term "antibody" is used in a broad sense and includes immunoglobulin or antibody molecules including human, humanized, composite and chimeric antibodies and antibody fragments that are monoclonal or polyclonal. In general, antibodies are proteins or peptide chains that exhibit binding specificity to a specific antigen. Antibody structures are well known. Immunoglobulins can be assigned to five major classes (i.e., IgA, IgD, IgE, IgG and IgM), depending on the heavy chain constant domain amino acid sequence. IgA and IgG are further sub-classified as the isotypes IgA1, IgA2, IgG1, IgG2, IgG3 and IgG4. Antibody light chains of vertebrate species can be assigned to one of two clearly distinct types, namely kappa and lambda, based on the amino acid sequences of their constant domains. Accordingly, the antibodies of the invention can contain a kappa or lambda light chain constant domain. According to particular embodiments, the antibodies disclosed herein include heavy and/or light chain constant regions from mouse or human antibodies. In addition to the heavy and light constant domains, antibodies contain an antigen-binding region that is made up of a light chain variable region and a heavy chain variable region, each of which contains three domains (i.e., complementarity determining regions 1-3; CDR1, CDR2, and CDR3). The light chain variable region domains are alternatively referred to as LCDR1, LCDR2, and LCDR3, and the heavy chain variable region domains are alternatively referred to as HCDR1, HCDR2, and HCDR3.

[0052] As used herein, the term an "isolated antibody" refers to an antibody which is substantially free of other antibodies having different antigenic specificities (e.g., an isolated antibody that specifically binds to Vβ17 is substantially free of antibodies that do not bind to Vβ17; an isolated antibody that specifically binds to CD123 is substantially free of antibodies that do not bind to CD123). In addition, an isolated antibody is substantially free of other cellular material and/or chemicals.

[0053] As used herein, the term "monoclonal antibody" refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally occurring mutations that can be present in minor amounts. The monoclonal antibodies disclosed herein can be made by the hybridoma method, phage display technology, single lymphocyte gene cloning technology, or by recombinant DNA methods. For example, the monoclonal antibodies can be produced by a hybridoma which includes a B cell obtained from a transgenic nonhuman animal, such as a transgenic mouse or rat, having a genome comprising a human heavy chain transgene and a light chain transgene.

[0054] As used herein, the term "antigen-binding fragment" refers to an antibody fragment such as, for example, a diabody, a Fab, a Fab', a F(ab')2, an Fv fragment, a disulfide stabilized Fv fragment (dsFv), a $(dsFv)_2$, a bispecific dsFv (dsFv-dsFv'), a disulfide stabilized diabody (ds diabody), a single-chain antibody molecule (scFv), a single domain antibody (sdab) an scFv dimer (bivalent diabody), a multispecific antibody formed from a portion of an antibody comprising one or more CDRs, a camelized single domain antibody, a nanobody, a domain antibody, a bivalent domain antibody, or any other antibody fragment that binds to an antigen but does not comprise a complete antibody structure. An antigen-binding fragment is capable of binding to the same antigen to which the parent antibody or a parent antibody fragment binds. According to particular embodiments, the antigen-binding fragment comprises a light chain variable region, a light chain constant region, and an Fd segment of the heavy chain. According to other particular embodiments, the antigen-binding fragment comprises Fab and F(ab').

[0055] As used herein, the term "humanized antibody" refers to a non-human antibody that is modified to increase the sequence homology to that of a human antibody, such that the antigen-binding properties of the antibody are retained, but its antigenicity in the human body is reduced.

[0056] As used herein, the term "multispecific antibody" refers to an antibody that comprises a plurality of immunoglobulin variable domain sequences, wherein a first immunoglobulin variable domain sequence of the plurality has binding specificity for a first epitope and a second immunoglobulin variable domain sequence of the plurality has binding specificity for a second epitope. In an embodiment, the first and second epitopes do not overlap or do not substantially overlap. In an embodiment, the first and second epitopes are on different antigens, *e.g.*, the different proteins (or different subunits of a multimeric protein). In an embodiment, a multispecific antibody comprises a third, fourth, or fifth immunoglobulin variable domain. In an embodiment, a multispecific antibody is a bispecific antibody molecule, a trispecific antibody molecule, or a tetraspecific antibody molecule.

[0057] As used herein, the term “bispecifc antibody” refers to a multispecific antibody that binds no more than two epitopes or two antigens. A bispecific antibody is characterized by a first immunoglobulin heavy and light chain pair which has binding specificity for a first epitope (e.g., an epitope on a Vβ17 antigen) and a second immunoglobulin heavy and light chain pair that has binding specificity for a second epitope (e.g., an epitope on a CD123 antigen). In an embodiment, the first and second epitopes are on different antigens, *e.g.*, the different proteins (or different subunits of a multimeric protein). In an embodiment, a bispecific antibody comprises a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a first epitope and a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a second epitope. In an embodiment, a bispecific antibody comprises a half antibody, or fragment thereof, having binding specificity for a first epitope and a half antibody, or fragment thereof, having binding specificity for a second epitope. In an embodiment, a bispecific antibody comprises a scFv, or fragment thereof, having binding specificity for a first epitope, and a scFv, or fragment thereof, having binding specificity for a second epitope. In an embodiment, the first epitope is located on Vβ17 and the second epitope is located on CD123. In an embodiment, the first epitope is located on Vβ17 and the second epitope is located on PD-1, PD-L1, CTLA-4, EGFR, HER-2, CD19, CD20, CD3 and/or other tumor associated immune suppressors or surface antigens.

[0058] The term "half antibody" as used herein refers to one immunoglobulin heavy chain associated with one immunoglobulin light chain. An exemplary half-antibody is depicted in SEQ ID NO: 28. One skilled in the art will readily appreciate that a half-antibody can encompass a fragment thereof and can also have an antigen binding domain consisting of a single variable domain, e.g., originating from a camelidae.

[0059] As used herein, the term “Vβ17” refers to a T cell receptor, which is expressed in response to an immune response on a cytotoxic T cell. Vβ17-expressing CD8+ T cells are commonly produced in response to influenza A virus exposure in a subject. Vβ17-expressing CD8+ T cells provide great recall in response to influenza exposure in the subject. The term “Vβ17” includes any Vβ17 variant, isoform, and species homolog, which is naturally expressed by cells (including T cells) or can be expressed on cells transfected with genes or cDNA encoding the polypeptide. Unless noted, preferably the Vβ17 is a human Vβ17. A human Vβ17 amino acid sequence is provided by GenBank Accession Number AAB49730.1.

[0060] The term "CD123" refers to a molecule that is found on cells which helps transmit the signal of interleukin-3, a soluble cytokine that is important in the immune system. CD123 can also be referred to as the "interleukin-3 receptor." The receptor belongs to the type I cytokine receptor family and is a heterodimer with a unique alpha chain paired with the common beta subunit (beta c or CD131). The CD123 receptor can be found on pluripotent progenitor cells and can induce tyrosine phosphorylation within the cell and promote proliferation and differentiation within hematopoietic cell lines. CD123 can also be expressed in acute myeloid leukemia (AML) subtypes. The term "CD123" includes any CD123 variant, isoform, and species homolog, which is naturally expressed by cells (including T cells) or can be expressed on cells transfected with genes or cDNA encoding those polypeptides, unless noted, preferably the "CD123" is a human CD123. A human CD123 amino acid sequence is provided by GenBank Accession Number AY789109.1.

[0061] As used herein, an antibody that "specifically binds to Vβ17" refers to an antibody that binds to a Vβ17, preferably a human Vβ17, with a KD of 1×10^{-7} M or less, preferably 1×10^{-8} M or less, more preferably 5×10^{-9} M or less, 1×10^{-9} M or less, 5×10^{-10} M or less, or 1×10^{-10} M or less. The term "KD" refers to the dissociation constant, which is obtained from the ratio of Kd to Ka (i.e., Kd/Ka) and is expressed as a molar concentration (M). KD values for antibodies can be determined using methods in the art in view of the present disclosure. For example, the KD of an antibody can be determined by using surface plasmon resonance, such as by using a biosensor system, e.g., a Biacore® system, or by using bio-layer interferometry technology, such as an Octet RED96 system.

[0062] As used herein, an antibody that "specifically binds to CD123" refers to an antibody that binds to a CD123, preferably a human CD123, with a KD of 1×10^{-7} M or less, preferably 1×10^{-8} M or less, more preferably 5×10^{-9} M or less, 1×10^{-9} M or less, 5×10^{-10} M or less, or 1×10^{-10} M or less. The term "KD" refers to the dissociation constant, which is obtained from the ratio of Kd to Ka (i.e., Kd/Ka) and is expressed as a molar concentration (M). KD values for antibodies can be determined using methods in the art in view of the present disclosure. For example, the KD of an antibody can be determined by using surface plasmon resonance, such as by using a biosensor system, e.g., a Biacore® system, or by using bio-layer interferometry technology, such as an Octet RED96 system.

[0063] The smaller the value of the KD of an antibody, the higher affinity that the antibody binds to a target antigen.

[0064] According to a particular aspect, the invention relates to an isolated Vβ17 bispecific antibody or antigen-binding fragment thereof comprising (a) a first heavy chain (HC1); (b) a second heavy chain (HC2); (c) a first light chain (LC1); and (d) a second light chain (LC2). The HC1 can be associated with the LC1 and the HC2 can be associated with LC2. The HC1 can comprise a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, respectively, and LC1 can comprise a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6, respectively.

[0065] The HC1 and LC1 form a binding site for a first antigen, and the HC2 and LC2 form a binding site for a second antigen. By way of an example, the binding site for the first antigen can bind to a Vβ17 on a CD8+ or CD4+ T cell, and the binding site for the second antigen can, for example, bind a tumor antigen present on the surface of a cancer cell. The binding of the Vβ17 bispecific antibody to Vβ17 present on the surface of the CD8+ or CD4+ T cell, and the binding of the tumor antigen present on the surface of the cancer cells can, for example, result in the killing of the cancer cell.

[0066] Also provided herein are anti-Vβ17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof comprising an anti-Vβ17 antibody or an antigen-binding fragment thereof and an anti-CD123 antibody or antigen-binding fragment thereof. In certain embodiments the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof comprises (a) a first heavy chain (HC1); (b) a second heavy chain (HC2); (c) a first light chain (LC1); and a second light chain (LC2). The HC1 is associated with the LC1 and the HC2 is associated with the LC2. In certain embodiments, the HC1 comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, respectively, and LC1 comprises a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6, respectively. In certain embodiments, the HC2 comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:34, SEQ ID NO:35, and SEQ ID NO:36, respectively, and LC2 comprises a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:37, SEQ ID NO:38, and SEQ ID NO:39, respectively

[0067] In certain embodiments, the HC1 can, for example, comprise an amino acid sequence of SEQ ID NO:13 and the LC1 can, for example, comprise an amino acid sequence of SEQ ID

NO:14 to form a binding site for a first antigen that specifically binds Vβ17. The HC2 can, for example, comprise an amino acid sequence of SEQ ID NO:15 and the LC2 can, for example, comprise an amino acid sequence of SEQ ID NO:16 to form a binding site for a second antigen that specifically binds CD123.

[0068] In certain embodiments, the Vβ17 is on the surface of a CD8+ or CD4+ T cell. In certain embodiments, the CD123 is on the surface of a cancer cell (e.g., a leukemia cell).

[0069] In some embodiments, the bispecific antibodies disclosed herein can take the form of a diabody, a cross-body, or a bispecific antibody obtained via a controlled Fab arm exchange as described herein.

[0070] In some embodiments, the bispecific antibodies include IgG-like molecules with complementary CH3 domains that promote heterodimerization; recombinant IgG-like dual targeting molecules, wherein the two sides of the molecule each contain the Fab fragment or part of the Fab fragment of at least two different antibodies; IgG fusion molecules, wherein full length IgG antibodies are fused to an extra Fab fragment or parts of Fab fragment; Fc fusion molecules, wherein single chain Fv molecules or stabilized diabodies are fused to heavy-chain constant-domains, Fc-regions or parts thereof; Fab fusion molecules, wherein different Fab-fragments are fused together; ScFv- and diabody-based and heavy chain antibodies (e.g., domain antibodies, nanobodies) wherein different single chain Fv molecules or different diabodies or different heavy-chain antibodies (e.g. domain antibodies, nanobodies) are fused to each other or to another protein or carrier molecule.

[0071] In some embodiments, IgG-like molecules with complementary CH3 domains molecules include the Triomab/Quadroma (Trion Pharma/Fresenius Biotech), the Knobs-into-Holes (Genentech), CrossMAbs (Roche) and the electrostatically-matched (Amgen), the LUZ-Y (Genentech), the Strand Exchange Engineered Domain body (SEEDbody) (EMD Serono), the Biclonic (Merus) and the DuoBody (Genmab A/S).

[0072] In some embodiments, recombinant IgG-like dual targeting molecules include Dual Targeting (DT)-Ig (GSK/Domantis), Two-in-one Antibody (Genentech), Cross-linked Mabs (Karmanos Cancer Center), mAb2 (F-Star) and CovX-body (CovX/Pfizer).

[0073] In some embodiments, IgG fusion molecules include Dual Variable Domain (DVD)-Ig (Abbott), IgG-like Bispecific (InnClone/Eli Lilly), Ts2Ab (MedImmune/AZ) and BsAb (Zymogenetics), HERCULES (Biogen Idec) and TvAb (Roche).

[0074] In some embodiments, Fc fusion molecules can include ScFv/Fc Fusions (Academic Institution), SCORPION (Emergent BioSolutions/Trubion, Zymogenetics/BMS), Dual Affinity Retargeting Technology (Fc-DART) (MacroGenics) and Dual(ScFv)$_2$-Fab (National Research Center for Antibody Medicine--China).

[0075] In some embodiments, Fab fusion bispecific antibodies include F(ab)$_2$ (Medarex/AMGEN), Dual-Action or Bis-Fab (Genentech), Dock-and-Lock (DNL) (ImmunoMedics), Bivalent Bispecific (Biotecnol) and Fab-Fv (UCB-Celltech). ScFv-, diabody-based, and domain antibodies, include but are not limited to, Bispecific T Cell Engager (BiTE) (Micromet), Tandem Diabody (Tandab) (Affimed), Dual Affinity Retargeting Technology (DART) (MacroGenics), Single-chain Diabody (Academic), TCR-like Antibodies (AIT, ReceptorLogics), Human Serum Albumin ScFv Fusion (Merrimack) and COMBODY (Epigen Biotech), dual targeting nanobodies (Ablynx), dual targeting heavy chain only domain antibodies.

[0076] Full length bispecific antibodies disclosed herein can be generated for example using Fab arm exchange (or half molecule exchange) between two mono specific bivalent antibodies by introducing substitutions at the heavy chain CH3 interface in each half molecule to favor heterodimer formation of two antibody half molecules having distinct specificity either *in vitro* in cell-free environment or using co-expression. The Fab arm exchange reaction is the result of a disulfide-bond isomerization reaction and dissociation-association of CH3 domains. The heavy-chain disulfide bonds in the hinge regions of the parent mono specific antibodies are reduced. The resulting free cysteines of one of the parent monospecific antibodies form an inter heavy-chain disulfide bond with cysteine residues of a second parent mono specific antibody molecule and simultaneously CH3 domains of the parent antibodies release and reform by dissociation-association. The CH3 domains of the Fab arms can be engineered to favor heterodimerization over homodimerization. The resulting product is a bispecific antibody having two Fab arms or half molecules, each binding a distinct epitope, i.e. an epitope on Vβ17 and an epitope on a tumor antigen.

[0077] "Homodimerization" as used herein refers to an interaction of two heavy chains having identical CH3 amino acid sequences. "Homodimer" as used herein refers to an antibody having two heavy chains with identical CH3 amino acid sequences.

[0078] "Heterodimerization" as used herein refers to an interaction of two heavy chains having non-identical CH3 amino acid sequences. "Heterodimer" as used herein refers to an antibody having two heavy chains with non-identical CH3 amino acid sequences.

[0079] The "knob-in-hole" strategy (see, e.g., PCT Inti. Publ. No. WO 2006/028936) can be used to generate full length bispecific antibodies. Briefly, selected amino acids forming the interface of the CH3 domains in human IgG can be mutated at positions affecting CH3 domain interactions to promote heterodimer formation. An amino acid with a small side chain (hole) is introduced into a heavy chain of an antibody specifically binding a first antigen and an amino acid with a large side chain (knob) is introduced into a heavy chain of an antibody specifically binding a second antigen. After co-expression of the two antibodies, a heterodimer is formed as a result of the preferential interaction of the heavy chain with a “hole” with the heavy chain with a “knob”. Exemplary CH3 substitution pairs forming a knob and a hole are (expressed as modified position in the first CH3 domain of the first heavy chain/modified position in the second CH3 domain of the second heavy chain): T366Y/F405A, T366W/ F405W, F405W/Y407A, T394W/Y407T, T394S/Y407A, T366W/T394S, F405W/T394S and T366W/T366S_L368A_Y407V.

[0080] Other strategies such as promoting heavy chain heterodimerization using electrostatic interactions by substituting positively charged residues at one CH3 surface and negatively charged residues at a second CH3 surface can be used, as described in US Pat. Publ. No. US2010/0015133; US Pat. Publ. No. US2009/0182127; US Pat. Publ. No. US2010/028637; or US Pat. Publ. No. US2011/0123532. In other strategies, heterodimerization can be promoted by the following substitutions (expressed as modified position in the first CH3 domain of the first heavy chain/modified position in the second CH3 domain of the second heavy chain): L351Y_F405AY407V/T394W, T366I_K392M_T394W/F405A_Y407V, T366L_K392M_T394W/F405A_Y407V, L351Y_Y407A/T366A_K409F, L351Y_Y407A/T366V K409F Y407A/T366A_K409F, or T350V_L351Y_F405A Y407V/T350V_T366L_K392L_T394W as described in U.S. Pat. Publ. No. US2012/0149876 or U.S. Pat. Publ. No. US2013/0195849.

[0081] In addition to methods described above, bispecific antibodies disclosed herein can be generated *in vitro* in a cell-free environment by introducing asymmetrical mutations in the CH3 regions of two mono specific homodimeric antibodies and forming the bispecific heterodimeric antibody from two parent monospecific homodimeric antibodies in reducing conditions to allow disulfide bond isomerization according to methods described in International Pat. Publ. No. W02011/131746. In the methods, the first monospecific bivalent antibody (e.g., anti-CD33 antibody) and the second monospecific bivalent antibody (e.g., anti-CD3 antibody) are engineered to have certain substitutions at the CH3 domain that promotes heterodimer stability; the antibodies are incubated together under reducing conditions sufficient to allow the cysteines in the hinge region to undergo disulfide bond isomerization; thereby generating the bispecific antibody by Fab arm exchange. The incubation conditions can optionally be restored to non-reducing conditions. Exemplary reducing agents that may be used are 2-mercaptoethylamine (2-MEA), dithiothreitol (DTT), dithioerythritol (DTE), glutathione, tris (2-carboxyethyl) phosphine (TCEP), L-cysteine and beta-mercaptoethanol, preferably a reducing agent selected from the group consisting of: 2-mercaptoethylamine, dithiothreitol and tris (2-carboxyethyl) phosphine. For example, incubation for at least 90 min at a temperature of at least 20° C in the presence of at least 25 mM 2-MEA or in the presence of at least 0.5 mM dithiothreitol at a pH from 5-8, for example at pH of 7.0 or at pH of 7.4 may be used.

[0082] In certain embodiments, the anti-Vβ17 antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, HCDR3, a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the polypeptide sequence of:

a. SEQ ID NOs:1, 2, 3, 4, 5, and 6, respectively;

and the anti-CD123 antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, HCDR3, a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the polypeptide sequence of:

1. SEQ ID NOs:34, 35, 36, 37, 38, and 39, respectively.

[0083] According to another particular aspect, the invention relates to an isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof that induces antibody-dependent cell-mediated cytotoxicity (ADCC). The bispecific antibody or antigen-binding fragment thereof can, for example, induce ADCC *in vitro*. The bispecific antibody or antigen-binding fragment thereof can induce ADCC with an EC_{50} of less than about 1 pM. In certain embodiments, the EC_{50} is less than about 1 pM, less than about 0.9 pM, less than about 0.8 pM, less than about 0.7 pM, less than about 0.6 pM, less than about 0.5 pM, less than about 0.4 pM, less than about 0.300 pM, less than about 0.2 pM, less than about 0.19 pM, less than about 0.18 pM, less than about 0.17 pM, less than about 0.16 pM, less than about 0.15 pM, less than about 0.14 pM, less than about 0.13 pM, less than about 0.12 pM, less than about 0.11 pM, less than about 0.1 pM, less than about 0.09 pM, less than about 0.08 pM, less than about 0.07 pM, less than about 0.06 pM, less than about 0.05 pM, less than about 0.04 pM, less than about 0.03 pM, less than about 0.02 pM, or less than about 0.01 pM. In certain embodiments, the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof comprises an IgG1, IgG2, IgG3, or IgG4 backbone. In one such embodiment, the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof has an antibody backbone of the IgG4 isotype.

[0084] In some embodiments described herein, immune effector properties of the anti-Vβ17/anti-CD123 bispecific antibodies can be enhanced or silenced through Fc modifications by techniques known to those skilled in the art. For example, Fc effector functions such as Clq binding, complement dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cell-mediated phagocytosis (ADCP), down regulation of cell surface receptors (e.g., B cell receptor; BCR), etc. may be provided and/or controlled by modifying residues in the Fc responsible for these activities.

[0085] "Antibody-dependent cell-mediated cytotoxicity" or "ADCC" refers to a cell-mediated reaction in which non-specific cytotoxic cells that express Fc receptors (FcRs) (e.g. Natural Killer (NK) cells, neutrophils, and macrophages) recognize bound antibody on a target cell and subsequently cause lysis of the target cell.

[0086] The ability of antibodies to induce ADCC can be enhanced by engineering their oligosaccharide component. Human IgG1 or IgG3 are N-glycosylated at Asn297 with the majority of the glycans in the well-known biantennary G0, G0F, G1, G1F, G2 or G2F forms. Antibodies produced by non-engineered CHO cells typically have a glycan fucose content of about at least 85%. The removal of the core fucose from the biantennary complex-type oligosaccharides attached to the Fc regions enhances the ADCC of antibodies via improved FcγRIIIa binding without altering antigen-binding or CDC activity. Such Abs can be achieved using different methods reported to lead to the successful expression of relatively high defucosylated antibodies bearing the biantennary complex-type of Fc oligosaccharides such as control of culture osmolality (Konno et al., Cytotechnology 64:249-65, 2012), application of a variant CHO line Lec13 as the host cell line (Shields et al., J Biol Chem 277:26733-26740, 2002), application of a variant CHO line EB66 as the host cell line (Olivier et al., MAbs; 2(4), 2010; Epub ahead of print; PMID:20562582), application of a rat hybridoma cell line YB2/0 as the host cell line (Shinkawa et al., J Biol Chem 278:3466-3473, 2003), introduction of small interfering RNA specifically against the α-1,6-fucosyltrasferase (FUT8) gene (Mori et al., Biotechnol Bioeng 88:901-908, 2004), or coexpression of β-1,4-N-acetylglucosaminyltransferase III and golgi α-mannosidase II or a potent alpha-mannosidase I inhibitor, kifunensine (Ferrara et al., J Biol Chem 281:5032-5036, 2006, Ferrara et al., Biotechnol Bioeng 93:851-861, 2006; Xhou et al., Biotechnol Bioeng 99:652-65, 2008).

[0087] In some embodiments described herein, ADCC elicited by the anti-Vβ17/anti-CD123 bispecific antibodies can also be enhanced by certain substitutions in the antibody Fc. Exemplary substitutions include, for example, substitutions at amino acid positions 256, 290, 298, 312, 356, 330, 333, 334, 360, 378 or 430 (residue numbering according to the EU index) as described in U.S. Pat. No. 6,737,056.

[0088] According to another particular aspect, the invention relates to an isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof capable of inducing T-cell dependent cytotoxicity in Vβ17-expressing cells and/or CD123-expressing cells. The bispecific antibody or antigen-binding fragment thereof can, for example, induce T-cell dependent cytotoxicity in Vβ17-expressing cells and/or CD123-expressing cells *in vitro* with an EC_{50} value of less than about 2nM. In certain embodiments, the EC_{50} is less than about 2.0nM, less than about 1.9nM, less than about 1.8nM, less than about 1.7nM, less than about 1.6nM, less than about 1.5nM, less than about 1.4nM, less than about 1.3nM, less than about 1.2nM, less than about 1.1nM, less than about 1.0nM, less than about 0.9nM, less than about 0.8nM, less than about 0.7nM, less than about 0.6nM, less than about 0.5nM, less than about 0.4nM, less than about 0.3nM, less than about 0.2nM, and less than about 0.1nM.

[0089] According to another particular aspect, the invention relates to an isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof, wherein the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof is chimeric.

[0090] According to another particular aspect, the invention relates to an isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof, wherein the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof is human or humanized.

[0091] In another general aspect, the invention relates to an isolated humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof. The isolated humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof comprises an amino acid sequence with at least 85%, preferably 90%, more preferably 95% or more, such as 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence of SEQ ID NO:28. In certain embodiments, the humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof comprises the amino acid sequence of SEQ ID NO:28.

[0092] In another general aspect, the invention relates to isolated nucleic acids encoding the monoclonal antibodies or antigen-binding fragments thereof disclosed herein. In another general aspect, the invention relates to isolated nucleic acids encoding the bispecific antibodies or antigen-binding fragments thereof disclosed herein. It will be appreciated by those skilled in the art that the coding sequence of a protein can be changed (e.g., replaced, deleted, inserted, etc.) without changing the amino acid sequence of the protein. Accordingly, it will be understood by those skilled in the art that nucleic acid sequences encoding monoclonal antibodies and/or bispecific antibodies disclosed herein can be altered without changing the amino acid sequences of the proteins.

[0093] In another general aspect, the invention relates to vectors comprising the isolated nucleic acids disclosed herein. Any vector known to those skilled in the art in view of the present disclosure can be used, such as a plasmid, a cosmid, a phage vector or a viral vector. In some embodiments, the vector is a recombinant expression vector such as a plasmid. The vector can include any element to establish a conventional function of an expression vector, for example, a promoter, ribosome binding element, terminator, enhancer, selection marker, and origin of replication. The promoter can be a constitutive, inducible or repressible promoter. A number of expression vectors capable of delivering nucleic acids to a cell are known in the art and can be used herein for production of an antibody or antigen-binding fragment thereof in the cell. Conventional cloning techniques or artificial gene synthesis can be used to generate a recombinant expression vector according to embodiments disclosed herein. Such techniques are well known to those skilled in the art in view of the present disclosure.

[0094] In another general aspect, the invention relates to host cells comprising the isolated nucleic acids encoding the monoclonal antibodies and/or bispecific antibodies or antigen-binding fragments thereof disclosed herein. Any host cell known to those skilled in the art in view of the present disclosure can be used for recombinant expression of antibodies or antigen-binding fragments thereof disclosed herein. In some embodiments, the host cells are E. coli TG1 or BL21 cells (for expression of, e.g., an scFv or Fab antibody), CHO-DG44 or CHO-K1 cells or HEK293 cells (for expression of, e.g., a full-length IgG antibody). According to particular embodiments, the recombinant expression vector is transformed into host cells by conventional methods such as chemical transfection, heat shock, or electroporation, where it is stably integrated into the host cell genome such that the recombinant nucleic acid is effectively expressed.

[0095] In another general aspect, the invention relates to a method of producing a bispecific antibody or antigen-binding fragment thereof disclosed herein. The methods comprise culturing a cell comprising a nucleic acid encoding the bispecific antibody or antigen-binding fragment thereof under conditions to produce a bispecific antibody or antigen-binding fragment thereof disclosed herein, and recovering the antibody or antigen-binding fragment thereof from the cell or cell culture (e.g., from the supernatant). Expressed antibodies or antigen-binding fragments thereof can be harvested from the cells and purified according to conventional techniques known in the art and as described herein.

Methods of use

[0096] In another general aspect, the invention relates to a method of targeting CD123 on the surface of a cancer cell, the method comprising exposing the cancer cell to an anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof.

[0097] The functional activity of bispecific antibodies and antigen-binding fragments thereof that bind Vβ17 and/or CD123 can be characterized by methods known in the art and as described herein. Methods for characterizing antibodies and antigen-binding fragments thereof that bind Vβ17 and/or CD123 include, but are not limited to, affinity and specificity assays including Biacore, ELISA, and OctetRed analysis; binding assays to detect the binding of antibodies to CD123 on cancer cells by FACS; binding assays to detect the binding of antibodies to Vβ17 on

CD8+ or CD4+ T cells. According to particular embodiments, the methods for characterizing antibodies and antigen-binding fragments thereof that bind Vβ17 and/or CD123 include those described below.

[0098] In another general aspect, the invention relates to a method of directing Vβ17-expressing CD8+ or CD4+ T cells to a cancer cell. The methods comprise contacting the Vβ17-expressing CD8+ or CD4+ T cell with a anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof, wherein the antibody or antibody fragment directs the Vβ17-expressing CD8+ or CD4+ T cell to a cancer cell having CD123 on its surface.

[0099] In another general aspect, the invention relates to a method for inhibiting growth or proliferation of cancer cells. The methods comprise contacting the Vβ17-expressing CD8+ T cells with a anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof , wherein contacting the cancer cells with the antibody or antibody fragment inhibits the growth or proliferation of the cancer cells.

[00100] According to embodiments of the invention, the described anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof can be provided in a buffered composition for storage or use. Suitable buffers for the storage of the described anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof would serve to maintain the stability of the antibody or antibody fragment by minimizing deterioration while stored, not promoting aggregation of the antibody or antibody fragment, or minimizing adhesion to the storage vessel.

EMBODIMENTS

[00101] This invention provides the following non-limiting embodiments.

[00102] Embodiment 1 is an isolated Vβ17 bispecific antibody or antigen-binding fragment thereof, the isolated Vβ17 bispecific antibody or antigen-binding fragment thereof comprising:

a. a first heavy chain (HC1);
b. a second heavy chain (HC2);
c. a first light chain (LC1); and
d. a second light chain (LC2),

wherein HC1 is associated with LC1 and HC2 is associated with LC2, and wherein HC1 comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, respectively, and LC1 comprises a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and

SEQ ID NO:6, respectively, to form a binding site for a first antigen, and wherein HC2 and LC2 form a binding site for a second antigen.

[00103] Embodiment 2 is the Vβ17 bispecific antibody or antigen-binding fragment thereof of embodiment 1, wherein the binding site for the first antigen binds to Vβ17 on a CD8+ or CD4+ T cell.

[00104] Embodiment 3 is the Vβ17 bispecific antibody or antigen-binding fragment thereof of embodiment 1 or 2, wherein the binding site for the second antigen binds to a tumor antigen present on the surface of a cancer cell.

[00105] Embodiment 4 is the Vβ17 bispecific antibody or antigen-binding fragment of any one of embodiments 1 to 3, wherein HC1 and LC1 are humanized.

[00106] Embodiment 5 is the Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 4, wherein HC2 and LC2 bind to CD123.

[00107] Embodiment 6 is the Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 5, wherein the bispecific antibody or antigen-binding fragment thereof is a IgG isotype.

[00108] Embodiment 7 is the Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 6, wherein the bispecific antibody or antigen-binding fragment thereof is a IgG4 isotype.

[00109] Embodiment 8 is the Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 7, wherein the bispecific antibody or antigen-binding fragment thereof induces CD8+ or CD4+ T-cell dependent cytotoxicity of a cancer cell *in vitro* with an EC_{50} of less than about 0.2 pM.

[00110] Embodiment 9 is an isolated nucleic acid encoding HC1 and LC1 of the Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 8.

[00111] Embodiment 10 is an isolated nucleic acid encoding HC2 and LC2 of the Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 8.

[00112] Embodiment 11 is a vector comprising the isolated nucleic acid of embodiment 9 or embodiment 10.

[00113] Embodiment 12 is a host cell comprising the vector of embodiment 11.

[00114] Embodiment 13 is a buffered composition comprising the isolated Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 8 and a buffered solution.

[00115] Embodiment 14 is an isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof comprising:

a. a first heavy chain (HC1);
b. a second heavy chain (HC2)
c. a first light chain (LC1); and
d. a second light chain (LC2),

wherein HC1 is associated with LC1 and HC2 is associated with LC2, and wherein HC1 comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, respectively, and LC1 comprises a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6, respectively, to form a binding site for a first antigen that specifically binds Vβ17, and wherein HC2 comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:34, SEQ ID NO:35, and SEQ ID NO:36, respectively, and LC2 comprises a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:37, SEQ ID NO:38, and SEQ ID NO:39, respectively, to form a binding site for a second antigen that specifically binds CD123.

[00116] Embodiment 15 is the isolated anti-Vb17/anti-CD123 bispecific antibody or antigen-binding fragment of embodiment 14, wherein HC1 comprises the amino acid sequence of SEQ ID NO:13 and LC1 comprises the amino acid sequence of SEQ ID NO:14, and wherein HC2 comprises the amino acid sequence of SEQ ID NO:15 and LC2 comprises the amino acid sequence of SEQ ID NO:16.

[00117] Embodiment 16 is the isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of embodiment 14 or embodiment 15, wherein the Vβ17 is on the surface of a CD8+ or CD4+ T cell.

[00118] Embodiment 17 is the isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 14 to 16, wherein the CD123 is on the surface of a cancer cell.

[00119] Embodiment 18 is the isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 14 to 17, wherein bispecific antibody or antigen-binding fragment thereof induces CD8+ or CD4+ T-cell dependent cytotoxicity of a cancer cell in vitro with an EC_{50} of less than about 0.2 pM.

[00120] Embodiment 19 is an isolated nucleic acid encoding the HC1 and LC1 of the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 14 to 18.

[00121] Embodiment 20 is an isolated nucleic acid encoding the HC2 and LC2 of the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 14 to 18.

[00122] Embodiment 21 is a vector comprising the isolated nucleic acid of embodiment 19 or embodiment 20.

[00123] Embodiment 22 is a host cell comprising the vector of embodiment 21.

[00124] Embodiment 23 is a buffered composition comprising the isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 14 to 18 and a buffered solution.

[00125] Embodiment 24 is a method of directing a Vβ17-expressing CD8+ or CD4+ T cell to a cancer cell, the method comprising contacting a Vβ17-expressing CD8+ or CD4+ T cell with the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 8 or 14 to 18, wherein contacting the Vβ17-expressing CD8+ or CD4+ T cell with the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof directs the Vβ17-expressing CD8+ or CD4+ T cell to a cancer cell having CD123 on its surface.

[00126] Embodiment 24(a) is the method of embodiment 24, wherein the Vβ17-expressing CD8+ or CD4+ T cell is contacted with an anti-Vβ17/anti-CD123 bispecific antibody of any one of embodiments 1 to 8 or 14 to 18.

[00127] Embodiment 24(b) is the method of embodiment 24, wherein the Vβ17-expressing CD8+ or CD4+ T cell is contacted with an anti-Vβ17/anti-CD123 bispecific antibody fragment of any one of embodiments 1 to 8 or 14 to 18.

[00128]

[00129] Embodiment 25 is a method for inhibiting growth or proliferation of cancer cells expressing CD123 on its surface, the method comprising contacting the cancer cells with the anti-Vβ17/anti-CD123 bispecific antibody or fragment thereof with any one of embodiments 1 to 8 or 14 to 18, wherein contacting the cancer cells with said antibody or antibody fragment inhibits the growth or proliferation of the cancer cells.

[00130] Embodiment 25(a) is the method of embodiments 25, wherein the CD123-expressing cancer cell is in the presence of a Vβ17-expressing CD8+ T cell while in contact with an anti-Vβ17/anti-CD123 bispecific antibody or fragment thereof.

[00131] Embodiment 25(b) is the method of embodiment 25 or 25(a), wherein the CD123-expressing cancer cell is contacted with an anti-Vβ17/anti-CD123 bispecific antibody of any one of embodiments 1 to 8 or 14 to 18.

[00132] Embodiment 25(c) is the method of embodiment 25 or 25(a), wherein the CD123-expressing cancer cell is contacted with an anti-Vβ17/anti-CD123 bispecific antibody fragment of any one of embodiments 1 to 8 or 14 to 18.

[00133] Embodiment 26 is a kit comprising a Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 8 and packaging for the same.

[00134] Embodiment 27 is a kit comprising an anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 14 to 18 and packaging for the same.

[00135] Embodiment 28 is a method of producing a Vβ17 bispecific antibody or antigen-binding fragment thereof, comprising culturing the host cell of embodiment 12 under conditions to produce the Vβ17 bispecific antibody or antigen-binding fragment thereof, and recovering the Vβ17 bispecific antibody or antigen-binding fragment thereof from the cell or culture.

[00136] Embodiment 29 is a method of producing an anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 14 to 18, comprising culturing the host cell of embodiment 22 under conditions to produce the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof, and recovering the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof from the cell or culture.

[00137] Embodiment 30 is an isolated humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof, the Vβ17 monoclonal antibody or antigen-binding fragment thereof comprising an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:28.

[00138] Embodiment 31 is isolated humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof of embodiment 30, wherein the Vβ17 monoclonal antibody or antigen-binding fragment thereof comprises the amino acid sequence of SEQ ID NO:28.

[00139] Embodiment 32 is an isolated nucleic acid encoding the humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof of embodiment 30 or embodiment 31.

[00140] Embodiment 33 is a vector comprising the isolated nucleic acid of embodiment 32.

[00141] Embodiment 34 is a host cell comprising the vector of embodiment 33.

[00142] Embodiment 35 is a buffered composition comprising the isolated humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof of embodiment 30 or embodiment 31.

EXAMPLES

[00143] The following examples are based on the premise that influenza virus derived peptide M1 is capable of expanding a select set of T cells. These cells express TCR- haplotype-Vβ17 and majority of these cells exhibit efficient cytotoxicity of tumor target cells. This ability is then harnessed using bispecific antibodies constructed such that one arm binds to the Vβ17 structure and the other arm binds to an antigen expressed by the cancer cells. Thus, the bispecific antibody bridges the effector and target cells together- resulting in cancer cell killing. This mechanism of action is described in the schematic outlined in FIG. 1.

[00144] The subsequent examples can be divided into the following categories: (1) Generation of bispecific antibodies capable of binding to the Vβ17 arm of T-cell receptors (TCR) on CTL (Examples 1 and 2); and (2) Evidence for bispecific antibody-enabled target cell killing by CTL expanded *in vitro* (Example 3).

[00145] Example 1: Human Framework Adaptation of anti-Vβ17 mAb E17.5F

[00146] The mouse IgG1 anti-human T cell receptor Vβ17 clone E17.5F was obtained from BeckmanCoulter, Inc. (Brea, CA). Sample preparation and LC/MSMS analysis were performed at Protea Bioscience Inc. (Morgantown, WV). The sample was reduced and alkylated, divided into seven aliquots, and proteolytically digested with Trypsin/LysC, Chymotrypsin, LysC, Pepsin, and AspN, Elastase, and Proteinase K enzymes. Resulting peptides were desalted using a ZipTip C18 Pipette Tips and separated on-line using reverse phase chromatography. Mass spectrometry was performed on Thermo Q-Exactive spectrometer using HCD fragmentation. MS data sets were analyzed using PEAKS software by matching *de novo* sequence tags to an IMGT-based antibody sequences database. Gaps in the sequence were assigned using Contig sequence assembly of *de novo* identified peptides. All CDRs and hyper-mutations were confirmed by inspecting the MS/MS spectra

[00147] The sequences obtained are shown in Tables 1 and 2.

[00148] Table 1: CDR Sequences of TCR Vβ17 clone E17.5F.

Antibody	**HCDR1**	**SEQ ID NO:**	**HCDR2**	**SEQ ID NO:**	**HCDR3**	**SEQ ID NO:**
E17.5F	GYSITSGYFWN	1	YISYDGSNN	2	PSPGTGYAVDY	3
Antibody	**LCDR1**	**SEQ ID NO:**	**LCDR2**	**SEQ ID NO:**	**LCDR3**	**SEQ ID NO:**
E17.5F	RSSQSLVHSNGNTYLH	4	KVSNRFS	5	SQSTHVPFT	6

[00149] Table 2: Heavy chain and light chain sequences of TCR Vb17 clone E17.5F.

mAb ID	**Heavy Chain Amino Acid Sequence**	**SEQ ID NO:**
B17B01	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFWNWIRQFPGNKLEWMGYISYDGSNNYNPSLKNRISITRDTSKNQFFLKLNSVTTEDTATYYCASPSPGTGYAVDYWGQGTSVTVSSAKTTPPSVYPLAPGSAAQTNSMVTLGCLVKGYFPEPVTVTWNSGSLSSGVHTFPAVLQSDLYTLSSSVTVPSSTWPSQTVTCNVAHPASSTKVDKKIVPRDCGCKPCICTVPEVSSVFIFPPKPKDVLTITLTPKVTCVVVDISKDDPEVQFSWFVDDVEVHTAQTKPREEQINSTFRSVSELPIMHQDWLNGKEFKCRVNSAAFPAPIEKTISKTYGRPKAPQVYTIPPPKEQMAKDKVSLTCMITNFFPEDITVEWQWNGQPAENYKNTQPIMDTDGSYFVYSKLNVQKSNWEAGNTFTCSVLHEG	7

	LHNHHTEKSLSHSPGK	
	Light Chain Amino Acid Sequence	**SEQ ID NO:**
B17B01	NVVMTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKFLIYKVSNRFSGVPDRFSGGGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFTFGSGTKLEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC	8

[00150] Changes were made in the sequences for the preparation of bispecific antibodies (Table 3). The changes include the following: (1) a framework mutation Asn1 of the heavy chain was not conserved, so the sequence has been modified to have the DVQLW sequence; (2) another mutation identified in the Fc, K337Y, was deemed uncharacteristic, and, thus, a construct without this mutation was synthesized; and (3) a potential secondary glycosylation site on the heavy chain was observed, and, thus, two versions of this mAb with and without the N-linked site (N82a, based on Chothia numbering) were synthesized.

[00151] Table 3: Heavy and Light Chain sequences for Vβ17 clone E17.5F antibody variants

mAb ID	**Heavy Chain Amino Acid Sequence**	**SEQ ID NO:**
B17B1	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFWNWIRQFPGNKLEWMGYISYDGSNNYNPSLKNRISITRDTSKNQFFLKLNSVTTEDTATYYCASPSPGTGYAVDYWGQGTSVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFLLYSKLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK	9
B17B2	DVQLKESGPGLVKPSQSLSVTCSVTGYSITSGYYWNWYRQFPGNKLEWMGYISYDGSNNYNPSLKNRISITRDTSKNQILLKLTYVTTEDTATYYCTRPSPGTGYAVDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFLLYSKLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK	11
	Light Chain Amino Acid Sequence	**SEQ ID NO:**
B17B1	NVVMTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKFLIYKVSNRFSGVPDRFSGGGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFTFGSGTKLEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC	10
B17B2	DIVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCSQSTHVPFTFGQGTKVEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC	12

[00152] The two antibodies (B17B1 and B17B2) were expressed in HEK293Expi cells. The supernatants were tested for Vβ17 binding (B17B1 and B17B2) and only B17B1 demonstrated binding. Thus, B17B1 was expressed having an IgG4 constant region with Fc substitutions.

[00153] The anti-human TCR Vβ17 mouse mAb B17B1 was humanized using the Human Framework Adaptation (HFA) method (Fransson J, et al. *J. Mol. Biol.* 2010; 398:214-231). To find the best combination of humanized heavy and light chains, several human V-region sequences were selected for testing (Table 4). Selection of human germlines was based solely on the overall sequence similarity to the mouse antibody in the framework (FR) region. Neither the CDR sequences, nor their length or canonical structures, were considered in this selection.

[00154] The CDR definition used in HFA is described in (Fransson J, et al. *J. Mol. Biol.* 2010; 398:214-231) and corresponds to the Martin's definition (Abhinandan KR and Martin AC. *Mol. Immunol.* 2008; 45:3832-3839). The CDRs (Table 1) were defined as described below (using the Chothia numbering scheme [Chothia C, and Lesk A. *J. Mol. Biol.* 1987; 196:901-917]):

HCDR1 (SEQ ID NO: 1)	26-35
HCDR2 (SEQ ID NO: 2)	50-58
HCDR3 (SEQ ID NO: 3)	95-102
LCDR1 (SEQ ID NO: 4)	24-34
LCDR2 (SEQ ID NO: 5)	50-56
LCDR3 (SEQ ID NO: 6)	89-97

[00155] The selected human germlines are provided in Table 4 (in the IMGT notation).

[00156] Table 4: VH and VL variants

Ab VH	**Sequence**	**SEQ ID NO:**
B17H1	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFWNWIRQFPGNKLEWMGYISYDGSNNYNPSLKNRISITRDTSKNQFFLKLNSVTTEDTATYYCASPSPGTGYAVDYWGQGTSVTVSS	25
B17H3	EVQLLESGGGLVQPGGSLRLSCAASGYSITSGYFWNWVRQAPGKGLEWVSYISYDGSNNYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKPSPGTGYAVDYWGQGTLVTVSS	19
B17H4	EVQLLESGGGLVQPGGSLRLSCAASGYSITSGYFWNWVRQAPGKGLEWVSYISYDGSNNYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASPSPGTGYAVDYWGQGTLVTVSS	20
B17H5	QVQLQESGPGLVKPSETLSLTCTVSGYSITSGYFWNWIRQPPGKGLEWIGYISYDGSNNYNPSLKSRVTISRDTSKNQFSLKLSSVTAADTAVYYCASPSPGTGYAVDYWGQGTLVTVSS	21
Ab VL	**Sequence**	**SEQ ID NO:**
B17L1	NVVMTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKFLIYKVSNRFSGVPDRFSGGGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFTFGSGTKLEIK	26
B17L3	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGNTYLHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPFTFGQGTKLEIK	22

B17L4	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGNTYLHWYQQKPGKAPKFLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPFTFGQGTKLEIK	23
B17L5	DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRFLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPFTFGQGTKLEIK	24

CDRs1-3 are underlined

[00157] "Back mutations" in several variants were introduced at FR positions that are known to be important for VL/VH pairing and CDR conformation. The selected human germlines are provided in Table 5 (in the IMGT notation), with the back mutations noted.

[00158] Table 5: The selected J-regions

J-region	**Sequence**	**SEQ ID NO:**
IGHJ1*01 HC	WGQGTLVTVSS	42
IGKJ2*01 LC	FGQGTKLEIK	43

[00159] Amino acid sequences of all nine pairwise combinations of three heavy chains and three light chains were back-translated to DNA, and cDNA was prepared using gene synthesis techniques (U.S. Pat. No. 6,670,127; U.S. Pat. No. 6,521,427). Heavy chain (HC) variable regions were subcloned onto human IgG4 constant region using an in-house expression vector with the CMV promoter using standard molecular biology techniques. Light chain (LC) variable regions were subcloned onto a human Lambda (λ) constant regions using an in-house expression vector with the CMV promoter using standard molecular biology techniques. Resulting plasmids were transfected into HEK EXPI cells (LifeTechnologies; Carlsbad, CA) and mAbs were expressed. Purification was by standard methods using a Protein A column (hiTrap MAbSelect SuRe column). After elution, the pools were dialyzed into D-PBS, pH 7.2.

[00160] Table 6**:** Heavy and Light chains of nine humanized Vβ17 antibodies

mAb	**Hc**	**SEQ ID NO:**	**Lc**	**SEQ ID NO:**	**Concentration (μg/mL)**
B17B14	B17H3	19	B17L3	22	686.3
B17B15	B17H3	19	B17L4	23	13.8
B17B16	B17H3	19	B17L5	24	14.6
B17B17	B17H4	20	B17L3	22	335.1
B17B18	B17H4	20	B17L4	23	45.2
B17B19	B17H4	20	B17L5	24	27.5
B17B20	B17H5	21	B17L3	22	602.1
B17B21	B17H5	21	B17L4	23	570.9
B17B22	B17H5	21	B17L5	24	320.5

[00161] The humanized antibodies were screened for binding to a TCRVβ17 (SEQID NO:27)/Va10.2-Fc (SEQ ID NO:44) fusion protein by ELISA. Biotinylated TCRVβ17/Va10.2-

Fc fusion protein was added to a streptavidin-coated ELISA plate. Unbound protein was washed away and mAb was added at a range of concentrations (0.01-10 µg/mL). Plates were washed and anti-kappa:HRP detection antibody was added. Plates were washed, chemiluminescent detection reagent was added, and the plates were read on a Perkin Elmer EnVision plate reader for luminescence. B17B20 and B17B21 showed positive binding to the TCR-Vβ17 protein. B17B22 showed weak binding to this protein. These antibodies were then purified as described above for further studies. B17B21 demonstrated the best binding to recombinant TCR-Vβ17 protein and to M1-stimulated T-cells and was thus chosen as the molecule for further functional studies, specifically T-cell re-directed cancer cell killing as a bispecific antibody.

[00162] Thus, the variable region sequence of B17B21 (anti-Vβ17) and I3RB217 (anti-CD123 antibody) was used to generate a bispecific antibody to be tested for T-cell re-directed killing of acute myeloid leukemia (AML) cells.

[00163] Example 2. Preparation of anti-Vβ17/anti-CD123 bispecific antibodies

[00164] VB11 (anti-Vβ17/anti-CD123) and VB13 (Vβ17 x Null) bispecific antibodies were produced as full-length antibodies in the knob-into-hole format as human IgG4, as previously described (Atwell et al. J. Mol. Biol. 270: 26-35, 1997). Nucleic acid sequences encoding variable regions were subcloned into a custom mammalian expression vectors containing constant region of IgG4 expression cassettes using standard PCR restriction enzyme based cloning techniques. The bispecific antibodies were expressed by transient transfection in Chinese hamster ovary cell line. The antibodies were initially purified by Mab Select SuRe Protein A column (GE healthcare, Piscataway, New Jersey) (Brown, Bottomley et al. 1998). The column was equilibrated with Phosphate Buffer Saline (PBS), pH 7.2 and loaded with fermentation supernatant at a flow rate of 2 mL/min. After loading, the column was washed with PBS (4 CV) followed by elution in 30 mM sodium acetate, pH 3.5. Fractions containing protein peaks as monitored by Absorbance at 280 nm in Akta Explorer (GE healthcare) were pooled together and were neutralized to pH 5.0 by adding 1% of 3M sodium acetate, pH 9.0. As a polishing step, the antibodies were purified on a preparative size exclusion chromatography (SEC) using a Superdex 200 column (GE healthcare). The integrity of the sample was assessed by endotoxin measurement and SDS polyacrylamide gel electrophoresis under reducing and non-reducing conditions. The final protein concentrations were 0.48 mg/ml for anti-Vβ17/anti-CD123 and 0.24 mg/mL for Vβ17 x Null. The final EU levels of anti-Vβ17/anti-CD123 and Vβ17 x Null based on these protein concentrations were 2.053 EU/mg and 4.219 EU/mg, respectively.

[00165] Table 7: Sequences of half antibodies expressed in CHO cells

mAb ID	'Knob' arm and 'hole' arm amino acid sequence	SEQ ID NO:

B17B21 (Vβ17 half Ab)	MAWVWTLLFLMAAAQSIQADIQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGNTYLHWYQQKPGKAPKFLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECGGSEGKSSGSGSESKSTEGKSSGSGSESKSTGGSQVQLQESGPGLVKPSETLSLTCTVSGYSITSGYFWNWIRQPPGKGLEWIGYISYDGSNNYNPSLKSRVTISRDTSKNQFSLKLSSVTAADTAVYYCASPSPGTGYAVDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSRLTVDKSRWQEGNVFSCSVMHEALHNRFTQKSLSLSLGK	28
I3RB217 (CD123 half Ab)	MAWVWTLLFLMAAAQSIQAEIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQDYGFPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECGGSEGKSSGSGSESKSTEGKSSGSGSESKSTGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVRQMPGKGLEWMGIIDPSDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARGDGSTDLDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK	30
B23B49 (Null half Ab)	MAWVWTLLFLMAAAQSIQAEIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQDYGFPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECGGSEGKSSGSGSESKSTEGKSSGSGSESKSTGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVRQMPGKGLEWMGIIDPSDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARGDGSTDLDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK	
	Half Antibody DNA sequence	
B17B21 (Vβ17 half Ab)	ATGGCCTGGGTGTGGACCCTGCTGTTCCTGATGGCCGCCGCCCAGAGCATCCAGGCCGACATCCAGATGACCCAGAGCCCAAGCAGCCTGAGCGCCAGCGTGGGCGACCGCGTGACCATCACCTGCCGCAGCAGCCAGAGCCTGGTGCACAGCAACGGCAACACCTACCTGCACTGGTACCAGCAGAAGCCAGGCAAGGCCCCAAAGTTCCTGATCTACAAGGTGAGCAACCGCTTCAGCGGCGTGCCAAGCCGCTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCAGAGGACTTCGCCACCTACTACTGCAGCCAGAGCACCCACGTGCCATTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAGCGCACCGTGGCCGCCCCAAGCGTGTTCATCTTCCCACCAAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCACGCGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACCGAGCAGGACAGCAAGGACAGCACCTACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACTACGAGAAGCACAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGAGCAGCCCAGTGACCAAGAGCTTCAACCGCGGCGAGTGCGGCGGCAGCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGGCGGCAGCCAGGTGCAGCTGCAGGAGAGCGGCCCAGGCCTGGTGAAGCCAAGCGAGACCCTGAGCCTGACCTGCACCGTGAGCGGCTACAGCATCACCAGCGGCTACTTCTGGAACTG	29

	GATCCGCCAGCCACCAGGCAAGGGCCTGGAGTGGATCGGCTACATCAGC TACGACGGCAGCAACAACTACAACCCAAGCCTGAAGAGCCGCGTGACCA TCAGCCGCGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGT GACCGCCGCCGACACCGCCGTGTACTACTGCGCCAGCCCAAGCCCAGGC ACCGGCTACGCCGTGGACTACTGGGGCCAGGGCACCCTGGTGACCGTGA GCAGCGCCAGCACCAAGGGCCCAAGCGTGTTCCCACTGGCCCCATGCAG CCGCAGCACCAGCGAGAGCACCGCCGCCCTGGGCTGCCTGGTGAAGGAC TACTTCCCAGAGCCAGTGACCGTGAGCTGGAACAGCGGCGCCCTGACCA GCGGCGTGCACACCTTCCCAGCCGTGCTGCAGAGCAGCGGCCTGTACAG CCTGAGCAGCGTGGTGACCGTGCCAAGCAGCAGCCTGGGCACCAAGACC TACACCTGCAACGTGGACCACAAGCCAAGCAACACCAAGGTGGACAAG CGCGTGGAGAGCAAGTACGGCCCACCATGCCCACCATGCCCAGCCCCAG AGGCCGCCGGCGGCCCAAGCGTGTTCCTGTTCCCACCAAAGCCAAAGGA CACCCTGATGATCAGCCGCACCCCAGAGGTGACCTGCGTGGTGGTGGAC GTGAGCCAGGAGGACCCAGAGGTGCAGTTCAACTGGTACGTGGACGGCG TGGAGGTGCACAACGCCAAGACCAAGCCACGCGAGGAGCAGTTCAACA GCACCTACCGCGTGGTGAGCGTGCTGACCGTGCTGCACCAGGACTGGCT GAACGGCAAGGAGTACAAGTGCAAGGTGAGCAACAAGGGCCTGCCAAG CAGCATCGAGAAGACCATCAGCAAGGCCAAGGGCCAGCCACGCGAGCC ACAGGTGTACACCCTGCCACCAAGCCAGGAGGAGATGACCAAGAACCA GGTGAGCCTGAGCTGCGCCGTGAAGGGCTTCTACCCAAGCGACATCGCC GTGGAGTGGGAGAGCAACGGCCAGCCAGAGAACAACTACAAGACCACC CCACCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGGTGAGCCGCCTGA CCGTGGACAAGAGCCGCTGGCAGGAGGGCAACGTGTTCAGCTGCAGCGT GATGCACGAGGCCCTGCACAACCGCTTCACCCAGAAGAGCCTGAGCCTG AGCCTGGGCAAGATGGCCTGGGTGTGGACCCTGCTGTTCCTGATGGCCG CCGCCCAGAGCATCCAGGCCGACATCCAGATGACCCAGAGCCCAAGCAG CCTGAGCGCCAGCGTGGGCGACCGCGTGACCATCACCTGCCGCAGCAGC CAGAGCCTGGTGCACAGCAACGGCAACACCTACCTGCACTGGTACCAGC AGAAGCCAGGCAAGGCCCCAAAGTTCCTGATCTACAAGGTGAGCAACCG CTTCAGCGGCGTGCCAAGCCGCTTCAGCGGCAGCGGCAGCGGCACCGAC TTCACCCTGACCATCAGCAGCCTGCAGCCAGAGGACTTCGCCACCTACTA CTGCAGCCAGAGCACCCACGTGCCATTCACCTTCGGCCAGGGCACCAAG CTGGAGATCAAGCGCACCGTGGCCGCCCCAAGCGTGTTCATCTTCCCACC AAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTG AACAACTTCTACCCACGCGAGGCCAAGGTGCAGTGGAAGGTGGACAACG CCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACCGAGCAGGACAGCA AGGACAGCACCTACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGA CTACGAGAAGCACAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTG AGCAGCCCAGTGACCAAGAGCTTCAACCGCGGCGAGTGCGGCGGCAGC GAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGAGGGC AAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGGCGGCAGCCAG GTGCAGCTGCAGGAGAGCGGCCCAGGCCTGGTGAAGCCAAGCGAGACC CTGAGCCTGACCTGCACCGTGAGCGGCTACAGCATCACCAGCGGCTACT TCTGGAACTGGATCCGCCAGCCACCAGGCAAGGGCCTGGAGTGGATCGG CTACATCAGCTACGACGGCAGCAACAACTACAACCCAAGCCTGAAGAGC CGCGTGACCATCAGCCGCGACACCAGCAAGAACCAGTTCAGCCTGAAGC TGAGCAGCGTGACCGCCGCCGACACCGCCGTGTACTACTGCGCCAGCCC AAGCCCAGGCACCGGCTACGCCGTGGACTACTGGGGCCAGGGCACCCTG GTGACCGTGAGCAGCGCCAGCACCAAGGGCCCAAGCGTGTTCCCACTGG CCCCATGCAGCCGCAGCACCAGCGAGAGCACCGCCGCCCTGGGCTGCCT GGTGAAGGACTACTTCCCAGAGCCAGTGACCGTGAGCTGGAACAGCGGC GCCCTGACCAGCGGCGTGCACACCTTCCCAGCCGTGCTGCAGAGCAGCG GCCTGTACAGCCTGAGCAGCGTGGTGACCGTGCCAAGCAGCAGCCTGGG CACCAAGACCTACACCTGCAACGTGGACCACAAGCCAAGCAACACCAAG GTGGACAAGCGCGTGGAGAGCAAGTACGGCCCACCATGCCCACCATGCC CAGCCCCAGAGGCCGCCGGCGGCCCAAGCGTGTTCCTGTTCCCACCAAA GCCAAAGGACACCCTGATGATCAGCCGCACCCCAGAGGTGACCTGCGTG GTGGTGGACGTGAGCCAGGAGGACCCAGAGGTGCAGTTCAACTGGTACG TGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCACGCGAGGAGC AGTTCAACAGCACCTACCGCGTGGTGAGCGTGCTGACCGTGCTGCACCA GGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGAGCAACAAGGG	

	CCTGCCAAGCAGCATCGAGAAGACCATCAGCAAGGCCAAGGGCCAGCCACGCGAGCCACAGGTGTACACCCTGCCACCAAGCCAGGAGGAGATGACCAAGAACCAGGTGAGCCTGAGCTGCGCCGTGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCAGAGAACAACTACAAGACCACCCCACCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGGTGAGCCGCCTGACCGTGGACAAGAGCCGCTGGCAGGAGGGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGCCCTGCACAACCGCTTCACCCAGAAGAGCCTGAGCCTGAGCCTGGGCAAGTGATAG	
I3RB217 (CD123 half Ab)	ATGGCCTGGGTGTGGACCCTGCTGTTCCTGATGGCCGCCGCCCAGAGCATCCAGGCCGAGATCGTGCTGACCCAGAGCCCAGGCACCCTGAGCCTGAGCCCAGGCGAGCGCGCCACCCTGAGCTGCCGCGCCAGCCAGAGCGTGAGCAGCAGCTACCTGGCCTGGTACCAGCAGAAGCCAGGCCAGGCCCCACGCCTGCTGATCTACGGCGCCAGCAGCCGCGCCACCGGCATCCCAGACCGCTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCCGCCTGGAGCCAGAGGACTTCGCCGTGTACTACTGCCAGCAGGACTACGGCTTCCCATGGACCTTCGGCCAGGGCACCAAGGTGGAGATCAAGCGCACCGTGGCCGCCCCAAGCGTGTTCATCTTCCCACCAAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCACGCGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACCGAGCAGGACAGCAAGGACAGCACCTACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACTACGAGAAGCACAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGAGCAGCCCAGTGACCAAGAGCTTCAACCGCGGCGAGTGCggcggcagcgagggcaagagcagcggcagcggcagcgagagcaagagcaccgagggcaagagcagcggcagcggcagcgagagcaagagcaccggcggcagcGAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCAGGCGAGAGCCTGAAGATCAGCTGCAAGGGCAGCGGCTACAGCTTCACCAGCTACTGGATCAGCTGGGTGCGCCAGATGCCAGGCAAGGGCCTGGAGTGGATGGGCATCATCGACCCAAGCGACAGCGACACCCGCTACAGCCCAAGCTTCCAGGGCCAGGTGACCATCAGCGCCGACAAGAGCATCAGCACCGCCTACCTGCAGTGGAGCAGCCTGAAGGCCAGCGACACCGCCATGTACTACTGCGCCCGCGGCGACGGCAGCACCGACCTGGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGCGCCAGCACCAAGGGCCCAAGCGTGTTCCCACTGGCCCCATGCAGCCGCAGCACCAGCGAGAGCACCGCCGCCCTGGGCTGCCTGGTGAAGGACTACTTCCCAGAGCCAGTGACCGTGAGCTGGAACAGCGGCGCCCTGACCAGCGGCGTGCACACCTTCCCAGCCGTGCTGCAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGGTGACCGTGCCAAGCAGCAGCCTGGGCACCAAGACCTACACCTGCAACGTGGACCACAAGCCAAGCAACACCAAGGTGGACAAGCGCGTGGAGAGCAAGTACGGCCCACCATGCCCACCATGCCCAGCCCCAGAGGCCGCCGGCGGCCCAAGCGTGTTCCTGTTCCCACCAAAGCCAAAGGACACCCTGATGATCAGCCGCACCCCAGAGGTGACCTGCGTGGTGGTGGACGTGAGCCAGGAGGACCCAGAGGTGCAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCACGCGAGGAGCAGTTCAACAGCACCTACCGCGTGGTGAGCGTGCTGACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGAGCAACAAGGGCCTGCCAAGCAGCATCGAGAAGACCATCAGCAAGGCCAAGGGCCAGCCACGCGAGCCACAGGTGTACACCCTGCCACCAAGCCAGGAGGAGATGACCAAGAACCAGGTGAGCCTGTGGTGCCTGGTGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCAGAGAACAACTACAAGACCACCCCACCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGTACAGCCGCCTGACCGTGGACAAGAGCCGCTGGCAGGAGGGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCCTGAGCCTGAGCCTGGGCAAG	31
B23B49 (Null half Ab)	ATGGCCTGGGTGTGGACCCTGCTGTTCCTGATGGCCGCCGCCCAGAGCATCCAGGCCGACATCGTGATGACCCAGAGCCCAGACAGCCTGGCCGTGAGCCTGGGCGAGCGCGCCACCATCAACTGCCGCGCCAGCCAGAGCGTGGACTACAACGGCATCAGCTACATGCACTGGTACCAGCAGAAGCCAGGCCAGCCACCAAAGCTGCTGATCTACGCCGCCAGCAACCCAGAGAGCGGCGTGCCAGACCGCTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGGCCGAGGACGTGGCCGTGTACTACTGCCAGCAGATCATCGAGGACCCATGGACCTTCGGCCAGGGCACCAAGGTGGAGATCAAGCGCACCGTGGCCGCCCCAAGCGTGTTCATCTTCCCACCAAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTGAACAACTTCTACCC	

	ACGCGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACCGAGCAGGACAGCAAGGACAGCACCTACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACTACGAGAAGCACAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGAGCAGCCCAGTGACCAAGAGCTTCAACCGCGGCGAGTGCGGCGGCAGCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGGCGGCAGCCAGATCACCCTGAAGGAGAGCGGCCCAACCCTGGTGAAGCCAACCCAGACCCTGACCCTGACCTGCACCTTCAGCGGCTTCAGCCTGAGCACCAGCGGCATGGGCGTGAGCTGGATCCGCCAGCCACCAGGCAAGGCCCTGGAGTGGCTGGCCCACATCTACTGGGACGACGACAAGCGCTACAACCCAAGCCTGAAGAGCCGCCTGACCATCACCAAGGACACCAGCAAGAACCAGGTGGTGCTGACCATGACCAACATGGACCCAGTGGACACCGCCACCTACTACTGCGCCCGCCTGTACGGCTTCACCTACGGCTTCGCCTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGCGCCAGCACCAAGGGCCCAAGCGTGTTCCCACTGGCCCCATGCAGCCGCAGCACCAGCGAGAGCACCGCCGCCCTGGGCTGCCTGGTGAAGGACTACTTCCCAGAGCCAGTGACCGTGAGCTGGAACAGCGGCGCCCTGACCAGCGGCGTGCACACCTTCCCAGCCGTGCTGCAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGGTGACCGTGCCAAGCAGCAGCCTGGGCACCAAGACCTACACCTGCAACGTGGACCACAAGCCAAGCAACACCAAGGTGGACAAGCGCGTGGAGAGCAAGTACGGCCCACCATGCCCACCATGCCCAGCCCCAGAGGCCGCCGGCGGCCCAAGCGTGTTCCTGTTCCCACCAAAGCCAAAGGACACCCTGATGATCAGCCGCACCCCAGAGGTGACCTGCGTGGTGGTGGACGTGAGCCAGGAGGACCCAGAGGTGCAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCACGCGAGGAGCAGTTCAACAGCACCTACCGCGTGGTGAGCGTGCTGACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGAGCAACAAGGGCCTGCCAAGCAGCATCGAGAAGACCATCAGCAAGGCCAAGGGCCAGCCACGCGAGCCACAGGTGTACACCCTGCCACCAAGCCAGGAGGAGATGACCAAGAACCAGGTGAGCCTGTGGTGCCTGGTGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCAGAGAACAACTACAAGACCACCCCACCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGTACAGCCGCCTGACCGTGGACAAGAGCCGCTGGCAGGAGGGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCCTGAGCCTGAGCCTGGGCAAG	

[00166] Table 8: Heavy and Light Chain Sequences for Vβ17 bispecific antibodies

Bispecific Antibody		**Amino Acid Sequence**
Anti-Vβ17/ anti-CD123	Heavy chain 1 B17B21 (SEQ ID NO: 13)	QVQLQESGPGLVKPSETLSLTCTVSGYSITSGYFWNWIRQPPGKGLEWIGYISYDGSNNYNPSLKSRVTISRDTSKNQFSLKLSSVTAADTAVYYCASPSPGTGYAVDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSRLTVDKSRWQEGNVFSCSVMHEALHNRFTQKSLSLSLGK
	Light Chain 1 B17B21 (SEQ ID NO: 14)	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGNTYLHWYQQKPGKAPKFLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	Heavy chain 2 I3RB217 (SEQ ID NO: 15)	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVRQMPGKGLEWMGIIDPSDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARGDGSTDLDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALT

		SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
	Light Chain 2 I3RB217 (SEQ ID NO: 16)	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQDYGFPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
Vβ17 x Null	Heavy chain 1 B17B21 (SEQ ID NO: 13)	QVQLQESGPGLVKPSETLSLTCTVSGYSITSGYFWNWIRQPPGKGLEWIGYISYDGSNNYNPSLKSRVTISRDTSKNQFSLKLSSVTAADTAVYYCASPSPGTGYAVDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSRLTVDKSRWQEGNVFSCSVMHEALHNRFTQKSLSLSLGK
	Light Chain 1 B17B21 (SEQ ID NO: 14)	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGNTYLHWYQQKPGKAPKFLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	Heavy chain 2 Null (SEQ ID NO: 17)	QITLKESGPTLVKPTQTLTLTCTFSGFSLSTSGMGVSWIRQPPGKALEWLAHIYWDDDKRYNPSLKSRLTITKDTSKNQVVLTMTNMDPVDTATYYCARLYGFTYGFAYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
	Light Chain 2 Null (SEQ ID NO: 18)	DIVMTQSPDSLAVSLGERATINCRASQSVDYNGISYMHWYQQKPGQPPKLLIYAASNPESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQIIEDPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

[00167] Example 3. Evaluation of binding and cytotoxic properties of anti-Vβ17/ anti-CD123 bispecific antibody using Kasumi-3 cells and human CD8$^+$ T cells

[00168] ***Stimulation and expansion of Vβ17$^+$ CD8$^+$ T cells from total PBMCs***

[00169] To expand Vβ17$^+$ CD8$^+$ T cells, whole PBMCs from HLA-A2 donor (HPU-08694) were stimulated with 1 μg/mL FLU MP 58 peptide (in DMSO). Frequency of Vβ17$^+$ cells among total CD8$^+$ T cells was determined on day 8 and 14 of the culture period. To enumerate the frequency of Vβ17$^+$ cells among total CD8$^+$ T cells, total live PBMCs were initially gated,

doublets were excluded, total $CD8^+$ T cells were gated and then $V\beta17^+$ cells were gated (FIG. 3A). Compared to the frequency of $V\beta17^+$ cells among total $CD8^+$ T cells on day 0, a substantial expansion of these cells were observed at day 8 of the culture period (FIG. 3B). A larger fraction of $CD8^+$ T cells on day 8 were $V\beta17^+$ cells (FIG. 3B) in this donor.

[00170] ***anti-Vβ17/anti-CD123 bispecific antibody binding assay***

[00171] On Kasumi-3 cells

[00172] To understand the binding kinetics of the anti-Vβ17/anti-CD123 bispecific antibody, Kasumi-3 cells were incubated with the anti-Vβ17/anti-CD123 bispecific antibody and Vβ*17XNULL* arm control at various concentrations (concentration range from 5 μg/mL to 0 μg/mL). Cell bound bispecific antibody was detected with mouse anti-human IgG4 Fc-PE secondary antibody. Table 9 shows the frequency of Kasumi-3 cells positive for PE (secondary antibody) when treated with different concentration of bispecific antibodies. The EC_{50} for anti-Vβ17/anti-CD123 and NULLXCD123 was determined as 6 and 42.7 nM respectively (Table 9).

[00173] Table 9: Binding affinity of Kasumi-3 cells for bispecific antibodies.

Conc.(ug/mL)	**anti-Vβ17/ anti-CD123**	**Vβ17XNULL**	**NULLXCD123**
5	87.37	-0.02	47.47
1.667	74.37	0.09	16.37
0.556	24.07	0.15	1.2
0.185	1.65	0.35	0.31
0.062	0.32	0.12	0.04
0.021	0.16	0.14	0.05
0.007	0.23	0.19	-0.06
0.002	0.04	-0.09	-0.04
0.001	0.09	0	-0.18
EC_{50} (μg/mL)	0.9	ND	6.4
EC_{50} (nM)	6	ND	42.7

[00174] Bispecific antibody binding affinities to Kasumi-3 cells were determined by flow cytometry. Half maximal effective concentration (EC_{50}) values were calculated as the bispecific concentration that generates 50% of maximal Binding (PE positive cells). ND: Not determined.

[00175] On enriched $CD8^+$ T cells

[00176] Enriched FLU MP 58 peptide stimulated $CD8^+$ T (from day 14 culture) cells were incubated with various concentrations of anti-Vβ17/anti-CD123 bispecific and Vβ17XNULL arm control antibodies. Mouse anti-human IgG4 Fc-PE secondary antibody was used to detect the bispecific antibody. Table 10 shows the frequency of $CD8^+$ T cells positive for PE (secondary antibody) when treated with different concentration of bispecific antibodies. The

EC_{50} for anti-Vβ17/anti-CD123, Vβ17XNULL, was determined as 9.0 nm, 18.7 nm respectively (Table 10).

[00177] Table 10: Binding activity of $CD8^+$ T cell for bispecific antibodies.

Conc.(μg/mL)	anti-Vβ17/ anti-CD123	Vβ17XNULL	NULLXCD123
20	74.7	76.2	0.1
10	72.4	75.4	0.4
5	70.8	64.6	0.3
2.5	64.8	42.5	0.5
1.25	38.0	32.4	0.4
0.625	41.4	21.7	-0.1
0.3125	26.5	11.8	0.8
0.15625	19.9	3.4	0.6
0.078125	10.8	1.8	0.7
EC_{50} (μg/mL)	1.35	2.80	ND
EC_{50} (nM)	9	18.7	ND

[00178] Bispecific antibody binding affinities to $CD8^+$ T cell were determined by flow cytometry. Half maximal effective concentration (EC_{50}) values were calculated as the antibody concentration that generates 50% of the maximal binding (PE positive cells). ND: Not Determined

[00179] ***Bispecific mediated cytotoxicity assay***

[00180] In order to analyze the potency of the anti-Vβ17/anti-CD123 bispecific antibody mediated cytotoxicity, CFSE labelled target (Kasumi-3) cells were co-cultured with stimulated $CD8^+$ T cells (effectors) from day 14 of culture at an effector to target (ET) ratio 0.5:1, 1:1, 5:1 for 14 and 24 hours with various concentrations of anti-Vβ17/anti-CD123 bispecific and Vβ17XNULL arm control antibody. CD123 expression on target Kasumi-3 cells were checked by using a commercially available anti-CD123 antibody. Target cells (Kasumi-3) were labelled with CFSE to identify them as $CFSE^+$ during flow cytometry analysis. Post co-culture period, 7-AAD was added to analyze the percentage of 7-AAD^+ $CFSE^+$ cells as a measure of cytotoxicity. Basal cytotoxicity observed in the absence of bispecific antibody was subtracted to obtain specific cytotoxicity in response to bispecific antibody. The assay was performed once with a single donor (HPU-08694). The EC_{50} for the anti-Vβ17/anti-CD123 bispecific antibody at 0.5:1, 1:1 and 5:1 ET ratios for 14-hour time point were 3.7, 0.1 and 0.133 pM respectively (Table 11).

[00181] Table 11: Summary of EC_{50} values for various bispecific antibodies upon co-culturing FLU MP 58 peptide stimulated $CD8^+$ T cell with Kasumi-3 cells at ET ratios 0.5:1, 1:1 and 5:1 for 14 hours.

	EC_{50} (ng/mL)		
Bispecific Ab	**E:T Ratio**	**E:T Ratio**	**E:T Ratio**

	(0.5:1)	**(1:1)**	**(5:1)**
NULLXCD123	**UD**	**UD**	**UD**
Vβ17XNULL	**UD**	**UD**	**UD**
Anti-Vβ17/anti-CD123	**0.55**	**0.015**	**0.02**

Bispecific Ab	**EC_{50} (pM)**		
	E:T Ratio (0.5:1)	**E:T Ratio (1:1)**	**E:T Ratio (5:1)**
NULLXCD123	**UD**	**UD**	**UD**
Vβ17XNULL	**UD**	**UD**	**UD**
anti-Vβ17/anti-CD123	**3.7**	**0.1**	**0.133**

UD: Undetectable, as the activity was too low for proper curve fitting.

[00182] The EC_{50} for the anti-Vβ17/anti-CD123 bispecific at 0.5:1,1:1 and 5:1 ET ratio for 24-hour time point were 0.4, 0.2 and 1.0 pM respectively (Table 12).

[00183] Table 12: Summary of EC_{50} values for various bispecific antibodies upon co-culturing FLU MP 58 peptide stimulated $CD8^+$ T cells with Kasumi-3 cells at ET ratios 0.5:1, 1:1 and 5:1 for 24 hours.

Bispecific Ab	**EC_{50} (ng/mL)**		
	E:T Ratio (0.5:1)	**E:T Ratio (1:1)**	**E:T Ratio (5:1)**
NULLXCD123	**UD**	**UD**	**UD**
Vβ17XNULL	**UD**	**UD**	**UD**
anti-Vβ17/anti-CD123	**0.06**	**0.03**	**0.15**

Bispecific Ab	**EC_{50} (pM)**		
	E:T Ratio (0.5:1)	**E:T Ratio (1:1)**	**E:T Ratio (5:1)**
NULLXCD123	**UD**	**UD**	**UD**
Vβ17XNULL	**UD**	**UD**	**UD**
anti-Vβ17/anti-CD123	**0.4**	**0.2**	**1.0**

UD: Undetectable

[00184] Similarly, anti-Vβ17/anti-CD123 bispecific mediated unstimulated $CD8^+$ T cell cytotoxicity was tested at ET ratio 0.5:1, 1:1, 5:1 for 14 (Table 13) and 24 (Table 14) hours. At 5 ng/ml anti-Vβ17/anti-CD123 bispecific concentration and 14-hour time point, unstimulated $CD8^+$ T cells at 0.5:1 and 1:1 ET ratio showed 2.8% and 9.8% target cell cytotoxicity respectively (Table 13), compared to 77% and 73% cytotoxicity by stimulated $CD8^+$ T cells. At 5:1 ET ratio, unstimulated $CD8^+$ T cells exhibited 31.65% target cytotoxicity, compared to 70.9% by stimulated $CD8^+$ T cells. Similar results were obtained from 24-hour time point (Table 12, 15, 16, and 17). At highest concentration (5 ng/ml) of anti-Vβ17/anti-CD123 bispecific tested, unstimulated CD8$^+$ T cells exhibited higher cytotoxicity towards target cells at a higher ET ratio.

[00185] Table 13: Cytotoxicity assay with unstimulated CD8$^+$ T cells at various ET ratios for 14 hours. Frequency of CFSE and 7-AAD positive cells when treated with different concentrations of bispecific antibodies.

Bispecific Ab	Conc (ng/mL)	E:T Ratio (0.5:1)	E:T Ratio (1:1)	E:T Ratio (5:1)
NULLXCD123	5	1.3	-0.6	-0.45
	0.005	1.3	-0.5	0.45
Vβ17XNULL	5	-0.6	-0.8	3.25
	0.005	-0.3	1	-1.35
anti-Vβ17/anti-CD123	5	2.8	9.8	31.65
	0.005	0.1	3.2	12.25

[00186] Table 14: Cytotoxicity assay with unstimulated CD8$^+$ T cells at various ET ratios for 24 hours. Frequency of CFSE and 7-AAD positive cells when treated with different concentrations of bispecific antibodies.

Unstimulated CD8+ T cells				
	Conc (ng/mL)	E:T Ratio (0.5:1)	E:T Ratio (1:1)	E:T Ratio (5:1)
NULLXCD123	5	-1.3	-0.55	-4.85
	0.005	-2	-0.85	-2.95
Vβ17XNULL	5	-0.8	-1.35	10.85
	0.005	-1	-1.05	-1.95
anti-Vβ17/anti-CD123	5	4.8	11.55	30.65
	0.005	1.5	1.75	10.95

[00187] Table 15: Cytotoxicity assay at 0.5:1 ET ratio (stimulated CD8$^+$ T cell: Kasumi-3 cells) upon incubation for 14 hrs. Frequency of CFSE and 7-AAD positive cells when treated with different concentrations of bispecific antibodies at 0.5:1 ET ratio for 14 hrs.

Conc.(ng/mL)	NULLXCD123	Vβ17XNULL	anti-Vβ17/ anti-CD123
50	3.47	2.57	77.07
5	2.67	2.17	77.47
0.5	-0.73	1.87	46.77
0.05	0.77	1.67	3.77
0.005	-0.03	1.47	1.97
0.0005	0.67	1.07	2.17
0.00005	1.67	0.17	0.17
0.000005	-0.43	3.27	0.87
EC_{50} (ng/mL)	ND	ND	0.55
EC_{50} (pM)	ND	ND	3.7

[00188] Half maximal effective concentration (EC_{50}) values were calculated as the antibody concentration that generates 50% of maximal cytotoxicity ($CFSE^+$ $7AAD^+$) cells. ND: Not Determined.

[00189] Table 16: Cytotoxicity assay at 1:1 ET ratio (stimulated $CD8^+$ T cell: Kasumi-3 cells) upon incubation for 14 hrs. Frequency of CFSE and 7-AAD positive cells when treated with different concentrations of bispecific antibodies at 11 ET ratio for 14 hrs.

Conc.(ng/mL)	NULLXCD123	Vβ17XNULL	anti-Vβ17/ anti-CD123
50	0.6	-0.5	76.0
5	0.1	0.9	73.0
0.5	1.0	0.9	77.9
0.05	0.4	1.8	59.4
0.005	1.8	0.9	36.8
0.0005	0.9	1.1	18.0
0.00005	0.7	0.9	6.1
0.000005	1.6	0.8	1.9
EC_{50} (ng/mL)	ND	ND	0.015
EC_{50} (pM)	ND	ND	0.1

[00190] Half maximal effective concentration (EC_{50}) values were calculated as the antibody concentration that generates 50% of maximal cytotoxicity ($CFSE^+$ $7AAD^+$) cells. ND: Not Determined

[00191] Table 17: Cytotoxicity assay at 5:1 E:T ratio (stimulated $CD8^+$ T cell: Kasumi-3 cells) upon incubation for 14 hrs. Frequency of CFSE and 7-AAD positive cells when treated with different concentrations of bispecific antibodies at 5:1 ET ratio for 14 hrs.

Conc.(ng/mL)	NULLXCD123	Vβ17XNULL	anti-Vβ17/ anti-CD123
50	2.3	0.0	70.2
5	3.1	2.7	70.9
0.5	1.8	4.4	74.5
0.05	3.0	1.5	73.2
0.005	2.1	1.6	2.5
0.0005	2.9	3.5	1.4
0.00005	3.2	5.5	2.5
0.000005	4.1	4.4	4.8
EC_{50} (ng/mL)	UD	UD	0.02
EC_{50} (pM)	UD	UD	0.13

[00192] Half maximal effective concentration (EC_{50}) values were calculated as the antibody concentration that generates 50% of maximal cytotoxicity ($CFSE^+$ $7AAD^+$) cells. UD: Undetectable.

[00193] It will be appreciated by those skilled in the art that changes could be made to the embodiments described above without departing from the broad inventive concept thereof. It is understood, therefore, that this invention is not limited to the particular embodiments disclosed, but it is intended to cover modifications within the spirit and scope of the present invention as defined by the present description.

SEQ ID NO:	Type	Species	Description	Sequence
1	PRT	mouse	B17B01-HCDR1	GYSITSGYFWN
2	PRT	mouse	B12B01-HCDR2	YISYDGSNN
3	PRT	mouse	B12B01-HCDR2	PSPGTGYAVDY
4	PRT	mouse	B17B01-LCDR1	RSSQSLVHSNGNTYLH
5	PRT	mouse	B12B01-LCDR2	KVSNRFS
6	PRT	mouse	B12B01-LCDR2	SQSTHVPFT
7	PRT	mouse	B17B01-HC	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFWNWIRQFPGNKLEWMGYISYDGSNNYNPSLKNRISITRDTSKNQFFLKLNSVTTEDTATYYCASPSPGTGYAVDYWGQGTSVTVSSAKTTPPSVYPLAPGSAAQTNSMVTLGCLVKGYFPEPVTVTWNSGSLSSGVHTFPAVLQSDLYTLSSSVTVPSSTWPSQTVTCNVAHPASSTKVDKKIVPRDCGCKPCICTVPEVSSVFIFPPKPKDVLTITLTPKVTCVVVDISKDDPEVQFSWFVDDVEVHTAQTKPREEQINSTFRSVSELPIMHQDWLNGKEFKCRVNSAAFPAPIEKTISKTYGRPKAPQVYTIPPPKEQMAKDKVSLTCMITNFFPEDITVEWQWNGQPAENYKNTQPIMDTDGSYFVYSKLNVQKSNWEAGNTFTCSVLHEGLHNHHTEKSLSHSPGK
8	PRT	mouse	B17B01-LC	NVVMTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKFLIYKVSNRFSGVPDRFSGGGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFTFGSGTKLEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC
9	PRT	mouse	B17B1-HC	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFWNWIRQFPGNKLEWMGYISYDGSNNYNPSLKNRISITRDTSKNQFFLKLNSVTTEDTATYYCASPSPGTGYAVDYWGQGTSVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFLLYSKLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
10	PRT	mouse	B17B1-LC	NVVMTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKFLIYKVSNRFSGVPDRFSGGGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFTFGSGTKLEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC
11	PRT	mouse	B17B2-HC	DVQLKESGPGLVKPSQSLSVTCSVTGYSITSGYYWNWYRQFPGNKLEWMGYISYDGSNNYNPSLKNRISITRDTSKNQILLKLTYVTTEDTATYYCTRPSPGTGYAVDYWGQGTLVTVSSASTKGPSVFPL

				APCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFLLYSKLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
12	PRT	mouse	B17B2-LC	DIVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCSQSTHVPFTFGQGTKVEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC
13	PRT	artificial	B17B21-HC	QVQLQESGPGLVKPSETLSLTCTVSGYSITSGYFWNWIRQPPGKGLEWIGYISYDGSNNYNPSLKSRVTISRDTSKNQFSLKLSSVTAADTAVYYCASPSPGTGYAVDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSRLTVDKSRWQEGNVFSCSVMHEALHNRFTQKSLSLSLGK
14	PRT	artificial	B17B21-LC	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGNTYLHWYQQKPGKAPKFLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
15	PRT	human	I3RB217-HC	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVRQMPGKGLEWMGIIDPSDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARGDGSTDLDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
16	PRT	human	I3RB217-LC	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQDYGFPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
17	PRT	human	Null-HC	QITLKESGPTLVKPTQTLTLTCTFSGFSLSTSGMGVSWIRQPPGKALEWLAHIYWDDDKRYNPSLKSRLTITKDTSKNQVVLTMTNMDPVDTATYYCA

				RLYGFTYGFAYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
18	PRT	human	Null-LC	DIVMTQSPDSLAVSLGERATINCRASQSVDYNGISYMHWYQQKPGQPPKLLIYAASNPESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQIIEDPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
19	PRT	artificial	B17H3	EVQLLESGGGLVQPGGSLRLSCAASGYSITSGYFWNWVRQAPGKGLEWVSYISYDGSNNYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKPSPGTGYAVDYWGQGTLVTVS
20	PRT	artificial	B17H4	EVQLLESGGGLVQPGGSLRLSCAASGYSITSGYFWNWVRQAPGKGLEWVSYISYDGSNNYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASPSPGTGYAVDYWGQGTLVTVSS
21	PRT	artificial	B17H5	QVQLQESGPGLVKPSETLSLTCTVSGYSITSGYFWNWIRQPPGKGLEWIGYISYDGSNNYNPSLKSRVTISRDTSKNQFSLKLSSVTAADTAVYYCASPSPGTGYAVDYWGQGTLVTVSS
22	PRT	artificial	B17L3	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGNTYLHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPFTFGQGTKLEIK
23	PRT	artificial	B17L4	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGNTYLHWYQQKPGKAPKFLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPFTFGQGTKLEIK
24	PRT	artificial	B17L5	DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRFLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPFTFGQGTKLEIK
25	PRT	artificial	B17H1	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFWNWIRQFPGNKLEWMGYISYDGSNNYNPSLKNRISITRDTSKNQFFLKLNSVTTEDTATYYCASPSPGTGYAVDYWGQGTSVTVSS
26	PRT	artificial	B17L1	NVVMTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKFLIYKVSNRFSGVPDRFSGGGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFTFGSGTKLEIK
27	PRT	human	TCR-Vβ17	MAWVWTLLFLMAAAQSIQAVDGGITQSPKYLFRKEGQNVTLSCEQNLNHDAMYWYRQDPGQGLRLIYYSQIVNDFQKGDIAEGYSVSREKKESFPLTVTSAQKNPTAFYLCASSSRSSYEQYFGPGTRLTVTEDLKNVFPPEVAVFEPSEAEISHTQKATLVCLATGFYPDHVELSWWVNGKEVHSGVSTDPQPLKEQPALNDSRYSLSSRLRVSATFWQNPRNHFRCQVQFYGLSENDEWTQDRAKPVTQIVSAEAWGRA

				DepkscdkthtcppcpapeLLggpsvflfppkpkdtlmisrtpevtcvvvDvshedpevkfnwyvdgvevhnaktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalpapiektiskakgqprepqvyVlppsreemtknqvslLclvkgfypsdiavewesngqpennyLtWppvldsdgsfflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspg
28	PRT	artificial	B17B21 half antibody	MAWVWTLLFLMAAAQSIQADIQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGNTYLHWYQQKPGKAPKFLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECGGSEGKSSGSGSESKSTEGKSSGSGSESKSTGGSQVQLQESGPGLVKPSETLSLTCTVSGYSITSGYFWNWIRQPPGKGLEWIGYISYDGSNNYNPSLKSRVTISRDTSKNQFSLKLSSVTAADTAVYYCASPSPGTGYAVDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSRLTVDKSRWQEGNVFSCSVMHEALHNRFTQKSLSLSLGK
29	DNA	artificial	B17B21 half antibody	ATGGCCTGGGTGTGGACCCTGCTGTTCCTGATGGCCGCCGCCCAGAGCATCCAGGCCGACATCCAGATGACCCAGAGCCCAAGCAGCCTGAGCGCCAGCGTGGGCGACCGCGTGACCATCACCTGCCGCAGCAGCCAGAGCCTGGTGCACAGCAACGGCAACACCTACCTGCACTGGTACCAGCAGAAGCCAGGCAAGGCCCCAAAGTTCCTGATCTACAAGGTGAGCAACCGCTTCAGCGGCGTGCCAAGCCGCTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCAGAGGACTTCGCCACCTACTACTGCAGCCAGAGCACCCACGTGCCATTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAGCGCACCGTGGCCGCCCCAAGCGTGTTCATCTTCCCACCAAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCACGCGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACCGAGCAGGACAGCAAGGACAGCACCTACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACTACGAGAAGCACAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGAGCAGCCCAGTGACCAAGAGCTTCAACCGCGGCGAGTGCGGCGGCAGCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGGCGGCAGCCAGGTGCAGCTGCAGGAGAGCGGCCCAGGCCTGGTGAAGCCAAGCGAGACCCTGAGCCTGACCTGCACCGTGAGCGGCTACAGCATCACCAGCGGCTACTTCTGGAACTGGATCCGCCAGCCACCAGGCAAGGGCCTGGAGTGGATCGGCTACATCAGCTACGACGGCAGCAACAACTACAACCCAAGCCTGAAGAGCCGCGTGACCATCAGCCGCGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGTGACCGCCGCCGACAC

				CGCCGTGTACTACTGCGCCAGCCCAAGCCCAGGCACCGGCTACGCCGTGGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGCGCCAGCACCAAGGGCCCAAGCGTGTTCCCACTGGCCCCATGCAGCCGCAGCACCAGCGAGAGCACCGCCGCCCTGGGCTGCCTGGTGAAGGACTACTTCCCAGAGCCAGTGACCGTGAGCTGGAACAGCGGCGCCCTGACCAGCGGCGTGCACACCTTCCCAGCCGTGCTGCAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGGTGACCGTGCCAAGCAGCAGCCTGGGCACCAAGACCTACACCTGCAACGTGGACCACAAGCCAAGCAACACCAAGGTGGACAAGCGCGTGGAGAGCAAGTACGGCCCACCATGCCCACCATGCCCAGCCCCAGAGGCCGCCGGCGGCCCAAGCGTGTTCCTGTTCCCACCAAAGCCAAAGGACACCCTGATGATCAGCCGCACCCCAGAGGTGACCTGCGTGGTGGTGGACGTGAGCCAGGAGGACCCAGAGGTGCAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCACGCGAGGAGCAGTTCAACAGCACCTACCGCGTGGTGAGCGTGCTGACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGAGCAACAAGGGCCTGCCAAGCAGCATCGAGAAGACCATCAGCAAGGCCAAGGGCCAGCCACGCGAGCCACAGGTGTACACCCTGCCACCAAGCCAGGAGGAGATGACCAAGAACCAGGTGAGCCTGAGCTGCGCCGTGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCAGAGAACAACTACAAGACCACCCCACCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGGTGAGCCGCCTGACCGTGGACAAGAGCCGCTGGCAGGAGGGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGCCCTGCACAACCGCTTCACCCAGAAGAGCCTGAGCCTGAGCCTGGGCAAGATGGCCTGGGTGTGGACCCTGCTGTTCCTGATGGCCGCCGCCCAGAGCATCCAGGCCGACATCCAGATGACCCAGAGCCCAAGCAGCCTGAGCGCCAGCGTGGGCGACCGCGTGACCATCACCTGCCGCAGCAGCCAGAGCCTGGTGCACAGCAACGGCAACACCTACCTGCACTGGTACCAGCAGAAGCCAGGCAAGGCCCCAAAGTTCCTGATCTACAAGGTGAGCAACCGCTTCAGCGGCGTGCCAAGCCGCTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCAGAGGACTTCGCCACCTACTACTGCAGCCAGAGCACCCACGTGCCATTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAGCGCACCGTGGCCGCCCCAAGCGTGTTCATCTTCCCACCAAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCACGCGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACCGAGCAGGACAGCAAGGACAGCACCTACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACTACGAGAAGCACAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGAGCAGCCCAGTGACCAAGAGCTTCAACCGCGGCGAGTGCGGCGGCAGCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGGCGGCAGCCAGGTGCAGCTGCAGGAGAGCGGCCCAGGCCTGGTGAAGCCAAGC

				GAGACCCTGAGCCTGACCTGCACCGTGAGCGGCTACAGCATCACCAGCGGCTACTTCTGGAACTGGATCCGCCAGCCACCAGGCAAGGGCCTGGAGTGGATCGGCTACATCAGCTACGACGGCAGCAACAACTACAACCCAAGCCTGAAGAGCCGCGTGACCATCAGCCGCGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGCGTGACCGCCGCCGACACCGCCGTGTACTACTGCGCCAGCCCAAGCCCAGGCACCGGCTACGCCGTGGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGCGCCAGCACCAAGGGCCCAAGCGTGTTCCCACTGGCCCCATGCAGCCGCAGCACCAGCGAGAGCACCGCCGCCCTGGGCTGCCTGGTGAAGGACTACTTCCCAGAGCCAGTGACCGTGAGCTGGAACAGCGGCGCCCTGACCAGCGGCGTGCACACCTTCCCAGCCGTGCTGCAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGGTGACCGTGCCAAGCAGCAGCCTGGGCACCAAGACCTACACCTGCAACGTGGACCACAAGCCAAGCAACACCAAGGTGGACAAGCGCGTGGAGAGCAAGTACGGCCCACCATGCCCACCATGCCCAGCCCCAGAGGCCGCCGGCGGCCCAAGCGTGTTCCTGTTCCCACCAAAGCCAAAGGACACCCTGATGATCAGCCGCACCCCAGAGGTGACCTGCGTGGTGGTGGACGTGAGCCAGGAGGACCCAGAGGTGCAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCACGCGAGGAGCAGTTCAACAGCACCTACCGCGTGGTGAGCGTGCTGACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGAGCAACAAGGGCCTGCCAAGCAGCATCGAGAAGACCATCAGCAAGGCCAAGGGCCAGCCACGCGAGCCACAGGTGTACACCCTGCCACCAAGCCAGGAGGAGATGACCAAGAACCAGGTGAGCCTGAGCTGCGCCGTGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCAGAGAACAACTACAAGACCACCCCACCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGGTGAGCCGCCTGACCGTGGACAAGAGCCGCTGGCAGGAGGGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGCCCTGCACAACCGCTTCACCCAGAAGAGCCTGAGCCTGAGCCTGGGCAAGTGATAG
30	PRT	artificial	I3RB217 half antibody	MAWVWTLLFLMAAAQSIQAEIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQDYGFPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECGGSEGKSSGSGSESKSTEGKSSGSGSESKSTGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVRQMPGKGLEWMGIIDPSDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARGDGSTDLDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPP

				VLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
31	DNA	artificial	I3RB217 half antibody	ATGGCCTGGGTGTGGACCCTGCTGTTCCTGATGGCCGCCGCCCAGAGCATCCAGGCCGAGATCGTGCTGACCCAGAGCCCAGGCACCCTGAGCCTGAGCCCAGGCGAGCGCGCCACCCTGAGCTGCCGCGCCAGCCAGAGCGTGAGCAGCAGCTACCTGGCCTGGTACCAGCAGAAGCCAGGCCAGGCCCCACGCCTGCTGATCTACGGCGCCAGCAGCCGCGCCACCGGCATCCCAGACCGCTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCCGCCTGGAGCCAGAGGACTTCGCCGTGTACTACTGCCAGCAGGACTACGGCTTCCCATGGACCTTCGGCCAGGGCACCAAGGTGGAGATCAAGCGCACCGTGGCCGCCCCAAGCGTGTTCATCTTCCCACCAAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCACGCGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACCGAGCAGGACAGCAAGGACAGCACCTACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACTACGAGAAGCACAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGAGCAGCCCAGTGACCAAGAGCTTCAACCGCGGCGAGTGCggcggcagcgagggcaagagcagcggcagcggcagcgagagcaagagcaccgagggcaagagcagcggcagcggcagcgagagcaagagcaccggcggcagcGAGGTGCAGCTGGTGCAGAGCGGCGCCGAGGTGAAGAAGCCAGGCGAGAGCCTGAAGATCAGCTGCAAGGGCAGCGGCTACAGCTTCACCAGCTACTGGATCAGCTGGGTGCGCCAGATGCCAGGCAAGGGCCTGGAGTGGATGGGCATCATCGACCCAAGCGACAGCGACACCCGCTACAGCCCAAGCTTCCAGGGCCAGGTGACCATCAGCGCCGACAAGAGCATCAGCACCGCCTACCTGCAGTGGAGCAGCCTGAAGGCCAGCGACACCGCCATGTACTACTGCGCCCGCGGCGACGGCAGCACCGACCTGGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGCGCCAGCACCAAGGGCCCAAGCGTGTTCCCACTGGCCCCATGCAGCCGCAGCACCAGCGAGAGCACCGCCGCCCTGGGCTGCCTGGTGAAGGACTACTTCCCAGAGCCAGTGACCGTGAGCTGGAACAGCGGCGCCCTGACCAGCGGCGTGCACACCTTCCCAGCCGTGCTGCAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGGTGACCGTGCCAAGCAGCAGCCTGGGCACCAAGACCTACACCTGCAACGTGGACCACAAGCCAAGCAACACCAAGGTGGACAAGCGCGTGGAGAGCAAGTACGGCCCACCATGCCCACCATGCCCAGCCCCAGAGGCCGCCGGCGGCCCAAGCGTGTTCCTGTTCCCACCAAAGCCAAAGGACACCCTGATGATCAGCCGCACCCCAGAGGTGACCTGCGTGGTGGTGGACGTGAGCCAGGAGGACCCAGAGGTGCAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCACGCGAGGAGCAGTTCAACAGCACCTACCGCGTGGTGAGCGTGCTGACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGAGCAACAAGGGCCTGCCAAGCAGCATCGAGAAGACCATCAGCAAGGCCAAGGGCCAGCCACGCGAGCCACAGGTGTACACCCTGCCACCAAGCCAGGAGGAGATGACCAAGAACCAGGTGAGCCTGTGG

				TGCCTGGTGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCAGAGAACAACTACAAGACCACCCCACCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGTACAGCCGCCTGACCGTGGACAAGAGCCGCTGGCAGGAGGGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCCTGAGCCTGAGCCTGGGCAAG
32	PRT	artificial	B23B49 half antibody	MAWVWTLLFLMAAAQSIQAEIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQDYGFPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECGGSEGKSSGSGSESKSTEGKSSGSGSESKSTGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVRQMPGKGLEWMGIIDPSDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARGDGSTDLDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
33	DNA	artificial	B23B49 half antibody	ATGGCCTGGGTGTGGACCCTGCTGTTCCTGATGGCCGCCGCCCAGAGCATCCAGGCCGACATCGTGATGACCCAGAGCCCAGACAGCCTGGCCGTGAGCCTGGGCGAGCGCGCCACCATCAACTGCCGCGCCAGCCAGAGCGTGGACTACAACGGCATCAGCTACATGCACTGGTACCAGCAGAAGCCAGGCCAGCCACCAAAGCTGCTGATCTACGCCGCCAGCAACCCAGAGAGCGGCGTGCCAGACCGCTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGGCCGAGGACGTGGCCGTGTACTACTGCCAGCAGATCATCGAGGACCCATGGACCTTCGGCCAGGGCACCAAGGTGGAGATCAAGCGCACCGTGGCCGCCCCAAGCGTGTTCATCTTCCCACCAAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCACGCGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACCGAGCAGGACAGCAAGGACAGCACCTACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACTACGAGAAGCACAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGAGCAGCCCAGTGACCAAGAGCTTCAACCGCGGCGAGTGCGGCGGCAGCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGGCGGCAGCCAGATCACCCTGAAGGAGAGCGGCCCAACCCTGGTGAAGCCAACCCAGACCCTGACCCTGACCTGCACCTTCAGCGGCTTCAGCCTGAGCACCAGCGGCATGGGCGTGAGCTGGATCCGCCAGCCACCAGGCAAGGCCCTGGAGTGGCTGGCCCACATCTACTGGGACGACGACAAGCGCT

				ACAACCCAAGCCTGAAGAGCCGCCTGACCATCACCAAGGACACCAGCAAGAACCAGGTGGTGCTGACCATGACCAACATGGACCCAGTGGACACCGCCACCTACTACTGCGCCCGCCTGTACGGCTTCACCTACGGCTTCGCCTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGCGCCAGCACCAAGGGCCCAAGCGTGTTCCCACTGGCCCCATGCAGCCGCAGCACCAGCGAGAGCACCGCCGCCCTGGGCTGCCTGGTGAAGGACTACTTCCCAGAGCCAGTGACCGTGAGCTGGAACAGCGGCGCCCTGACCAGCGGCGTGCACACCTTCCCAGCCGTGCTGCAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGGTGACCGTGCCAAGCAGCAGCCTGGGCACCAAGACCTACACCTGCAACGTGGACCACAAGCCAAGCAACACCAAGGTGGACAAGCGCGTGGAGAGCAAGTACGGCCCACCATGCCCACCATGCCCAGCCCCAGAGGCCGCCGGCGGCCCAAGCGTGTTCCTGTTCCCACCAAAGCCAAAGGACACCCTGATGATCAGCCGCACCCCAGAGGTGACCTGCGTGGTGGTGGACGTGAGCCAGGAGGACCCAGAGGTGCAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCACGCGAGGAGCAGTTCAACAGCACCTACCGCGTGGTGAGCGTGCTGACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGAGCAACAAGGGCCTGCCAAGCAGCATCGAGAAGACCATCAGCAAGGCCAAGGGCCAGCCACGCGAGCCACAGGTGTACACCCTGCCACCAAGCCAGGAGGAGATGACCAAGAACCAGGTGAGCCTGTGGTGCCTGGTGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCAGAGAACAACTACAAGACCACCCCACCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGTACAGCCGCCTGACCGTGGACAAGAGCCGCTGGCAGGAGGGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCCTGAGCCTGAGCCTGGGCAAG
34	PRT	Artificial	HCDR1	SYWIS
35	PRT	Artificial	HCDR2	IIDPSDSDTRYSPSFQG
36	PRT	Artificial	HCDR3	GDGSTDLDY
37	PRT	Artificial	LCDR1	RASQSVSSSYL
38	PRT	Artificial	LCDR2	GASSRAT
39	PRT	Artificial	LCDR3	QQDYGFPWT
40	PRT	Artificial	HC	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVRQMPGKGLEWMGIIDPSDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARGDGSTDLDYWGQGTLVTVSS
41	PRT	Artificial	LC	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQDYGFPWTFGQGTKVEIK
42	PRT	Artificial	IGHJ1*01 HC	WGQGTLVTVSS
43	PRT	Artificial	IGKJ2*01 LC	FGQGTKLEIK
44	PRT	Artificial	Va10.2_Fc	MAWVWTLLFLMAAAQSIQAQLLEQSPQFLSIQEGENLTVYCNSSSVFSSLQWYRQEPGEGPVLLVTVVTGGEVKKLKRLTFQFGDARKDSSLHITAAQPGDTGLYLCAGAGSQGNLIFGKGTKLSVKPNIQNPDPAVYQLRDSKSSDKSVCLFTDFDSQTNVSQSKDSDVYITDKTVLDMRSMDFKSNSAVAWSNKS

				DFACANAFNNSIIPEDTFFPSepkscdkthtcppcpapeLLggpsvflfppkpkdtlmisrtpevtcvvvDvshedpevkfnwyvdgvevhnaktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalpapiektiskakgqprepqvyVYppsreemtknqvsltclvkgfypsdiavewesngqpennykttppvldsdgsfAlVskltvdksrwqqgnvfscsvmhealhnhytqkslslspg

CLAIMS

1. An isolated Vβ17 bispecific antibody or antigen-binding fragment thereof, the isolated Vβ17 bispecific antibody or antigen-binding fragment thereof comprising:

   a. a first heavy chain (HC1);
   b. a second heavy chain (HC2);
   c. a first light chain (LC1); and
   d. a second light chain (LC2),

wherein HC1 is associated with LC1 and HC2 is associated with LC2, and wherein HC1 comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, respectively, and LC1 comprises a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6, respectively, to form a binding site for a first antigen, and wherein HC2 and LC2 form a binding site for the second antigen.

2. The Vβ17 bispecific antibody or antigen-binding fragment thereof of claim 1, wherein the binding site for the first antigen binds to Vβ17 on a CD8+ or CD4+ T cell.

3. The Vβ17 bispecific antibody or antigen-binding fragment thereof of claim 1 or 2, wherein the binding site for the second antigen binds to a tumor antigen present on the surface of a cancer cell.

4. The Vβ17 bispecific antibody or antigen-binding fragment of any one of claims 1 to 3, wherein HC1 and LC1 are humanized.

5. The Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of claims 1 to 4, wherein HC2 and LC2 bind to CD123.

6. The Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of claims 1 to 5, wherein the bispecific antibody or antigen-binding fragment thereof is a IgG isotype.

7. The Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of claims 1 to 6, wherein the bispecific antibody or antigen-binding fragment thereof is a IgG4 isotype.

8. The Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of claims 1 to 7, wherein the bispecific antibody or antigen-binding fragment thereof induces CD8+ or CD4+ T-cell dependent cytotoxicity of a cancer cell *in vitro* with an EC_{50} of less than about 0.2 pM.

9. An isolated nucleic acid encoding the HC1 and the LC1 of the Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of claims 1 to 8.

10. An isolated nucleic acid encoding the HC2 and the LC2 of the Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of claims 1 to 8.

11. A vector comprising the isolated nucleic acid of claim 9 or claim 10.

12. A host cell comprising the vector of claim 11.

13. An isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof comprising:

a. a first heavy chain (HC1);
b. a second heavy chain (HC2)
c. a first light chain (LC1); and
d. a second light chain (LC2),

wherein HC1 is associated with LC1 and HC2 is associated with LC2, and wherein HC1 comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, respectively, and LC1 comprises a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6, respectively, to form a binding site for a first antigen that specifically binds Vβ17, and wherein HC2 comprises a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO:34, SEQ ID NO:35, and SEQ ID NO:36, respectively, and LC2 comprises a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO:37, SEQ ID NO:38, and SEQ ID NO:39, respectively, to form a binding site for a second antigen that specifically binds CD123.

14. The isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of claim 13, wherein HC1 comprises the amino acid sequence of SEQ ID NO:13 and LC1 comprises the amino acid sequence of SEQ ID NO:14, and wherein HC2 comprises the amino acid sequence of SEQ ID NO:15 and LC2 comprises the amino acid sequence of SEQ ID NO:16.

15. The isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of claim 13 or 14, wherein the Vβ17 is on the surface of a CD8+ or CD4+ T cell.

16. The isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of claims 13 to 15, wherein the CD123 is on the surface of a cancer cell or a CD34+ stem cell.

17. The isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of claims 13 to 16, wherein bispecific antibody or antigen-binding fragment

thereof induces CD8+ or CD4+ T-cell dependent cytotoxicity of a cancer cell *in vitro* with an EC_{50} of less than about 0.2 pM.

18. An isolated nucleic acid encoding the HC1 and LC1 of the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of claims 13 to 17.

19. An isolated nucleic acid encoding the HC2 and LC2 of the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of claims 13 to 18.

20. A vector comprising the isolated nucleic acid of claim 18 or 19.

21. A host cell comprising the vector of claim 20.

22. A buffered composition comprising the isolated anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of claims 13 to 17.

23. A method of directing a Vβ17-expressing CD8+ or CD4+ T cell to a cancer cell, the method comprising contacting a Vβ17-expressing CD8+ or CD4+ T cell with the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of claim 13, wherein contacting the Vβ17-expressing CD8+ or CD4+ T cell with the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof directs the Vβ17-expressing CD8+ or CD4+ T cell to a cancer cell.

24. A method for inhibiting growth or proliferation of cancer cells, the method comprising contacting the cancer cells with the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of claim 13, wherein contacting the cancer cells with the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof inhibits the growth or proliferation of the cancer cells.

25. The method of claim 23 or 24, wherein the cancer cell is a CD123-expressing cancer cell.

26. A kit comprising a Vβ17 bispecific antibody or antigen-binding fragment thereof of any one of claims 1 to 8 and packaging for the same.

27. A kit comprising an anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of claims 13 to 17 and packaging for the same.

28. A method of producing a Vβ17 bispecific antibody or antigen-binding fragment thereof comprising culturing the host cell of claim 12 to produce the Vβ17 bispecific antibody or antigen-binding fragment thereof, and recovering the Vβ17 bispecific antibody or antigen-binding fragment thereof from the cell or culture.

29. A method of producing an anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof comprising culturing the host cell of claim 21 to produce the anti-Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof, and recovering the anti-

Vβ17/anti-CD123 bispecific antibody or antigen-binding fragment thereof from the cell or culture.

30. An isolated humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof, the humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof comprising an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:28.

31. The isolated humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof of claim 30, wherein the humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof comprises the amino acid sequence of SEQ ID NO:28.

32. An isolated nucleic acid encoding the isolated humanized Vβ17 monoclonal antibody or antigen-binding fragment thereof of claim 30 or 31.

33. A vector comprising the isolated nucleic acid of claim 32.

34. A host cell comprising the vector of claim 33.

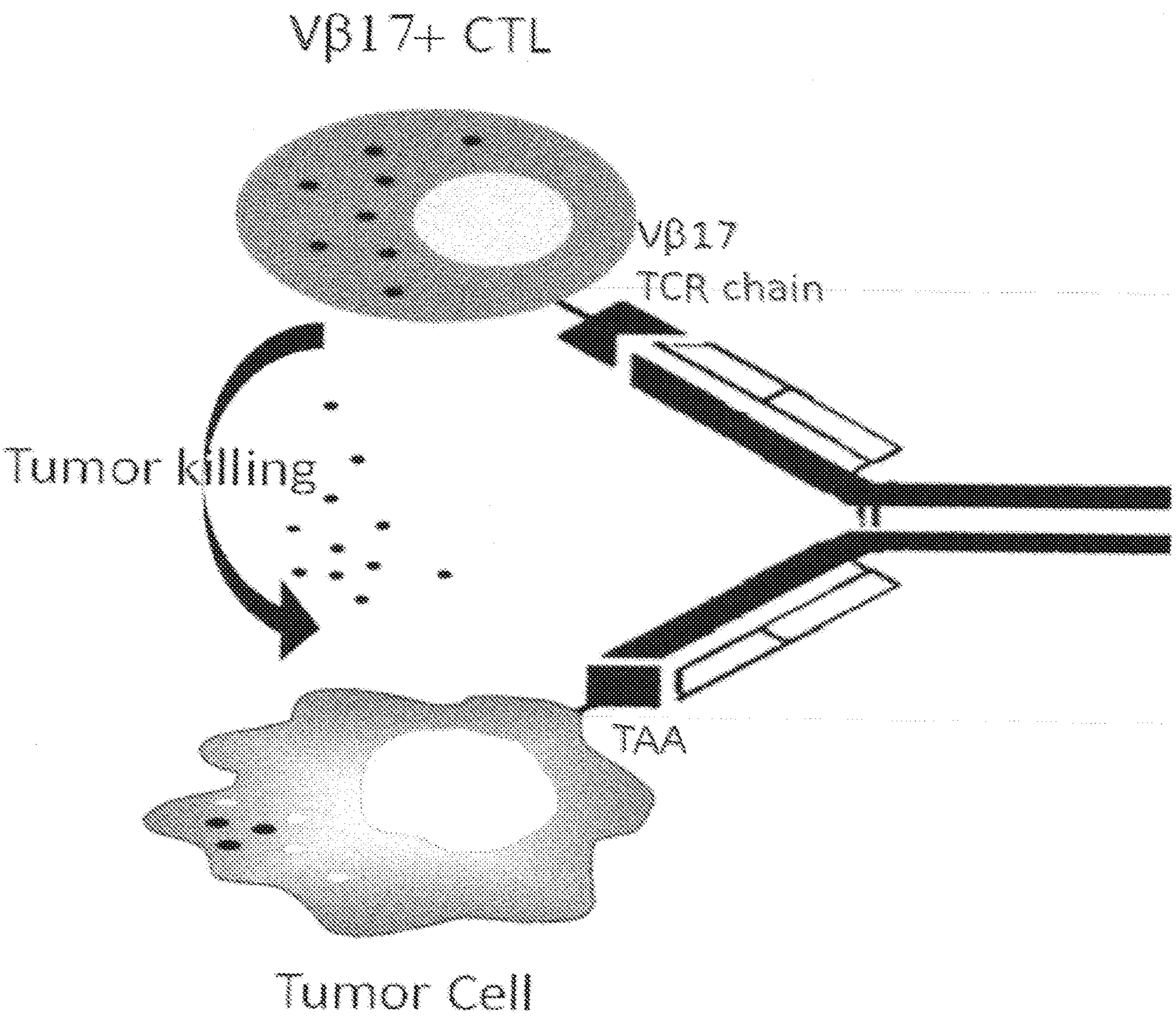


FIG. 1

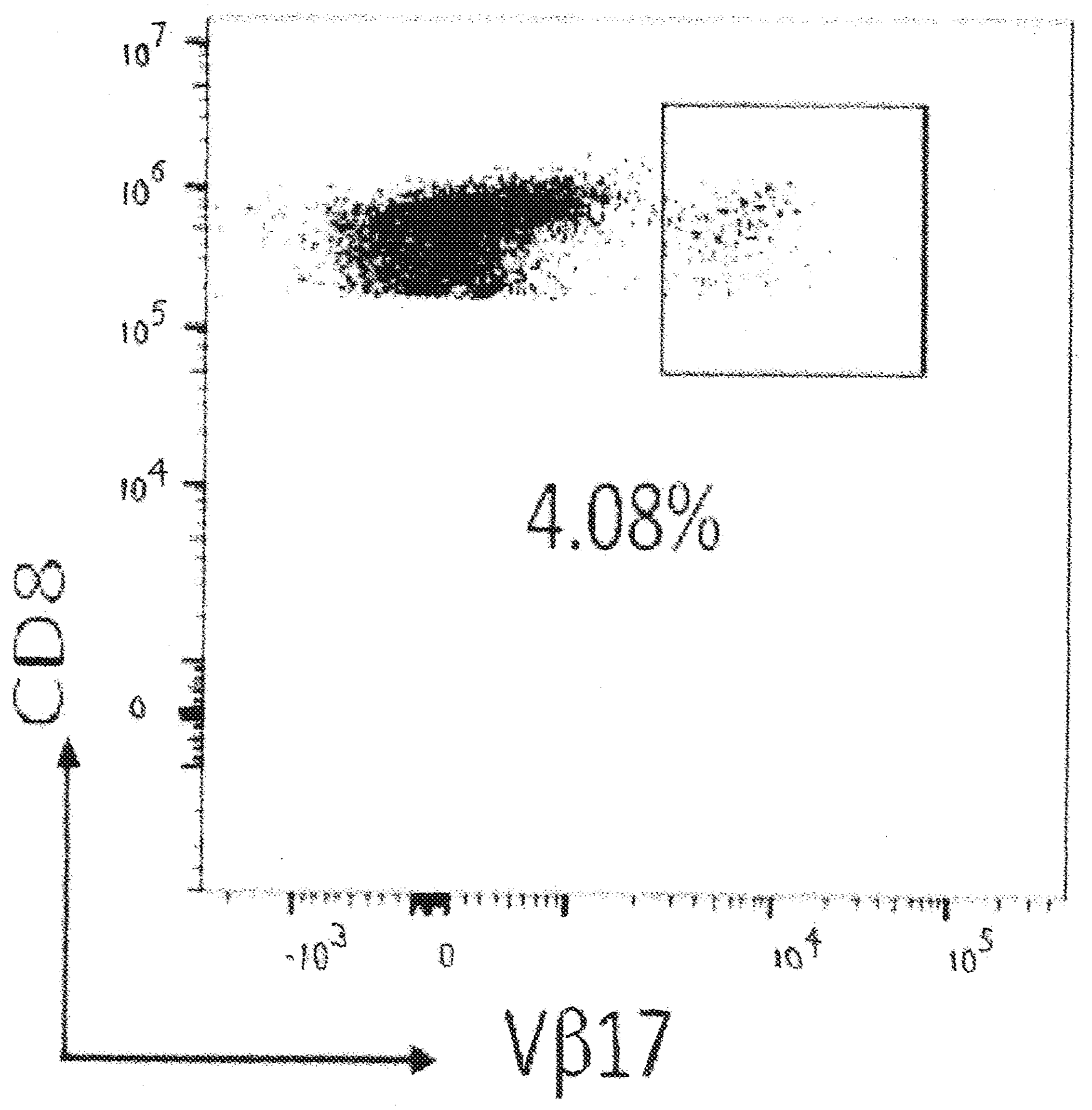


FIG. 2A

Donor	HLA status	% of Vβ17$^+$ in CD8 T cells (Day 0)	% of Vβ17$^+$ in CD8 T cells (Day 14)
HPU-03033	A2	5.45	14.4
HPU-07540	A2	3.70	34.4
HPU-08694	A2	3.88	75
17043595	A*0201	2	15
14035473	A*0201	2.8	40.7
15036948	A*0201	3.64	43.0

FIG. 2B

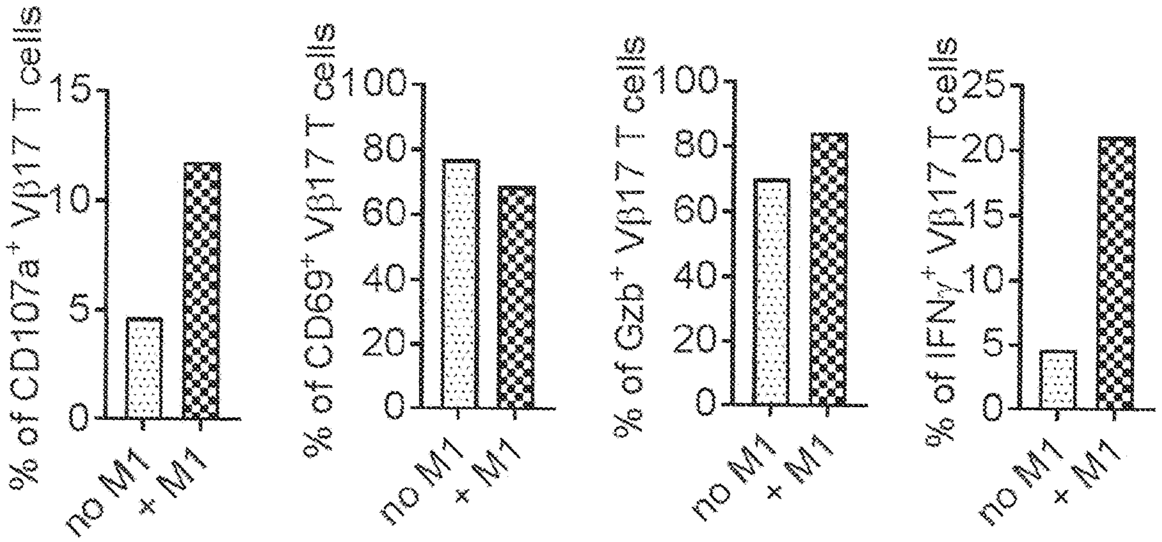
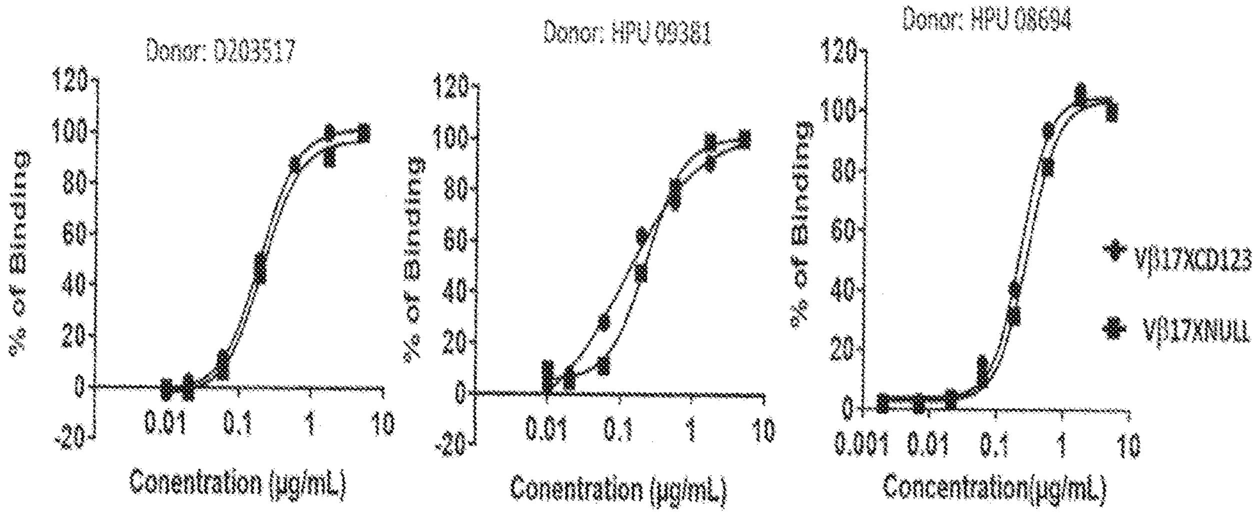


FIG. 3

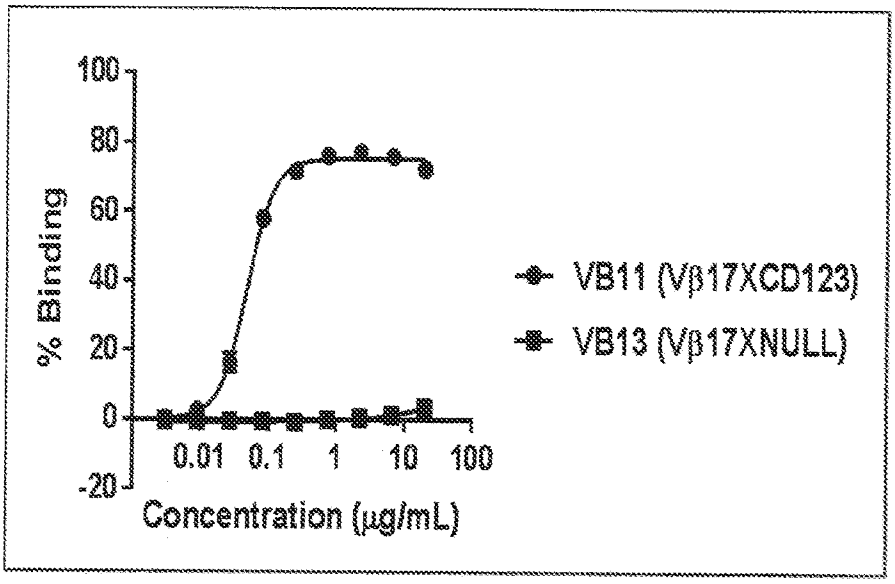


	Vβ17XCD123	Vβ17XNULL
EC$_{50}$ (nM)	1.26	1.4

	Vβ17XCD123	Vβ17XNULL
EC$_{50}$ (nM)	0.8	1.5

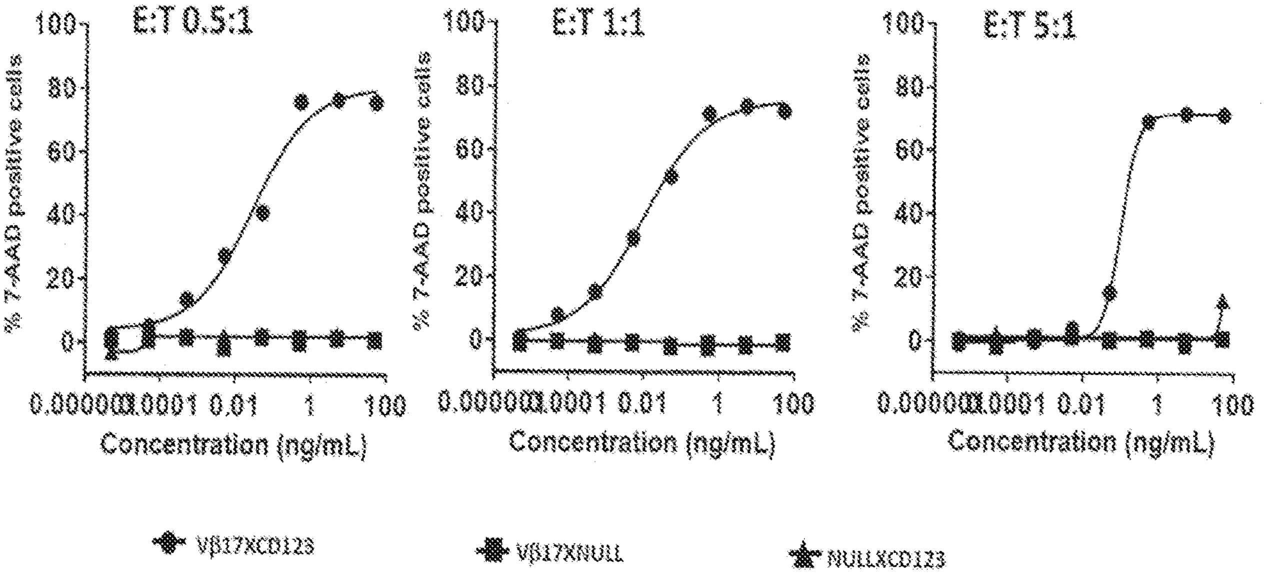
	Vβ17XCD123	Vβ17XNULL
EC$_{50}$ (nM)	1.9	1.5

FIG. 4



	Vβ17XCD123	Vβ17XNULL
EC_{50} (nM)	0.33	ND

FIG. 5



EC$_{50}$ (pM)

ET ratio	0.5:1	1:1	5:1
NULLXCD123	ND	ND	ND
Vβ17XNULL	ND	ND	ND
Vβ17XCD123	0.4	0.2	1.0

FIG. 6

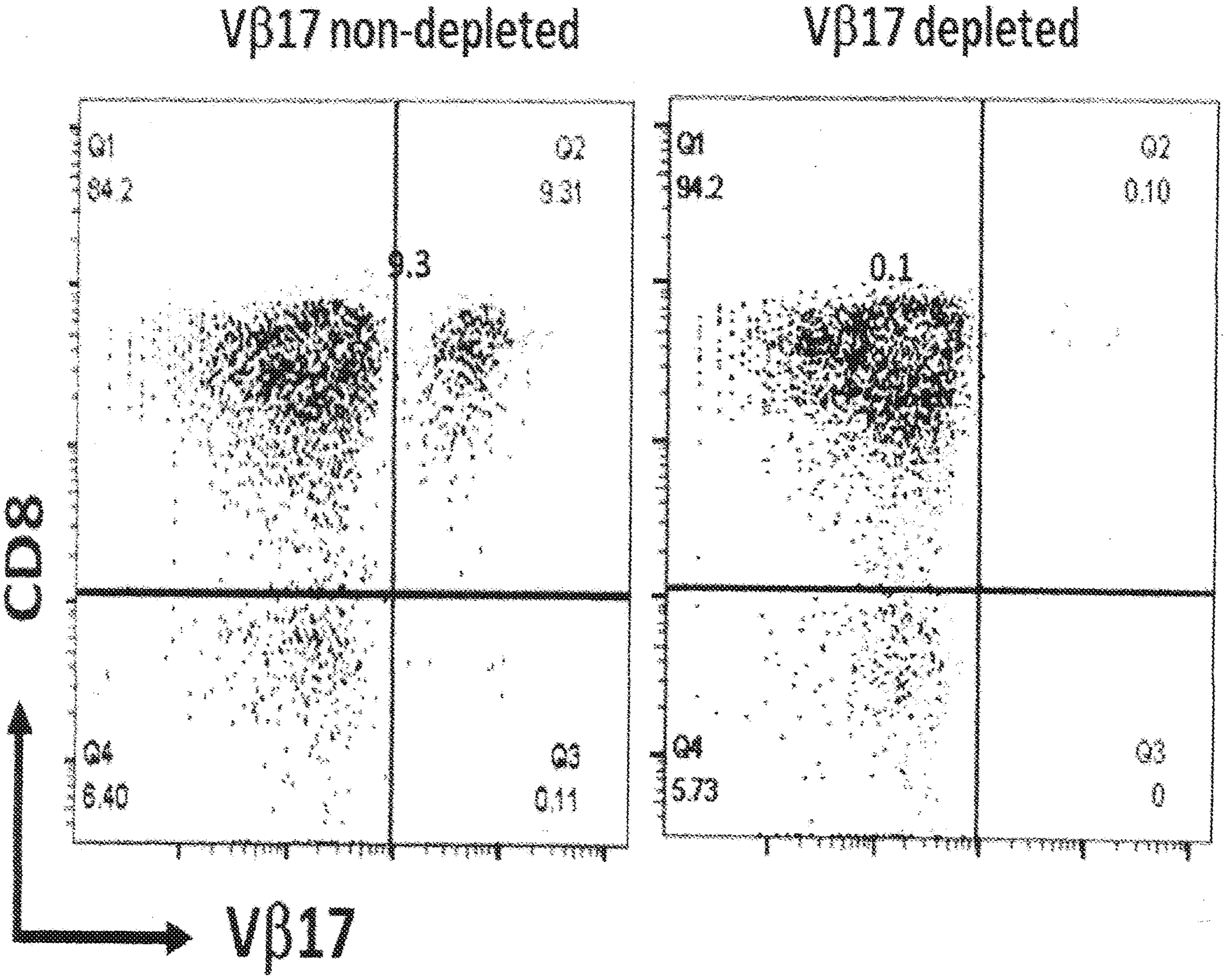
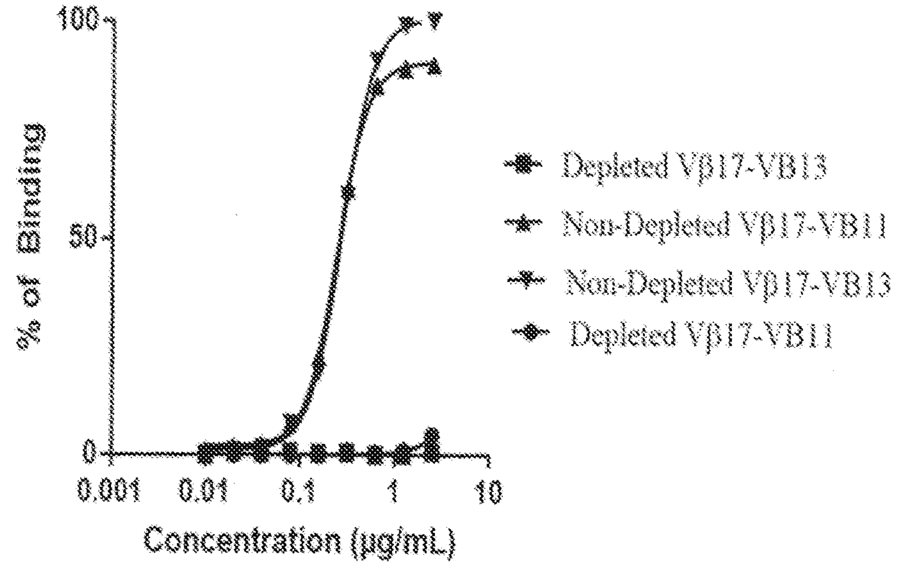
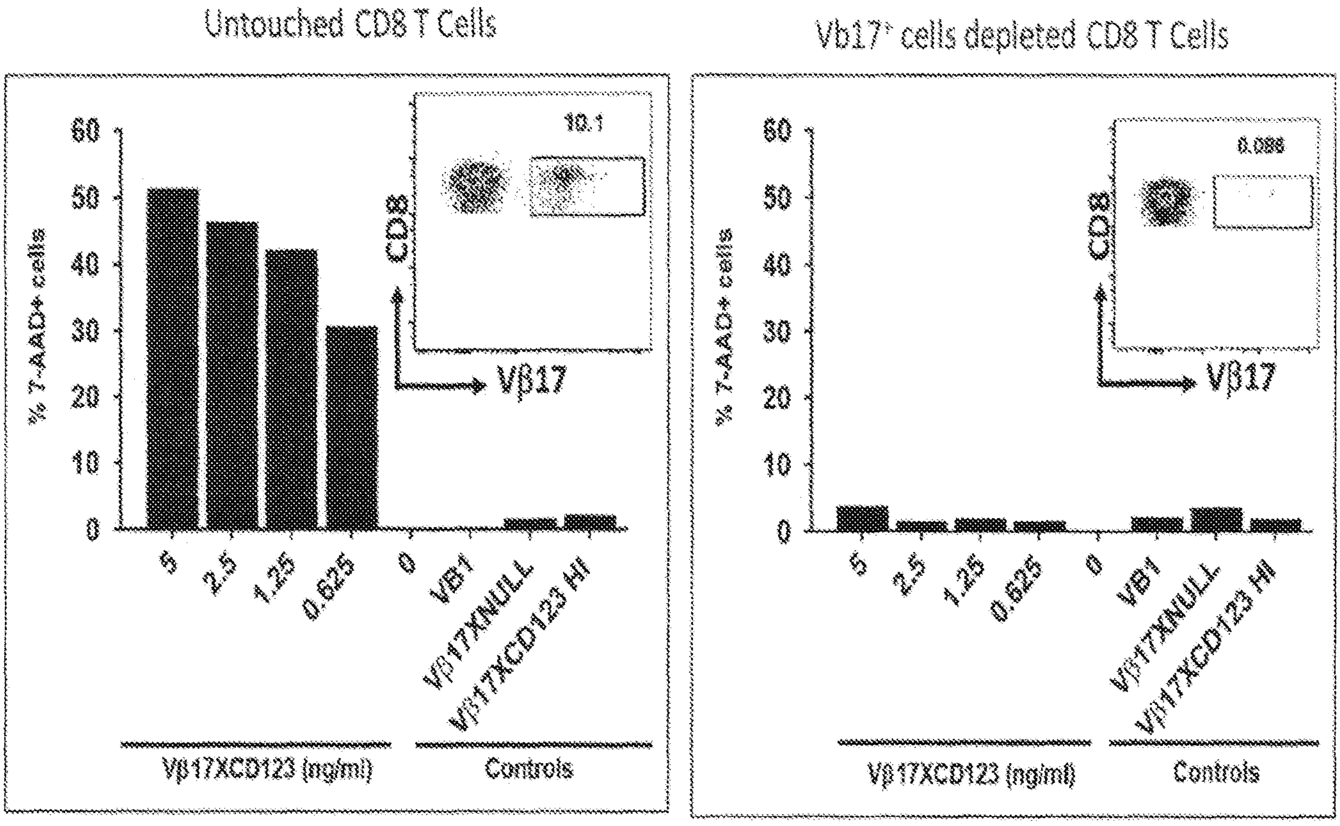

Vβ17 non-depleted
Vβ17 depleted
Q1
94.2
Q2
9.31
9.3
Q4
6.40
Q3
0.11
Q1
94.2
Q2
0.10
0.1
Q4
5.73
Q3
0
CD8
Vβ17

FIG. 7A



	EC50 (nM)
VB11	12.2
VB13	12.6

FIG. 7B



Untouched CD8 T Cells

Vb17⁺ cells depleted CD8 T Cells

- VB1: NULLXCD123
- Vβ17XCD123 HI: Heat denatured Vβ17XCD123 (at 95°C for 6 minutes)

FIG. 8

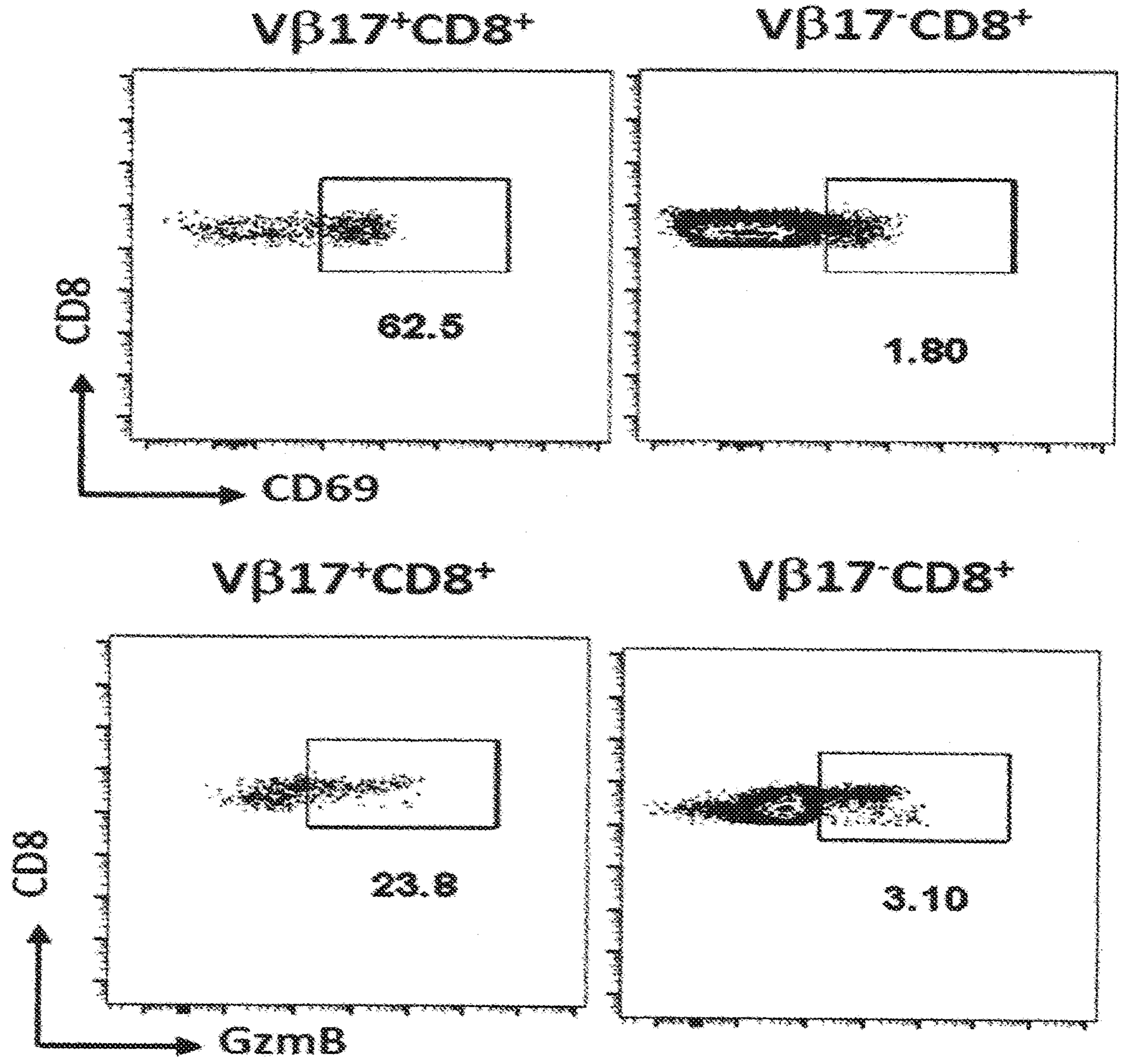

Vβ17⁺CD8⁺
Vβ17⁻CD8⁺
CD8
CD69
62.5
1.80
Vβ17⁺CD8⁺
Vβ17⁻CD8⁺
CD8
GzmB
23.8
3.10

FIG. 9A

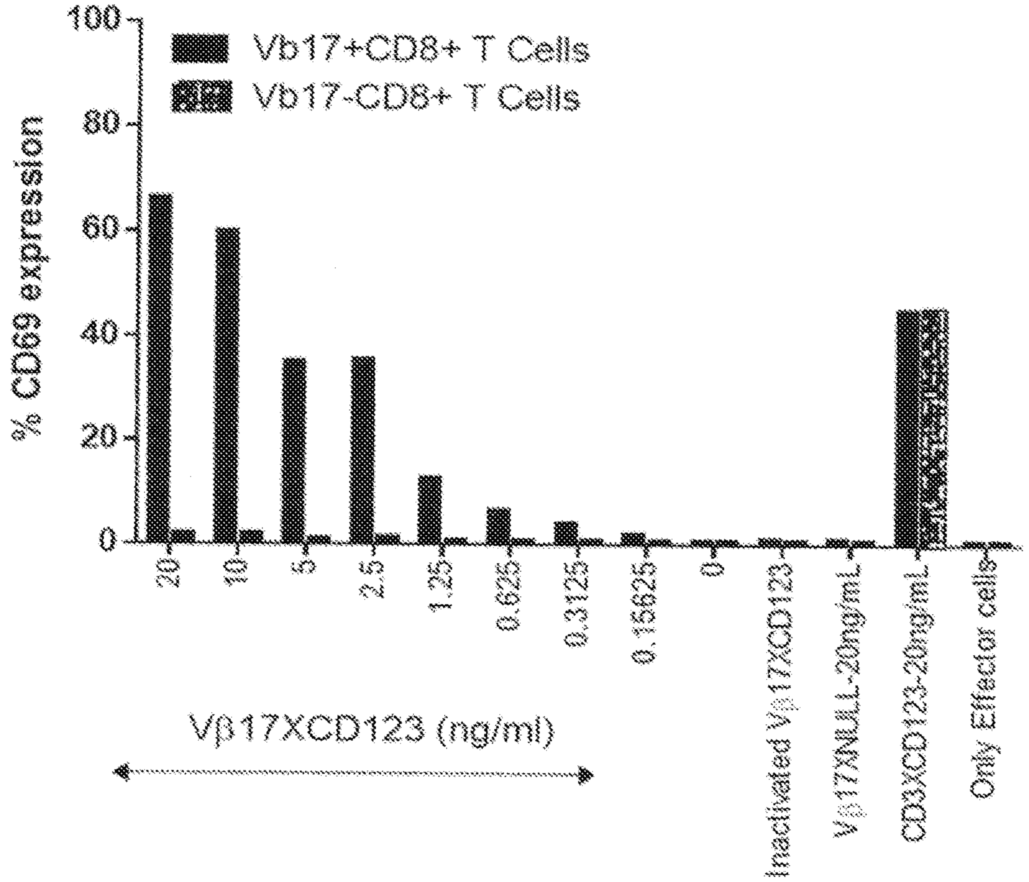

100
80
60
40
20
0
% CD69 expression
Vb17+CD8+ T Cells
Vb17-CD8+ T Cells
20
10
5
2.5
1.25
0.625
0.3125
0.15625
0
Inactivated Vβ17XCD123
Vβ17XNULL-20ng/mL
CD3XCD123-20ng/mL
Only Effector cells
Vβ17XCD123 (ng/ml)

FIG. 9B

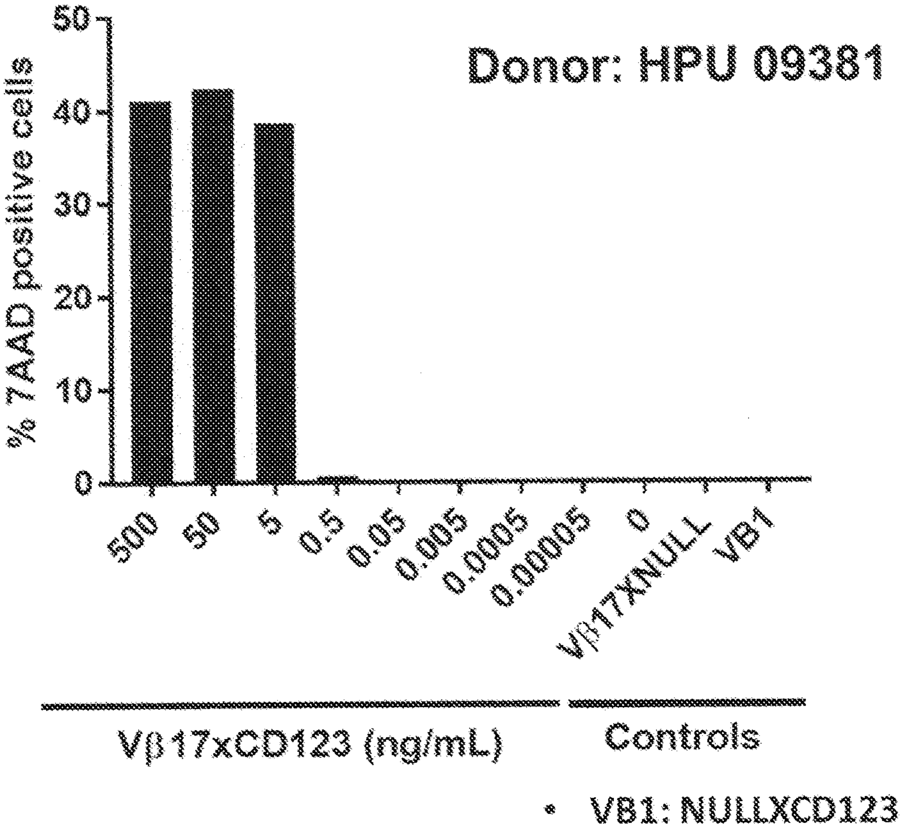

Donor: HPU 09381
% 7AAD positive cells
50
40
30
20
10
0
500
50
5
0.5
0.05
0.005
0.0005
0.00005
0
Vβ17XNULL
VB1
Vβ17xCD123 (ng/mL)
Controls
• VB1: NULLXCD123

FIG. 10

SEQUENCE LISTING

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<110>  Janssen Biotech, Inc.

<120>  Anti-VB17/Anti-CD123 Bispecific Antibodies and Uses Thereof

<130>  PRD4012WOPCT

<150>  US62/816,464
<151>  2019-03-11

<160>  44

<170>  PatentIn version 3.5

<210>  1
<211>  11
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17B01 HCDR1

<400>  1

Gly Tyr Ser Ile Thr Ser Gly Tyr Phe Trp Asn
1               5                   10


<210>  2
<211>  9
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17B01 HCDR2

<400>  2

Tyr Ile Ser Tyr Asp Gly Ser Asn Asn
1               5


<210>  3
<211>  11
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17B01 HCDR3

<400>  3

Pro Ser Pro Gly Thr Gly Tyr Ala Val Asp Tyr
1               5                   10


<210>  4
<211>  16
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17B01 LCDR1

<400>  4

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
```

1   5   10   15

<210> 5
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> B17B01 LCDR2

<400> 5

Lys Val Ser Asn Arg Phe Ser
1   5

<210> 6
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> B17B01 LCDR3

<400> 6

Ser Gln Ser Thr His Val Pro Phe Thr
1   5

<210> 7
<211> 444
<212> PRT
<213> Artificial Sequence

<220>
<223> B17B01 Heavy Chain

<400> 7

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

Ser Leu Ser Leu Thr Cys Ser Val Ala Gly Tyr Ser Ile Thr Ser Gly
            20   25   30

Tyr Phe Trp Asn Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
        35   40   45

Met Gly Tyr Ile Ser Tyr Asp Gly Ser Asn Asn Tyr Asn Pro Ser Leu
    50   55   60

Lys Asn Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65   70   75   80

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

Ala Ser Pro Ser Pro Gly Thr Gly Tyr Ala Val Asp Tyr Trp Gly Gln
            100   105   110

```
Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr Pro Pro Ser Val
        115                 120                 125

Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser Met Val Thr
    130                 135                 140

Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Val Thr
145                 150                 155                 160

Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Pro Ser
            180                 185                 190

Ser Thr Trp Pro Ser Gln Thr Val Thr Cys Asn Val Ala His Pro Ala
        195                 200                 205

Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp Cys Gly Cys
    210                 215                 220

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

Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys Val
                245                 250                 255

Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val Gln Phe
            260                 265                 270

Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr Lys Pro
        275                 280                 285

Arg Glu Glu Gln Ile Asn Ser Thr Phe Arg Ser Val Ser Glu Leu Pro
    290                 295                 300

Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg Val
305                 310                 315                 320

Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr
                325                 330                 335

Tyr Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro Lys
            340                 345                 350

Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile Thr Asn
        355                 360                 365

Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly Gln Pro
    370                 375                 380

Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr Asp Gly Ser
```

```
385                 390                 395                 400


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


Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His Asn His
            420                 425                 430


His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
        435                 440


<210>  8
<211>  219
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17B01 Light Chain

<400>  8

Asn Val 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 Phe Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Glu 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 Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
        115                 120                 125


Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe
    130                 135                 140


Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
145                 150                 155                 160


Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
                165                 170                 175
```

Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
            180   185   190

Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
        195   200   205

Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
    210   215

<210> 9
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<223> B17B1 Heavy Chain

<400> 9

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

Ser Leu Ser Leu Thr Cys Ser Val Ala Gly Tyr Ser Ile Thr Ser Gly
            20   25   30

Tyr Phe Trp Asn Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
        35   40   45

Met Gly Tyr Ile Ser Tyr Asp Gly Ser Asn Asn Tyr Asn Pro Ser Leu
    50   55   60

Lys Asn Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65   70   75   80

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

Ala Ser Pro Ser Pro Gly Thr Gly Tyr Ala Val Asp Tyr Trp Gly Gln
            100   105   110

Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115   120   125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130   135   140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145   150   155   160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165   170   175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180   185   190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195   200   205

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

Pro Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
225   230   235   240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245   250   255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260   265   270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275   280   285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290   295   300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305   310   315   320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325   330   335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340   345   350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355   360   365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370   375   380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385   390   395   400

Asp Gly Ser Phe Leu Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405   410   415

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420   425   430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
        435   440   445

<210> 10
<211> 219
<212> PRT
<213> Artificial Sequence

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<220>
<223>  B17B1 Light Chain

<400>  10

Asn Val 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 Phe Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Glu 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 Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
        115                 120                 125


Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe
    130                 135                 140


Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
145                 150                 155                 160


Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
                165                 170                 175


Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
            180                 185                 190


Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
        195                 200                 205


Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
    210                 215


<210>  11
<211>  447
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17B2 Heavy Chain
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<400>  11

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


Ser Leu Ser Val Thr Cys Ser Val Thr Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30


Tyr Tyr Trp Asn Trp Tyr Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
        35                  40                  45


Met Gly Tyr Ile Ser Tyr Asp Gly Ser Asn Asn Tyr Asn Pro Ser Leu
    50                  55                  60


Lys Asn Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Ile Leu
65                  70                  75                  80


Leu Lys Leu Thr Tyr Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys
                85                  90                  95


Thr Arg Pro Ser Pro Gly Thr Gly Tyr Ala Val Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125


Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140


Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160


Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175


Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190


Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205


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


Pro Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
225                 230                 235                 240


Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255


Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260                 265                 270
```

```
Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285


Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300


Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320


Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335


Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350


Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365


Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380


Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400


Asp Gly Ser Phe Leu Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415


Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430


His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
        435                 440                 445


<210>  12
<211>  219
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17B2 Light Chain

<400>  12

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Arg Ser Ser Gln Ser Leu Val His Ser
            20                  25                  30


Asn Gly Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Pro
        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 Thr Ile
65                  70                  75                  80

Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Ser Gln Ser
                85                  90                  95

Thr His Val Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105                 110

Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
        115                 120                 125

Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
145                 150                 155                 160

Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
                165                 170                 175

Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
            180                 185                 190

Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
        195                 200                 205

Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
    210                 215


<210>  13
<211>  447
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17B21 Heavy Chain

<400>  13

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30

Tyr Phe Trp Asn Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Asp Gly Ser Asn Asn Tyr Asn Pro Ser Leu
    50                  55                  60
```

```
Lys Ser Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Pro Ser Pro Gly Thr Gly Tyr Ala Val Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205

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

Pro Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
```

            340   345   350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser Cys Ala
        355   360   365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370   375   380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385   390   395   400

Asp Gly Ser Phe Phe Leu Val Ser Arg Leu Thr Val Asp Lys Ser Arg
                405   410   415

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420   425   430

His Asn Arg Phe Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
        435   440   445

<210> 14
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> B17B21 Light Chain

<400> 14

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 Ser Ser Gln Ser Leu Val His Ser
            20   25   30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala
        35   40   45

Pro Lys Phe Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50   55   60

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65   70   75   80

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Ser Gln Ser
                85   90   95

Thr His Val Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100   105   110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115   120   125

```
Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140


Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160


Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175


Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190


Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205


Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210>  15
<211>  445
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I3RB217 Heavy Chain

<400>  15

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


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30


Trp Ile Ser Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Ile Ile Asp Pro Ser Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60


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


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Asp Gly Ser Thr Asp Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        115                 120                 125


Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly
    130                 135                 140
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Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys
    210                 215                 220

Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu
225                 230                 235                 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
                245                 250                 255

Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln
            260                 265                 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
        275                 280                 285

Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu
    290                 295                 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305                 310                 315                 320

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
                325                 330                 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
            340                 345                 350

Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys
        355                 360                 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
    370                 375                 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385                 390                 395                 400

Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
                405                 410                 415
```

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

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

<210> 16
<211> 215
<212> PRT
<213> Artificial Sequence

<220>
<223> I3RB217 Light Chain

<400> 16

Glu Ile Val Leu Thr Gln Ser Pro Gly 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 Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

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

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Gly Phe Pro
85 90 95

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

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

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190

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

```
Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210>  17
<211>  447
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Null Heavy Chain

<400>  17

Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
1               5                   10                  15


Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
            20                  25                  30


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


Trp Leu Ala His Ile Tyr Trp Asp Asp Asp Lys Arg Tyr Asn Pro Ser
    50                  55                  60


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


Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
                85                  90                  95


Cys Ala Arg Leu Tyr Gly Phe Thr Tyr Gly Phe Ala Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125


Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140


Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160


Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175


Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190


Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205


Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
    210                 215                 220
```

Pro Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
225 230 235 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
260 265 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
290 295 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
325 330 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu
355 360 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
435 440 445

<210> 18
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<223> Null Light Chain

<400> 18

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly

```
1               5                   10                  15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Gln Ser Val Asp Tyr Asn
            20                  25                  30

Gly Ile Ser Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35                  40                  45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Pro Glu Ser Gly Val Pro Asp
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ile Ile
                85                  90                  95

Glu Asp Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105                 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190

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

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210>  19
<211>  119
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17H3

<400>  19

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30


Tyr Phe Trp Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45


Val Ser Tyr Ile Ser Tyr Asp Gly Ser Asn Asn Tyr Ala Asp Ser Val
    50                  55                  60


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


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


Ala Lys Pro Ser Pro Gly Thr Gly Tyr Ala Val Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser
        115


<210>  20
<211>  120
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17H4

<400>  20

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30


Tyr Phe Trp Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45


Val Ser Tyr Ile Ser Tyr Asp Gly Ser Asn Asn Tyr Ala Asp Ser Val
    50                  55                  60


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


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


Ala Ser Pro Ser Pro Gly Thr Gly Tyr Ala Val Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

```
<210>  21
<211>  120
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17H5

<400>  21

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


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30


Tyr Phe Trp Asn Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45


Ile Gly Tyr Ile Ser Tyr Asp Gly Ser Asn Asn Tyr Asn Pro Ser Leu
    50                  55                  60


Lys Ser Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80


Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ser Pro Ser Pro Gly Thr Gly Tyr Ala Val Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  22
<211>  112
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17L3

<400>  22

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 Ser Ser Gln Ser Leu Val His Ser
            20                  25                  30


Asn Gly Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala
        35                  40                  45


Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60
```

```
Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65                  70                  75                  80


Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Ser Gln Ser
                85                  90                  95


Thr His Val Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


<210>  23
<211>  112
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17L4

<400>  23

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 Ser Ser Gln Ser Leu Val His Ser
            20                  25                  30


Asn Gly Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala
        35                  40                  45


Pro Lys Phe Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60


Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65                  70                  75                  80


Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Ser Gln Ser
                85                  90                  95


Thr His Val Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


<210>  24
<211>  112
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17L5

<400>  24

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1               5                   10                  15


Gln Pro 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 Phe Gln Gln Arg Pro Gly Gln Ser
```

```
        35                  40                  45


Pro Arg Phe 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 Val Gly Val Tyr Tyr Cys Ser Gln Ser
                85                  90                  95


Thr His Val Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


<210>  25
<211>  120
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17H1

<400>  25

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


Ser Leu Ser Leu Thr Cys Ser Val Ala Gly Tyr Ser Ile Thr Ser Gly
            20                  25                  30


Tyr Phe Trp Asn Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
        35                  40                  45


Met Gly Tyr Ile Ser Tyr Asp Gly Ser Asn Asn Tyr Asn Pro Ser Leu
    50                  55                  60


Lys Asn Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65                  70                  75                  80


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


Ala Ser Pro Ser Pro Gly Thr Gly Tyr Ala Val Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Ser Val Thr Val Ser Ser
        115                 120


<210>  26
<211>  112
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17L1
```

```
<400>  26

Asn Val 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 Phe Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Glu 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 Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


<210>  27
<211>  493
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  TCR-Vbeta17_Fc fusion

<400>  27

Met Ala Trp Val Trp Thr Leu Leu Phe Leu Met Ala Ala Ala Gln Ser
1               5                   10                  15


Ile Gln Ala Val Asp Gly Gly Ile Thr Gln Ser Pro Lys Tyr Leu Phe
            20                  25                  30


Arg Lys Glu Gly Gln Asn Val Thr Leu Ser Cys Glu Gln Asn Leu Asn
        35                  40                  45


His Asp Ala Met Tyr Trp Tyr Arg Gln Asp Pro Gly Gln Gly Leu Arg
    50                  55                  60


Leu Ile Tyr Tyr Ser Gln Ile Val Asn Asp Phe Gln Lys Gly Asp Ile
65                  70                  75                  80


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


Thr Val Thr Ser Ala Gln Lys Asn Pro Thr Ala Phe Tyr Leu Cys Ala
            100                 105                 110


Ser Ser Ser Arg Ser Ser Tyr Glu Gln Tyr Phe Gly Pro Gly Thr Arg
```

```
        115                 120                 125

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

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

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

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

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

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

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

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

Ala Trp Gly Arg Ala Asp Glu Pro Lys Ser Cys Asp Lys Thr His Thr
            260                 265                 270

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
        275                 280                 285

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
    290                 295                 300

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
305                 310                 315                 320

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
                325                 330                 335

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
            340                 345                 350

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
        355                 360                 365

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
    370                 375                 380

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Val Leu Pro Pro
385                 390                 395                 400
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```
Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Leu Cys Leu Val
                405                 410                 415


Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
            420                 425                 430


Gln Pro Glu Asn Asn Tyr Leu Thr Trp Pro Pro Val Leu Asp Ser Asp
        435                 440                 445


Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
    450                 455                 460


Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
465                 470                 475                 480


Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
                485                 490


<210>  28
<211>  719
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  B17B21 half antibody

<400>  28

Met Ala Trp Val Trp Thr Leu Leu Phe Leu Met Ala Ala Ala Gln Ser
1               5                   10                  15


Ile Gln Ala Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
            20                  25                  30


Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ser Ser Gln Ser Leu
        35                  40                  45


Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro
    50                  55                  60


Gly Lys Ala Pro Lys Phe Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
65                  70                  75                  80


Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
                85                  90                  95


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


Ser Gln Ser Thr His Val Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu
        115                 120                 125


Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
```

```
    130                 135                 140


Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
145                 150                 155                 160


Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
                165                 170                 175


Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
            180                 185                 190


Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
        195                 200                 205


Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
    210                 215                 220


Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Gly
225                 230                 235                 240


Ser Glu Gly Lys Ser Ser Gly Ser Gly Ser Glu Ser Lys Ser Thr Glu
                245                 250                 255


Gly Lys Ser Ser Gly Ser Gly Ser Glu Ser Lys Ser Thr Gly Gly Ser
            260                 265                 270


Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
        275                 280                 285


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Gly
    290                 295                 300


Tyr Phe Trp Asn Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
305                 310                 315                 320


Ile Gly Tyr Ile Ser Tyr Asp Gly Ser Asn Asn Tyr Asn Pro Ser Leu
                325                 330                 335


Lys Ser Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser
            340                 345                 350


Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
        355                 360                 365


Ala Ser Pro Ser Pro Gly Thr Gly Tyr Ala Val Asp Tyr Trp Gly Gln
    370                 375                 380


Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
385                 390                 395                 400


Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
                405                 410                 415
```

```
Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
            420                 425                 430

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
        435                 440                 445

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
    450                 455                 460

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
465                 470                 475                 480

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
                485                 490                 495

Pro Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
            500                 505                 510

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
        515                 520                 525

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
    530                 535                 540

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
545                 550                 555                 560

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
                565                 570                 575

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
            580                 585                 590

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
        595                 600                 605

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
    610                 615                 620

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser Cys Ala
625                 630                 635                 640

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
                645                 650                 655

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
            660                 665                 670

Asp Gly Ser Phe Phe Leu Val Ser Arg Leu Thr Val Asp Lys Ser Arg
        675                 680                 685
```

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
690 695 700

His Asn Arg Phe Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
705 710 715

<210> 29
<211> 4320
<212> DNA
<213> Artificial Sequence

<220>
<223> B17B21 half antibody

<400> 29
atggcctggg tgtggaccct gctgttcctg atggccgccg cccagagcat ccaggccgac 60

atccagatga cccagagccc aagcagcctg agcgccagcg tgggcgaccg cgtgaccatc 120

acctgccgca gcagccagag cctggtgcac agcaacggca acacctacct gcactggtac 180

cagcagaagc caggcaaggc ccccaaagttc ctgatctaca aggtgagcaa ccgcttcagc 240

ggcgtgccaa gccgcttcag cggcagcggc agcggcaccg acttcaccct gaccatcagc 300

agcctgcagc cagaggactt cgccacctac tactgcagcc agagcaccca cgtgccattc 360

accttcggcc agggcaccaa gctggagatc aagcgcaccg tggccgcccc aagcgtgttc 420

atcttcccac caagcgacga gcagctgaag agcggcaccg ccagcgtggt gtgcctgctg 480

aacaacttct acccacgcga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc 540

ggcaacagcc aggagagcgt gaccgagcag gacagcaagg acagcaccta cagcctgagc 600

agcaccctga ccctgagcaa ggccgactac gagaagcaca aggtgtacgc ctgcgaggtg 660

acccaccagg gcctgagcag cccagtgacc aagagcttca accgcggcga gtgcggcggc 720

agcgagggca agagcagcgg cagcggcagc gagagcaaga gcaccgaggg caagagcagc 780

ggcagcggca gcgagagcaa gagcaccggc ggcagccagg tgcagctgca ggagagcggc 840

ccaggcctgg tgaagccaag cgagaccctg agcctgacct gcaccgtgag cggctacagc 900

atcaccagcg gctacttctg gaactggatc cgccagccac caggcaaggg cctggagtgg 960

atcggctaca tcagctacga cggcagcaac aactacaacc caagcctgaa gagccgcgtg 1020

accatcagcc gcgacaccag caagaaccag ttcagcctga agctgagcag cgtgaccgcc 1080

gccgacaccg ccgtgtacta ctgcgccagc ccaagcccag gcaccggcta cgccgtggac 1140

tactggggcc agggcaccct ggtgaccgtg agcagcgcca gcaccaaggg cccaagcgtg 1200

ttcccactgg ccccatgcag ccgcagcacc agcgagagca ccgccgccct gggctgcctg 1260

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ggcgtgcaca ccttcccagc cgtgctgcag agcagcggcc tgtacagcct gagcagcgtg 1380

gtgaccgtgc caagcagcag cctgggcacc aagacctaca cctgcaacgt ggaccacaag 1440

ccaagcaaca ccaaggtgga caagcgcgtg gagagcaagt acggcccacc atgcccacca 1500

tgcccagccc cagaggccgc cggcggccca agcgtgttcc tgttcccacc aaagccaaag 1560 gacaccctga tgatcagccg caccccagag gtgacctgcg tggtggtgga cgtgagccag 1620

gaggacccag aggtgcagtt caactggtac gtggacggcg tggaggtgca caacgccaag 1680

accaagccac gcgaggagca gttcaacagc acctaccgcg tggtgagcgt gctgaccgtg 1740

ctgcaccagg actggctgaa cggcaaggag tacaagtgca aggtgagcaa caagggcctg 1800

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gtgaagggct tctacccaag cgacatcgcc gtggagtggg agagcaacgg ccagccagag 1980

aacaactaca agaccacccc accagtgctg gacagcgacg gcagcttctt cctggtgagc 2040

cgcctgaccg tggacaagag ccgctggcag gagggcaacg tgttcagctg cagcgtgatg 2100

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gcctgggtgt ggaccctgct gttcctgatg gccgccgccc agagcatcca ggccgacatc 2220

cagatgaccc agagcccaag cagcctgagc gccagcgtgg gcgaccgcgt gaccatcacc 2280

tgccgcagca gccagagcct ggtgcacagc aacggcaaca cctacctgca ctggtaccag 2340

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accctgccac caagccagga ggagatgacc aagaaccagg tgagcctgag ctgcgccgtg   4080

aagggcttct acccaagcga catcgccgtg gagtgggaga gcaacggcca gccagagaac   4140

aactacaaga ccaccccacc agtgctggac agcgacggca gcttcttcct ggtgagccgc   4200

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<210> 30
<211> 713
<212> PRT
<213> Artificial Sequence

<220>
<223> I3RB217 half antibody

<400> 30

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Met Ala Trp Val Trp Thr Leu Leu Phe Leu Met Ala Ala Ala Gln Ser
1               5                   10                  15


Ile Gln Ala Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu
            20                  25                  30


Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val
        35                  40                  45


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


Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp
65                  70                  75                  80


Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
                85                  90                  95


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


Gly Phe Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
        115                 120                 125


Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
    130                 135                 140
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Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
145                 150                 155                 160

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
                165                 170                 175

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

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
        195                 200                 205

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
    210                 215                 220

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Gly Ser Glu Gly Lys
225                 230                 235                 240

Ser Ser Gly Ser Gly Ser Glu Ser Lys Ser Thr Glu Gly Lys Ser Ser
                245                 250                 255

Gly Ser Gly Ser Glu Ser Lys Ser Thr Gly Gly Ser Glu Val Gln Leu
            260                 265                 270

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu Ser Leu Lys Ile
        275                 280                 285

Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr Trp Ile Ser Trp
    290                 295                 300

Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met Gly Ile Ile Asp
305                 310                 315                 320

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

Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr Leu Gln Trp Ser
            340                 345                 350

Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala Arg Gly Asp
        355                 360                 365

Gly Ser Thr Asp Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
    370                 375                 380

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys
385                 390                 395                 400

Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys
                405                 410                 415
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Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
            420                 425                 430

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
        435                 440                 445

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
    450                 455                 460

Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val
465                 470                 475                 480

Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro
                485                 490                 495

Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
            500                 505                 510

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
        515                 520                 525

Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr
    530                 535                 540

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
545                 550                 555                 560

Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                565                 570                 575

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            580                 585                 590

Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        595                 600                 605

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met
    610                 615                 620

Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro
625                 630                 635                 640

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                645                 650                 655

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            660                 665                 670

Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val
        675                 680                 685
```

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
690 695 700

Lys Ser Leu Ser Leu Ser Leu Gly Lys
705 710

<210> 31
<211> 2139
<212> DNA
<213> Artificial Sequence

<220>
<223> I3RB217 half antibody

<400> 31
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atcgtgctga cccagagccc aggcaccctg agcctgagcc caggcgagcg cgccaccctg 120

agctgccgcg ccagccagag cgtgagcagc agctacctgg cctggtacca gcagaagcca 180

ggccaggccc cacgcctgct gatctacggc gccagcagcc gcgccaccgg catcccagac 240

cgcttcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagccg cctggagcca 300

gaggacttcg ccgtgtacta ctgccagcag gactacggct tcccatggac cttcggccag 360

ggcaccaagg tggagatcaa gcgcaccgtg gccgccccaa gcgtgttcat cttcccacca 420

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ccacgcgagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 540

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ctgagcagcc cagtgaccaa gagcttcaac cgcggcgagt gcggcggcag cgagggcaag 720

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tggatcagct gggtgcgcca gatgccaggc aagggcctgg agtggatggg catcatcgac 960

ccaagcgaca gcgacacccg ctacagccca agcttccagg gccaggtgac catcagcgcc 1020

gacaagagca tcagcaccgc ctacctgcag tggagcagcc tgaaggccag cgacaccgcc 1080

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cagttcaaca gcacctaccg cgtggtgagc gtgctgaccg tgctgcacca ggactggctg 1740

aacggcaagg agtacaagtg caaggtgagc aacaagggcc tgccaagcag catcgagaag 1800

accatcagca aggccaaggg ccagccacgc gagccacagg tgtacaccct gccaccaagc 1860

caggaggaga tgaccaagaa ccaggtgagc ctgtggtgcc tggtgaaggg cttctaccca 1920

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ccaccagtgc tggacagcga cggcagcttc ttcctgtaca gccgcctgac cgtggacaag 2040

agccgctggc aggagggcaa cgtgttcagc tgcagcgtga tgcacgaggc cctgcacaac 2100

cactacaccc agaagagcct gagcctgagc ctgggcaag 2139

<210> 32
<211> 713
<212> PRT
<213> Artificial Sequence

<220>
<223> B23B49 half antibody

<400> 32

Met Ala Trp Val Trp Thr Leu Leu Phe Leu Met Ala Ala Ala Gln Ser
1   5   10   15

Ile Gln Ala Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu
            20   25   30

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val
        35   40   45

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

Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp
65   70   75   80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
                85   90   95

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

Gly Phe Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
        115   120   125

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
    130   135   140

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
145   150   155   160

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Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
                165                 170                 175

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

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
        195                 200                 205

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
    210                 215                 220

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Gly Ser Glu Gly Lys
225                 230                 235                 240

Ser Ser Gly Ser Gly Ser Glu Ser Lys Ser Thr Glu Gly Lys Ser Ser
                245                 250                 255

Gly Ser Gly Ser Glu Ser Lys Ser Thr Gly Gly Ser Glu Val Gln Leu
            260                 265                 270

Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu Ser Leu Lys Ile
        275                 280                 285

Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr Trp Ile Ser Trp
    290                 295                 300

Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met Gly Ile Ile Asp
305                 310                 315                 320

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

Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr Leu Gln Trp Ser
            340                 345                 350

Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala Arg Gly Asp
        355                 360                 365

Gly Ser Thr Asp Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
    370                 375                 380

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys
385                 390                 395                 400

Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys
                405                 410                 415

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
            420                 425                 430
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Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
        435                 440                 445

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
    450                 455                 460

Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val
465                 470                 475                 480

Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro
                485                 490                 495

Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
            500                 505                 510

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
        515                 520                 525

Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr
    530                 535                 540

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
545                 550                 555                 560

Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                565                 570                 575

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            580                 585                 590

Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        595                 600                 605

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met
    610                 615                 620

Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro
625                 630                 635                 640

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                645                 650                 655

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            660                 665                 670

Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val
        675                 680                 685

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
    690                 695                 700
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Lys Ser Leu Ser Leu Ser Leu Gly Lys
705   710

<210> 33
<211> 2154
<212> DNA
<213> Artificial Sequence

<220>
<223> B23B49 half antibody

<400> 33
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aactgccgcg ccagccagag cgtggactac aacggcatca gctacatgca ctggtaccag   180

cagaagccag gccagccacc aaagctgctg atctacgccg ccagcaaccc agagagcggc   240

gtgccagacc gcttcagcgg cagcggcagc ggcaccgact tcaccctgac catcagcagc   300

ctgcaggccg aggacgtggc cgtgtactac tgccagcaga tcatcgagga cccatggacc   360

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aacagccagg agagcgtgac cgagcaggac agcaaggaca gcacctacag cctgagcagc   600

accctgaccc tgagcaaggc cgactacgag aagcacaagg tgtacgcctg cgaggtgacc   660

caccagggcc tgagcagccc agtgaccaag agcttcaacc gcggcgagtg cggcggcagc   720

gagggcaaga gcagcggcag cggcagcgag agcaagagca ccgagggcaa gagcagcggc   780

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gtggacaccg ccacctacta ctgcgcccgc ctgtacggct tcacctacgg cttcgcctac   1140

tggggccagg gcaccctggt gaccgtgagc agcgccagca ccaagggccc aagcgtgttc   1200

ccactggccc catgcagccg cagcaccagc gagagcaccg ccgccctggg ctgcctggtg   1260

aaggactact tcccagagcc agtgaccgtg agctggaaca gcggcgccct gaccagcggc   1320

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gacccagagg tgcagttcaa ctggtacgtg gacggcgtgg aggtgcacaa cgccaagacc   1680

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agcagcatcg agaagaccat cagcaaggcc aagggccagc cacgcgagcc acaggtgtac     1860

accctgccac caagccagga ggagatgacc aagaaccagg tgagcctgtg gtgcctggtg     1920

aagggcttct acccaagcga catcgccgtg gagtgggaga gcaacggcca gccagagaac     1980

aactacaaga ccaccccacc agtgctggac agcgacggca gcttcttcct gtacagccgc     2040

ctgaccgtgg acaagagccg ctggcaggag ggcaacgtgt tcagctgcag cgtgatgcac     2100

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<210>  34
<211>  5
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I3RB217 HCDR1

<400>  34

Ser Tyr Trp Ile Ser
1               5


<210>  35
<211>  17
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I3RB217 HCDR2

<400>  35

Ile Ile Asp Pro Ser Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln
1               5                   10                  15


Gly



<210>  36
<211>  9
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I3RB217 HCDR3

<400>  36

Gly Asp Gly Ser Thr Asp Leu Asp Tyr
1               5


<210>  37
<211>  11
<212>  PRT
<213>  Artificial Sequence

<220>
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<223>  I3RB217 LCDR1

<400>  37

Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu
1               5                   10


<210>  38
<211>  7
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I3RB217 LCDR2

<400>  38

Gly Ala Ser Ser Arg Ala Thr
1               5


<210>  39
<211>  9
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I3RB217 LCDR3

<400>  39

Gln Gln Asp Tyr Gly Phe Pro Trp Thr
1               5


<210>  40
<211>  118
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I3RB217 HC

<400>  40

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


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30


Trp Ile Ser Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Ile Ile Asp Pro Ser Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60


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


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
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Ala Arg Gly Asp Gly Ser Thr Asp Leu Asp Tyr Trp Gly Gln Gly Thr
            100   105   110

Leu Val Thr Val Ser Ser
        115

<210> 41
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> I3RB217 LC

<400> 41

Glu Ile Val Leu Thr Gln Ser Pro Gly 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 Ser Ser
            20   25   30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35   40   45

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

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65   70   75   80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Gly Phe Pro
                85   90   95

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 42
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> IGHJ1*01 HC

<400> 42

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1   5   10

<210> 43
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> IGKJ2*01 LC

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<400>  43

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
1               5                   10


<210>  44
<211>  449
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Va10.2_Fc fusion

<400>  44

Met Ala Trp Val Trp Thr Leu Leu Phe Leu Met Ala Ala Ala Gln Ser
1               5                   10                  15


Ile Gln Ala Gln Leu Leu Glu Gln Ser Pro Gln Phe Leu Ser Ile Gln
            20                  25                  30


Glu Gly Glu Asn Leu Thr Val Tyr Cys Asn Ser Ser Ser Val Phe Ser
        35                  40                  45


Ser Leu Gln Trp Tyr Arg Gln Glu Pro Gly Glu Gly Pro Val Leu Leu
    50                  55                  60


Val Thr Val Val Thr Gly Gly Glu Val Lys Lys Leu Lys Arg Leu Thr
65                  70                  75                  80


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


Ala Gln Pro Gly Asp Thr Gly Leu Tyr Leu Cys Ala Gly Ala Gly Ser
            100                 105                 110


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


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


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


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


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


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


Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser Glu Pro Lys Ser Cys Asp
```

```
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Val Tyr Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Ala Leu Val Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly
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