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(54) **ANTI-VBETA17/ANTI-CD123 BISPECIFIC ANTIBODIES**

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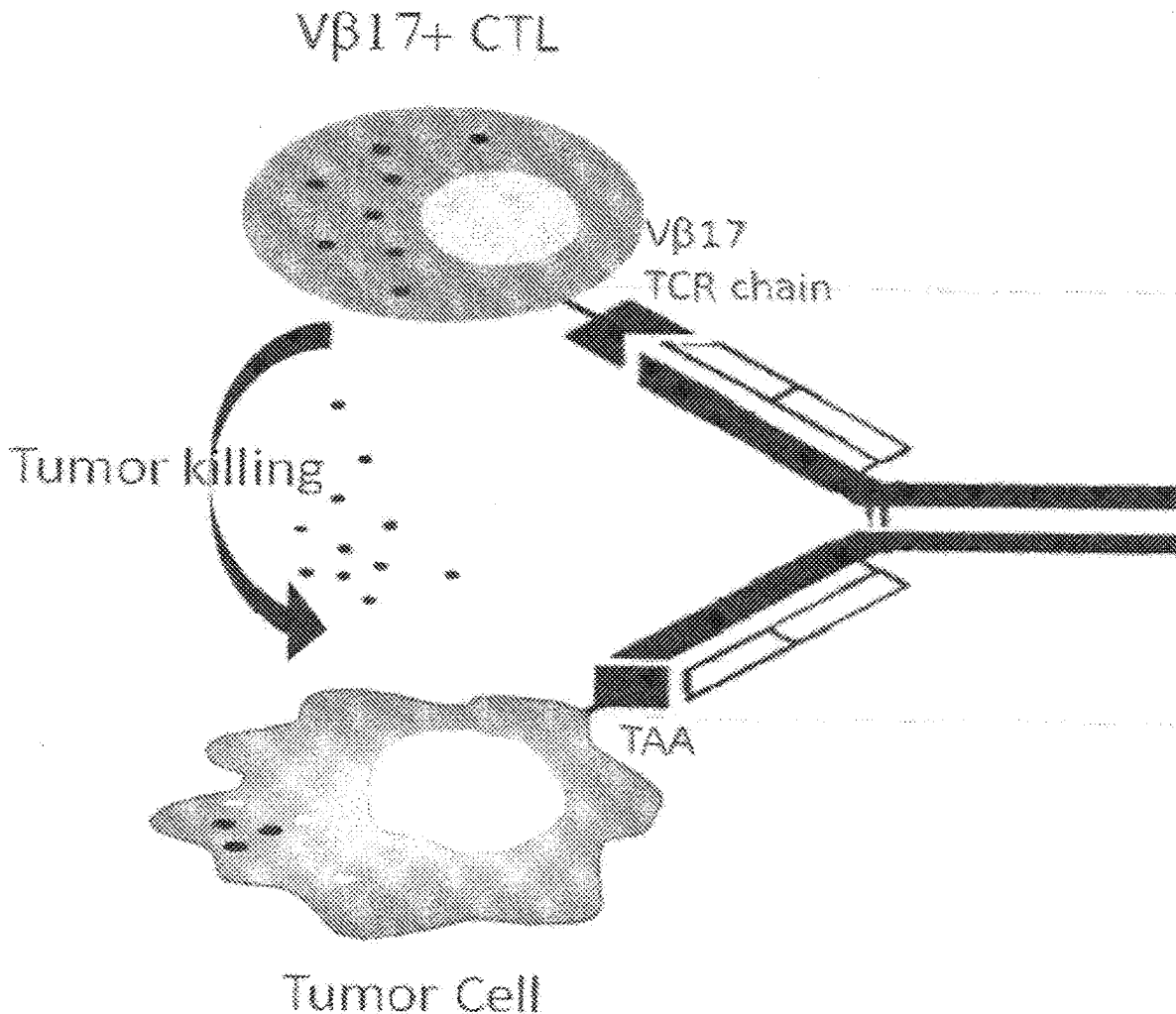
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(57)

ABSTRACT

Anti-V β 17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof are described. Also described are nucleic acids encoding the antibodies, compositions comprising the antibodies, methods of producing the antibodies, and methods of using the antibodies.

Specification includes a Sequence Listing.



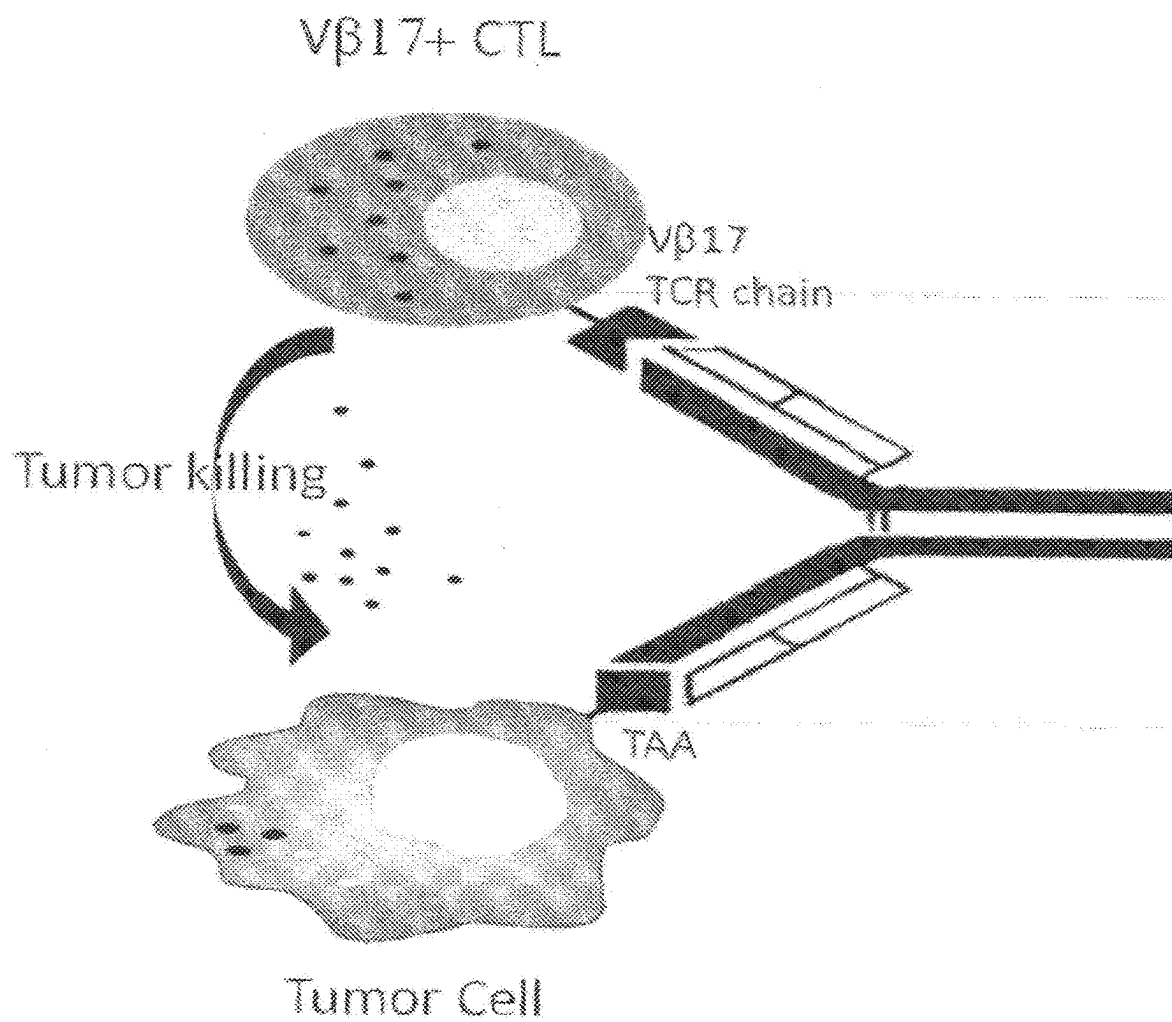


FIG. 1

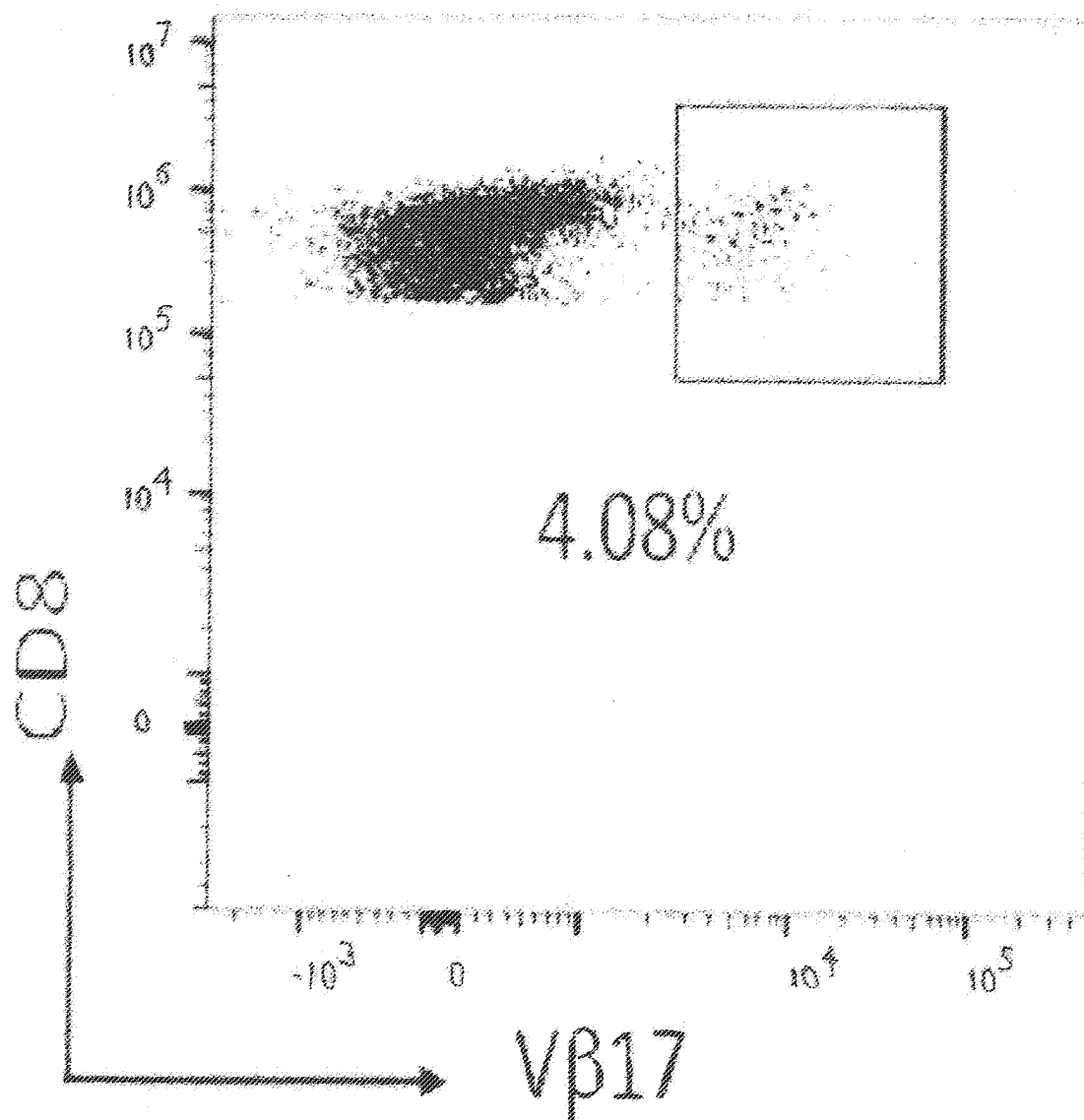


FIG. 2A

Donor	HLA status	% of V β 17 ⁺ in CD8 T cells (Day 0)	% of V β 17 ⁺ 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

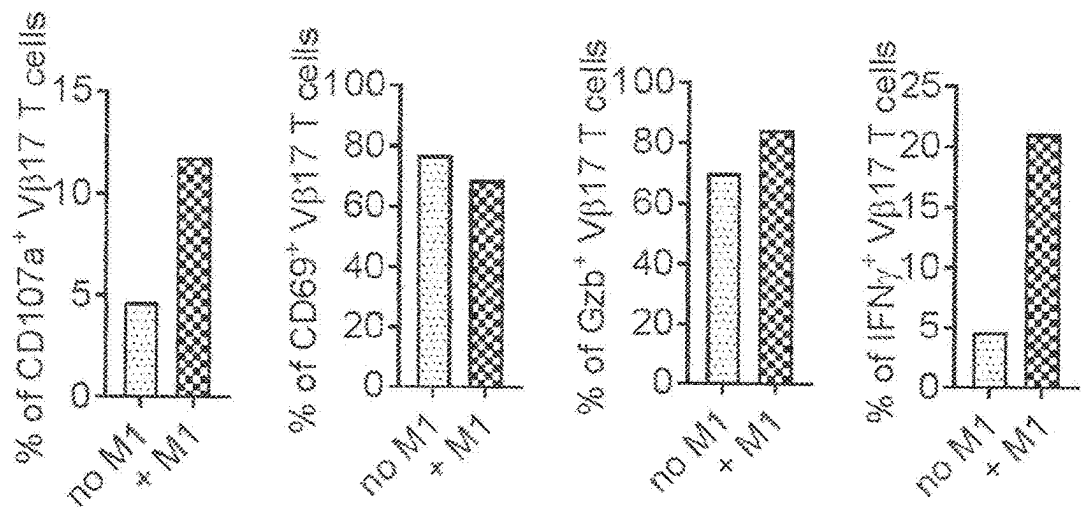


FIG. 3

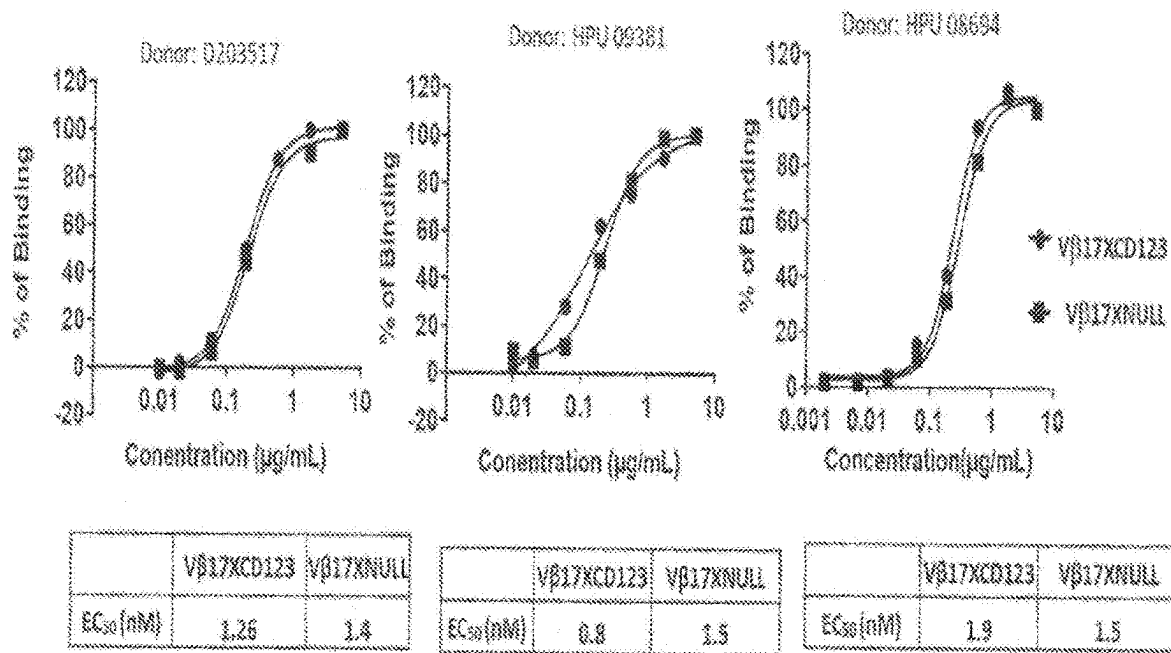
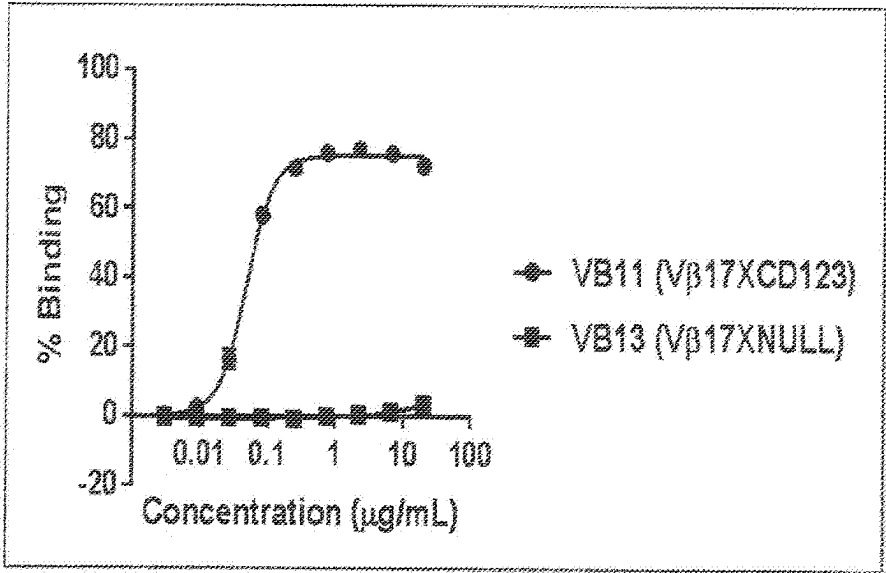
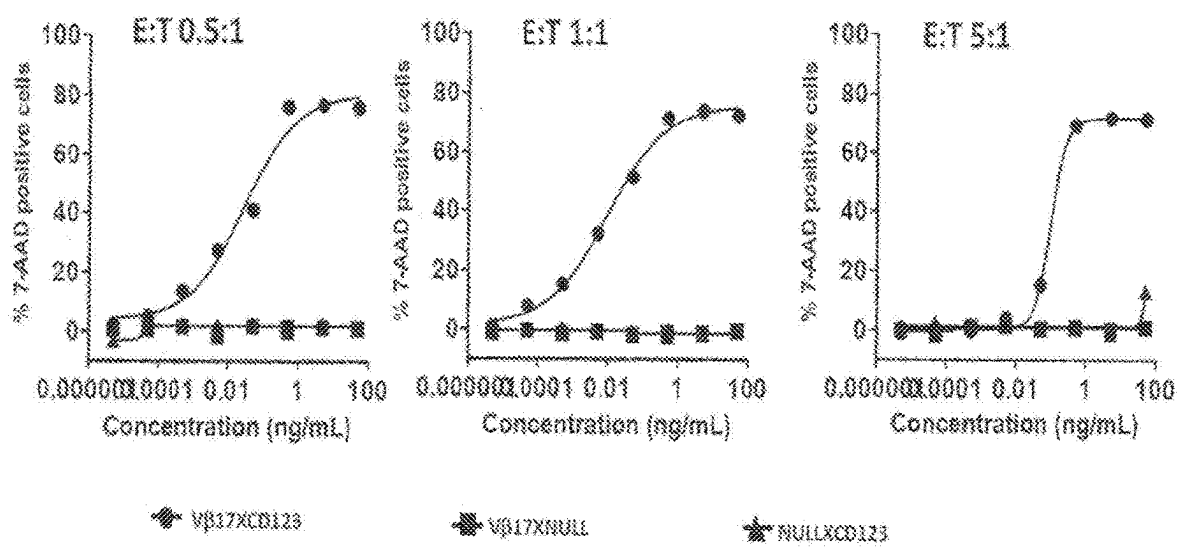


FIG. 4



	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
VB17XNULL	ND	ND	ND
VB17XCD123	0.4	0.2	1.0

FIG. 6

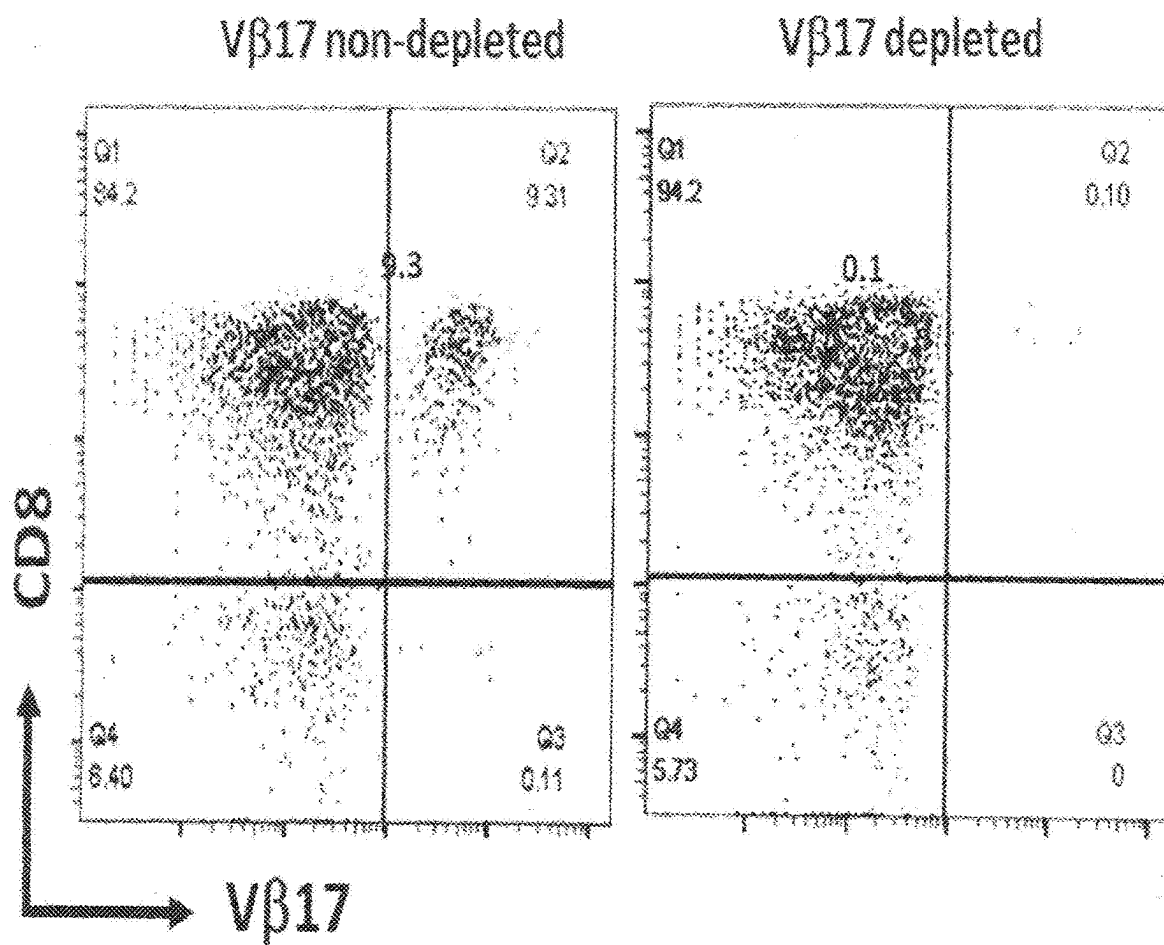
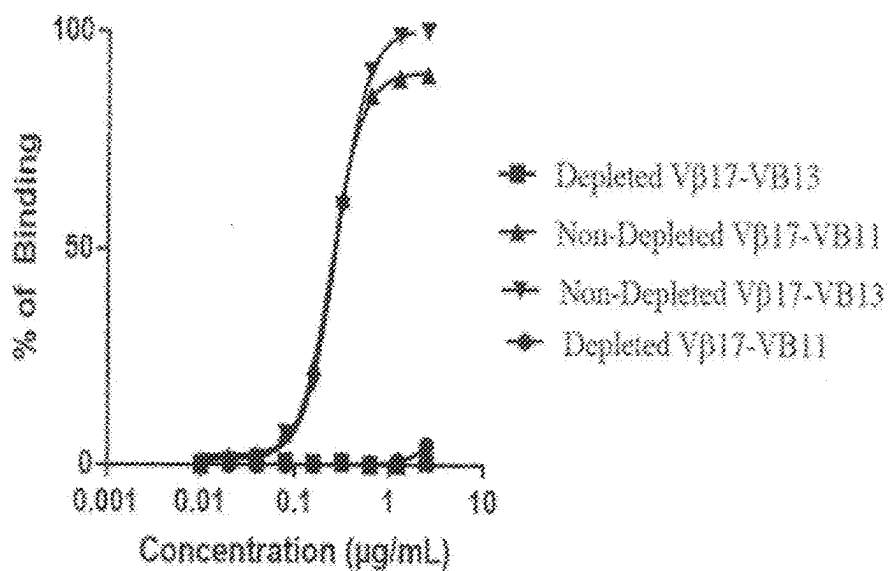


FIG. 7A



	EC50 (nM)
VB11	12.2
VB13	12.6

FIG. 7B

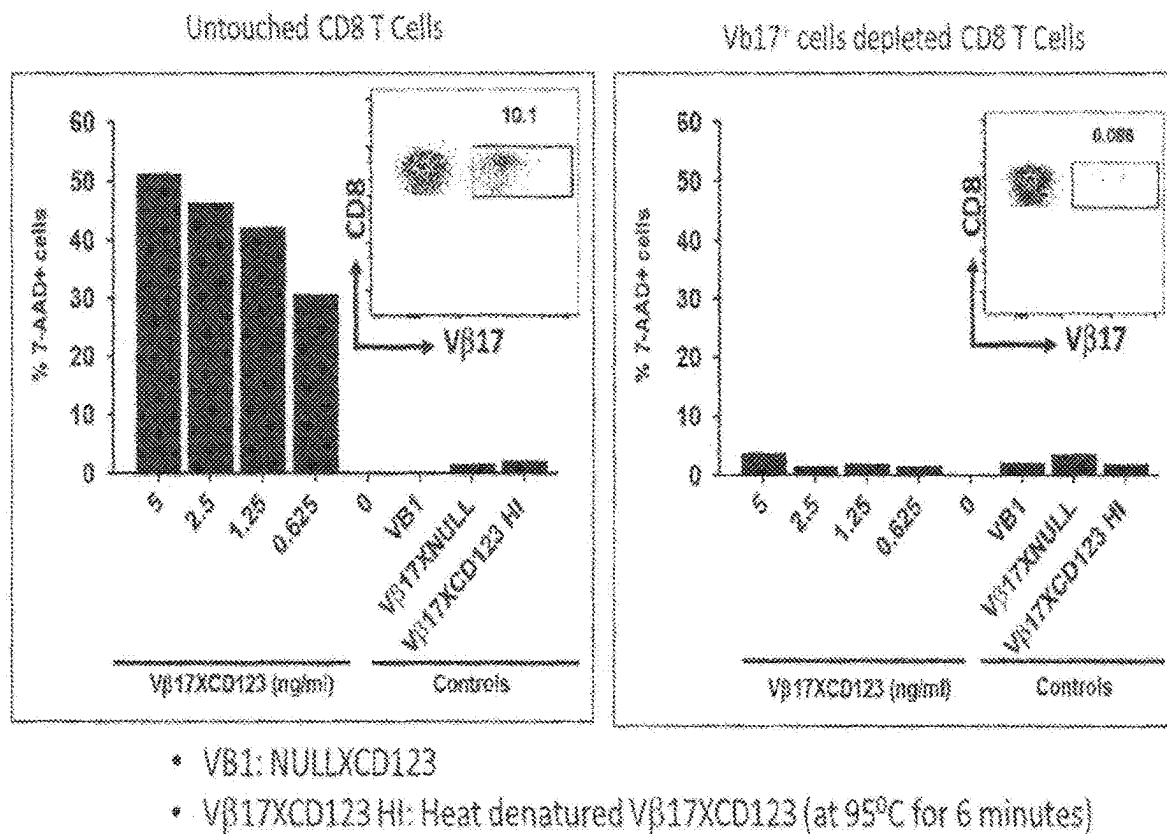


FIG. 8

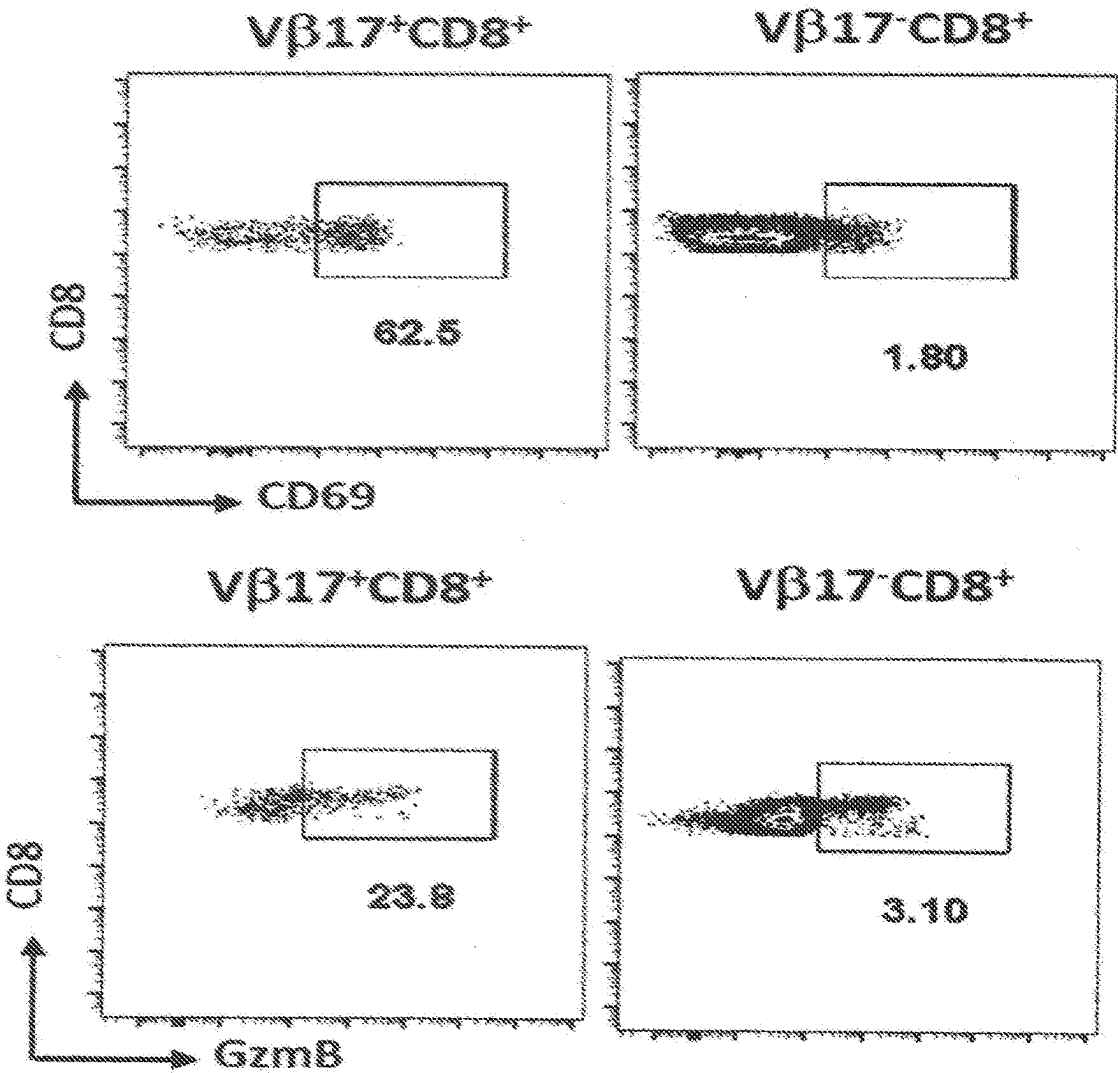


FIG. 9A

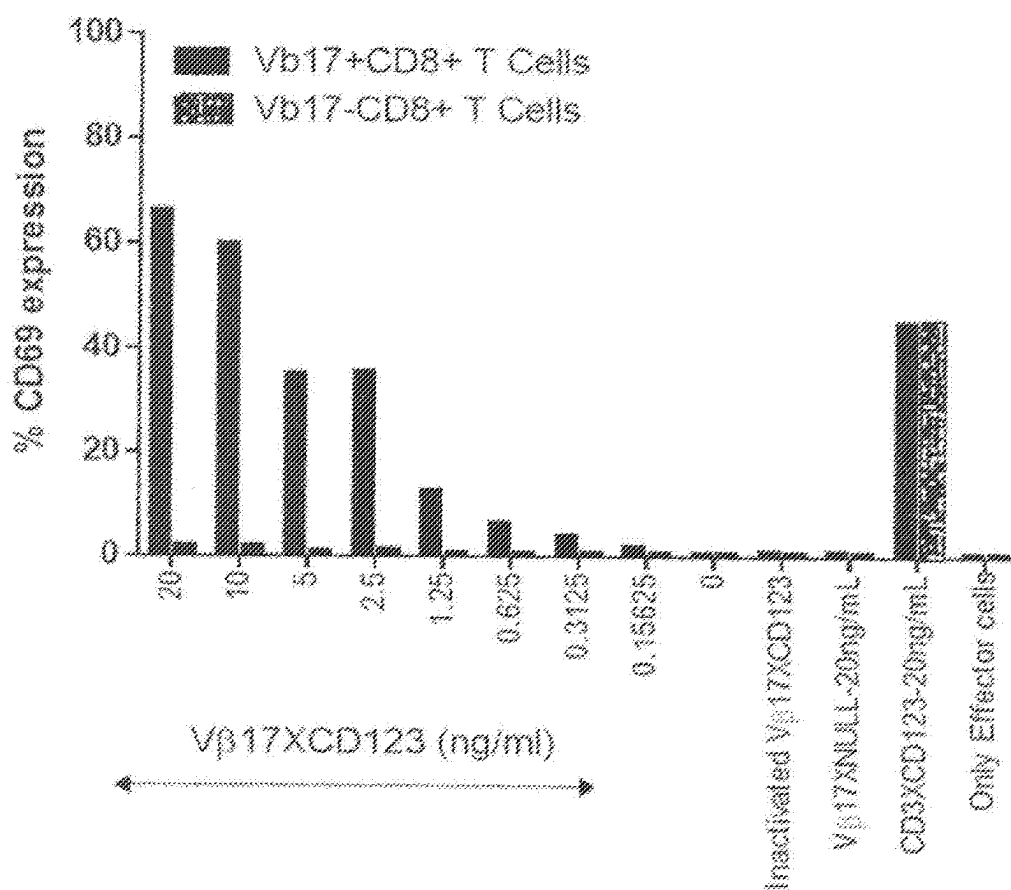


FIG. 9B

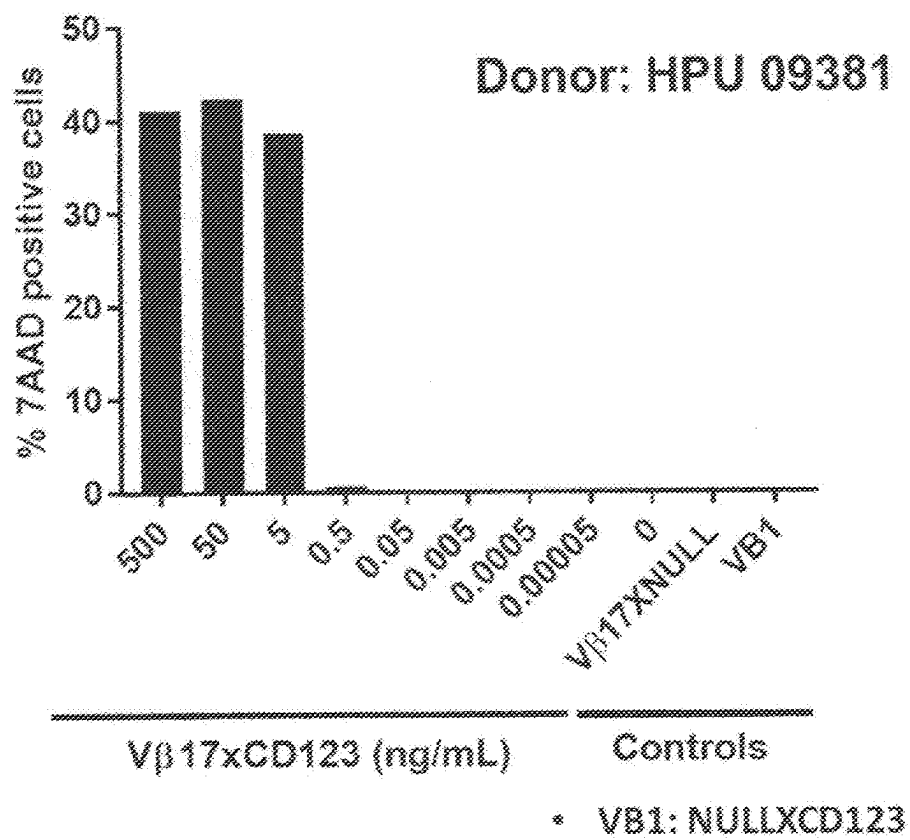


FIG. 10

ANTI-VBETA17/ANTI-CD123 BISPECIFIC ANTIBODIES

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation of U.S. patent application Ser. No. 17/437,771, filed on Sep. 9, 2021, which is the U.S. National Stage Application under 35 U.S.C. § 371 of International Patent Application No. PCT/IB2020/000342, filed on Mar. 11, 2020, which claims the benefit of U.S. Provisional Application No. 62/816,464, filed on Mar. 11, 2019, the disclosure of each of which is incorporated by reference herein 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. The contents of the electronic sequence listing (065768.133US3.xml; size 72,235 bytes; and creation date Feb. 24, 2025) 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:

- [0008]** a. a first heavy chain (HC1);
- [0009]** b. a second heavy chain (HC2);
- [0010]** c. a first light chain (LC1); and
- [0011]** 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.

[0012] 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.

[0013] In certain embodiments, HC2 and LC2 bind to CD123.

[0014] In certain embodiments, the bispecific antibody or antigen-binding fragment thereof is an IgG isotype, such as IgG4.

[0015] 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.

[0016] 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:

- [0017]** a. a first heavy chain (HC1);
- [0018]** b. a second heavy chain (HC2)
- [0019]** c. a first light chain (LC1); and
- [0020]** 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. 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 V β 17 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.

[0021] In certain embodiments, the anti-V β 17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof are chimeric, partially humanized, or fully humanized.

[0022] Also provided are isolated humanized V β 17 monoclonal antibodies or antigen-binding fragments thereof. The isolated humanized V β 17 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 V β 17 monoclonal antibody or antigen-binding fragment thereof comprises an amino acid sequence of SEQ ID NO:28.

[0023] 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.

[0024] 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.

[0025] Also provided are host cells comprising the vectors comprising the isolated nucleic acids disclosed herein.

[0026] Also provided are methods of directing a V β 17-expressing CD8+ or CD4+ T cell to a cancer cell. The methods comprise contacting a V β 17-expressing CD8+ or CD4+ T cell with a anti-V β 17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof disclosed herein. Contacting the V β 17-expressing CD8+ or CD4+ T cell with the anti-V β 17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof can direct the V β 17-expressing CD8+ or CD4+ T cell to a cancer cell.

[0027] 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.

[0028] 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.

[0029] 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.

[0030] Also provided are kits comprising bispecific antibodies or antigen-binding fragments thereof disclosed herein and packaging for the same.

BRIEF DESCRIPTION OF THE DRAWINGS

[0031] 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.

[0032] FIG. 1 shows a schematic demonstrating the binding of an anti-V β 17/anti-tumor antigen bispecific antibody to recruit T-cells to a cancer cell and to induce cancer cell death.

[0033] FIGS. 2A-2B shows that V β 17+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 V β 17 (V β 17+) on the cells surface from healthy subjects. FIG. 2B shows HLA sub-type of various donors and presence of percent V β 17+ CD8+ T cells identified as day 0, and after in vitro expansion with M1 peptide for 14 days (Day 14).

[0034] FIG. 3 shows V β 17+CD8+ T cells have hallmarks of killer cytotoxic cells. Bar graph indicates expression of CD107a, CD69, Granzyme B (Gzb) and Interferon- γ (IFN γ) on gated PBMCs for CD8+ T cells expressing V β 17 (V β 17+) on the cell surface at day 0 (no M1) and at day 14 after stimulation with M1 peptide (+M1).

[0035] FIG. 4 shows binding of V β 11 [anti-V β 17/anti-CD123] bispecific as well as V β 13 [V β 17 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 EC₅₀ values for binding in nM.

[0036] FIG. 5 shows binding of V β 17 and CD123 bispecific (V β 11) as well as V β 17 null control bispecific (V β 13) antibodies to AML cancer cell line. Data presented shows binding of bispecific antibodies to Kasumi3 AML cell line. The table below the graph presents EC₅₀ values for binding in nM.

[0037] FIG. 6 shows redirection of V β 17+ 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 ET ratio 5:1 and

dose titration of bispecific antibodies. The table below the graphs shows EC₅₀ values calculated from the above graphs given in pM.

[0038] FIGS. 7A-7B show specific binding of an anti-Vβ17/anti-CD123 bispecific antibody (Vβ11) and a Vβ17 null bispecific antibody (Vβ13) 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 (Vβ11) and a Vβ17 null bispecific antibody (Vβ13) to CD8+ T cells from FIG. 7A. A dose response of bispecific antibodies is shown in the figure. The table below the graph shows EC₅₀ values for binding calculated from the above graph given in nM.

[0039] 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 effector 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.

[0040] 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.

[0041] 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

[0042] 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.

[0043] 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.

[0044] 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 sub-ranges, all individual numerical values within that range, including integers within such ranges and fractions of the values unless the context clearly indicates otherwise.

[0045] 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.

[0046] 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.

[0047] 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).

[0048] 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.”

[0049] 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.

[0050] 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 V β 17 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.

[0051] 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.

[0052] 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)).

[0053] 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.

[0054] 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)).

[0055] 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.

[0056] 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.

Antibodies

[0057] Described herein are isolated anti-V β 17 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-V β 17/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 V β 17 and/or CD123, high specificity to V β 17 and/or CD123, and the ability to treat or prevent cancer when administered alone or in combination with other anti-cancer therapies.

[0058] 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.

[0059] 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 V β 17 is substantially free of antibodies that do not bind to V β 17; 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.

[0060] 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.

[0061] 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').

[0062] 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.

[0063] 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.

[0064] As used herein, the term “bispecific 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 V β 17 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 V β 17 and the second epitope is located on CD123. In an embodiment, the first epitope is located on V β 17 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.

[0065] 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.

[0066] As used herein, the term “V β 17” refers to a T cell receptor, which is expressed in response to an immune response on a cytotoxic T cell. V β 17-expressing CD8⁺ T cells are commonly produced in response to influenza A virus exposure in a subject. V β 17-expressing CD8⁺ T cells provide great recall in response to influenza exposure in the subject. The term “V β 17” includes any V β 17 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 V β 17 is a human V β 17. A human V β 17 amino acid sequence is provided by GenBank Accession Number AAB49730.1.

[0067] 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.

[0068] As used herein, an antibody that “specifically binds to V β 17” refers to an antibody that binds to a V β 17, preferably a human V β 17, 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.

[0069] 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.

[0070] The smaller the value of the KD of an antibody, the higher affinity that the antibody binds to a target antigen.

[0071] According to a particular aspect, the invention relates to an isolated V β 17 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.

[0072] 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 V β 17 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 V β 17 bispecific antibody to V β 17 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.

[0073] Also provided herein are anti-V β 17/anti-CD123 bispecific antibodies or antigen-binding fragments thereof comprising an anti-V β 17 antibody or an antigen-binding fragment thereof and an anti-CD123 antibody or antigen-binding fragment thereof. In certain embodiments the anti-V β 17/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.

[0074] 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 V β 17. 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.

[0075] In certain embodiments, the V β 17 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).

[0076] 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.

[0077] 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 mol-

ecules 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.

[0078] 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).

[0079] 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).

[0080] 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).

[0081] 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).

[0082] In some embodiments, Fab fusion bispecific antibodies include F(ab)₂ (Medarex/AMGEN), Dual-Action or Bis-Fab (Genentech), Dock-and-Lock (DNL®) (Immuno-Medics), Bivalent Bispecific (Biotecnoland 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®) (Aflimed), 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.

[0083] 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.

[0084] “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.

[0085] “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.

[0086] The “knob-in-hole” strategy (see, e.g., PCT Int. 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.

[0087] 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, T366L_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.

[0088] 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. WO2011/131746. 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.

[0089] In certain embodiments, the anti-V β 17 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:

[0090] 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:

[0091] 1. SEQ ID NOs: 34, 35, 36, 37, 38, and 39, respectively.

[0092] According to another particular aspect, the invention relates to an isolated anti-V β 17/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 EC₅₀ of less than about 1 pM. In certain embodiments, the EC₅₀ 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-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof comprises an IgG1, IgG2, IgG3, or IgG4 backbone. In one such embodiment, the anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof has an antibody backbone of the IgG4 isotype.

[0093] In some embodiments described herein, immune effector properties of the anti-V β 17/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 C1q 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.

[0094] “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.

[0095] 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 Fc γ RIIIa 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-fucosyltransferase (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 α -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).

[0096] In some embodiments described herein, ADCC elicited by the anti-V β 17/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.

[0097] According to another particular aspect, the invention relates to an isolated anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof capable of inducing T-cell dependent cytotoxicity in V β 17-expressing cells and/or CD123-expressing cells. The bispecific antibody or antigen-binding fragment thereof can, for example, induce T-cell dependent cytotoxicity in V β 17-expressing cells and/or CD123-expressing cells in vitro with an EC₅₀ value of less than about 2 nM. In certain embodiments, the EC₅₀ is less than about 2.0 nM, less than about 1.9 nM, less than about 1.8 nM, less than about 1.7 nM, less than about 1.6 nM, less than about 1.5 nM, less than about 1.4 nM, less than about 1.3 nM, less than about 1.2 nM, less than about 1.1 nM, less than about 1.0 nM, less than about 0.9 nM, less than about 0.8 nM, less than about 0.7 nM, less than about 0.6 nM, less than about 0.5 nM, less than about 0.4 nM, less than about 0.3 nM, less than about 0.2 nM, and less than about 0.1 nM.

[0098] According to another particular aspect, the invention relates to an isolated anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof, wherein the anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof is chimeric.

[0099] According to another particular aspect, the invention relates to an isolated anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof, wherein the anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof is human or humanized.

[0100] In another general aspect, the invention relates to an isolated humanized V β 17 monoclonal antibody or antigen-binding fragment thereof. The isolated humanized V β 17 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 V β 17 monoclonal antibody or antigen-binding fragment thereof comprises the amino acid sequence of SEQ ID NO:28.

[0101] 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.

[0102] 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.

[0103] 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 electropo-

ration, where it is stably integrated into the host cell genome such that the recombinant nucleic acid is effectively expressed.

[0104] 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

[0105] 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-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof.

[0106] The functional activity of bispecific antibodies and antigen-binding fragments thereof that bind V β 17 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 V β 17 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 V β 17 on CD8+ or CD4+ T cells. According to particular embodiments, the methods for characterizing antibodies and antigen-binding fragments thereof that bind V β 17 and/or CD123 include those described below.

[0107] In another general aspect, the invention relates to a method of directing V β 17-expressing CD8+ or CD4+ T cells to a cancer cell. The methods comprise contacting the V β 17-expressing CD8+ or CD4+ T cell with a anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof, wherein the antibody or antibody fragment directs the V β 17-expressing CD8+ or CD4+ T cell to a cancer cell having CD123 on its surface.

[0108] In another general aspect, the invention relates to a method for inhibiting growth or proliferation of cancer cells. The methods comprise contacting the V β 17-expressing CD8+ T cells with a anti-V β 17/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.

[0109] According to embodiments of the invention, the described anti-V β 17/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-V β 17/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

[0110] This invention provides the following non-limiting embodiments.

[0111] Embodiment 1 is an isolated V β 17 bispecific antibody or antigen-binding fragment thereof, the isolated V β 17 bispecific antibody or antigen-binding fragment thereof comprising:

- [0112] a. a first heavy chain (HC1);
- [0113] b. a second heavy chain (HC2);
- [0114] c. a first light chain (LC1); and
- [0115] 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.

[0116] Embodiment 2 is the V β 17 bispecific antibody or antigen-binding fragment thereof of embodiment 1, wherein the binding site for the first antigen binds to V β 17 on a CD8+ or CD4+ T cell.

[0117] Embodiment 3 is the V β 17 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.

[0118] Embodiment 4 is the V β 17 bispecific antibody or antigen-binding fragment of any one of embodiments 1 to 3, wherein HC1 and LC1 are humanized.

[0119] Embodiment 5 is the V β 17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 4, wherein HC2 and LC2 bind to CD123.

[0120] Embodiment 6 is the V β 17 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.

[0121] Embodiment 7 is the V β 17 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.

[0122] Embodiment 8 is the V β 17 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 EC₅₀ of less than about 0.2 pM.

[0123] Embodiment 9 is an isolated nucleic acid encoding HC1 and LC1 of the V β 17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 8.

[0124] Embodiment 10 is an isolated nucleic acid encoding HC2 and LC2 of the V β 17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 8.

[0125] Embodiment 11 is a vector comprising the isolated nucleic acid of embodiment 9 or embodiment 10.

[0126] Embodiment 12 is a host cell comprising the vector of embodiment 11.

[0127] Embodiment 13 is a buffered composition comprising the isolated V β 17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 8 and a buffered solution.

[0128] Embodiment 14 is an isolated anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof comprising:

- [0129] a. a first heavy chain (HC1);
- [0130] b. a second heavy chain (HC2)
- [0131] c. a first light chain (LC1); and
- [0132] 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 V β 17, 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.

[0133] Embodiment 15 is the isolated anti-V β 17/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.

[0134] Embodiment 16 is the isolated anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of embodiment 14 or embodiment 15, wherein the V β 17 is on the surface of a CD8+ or CD4+ T cell.

[0135] Embodiment 17 is the isolated anti-V β 17/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.

[0136] Embodiment 18 is the isolated anti-V β 17/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 EC₅₀ of less than about 0.2 pM.

[0137] Embodiment 19 is an isolated nucleic acid encoding the HC1 and LC1 of the anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 14 to 18.

[0138] Embodiment 20 is an isolated nucleic acid encoding the HC2 and LC2 of the anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 14 to 18.

[0139] Embodiment 21 is a vector comprising the isolated nucleic acid of embodiment 19 or embodiment 20.

[0140] Embodiment 22 is a host cell comprising the vector of embodiment 21.

[0141] Embodiment 23 is a buffered composition comprising the isolated anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 14 to 18 and a buffered solution.

[0142] Embodiment 24 is a method of directing a V β 17-expressing CD8+ or CD4+ T cell to a cancer cell, the method comprising contacting a V β 17-expressing CD8+ or CD4+ T cell with the anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 8 or 14 to 18, wherein contacting the V β 17-expressing CD8+ or CD4+ T cell with the anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof directs the V β 17-expressing CD8+ or CD4+ T cell to a cancer cell having CD123 on its surface.

[0143] Embodiment 24(a) is the method of embodiment 24, wherein the V β 17-expressing CD8+ or CD4+ T cell is contacted with an anti-V β 17/anti-CD123 bispecific antibody of any one of embodiments 1 to 8 or 14 to 18.

[0144] Embodiment 24(b) is the method of embodiment 24, wherein the V β 17-expressing CD8+ or CD4+ T cell is contacted with an anti-V β 17/anti-CD123 bispecific antibody fragment of any one of embodiments 1 to 8 or 14 to 18.

[0145] 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-V β 17/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.

[0146] Embodiment 25 (a) is the method of embodiments 25, wherein the CD123-expressing cancer cell is in the presence of a V β 17-expressing CD8+ T cell while in contact with an anti-V β 17/anti-CD123 bispecific antibody or fragment thereof.

[0147] Embodiment 25 (b) is the method of embodiment 25 or 25 (a), wherein the CD123-expressing cancer cell is contacted with an anti-V β 17/anti-CD123 bispecific antibody of any one of embodiments 1 to 8 or 14 to 18.

[0148] Embodiment 25 (c) is the method of embodiment 25 or 25 (a), wherein the CD123-expressing cancer cell is contacted with an anti-V β 17/anti-CD123 bispecific antibody fragment of any one of embodiments 1 to 8 or 14 to 18.

[0149] Embodiment 26 is a kit comprising a V β 17 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 1 to 8 and packaging for the same.

[0150] Embodiment 27 is a kit comprising an anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of any one of embodiments 14 to 18 and packaging for the same.

[0151] Embodiment 28 is a method of producing a V β 17 bispecific antibody or antigen-binding fragment thereof, comprising culturing the host cell of embodiment 12 under conditions to produce the V β 17 bispecific antibody or antigen-binding fragment thereof, and recovering the V β 17 bispecific antibody or antigen-binding fragment thereof from the cell or culture.

[0152] Embodiment 29 is a method of producing an anti-V β 17/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-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof, and recovering the anti-V β 17/anti-CD123 bispecific antibody or antigen-binding fragment thereof from the cell or culture.

[0153] Embodiment 30 is an isolated humanized V β 17 monoclonal antibody or antigen-binding fragment thereof,

the V β 17 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.

[0154] Embodiment 31 is isolated humanized V β 17 monoclonal antibody or antigen-binding fragment thereof of embodiment 30, wherein the V β 17 monoclonal antibody or antigen-binding fragment thereof comprises the amino acid sequence of SEQ ID NO:28.

[0155] Embodiment 32 is an isolated nucleic acid encoding the humanized V β 17 monoclonal antibody or antigen-binding fragment thereof of embodiment 30 or embodiment 31.

[0156] Embodiment 33 is a vector comprising the isolated nucleic acid of embodiment 32.

[0157] Embodiment 34 is a host cell comprising the vector of embodiment 33.

[0158] Embodiment 35 is a buffered composition comprising the isolated humanized V β 17 monoclonal antibody or antigen-binding fragment thereof of embodiment 30 or embodiment 31.

EXAMPLES

[0159] 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-V β 17 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 V β 17 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.

[0160] The subsequent examples can be divided into the following categories: (1) Generation of bispecific antibodies capable of binding to the V β 17 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).

Example 1: Human Framework Adaptation of Anti-V β 17 mAb E17.5F

[0161] The mouse IgG1 anti-human T cell receptor V β 17 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

[0162] The sequences obtained are shown in Tables 1 and 2.

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	GYSITSGYFVN	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

TABLE 2

Heavy chain and light chain sequences of TCR Vb17 clone E17.5F.		
mAb ID	Heavy Chain Amino Acid Sequence	SEQ ID NO:
B171B01	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFVNWIRQFPGNKLEWMGYIS YDGSNNYNPSLKNRISITRDTSKNQFFLKLNSVTTEDTATYYCASPSPGTGYA VDYWGGTSTVTSSAKTTPPSVYPLAPGSAQTNSMVTGCLVKGYFPEPVTV TWNSSGLSSGVHTFPFVAVLQSDLYTLSSSVTVPSSTWPSQTVTCNVAHPASSTK VDKKIVPRDCGCKPCICTVPEVSSVFIFPPKPKDVLITITLTPKVTCTVVDISK DDPEVQFSWFVDDVEVHTAQTKPREEQINSTFRSVSELPIMHQDWLNGKEFKC RVNSAAPPAPIEKTISKTYGRPKAPQVYTIPPPKEQMAKDKVSLTCMITNFFP EDITVEWQWNGQPAENYKNTQPIMDTDGSYFVYSKLVQKSNWEAGNTFTCSV LHEGLHNHHTKSLSHSPGK	7
Light Chain Amino Acid Sequence		SEQ ID NO:
B17B01	NVVMQTPLSLFVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKFLI YKVSNRFSGVDPDRFSGGGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFTFGSG TKLEIKRADAAPTVISIFPPSSEQLTSGGASVVCFLNNFYPKDINVKKIDGSE RQNGVLNSWTDQDSKDYSTMSSTLTTLTKDEYERHNSYTCATHKSTSTSPIVK SFNRNEC	8

[0163] 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 uncharacter-

istic, 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.

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	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFVNWIRQFPGNKLEWMGYIS YDGSNNYNPSLKNRISITRDTSKNQFFLKLNSVTTEDTATYYCASPSPGTGYA VDYWGGTSTVTSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTITCNVDHKPSNTK VDKRVESKYGPPCPCPAPEAAGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVS QEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE YKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTTTPVLDSDGSFLLYSKLTVDKSRWQEGNVFSC SVMHEALHNHYTQKSLSLSLGK	9
B17B2	DVQLKESGPGLVKPSQSLSVTCSVTGYSITSGYYNWNWRQFPGNKLEWMGYI SYDGSNNYNPSLKNRISITRDTSKNQILLKLTYYTTEDTATYYCTRPSPGTGYA VDYWGGTTLVTSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTITCNVDHKPSNTK VDKRVESKYGPPCPCPAPEAAGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVS QEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE YKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTTTPVLDSDGSFLLYSKLTVDKSRWQEGNVFSC SVMHEALHNHYTQKSLSLSLGK	11

TABLE 3-continued

Heavy and Light Chain sequences for V β 17 clone E17.5F antibody variants		
	Light Chain Amino Acid Sequence	SEQ ID NO:
B17B1	NVVMQTPTPLSLPVS LGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKFLIY KVSNRFGVDPDRFSGGGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFTFGSGTK LEIKRADAAPT VSI FPPSSEQLTSGGASVVCFLNNFY PKDINVKWKIDGSE RQN GVLNSWTDQDSKDYMSSTLT LTKDEYERHNSYTCEATHKTSTSPIVKSPN RNEC	10
B17B2	DIVMTQSPDLSAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLI YKVSNRFGVDPDRFSGGGSGTDFTLTISSLQAEDVAVYYCSQSTHVPFTFGQGT KVEIKRADAAPT VSI FPPSSEQLTSGGASVVCFLNNFY PKDINVKWKIDGSE RQ NGVLNSWTDQDSKDYMSSTLT LTKDEYERHNSYTCEATHKTSTSPIVKSF NRNEC	12

[0164] The two antibodies (B17B1 and B17B2) were expressed in HEK293Expi cells. The supernatants were tested for V β 17 binding (B17B1 and B17B2) and only B17B1 demonstrated binding. Thus, B17B1 was expressed having an IgG4 constant region with Fc substitutions.

[0165] The anti-human TCR V β 17 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.

[0166] 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 K R and Martin A C. *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	

[0167] The selected human germlines are provided in Table 4 (in the IMGT notation).

TABLE 4

VH and VL variants		
Ab	VH Sequence	SEQ ID NO:
B17H1	NVQLQESGPGLVKPSQSLSLTCTVSVAGYSITSYGFWNWIRQFPGNKLEWMG YSIYDGSNNYNPSLKNRISITRDTSKNQFFLKLNSVTEDTATYYCASPSP GTGYAVDYWGQGTSTVTVSS	25
B17H3	EVQLLES GGGVLVQPGGSLRLSCAASGYSITSGYFNNWVRQAPGKGLEWVS ISYDGSNNYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCAKPSPG TGYAVDYWGQGTSTVTVSS	19
B17H4	EVQLLES GGGVLVQPGGSLRLSCAASGYSITSGYFNNWVRQAPGKGLEWVS ISYDGSNNYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCAKPSPG TGYAVDYWGQGTSTVTVSS	20
B17H5	QVQLVQESGPGLVKPSQSLSLTCTVSVAGYSITSGYFNNWIRQFPGNKLEWIG YISYDGSNNYNPSLKRVTISRDTSKNQFSLKLSSVTAADTAVYYCASPSP GTGYAVDYWGQGTSTVTVSS	21
Ab	VL Sequence	SEQ ID NO:
B17L1	NVVMQTPTPLSLPVS LGDQASISVRSSQSLVHSNGNTYLHWYLQKPGQSPKF LIYKVSNRFGVDPDRFSGGGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFT FGSGTKLEIK	26

TABLE 4-continued

VH and VL variants		
B17L3	DIQMTQSPSSLSASVGRVTITCRSSQSLVHSNGNTYLHWYQQKPGKAPKL LIYKVSNNRFGVPSRFSGSGSGTDFTLTISLQPEDFATYYCSQSTHVPFT FGQGTKLEIK	22
B17L4	DIQMTQSPSSLSASVGRVTITCRSSQSLVHSNGNTYLHWYQQKPGKAPKF LIYKVSNNRFGVPSRFSGSGSGTDFTLTISLQPEDFATYYCSQSTHVPFT FGQGTKLEIK	23
B17L5	DVVMTQSPPLSLPVTLGQPAISCRSSQSLVHSNGNTYLHWYQQKPGQSPRF LIYKVSNNRFGVPSRFSGSGSGTDFTLTISRVEAEDVGVYYCSQSTHVPFT FGQGTKLEIK	24

CRSs1-3 are underlined

[0168] “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.

TABLE 5

The selected J-regions		
J-region	Sequence	SEQ ID NO:
IGHJ1*01 HC	WGQGT ¹ LVTVSS	42
IGKJ2*01 LC	FGQGT ¹ KLEIK	43

[0169] 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. Nos. 6,670,127; 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 (2) 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 (Life Technologies; 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.

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

[0170] The humanized antibodies were screened for binding to a TCRVβ17 (SEQ ID 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.

[0171] 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.

Example 2. Preparation of Anti-Vβ17/Anti-CD123 Bispecific Antibodies

[0172] VB11 (anti-Vβ17/anti-CD123) and VB13 (Vβ17× 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×Null. The final EU levels of anti-Vβ17/anti-CD123 and Vβ17×Null based on these protein concentrations were 2.053 EU/mg and 4.219 EU/mg, respectively.

TABLE 7

Sequences of half antibodies expressed in CHO cells		
mAb ID	SEQ ID NO:	
'Knob' arm and 'hole' arm amino acid sequence		
B17B21 (Vβ17 half Ab)	28	MAWVWTLFLMAAAQSIQADIQMTQSPSSLSASVGDRTITCRSSQSLVHS NGNTYLHWYQQKPKGKAPFLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCSQSTHVPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGT ASVVCCLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECGSGEGKSSGSGSEKST EGKSSGSGSEKSTGGSQVQLQESGPGLVKPSSETLSLTCTVSGYSITSGYF WNWIRQPPGKLEWIGYISYDGSNNYNPSLKSRVTISRDTSKNQFSLKLSS VTAADTAVYYCASPSPTGYAVDYWGQGLTVTVSSASTKGPSVFPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTCTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGP SVFLFPPKPKDITLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKT KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIKAK GQPREPQVYITLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNY KTPPVPVLDSDGSFFLVSRLLTVDKSRWQEGNVFSCSVMEALHNHRTQKSL LSLGGK
I3RB217 (CD123 half Ab)	30	MAWVWTLFLMAAAQSIQAEIVLTQSPGTLSSLSPGERATLSCRASQSVSSS YLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPED FAVYYCQQDYGFPPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV CLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKA DYEKHKVYACEVTHQGLSSPVTKSFNRGECGSGEGKSSGSGSEKSTEGKS SGSGSEKSTGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVR QMPKGLIEWMGIIDPSDSITRYSPSPQGGVTISADKSIISTAYLQWSSLKAS DTAMYYCARGDGSITDLDYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSE AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS SSLGKTCTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPPSVFLFP PKPKDITLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKT KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPREP QVYITLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTPPVP LDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHNTQKSLSLSLGGK
B23B49 (Null half Ab)		MAWVWTLFLMAAAQSIQAEIVLTQSPGTLSSLSPGERATLSCRASQSVSSS YLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPED FAVYYCQQDYGFPPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV CLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKA DYEKHKVYACEVTHQGLSSPVTKSFNRGECGSGEGKSSGSGSEKSTEGKS SGSGSEKSTGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVR QMPKGLIEWMGIIDPSDSITRYSPSPQGGVTISADKSIISTAYLQWSSLKAS DTAMYYCARGDGSITDLDYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSE AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS SSLGKTCTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPPSVFLFP PKPKDITLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKT KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPREP QVYITLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTPPVP LDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHNTQKSLSLSLGGK
Half Antibody DNA sequence		
B17B21 (Vβ17 half Ab)	29	ATGGCCTGGGTGTGGACCTGCTGTTCTGATGGCCGCCGCCAGAGCATC CAGGCCGACATCCAGATGACCCAGAGCCCAAGCAGCCTGAGCGCCAGCGTG GGCAGCGCGTGAACATCACTGCGCAGCAGCAGCAGCAGCCTGGTGACAGC AACGGCAACACCTACCTGCACTGGTACCAGCAGAAGCCAGGCCAAGCCCCA AAGTTCCTGATCTACAAGGTGAGCAACCGCTTCAGCGCGCTGCCAAGCCGC TTCAGCGGCAGCGGCAGCGGCACCGACTTCACCTGACCATCAGCAGCCTG CAGCCAGAGGACTTCGCCACCTACTACTGAGCAGCAGCAGCAGCAGCAGTGC TTCACCTTCGGCCAGGCCACCAAGCTGGAGATCAAGCGCACCGTGGCGCC CCAAGCGTGTTCATCTTCCACCAAGCGACGAGCAGTGAAGAGCGGCAC GCCAGCGTGGTGTGCTGCTGAACAACCTTCTACCCAGCGAGGCCAAGGTG CAGTGGAAAGGTGGACAACGCCCTGCAAGAGCGGCAACAGCCAGGAGAGCGTG ACCGAGCAGGACAGCAAGGACAGCAGCTACAGCTGAGCAGCAGCAGCTGACC CTGAGCAAGGCCGACTACGAGAAGCACAAGGTGTACGCTGCGAGGTGACC CACCAGGGCCTGAGCAGCCAGTGACCAAGAGCTTCAACCGCGCGAGTG GGCGGCAGCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACC GAGGGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCAGCGGCAGC CAGGTGACGTGACGAGAGCGGCCAGCGCTGGTGAAGCAAGCGAGAC

TABLE 7-continued

Sequences of half antibodies expressed in CHO cells	
mAb ID	SEQ ID NO:
	CTGAGCCTGACCTGCACCGTGAGCGGCTACAGCATCACCAGCGGCTACTTC TGGAACTGGATCCGCCAGCCACCAGGCAAGGGCTGGAGTGGATCGGCTAC ATCAGCTACGACGGCAGCAACAACACCAACCCAGCCTGAAGAGCCGCGTG ACCATCAGCCGCGACACCAGCAAGAACCAGTTCAGCCTGAAGCTGAGCAGC GTGACCGCCGCGACACCGCGGTGTACTACTGCGCCAGCCCAAGCCAGGC ACCGGCTACGCCGTGGACTACTGGGGCCAGGGCACCCCTGGTGACCGTGAGC AGCGCCAGCACCAAGGGCCCAAGCGTGTTCCTCACTGGCCCCATGCAGCCGC AGCACCAGCGAGAGCACCGCCGCCCTGGGCTGCCCTGGTGAAGGACTACTTC CCAGAGCCAGTGACCGTGAGCTGGAACAGCGCGCCCTGACCAGCGCGTG CACACCTTCCCAGCCGTGCTGCAGAGCAGCGGCTGTACAGCCTGAGCAGC GTGGTGACCGTGCCCAAGCAGCAGCCTGGGCACCAAGACCTACACCTGCAAC GTGGACCACAAGCCAAGCAACACCAGGTGGACAAGCGCTGGAGAGCAAG TACGGCCACCATTGCCACCATGCCCCAGCCCCAGAGGGCCCGCGCGGCCA AGCGTGTTCCTGTTCACCAACAAGCCAAGGACACCCGTGATGATCAGCCGC ACCCCAGAGGTGACCTGCGTGGTGGTGGAGCTGAGCCAGGAGGACCCAGAG GTGCAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACC AAGCCACGCGAGGAGCAGTTCAACAGCACCTACCGCGTGGTGAGCGTGCTG ACCGTGCTGCACACGAGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTG AGCAACAAGGGCCTGCCAAGCAGCATCGAGAAGACCATCAGCAAGGCCAAG GGCCAGCCACGCGAGCCACAGGTGTACACCCCTGCCACCAAGCCAGGAGGAG ATGACCAAGAACCAGGTGAGCCTGAGCTGCGCCGTGAAGGGCTTCTACCCA AGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCAGAGAACAACTAC AAGACCACCCACCAGTGCTGGACAGCGACGGCAGCTTCTTCTTGGTGAGC CGCCTGACCGTGGACAAGAGCCCGCTGGCAGGAGGGCAACGTGTTTCACTGC AGCGTGATGCACAGGCGCTGCACAAACCGCTTACCCAGAAGAGCTGAGC CTGAGCCTGGGCAAGATGGCTGGGTGTGGACCTGCTGTTCCTGATGGCC GCCGCCAGAGCATCCAGGCCGACATCCAGATGACCCAGAGCCCAAGCAGC CTGAGCGCCAGCGTGGGCGACCGCGTGACCATCACTGCCGACAGCAGCAG AGCCTGGTGACAGCAACGGCAACACCTACCTGCACTGGTACCAGCAGAAG CCAGGCAAGGCCCAAGATTCTGTATCTACAGGTGAGCAACCGCTTCAAGC GGCGTGCCCAAGCCGCTTCAAGCGCAGCGCAGCGGACCGCACTTCAACCTG ACCATCAGCAGCCTGCAGCCAGAGGACTTCGCCACCTACTACTGCAGCCAG AGCACCACGTGCCATTCACTTTCGGCCAGGGCACCAAGCTGGAGATCAAG CGCACCGTGGCCGCCCCAAGCGTGTTCATCTTCCCACCAAGCGACGAGCAG CTGAAGAGCGGCACCGCCAGCGTGGTGTGCTGCTGAACAACCTTCTACCCA CGCGAGGCCAAGGTGCAGTGGAGGTGGACAACGCCCTGCAGAGCGGCAAC AGCCAGGAGAGCGTGACCGAGCAGGACAGCAAGGACAGCACCTACAGCCTG AGCAGCACCTTGACCTGAGCAAGGCCGACTACGAGAAGCACAAGGTGTAC GCCTGCGAGGTGACCCACAGGGCCTGAGCAGCCAGTGACCAAGAGCTTC AACC CGCGCGAGTGCGGCGGACGAGGGCAAGAGCAGCGGACGCGGACG GAGAGCAAGAGCACCGAGGGCAAGAGCAGCGGACGCGGACGAGAGCAAG AGCAACCGCGGCGAGCCAGGTGCAGCTGCAAGGAGAGCGGCCAGGCTTGGTG AAGCCAAGCGAGACCTGAGCCTGACCTGCACCGTGAGCGGCTACAGCATC ACCAGCGGCTACTTCTGGAATGGATCCGCCAGCCACAGGCAAGGGCCTG GAGTGGATCGGCTACATCAGCTACGACGGCAGCAACAATAACAACCAAGC CTGAAGAGCCGCGTGACCATCAGCCGCGACACCAAGCAAGAACAGTTTCAAGC CTGAAGCTGAGCAGCGTGACCGCGCGACACCGCCGTGTACTACTGCGCC AGCCCAAGCCCAGGCACCGCTACGCGTGGACTACTGGGGCCAGGGCACCC CTGGTGACCGTGAGCAGCGCCAGCACCAAGGGCCCAAGCGTGTTCCTACTG GCCCATGTCAGCCGAGCACCAGCGAGAGCACCGCCGCCCTGGGCTGCTG GTGAAGGACTACTTCCCAGAGCCAGTGACCGTGAGCTGGAACAGCGGCGCC CTGACCAGCGGCGTGCAACCTTCCCAGCCGTGCTGCAGAGCAGCGGCTG TACAGCCTGAGCAGCGTGGTGACCGTGCCAAAGCAGCAGCCTGGGCACCAAG ACCTACACCTGCAACGTGGACCAAGCCAAAGCAACCAAGGTGGACAAG CGCGTGGAGAGCAAGTACGGCCACCATGCCCCACCATGCCAGCCCCAGAG GCCGCCGCGGCGCCCAAGCGTGTTCCTGTTCACCAAGCCAAAGGACACC CTGATGATCAGCCGACCCAGAGGTGACCTGCGTGGTGGTGGAGCTGAGC CAGGAGGACCCAGAGGTGAGTTCAACTGTGTGACGTGGACGGCGTGGAGGTG CACAACGCCAAGACCAAGCCACGCGAGGAGAGTTCAACAGCACCTACCGC GTGGTGAGCGTGTGACCGTGTGCACACAGGACTGGCTGAACGGCAAGGAG TACAAGTGCAAGGTGAGCAACAAGGGCTGCCAAGCAGCATCGAGAAGACC ATCAGCAAGGCCAAGGGCCAGCCACGCGAGCCACAGGTGTACACCTTGCCA CCAAGCCAGGAGGAGATGACCAAGAACAGGTGAGCCTGAGCTGCGCCGTG AAGGGCTTCTACCAAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAG CCAGAGAACAACTACAAGACACCCACACAGTGCTGGACAGCGACGGCAGC TTCTTCTTGGTGAGCCGCTGACCGTGGACAAGAGCCGCTGGCAGGAGGGC AACGTGTTCAGCTGACGCGTGATGCACAGAGGCCCTGCACAACCGCTTACCC CAGAAGAGCCTGAGCCTGAGCCTGGGCAAGTGATAG

TABLE 7-continued

Sequences of half antibodies expressed in CHO cells		
mAb ID		SEQ ID NO:
I3RB217 (CD123 half Ab)	ATGGCCTGGGTGTGGACCTGCTGTTCTGATGGCCGCCGCCAGAGCATC CAGGCCGAGATCGTGTGACCCAGAGCCAGGCACCTGAGCCTGAGCCCA GGCGAGCGCGCCACCTGAGCTGCCGCGCCAGCCAGAGCGTGAGCAGCAGC TACCTGGCCTGGTACCAGCAGAAGCCAGGCCAGGCCCCACGCTGCTGATC TACGCGCCAGCAGCCGCGCCACCGGCATCCAGACCGCTTCAGCGGCAGC GGCAGCGGCACCGACTTCACCTGACCATCAGCCGCTGGAGCCAGAGGAC TTCGCCGTGTACTACTGCCAGCAGGACTACGGCTTCCCATGGACCTTCGGC CAGGGCACCAAGGTGGAGATCAAGCGCACCTGGCCGCCCAAGCGTGTTC ATCTTCCACCAAGCGCAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTG TGCTGTGTGAACAACCTTACCCACGCGAGGCCAAGGTGACGTGGAAGGTG GACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACCGAGCAGGAC AGCAAGGACAGCACCTACAGCCTGAGCAGCACCTGACCTGAGCAAGGCC GACTACGAGAAGCACCAAGGTGTACGCTGCGAGGTGACCCACAGGCCCTG AGCAGCCCAAGTGACCAAGAGCTTCAACCGCGCGAGTGCGCGGcagcgag ggcaagagcagcggcagcgagcagcgagagcaagagcaccgagggcgaagagc agcggcagcggcagcgagagcaagagcaccggcgagcagcGAGGTGACGTG GTGCAGAGCGCGCGCGAGGTGAAGAAGCCAGGCCAGAGCCTGAAGATCAGC TGCAAGGGCAGCGGCTACAGCTTACAGCTACTGGATCAGCTGGGTGCGC CAGATGCCAGGCAAGGGCCTGGAGTGGATGGGCATCATCGACCCAAAGCGAC AGCGACACCCGCTACAGCCCAAGCTTCCAGGCCAGGTGACCATCAGCGCC GACAAGAGCATCAGCACCGCTACCTGACGTGGAGCAGCCTGAAGGCCAGC GACACCGCCATGTACTACTGCGCCCGCGGCGACGGCAGCACCGACCTGGAC TACTGGGGCCAGGGCACCTGGTGACCGTGAGCAGCGCCAGCACCAAGGGC CCAAGCGTGTTCCTACTGGCCCCATGCAGCCGCGAGCACCGAGAGCAGC GCCGCCCTGGGTGCTGGTGAAGGACTACTTCCAGAGCCAGTGACCGTG AGCTGGAACAGCGCGCCCTGACCAAGCGCGTGACACCTTCCAGCCGTG CTGCAGAGCAGCGGCTGTACAGCCTGAGCAGCGTGGTGACCGTGCCAAGC AGCAGCCTGGGCACCAAGACCTACACCTGCACAGTGGACCAAGCCAAAGC AACACCAAGGTGGACAAGCGCTGGAGAGCAAGTACGGCCCAACATGCCCA CCATGCCCAGCCCCAGAGGCCGCGCGGCGGCCAAGCGTGTTCCTGTTCCCA CCAAAGCCAAAGGACACCTGATGATCAGCCGACCCAGAGGTGACCTGC GTGGTGGTGGACGTGAGCCAGGAGGACCCAGAGGTGCAAGTTCAACTGGTAC GTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCACGCGAGGAGCAG TTCAACAGCACCTACCGCGTGGTGAGCGTGCTGACCGTGCTGACACAGGAC TGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGAGCAACAAGGGCTTCCCA AGCAGCATCGAGAAGACCATCAGCAAGGCCAAGGGCCAGCCACGCGAGCCA CAGGTGTACACCTGCCACCAAGCCAGGAGGAGATGACCAAGAACCAGGTG AGCCTGTGGTGGCTGGTGAAGGGCTTCAACCAAGCGACATCGCCGTGGAG TGGGAGAGCAACGGCCAGCCAGAGAACAACCTACAAGACCAACCCACAGTG CTGGACAGCGACGGCAGCTTCTTCTGTACAGCCGCTGACCGTGGACAAG AGCCGCTGGCAGGAGGGCAACGTGTTACGTGACGCGTGATGCACGAGGCC CTGCACAACCACTACACCCAGAAGAGCCTGAGCCTGAGCCTGGGCAAG	31
B23B49 (Null half Ab)	ATGGCCTGGGTGTGGACCTGCTGTTCTGATGGCCGCCGCCAGAGCATC CAGGCCGACATCGTGTGACCCAGAGCCAGACAGCCTGGCCGTGAGCCTG GGCGAGCGCGCCACCATCACTGCCGCGCCAGCCAGAGCGTGGACTACAAC GGCATCAGCTACATGCACCTGGTACCAGCAGAAGCCAGGCCAGCCACCAAG CTGCTGATCTACGCCGCGCAGCAACCCAGAGAGCGGCGTGCCAGACCGCTT AGCGGCAGCGCGCAGCGGCACCGACTTACCCCTGACCATCAGCAGCCTGCAG GCCAGGACGTGGCCGTGTACTACTGCCAGCAGATCATCAGGACCCATGG ACCTTCGGCCAGGGCACCAAGGTGGAGATCAAGCGCACCGTGGCCGCCCA AGCGTGTTCATCTTCCACCAAGCGACGAGCAGCTGAAGAGCGGCACCGCC AGCGTGGTGTGCTGCTGTAACAACCTTACCCACGCGAGGCCAAGGTGCAG TGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACC GAGCAGGACAGCAAGGACAGCACCTACAGCCTGAGCAGCACCTGACCCCTG AGCAAGGCCGACTACGAGAAGCACAAAGGTGTACCGCTGCGAGGTGACCCAC CAGGGCCTGAGCAGCCAGTGACCAAGAGCTTCAACCGCGCGAGTGCGGC GGCAGCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGCAAGAGCACCGAG GGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGCGCGCAGCAG ATCACCTGAAGGAGAGCGGCCAACCTTGGTGAAGCCAAACAGACCTTG ACCCTGACCTGCACCTTCAGCGGCTTACGCTGAGCACCAGCGCATGGGC GTGAGCTGGATCCGCCAGCCACAGGCCAAGGCCCTGGAGTGGCTGGCCAC ATCTACTGGGACGACGACAAGCGCTACAACCAAGCCTGAAGAGCGCGCTG ACCATCACCAAGGACACAGCAAGAACCAGGTGGTGTGACCATGACCAAC ATGGACCCAGTGGACACCGCCACCTACTACTGCGCCCGCTGTACGGCTTC ACCTACGGCTTCGCTACTGGGGCCAGGGCACCTGGTGACCGTGAGCAGC GCCAGCACCAAGGGCCCAAGCGTGTTCCTACTGGCCCCATGCAGCCGAGC ACCAGCGAGAGCACCGCCGCTGGGCTGCTGGTGAAGGACTACTTCCCA GAGCCAGTGACCGTGAGCTGGAAACAGCGCGCCCTGACAGCGCGCTGCAC ACCTTCCAGCCGCTGCTGCAGAGCAGCGGCCGTGTACAGCCTGAGCAGCGTG GTGACCGTGCCAAAGCAGCAGCCTGGGCCAACAGACCTACACCTGCAACGTG GACCACAAGCCAAAGCAACACCAAGGTGGACAAGCGCGTGGAGAGCAAGTAC	

TABLE 7-continued

Sequences of half antibodies expressed in CHO cells	
mAb ID	SEQ ID NO:
	GGCCCAACCATGCCACCATGCCAGCCCCAGAGGCCGCCGGCGGCCCAAGC GTGTTCTCTGTTCCCAAGCAAAGGACACCTGATGATCAGCCGACCC CCAGAGGTGACCTGCGTGGTGGTGGACGTGAGCCAGGAGGCCAGAGGTG CAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAG CCACGCGAGGAGCAGTTCAACAGCACCTACCGCGTGGTGGACGTGCTGACC GTGCTGCACCAAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGAGC AACCAAGGGCCTGCCAAGCAGCATCGAGAAGACCATCAGCAAGGCCAAGGGC CAGCCACGCGAGCCACAGGTGTACACCTGCCACCAAGCCAGGAGGAGATG ACCAAGAACCAGGTGAGCCTGTGGTGCCTGGTGAAGGGCTTCTACCAAGC GACATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCAGAGAACAACACTACAAG ACCACCCCAACAGTGTGCTGGACAGCGACGGCAGCTTCTTCTGTACAGCCGC CTGACCGTGGACAAGAGCCGCTGGCAGGAGGGCAACGTGTTGAGCTGAGC GTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCCTGAGCCTG AGCCTGGGCAAG

TABLE 8

Heavy and Light Chain Sequences for V β 17 bispecific antibodies		
Bispecific Antibody		Amino Acid Sequence
Anti-V β 17/ anti-CD123	Heavy chain 1 B17B21 (SEQ ID NO: 13)	QVQLQESGPGLVKPSSETLSLTCTVSGYSITSGYFNNWIRQPP GKGLEWIGYISYDGSNNYNPSLKSRVTISRDTSKNQFSLKLS SVTAADTAVYYCASPSPGTGYAVDYWGQGLTVTVSSASTKGP SVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYYTCNVDHKPS NTKVDKRVESKYGPCCPPCPAPEAAGGPSVFLFPPKPKDTLM ISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREE QFNSTYRVVSVLTVHLQDNLNGKEYCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLSCAVKGFYPSDIA VEWESNGQPENNYKTPPVLDSDGSFFLVSRSLTVDKSRWQEG NVFSCVMHEALHNRFTQKSLSLSLGK
	Light Chain 1 B17B21 (SEQ ID NO: 14)	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGNTYLHWYQ QKPGKAPKFLIYKVSNNRFGVPSRFGSGSGTDFTLTISSLQ PEDFATYYCSQSTHVPFTFGQGTGLEIKRTVAAPSVFIFPPPS DEQLKSGTASVCLLNNFYPREAKVQWKVDNALQSGNSQESV TEQDSKDSYSLSTLTLSKADYEKHKVYACEVTHQGLSSPV TKSFNREGC
	Heavy chain 2 I3RB217 (SEQ ID NO: 15)	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVRQMPG KGLEWMGIIDPSDSDTRYSPFQGVTTISADKSI STAYLQWS SLKASDTAMYYCARGDGTDLDYWGQGLTVTVSSASTKGPSV FPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYYTCNVDHKPSNT KVDKRVESKYGPCCPPCPAPEAAGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVHLQDNLNGKEYCKVSNKGLPSSIEKTI SK AKGQPREPQVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLVSRSLTVDKSRWQEGNV FSCVMHEALHNHYTQKSLSLSLGK
	Light Chain 2 I3RB217 (SEQ ID NO: 16)	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPG QAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDF AVYYCQQDYGFPTFGQGTKEIKRTVAAPSVFIFPPSDEQL KSGTASVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSF NRGEC
V β 17 x Null	Heavy chain 1 B17B21 (SEQ ID NO: 13)	QVQLQESGPGLVKPSSETLSLTCTVSGYSITSGYFNNWIRQPP GKGLEWIGYISYDGSNNYNPSLKSRVTISRDTSKNQFSLKLS SVTAADTAVYYCASPSPGTGYAVDYWGQGLTVTVSSASTKGP SVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYYTCNVDHKPS NTKVDKRVESKYGPCCPPCPAPEAAGGPSVFLFPPKPKDTLM ISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREE QFNSTYRVVSVLTVHLQDNLNGKEYCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLSCAVKGFYPSDIA VEWESNGQPENNYKTPPVLDSDGSFFLVSRSLTVDKSRWQEG NVFSCVMHEALHNRFTQKSLSLSLGK

TABLE 8-continued

Heavy and Light Chain Sequences for V β 17 bispecific antibodies	
Bispecific Antibody	Amino Acid Sequence
Light Chain 1 B17B21 (SEQ ID NO: 14)	DIQMTQSPSSLSASVGDRTTITCRSSQSLVHSNGNTYLHWYQ QKPGKAPKFLIYKVSNRFSVPSRFSGSGSGTDFTLTISSLQ PEDFATYYCSQSTHVPFTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESV TEQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPV TKSFNRGEC
Heavy chain 2 Null (SEQ ID NO: 17)	QITLKESGPTLVKPTQTTLTCTFSGFSLSTSGMGVSWIRQP PGKALEWLAHIYWDDDKRYNPSLKSRLTITKDTSKNQVVLTM TNMDPVDATYYCARLYGFTYGFAYWGQGTLLTVTSASTKGP SVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALT GVHTFPAVLQSSGLYSLSSVTVPSSSLGKTITCTNVDHKPS NTKVDKRVESKYGPPCPCPAPEAAGGPSVFLFPPKPKDTLM ISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREE QFNSTYRVVSVLTVHLQDNLNGKEYKKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIA VEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEG NVFSCSVMEALHNNHTQKSLSLSLGK
Light Chain 2 Null (SEQ ID NO: 18)	DIVMTQSPDLSAVSLGERATINCRASQSVDYNGISYHMYQQ KPGQPPKLLIYAASNPESGVPRFSGSGSGTDFTLTISSLQA EDVAVYYCQQLIEDPWTFGQGTKVEIKRTVAAPSVFIFPPSD EQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVT EQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVT KSFNRGEC

Example 3. Evaluation of Binding and Cytotoxic Properties of Anti-V β 17/Anti-CD123 Bispecific Antibody Using Kasumi-3 Cells and Human CD8+ T Cells

Stimulation and Expansion of V β 17+CD8+ T Cells from Total PBMCs

[0173] To expand V β 17+CD8+ T cells, whole PBMCs from HLA-A2 donor (HPU-08694) were stimulated with 1 μ g/mL FLU MP 58 peptide (in DMSO). Frequency of V β 17+ cells among total CD8+ T cells was determined on day 8 and 14 of the culture period. To enumerate the frequency of V β 17+ cells among total CD8+ T cells, total live PBMCs were initially gated, doublets were excluded, total CD8+ T cells were gated and then V β 17+ cells were gated (FIG. 3A). Compared to the frequency of V β 17+ 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 β 17+ cells (FIG. 3B) in this donor.

Anti-V β 17/Anti-CD123 Bispecific Antibody Binding Assay

On Kasumi-3 Cells

[0174] To understand the binding kinetics of the anti-V β 17/anti-CD123 bispecific antibody, Kasumi-3 cells were incubated with the anti-V β 17/anti-CD123 bispecific antibody and V β 17xNULL arm control at various concentrations (concentration range from 5 μ g/mL to 0 μ g/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 EC₅₀ for anti-V β 17/anti-CD123 and NULLxCD123 was determined as 6 and 42.7 nM respectively (Table 9).

TABLE 9

Binding affinity of Kasumi-3 cells for bispecific antibodies.			
Conc. (μ g/mL)	anti-V β 17/		
	anti-CD123	V β 17xNULL	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 (μ g/mL)	0.9	ND	6.4
EC ₅₀ (nM)	6	ND	42.7

[0175] Bispecific antibody binding affinities to Kasumi-3 cells were determined by flow cytometry. Half maximal effective concentration (EC₅₀) values were calculated as the bispecific concentration that generates 50% of maximal Binding (PE positive cells). ND: Not determined.

On Enriched CD8+ T Cells

[0176] Enriched FLU MP 58 peptide stimulated CD8+ T (from day 14 culture) cells were incubated with various concentrations of anti-V β 17/anti-CD123 bispecific and V β 17xNULL 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 EC₅₀ for anti-V β 17/anti-CD123, V β 17xNULL, was determined as 9.0 nm, 18.7 nm respectively (Table 10).

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

[0177] Bispecific antibody binding affinities to CD8⁺ T cell were determined by flow cytometry. Half maximal effective concentration (EC₅₀) values were calculated as the antibody concentration that generates 50% of the maximal binding (PE positive cells). ND: Not Determined

Bispecific Mediated Cytotoxicity Assay

[0178] 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 EC₅₀ 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).

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.			
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	0.55	0.015	0.02

TABLE 11-continued

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.			
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.

[0179] The EC₅₀ 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).

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

[0180] 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.

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

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

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

[0181] Half maximal effective concentration (EC₅₀) values were calculated as the antibody concentration that generates 50% of maximal cytotoxicity (CFSE⁺7AAD⁺) cells. ND: Not Determined.

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 1:1 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

[0182] Half maximal effective concentration (EC₅₀) values were calculated as the antibody concentration that generates 50% of maximal cytotoxicity (CFSE⁺7AAD⁺) cells. ND: Not Determined

TABLE 17

Cytotoxicity assay at 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 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

[0183] Half maximal effective concentration (EC₅₀) values were calculated as the antibody concentration that generates 50% of maximal cytotoxicity (CFSE⁺7AAD⁺) cells. UD: Undetectable.

[0184] 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	GYSITSGYFVN
2	PRT	mouse	B12B01-HCDR2	YISYDGSNN
3	PRT	mouse	B12B01-HCDR2	PSPGTGYAVDY
4	PRT	mouse	B17B01-LCDR1	RSSQSLVHNSNGNTYLH
5	PRT	mouse	B12B01-LCDR2	KVSNRFS
6	PRT	mouse	B12B01-LCDR2	SQSTHVPFT
7	PRT	mouse	B17B01-HC	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFVNWIRQFPGNKLEWMGY ISYDGSNNYNPSLKNRISITRDTSKNQFFLKLSVTTEDTATYYCASPSPG TGYAVDYWGQGSTVTVSSAKTTPPSVYPLAPGSAQAQTNMVTGLCLVKGYF PEPVTVTWNSGSLSSGVHTFPAVLQSDLYTLSSSVTVPSSTWPSQTVTCNV AHPASSTKVDDKIIVPRDCGCKPCICTVPEVSSVFIFPPKPKDVLTIITLTPK VTCVVVDISKDDPEVQFSWFVDDVEVHTAQTTPREEQINSTRSVSELPIM HQDWLNGKEFKCRVNSAAPPAPIEKTSKTYGRPKAPQVYTIPTPPKEQMAK DKVSLTCMITNFFPEDITVEWQWNGQPAENYKNTQPIMDTDGSYFVYSKLN VQKSNWEAGNTFTCSVLHEGLHNHHTKSLSHSPGK
8	PRT	mouse	B17B01-LC	NVVMQTPLSLPVSLSLGDQASISCRSSQSLVHNSNGNTYLHWYLQKPGQSPKF LIYKVSNNRFSVGPDRFSGGGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFT FGSGTKLEIKRADAAPTVISIFPPSSEQLTSGGASVVCFLNNFYPKDINVVKW KIDGGERQNGVLNSWTDQDSKDYMSSTLTTLTKDEYERHNSYTCEATHK TSTSPIVKSFNRECE
9	PRT	mouse	B17B1-HC	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFVNWIRQFPGNKLEWMGY ISYDGSNNYNPSLKNRISITRDTSKNQFFLKLSVTTEDTATYYCASPSPG TGYAVDYWGQGSTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCN VDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFLLYS KLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLGK
10	PRT	mouse	B17B1-LC	NVVMQTPLSLPVSLSLGDQASISCRSSQSLVHNSNGNTYLHWYLQKPGQSPKF LIYKVSNNRFSVGPDRFSGGGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFT FGSGTKLEIKRADAAPTVISIFPPSSEQLTSGGASVVCFLNNFYPKDINVVKW KIDGGERQNGVLNSWTDQDSKDYMSSTLTTLTKDEYERHNSYTCEATHK TSTSPIVKSFNRECE
11	PRT	mouse	B17B2-HC	DVQLKESGPGLVKPSQSLSVTCSVTGYSITSGYYNWNWYRQFPGNKLEWMGY ISYDGSNNYNPSLKNRISITRDTSKNQILLKLTIVTTEDTATYYCTRPSPG TGYAVDYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCN VDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFLLYS KLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLGK
12	PRT	mouse	B17B2-LC	DIVMTQSPDSLAVSLGERATINCRSSQSLVHNSNGNTYLHWYQKPGQPPKL LIYKVSNNRFSVGPDRFSGGGSGTDFTLTISSLQAEADVYYCSQSTHVPFT FGQGTKEIKRADAAPTVISIFPPSSEQLTSGGASVVCFLNNFYPKDINVVKW KIDGGERQNGVLNSWTDQDSKDYMSSTLTTLTKDEYERHNSYTCEATHK TSTSPIVKSFNRECE
13	PRT	artificial	B17B21-HC	QVQLQESGPGLVKPSSETLSLTCTVSGYSITSGYFVNWIRQPPGKGLEWIGY ISYDGSNNYNPSLKSRTISRDTSKNQFLKLSVTAADTAVYYCASPSPG TGYAVDYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCN VDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEE MTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFLLVS RLTVDKSRWQEGNVFSCVMHEALHNRTQKSLSLSLGK
14	PRT	artificial	B17B21-LC	DIQMTQSPSSLSASVGRVTITCRSSQSLVHNSNGNTYLHWYQKPGKAPKF LIYKVSNNRFSVGPDRFSGGGSGTDFTLTISLQPEDFATYYCSQSTHVPFT FGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCFLNNFYPREAKVQW KVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQ GLSSPVTKSFNRGEC

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SEQ ID NO:	Type	Species	Description	Sequence
15	PRT	human	I3RB217-HC	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVRQMPGKGLEWMGII DPSDDTRYSPSFQGGVTSADKSIISTAYLQWSSSLKASDTAMYYCARGDGS TDLDYWGQGTLLTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTTKTYTCNVD HKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPE EVTCTVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTV LHQDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPREPQVYTLPPSQEEMT KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRL TVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK
16	PRT	human	I3RB217-LC	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYG ASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQDDYGFPTWTFGQG TKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQGLSS PVTKSFNRGEC
17	PRT	human	Null-HC	QITLKESGPTLVKPTQTLTCTCFSGFSLSTSGMGVSWIRQPPGKALEWLA HIYWDGDKRYNPSLKSRLTITKDTSKNQVVLMTNMDPVDATATYYCARLYG FTYGFAYWGQGTLLTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTTKTYTCN VDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPREPQVYTLPPSQEE MTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYS RLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK
18	PRT	human	Null-LC	DIVMTQSPDLSAVSLGERATINCRASQSVVDYNGISYMHWYQQKPGQPPKLL IYAASNPESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQIIEDPWF GQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQG LSSPVTKSFNRGEC
19	PRT	artificial	B17H3	EVQLLESQGGGLVQPGGSLRLSCAASGYSITSGYFNNWVRQAPGKGLEWVS YISYDGSNNYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAKPS PGTGYAVDYWGQGTLLTVTS
20	PRT	artificial	B17H4	EVQLLESQGGGLVQPGGSLRLSCAASGYSITSGYFNNWVRQAPGKGLEWVS YISYDGSNNYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCASPSPG TGYAVDYWGQGTLLTVSS
21	PRT	artificial	B17H5	QVQLQESGPGLVKPSETLSLTCTVSGYSITSGYFNNWIRQPPGKGLEWIGY ISYDGSNNYNPSLKSRLTISRDTSKNQFSLKLSVTAADTAVYYCASPSPG TGYAVDYWGQGTLLTVSS
22	PRT	artificial	B17L3	DIQMTQSPSSLSASVGDRTITCRSSQSLVHSGNGNTYLHWYQQKPGKAPKL LIYKVSNNRFGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHPFFT FGQGTKLEIK
23	PRT	artificial	B17L4	DIQMTQSPSSLSASVGDRTITCRSSQSLVHSGNGNTYLHWYQQKPGKAPKF LIYKVSNNRFGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHPFFT FGQGTKLEIK
24	PRT	artificial	B17L5	DVVMTQSPSLPLVTLGQPASISCRSSQSLVHSGNGNTYLHWYQQKPGQSPRF LIYKVSNNRFGVPSRFSGSGSGTDFTLTISRVEAEDLGVYFCSQSTHPFFT FGQGTKLEIK
25	PRT	artificial	B17H1	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFNNWIRQFPGNKLEWMGY ISYDGSNNYNPSLKNRISITRDTSKNQFSLKLSVTTEDTATYYCASPSPG TGYAVDYWGQGSTVTVSS
26	PRT	artificial	B17L1	NVVMTQTPSLPLVSLGDQASISCRSSQSLVHSGNGNTYLHWYQQKPGQSPKF LIYKVSNNRFGVPSRFSGSGSGTEFTLKISRVEAEDLGVYFCSQSTHPFFT FGSGTKLEIK
27	PRT	human	TCR-V β 17	MAWVWTLFLFLMAAAQSIQAVDGGITQSPKYLFRKEGQNVTLSCQNLNHDA MYWYRQDPGQGLRLIYYSQIVNDFQKGDIAEGYSVSREKKESFPLTVTSAQ KNPTAFYLCASSRSRSYEQYFGPGTRLTVTEDLKNVFPPEVAVFEPSEAEI SHTQKATLVCLATGFYPDHVELSWWVNGKEVHSGVSTDPQLKEQPALNDS RYSLSRLRVSATFWQNPNNHFRQCQVQFYGLSENDEWTDRAKPVTVQVSA EAWGRADepkscdkthtccppcpapeLLggpsvflfppkpkdtlmisrtpev tcvvvDvshedpevkfnwyvdgvevhnaktkpreeqynstyrvvsvltvlh qdwlngkeykckvsnkalpapiektiskakgqprepqvyVlppsreemtkn

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SEQ ID NO:	Type	Species	Description	Sequence
				qvslLclvkgyfypsdiavewesngqpennyLtWppvldsdsdgsfflyskltv dksnvqggnvfscsvmhealhnhytqklslsppg
28	PRT	artificial	B17B21 half antibody	MAWVWTLFLMAAAQSIQADIQMTQSPSSLSASVGDRTITCRSSQSLVHS NGNTYLHWYQQKPKGKAPFLIYKVNRFSGVPSRFSGSGSGTDFTLTISL QPEDFATYYCSQSTHVPTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGT ASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSLSTLT LSKADYEEKHKVYACEVTHQGLSSPVTKSFNRGECGSGEGKSSGSGSESKST EGKSSGSGSESKSTGGSQVQLQESGPGLVKPSSETLSLTCTVSGYSITSGYF WNWIRQPPGKGLEWIGYISYDGSNNYNPSLKSRTISRDTSKNQFSKLSS VTAADTAVYYCASPSPTGYAVDYWGQGLTVTVSSASTKGPSVFPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGP SVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKT KPREEQFNSTYRVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIIEKTSKAK GQPREPQVYTLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFPLVSRLLTVDKSRWQEGNVFSCSVMHEALHNRPTQKSLSL LSLGK
29	DNA	artificial	B17B21 half antibody	ATGGCCTGGGTGTGGACCTGCTGTTCTCTGATGGCCGCCGCCAGAGCATC CAGGCCGACATCCAGATGACCCAGAGCCCAAGCAGCCTGAGCGCCAGCGTG GCGACCCGCTGACCATCACTGCCGCGAGCAGCAGAGCCTGGTGCACAGC AACGGCAACACCTACCTGCCTGGTACCAGCAGAAGCCAGGCAAGGCCCCA AAGTTCCTGATCTACAAGGTGAGCAACCGCTTCAGCGCGCTGCCAAGCCGC TTCAGCGCGAGCGCAGCGCACCGCACTTCACTGACCATCAGCAGCCTG CAGCCAGAGGACTTCGCCACCTACTACTGTCAGCCAGAGCACCCAGTGCCA TTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAGCGCACCGTGGCCGCC CCAAGCGTGTTCATCTTCCACCAAGCGACGAGCAGCTGAAGAGCGGACCC GCCAGCGTGGTGTGCTGCTGAACAACTTCTACCCACGCGAGGCCAAGGTG CAGTGGAAAGGTGGACAACGCCCTGACAGCGCGCAACAGCCAGGAGAGCGTG ACCGAGCAGGACAGCAAGGACAGCACCTACAGCCTGAGCAGCACCTGACC CTGAGCAAGGCCGACTACGAGAAGCACAAAGGTGTACGCCCTGCGAGGTGACC CACCAGGGCCTGAGCAGCCAGTGAACAGAGCTTCAACCGCGCGAGTGC GGCGCGCAGCGAGGCAAGAGCAGCGCGCAGCGCAGCAGAGCAGAGCACCC GAGGCAAGAGCAGCGCGCAGCGCAGCGAGCAGCAAGAGCACCGCGCGCAGC CAGGTGTCAGCTGCAGAGAGCGGCCAGGCCCTGGTGAAGCCAAAGCAGACC CTGAGCCTGACCTGCACCGTGAGCGGCTACAGCATCACCAGCGGCTACTTC TGGAAGTGGATCCGCCAGCCACCAGGCAAGGGCCTGGAGTGGATCGGCTAC ATCAGCTACGACGCGCAGCAACAATAACAACCAAGCCTGAAGAGCCGCGTG ACCATCAGCGCGCAGCACAGCAAGAACAGTTACGCCCTGAAGCTGAGCAGC GTGACCGCGCGCAGCACCGCGCTGTACTACTGCGCCAGCCCAAGCCAGGC ACCGGCTACGCGCTGGACTACTGGGGCCAGGGCACCTTGGTGACCGTGAGC AGCGCCAGCACCAAGGGCCCCAAGCGTGTTCCTACTGGCCCCATGCGCGCGC AGCACCGCAGAGCAGCACCGCGCCTGGGCTGCCTGGTGAAGGACTACTTC CCAGAGCCAGTGACCGTGAGCTGGAACAGCGCGCGCTGACAGCGCGGTG CACACCTTCCAGCGGTGCTGCAGAGCAGCGGCTGTACAGCCTGAGCCAGC GTGGTGACCGTGCCAAAGCAGCAGCCTGGGCACCAAGACCTACACCTGCAAC GTGGACCAACAAGCAAGCAACCAAGGTGGACAAGCGCGTGAGAGAGCAAG TACGGCCACCATGCCCACCATGCCAGCCCCAGAGGCCGCCCGCGCGCCCA AGCGTGTTCCTGTTCACCAAAAGCCAAAGGACACCTGATGATCAGCCGC ACCCAGAGGTGACCTGCGTGGTGGTGGACGTGAGCCAGGAGGACCCAGAG GTGCAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACC AAGCCACGCGAGGAGCAGTTCAACAGCACCTACCGCGTGGTGGAGTGTCTG ACCGTGTCTGACACAGGACTGGCTGAACGGCAAGGAGTACAAGTGAAGGTG AGCAACAAGGGCCTGCCAAGCAGCATCGAGAAGACCATCAGCAAGGCCAAG GGCCAGCCACGCGAGCCACAGGTGTACACCTGCCACCAAGCCAGGAGGAG ATGACCAAGAACAGGTGAGCTGAGCTGCGCCGTGAAGGGCTTCTACCCCA AGCGACATCGCCGTGGAGTGGAGAGCAACGGCCAGCCAGAGAACCACTAC AAGACCACCCACAGTGTGGACAGCGACGGCAGCTTCTTCTGGTGGAGC CGCCTGACCGTGGAACAAGAGCGCTGGCAGGAGGGCAACGTGTTGAGTGC AGCGTGTGACAGAGGCCCTGCACAACCGCTTACCCAGAAGAGCCTGAGC CTGAGCCTGGGCAAGATGGCCTGGGTGTGGACCTGCTGTTCTGATGGCC GCCGCCAGAGCATCCAGGCCAGACATCCAGATGACCCAGAGCCCAAGCAGC CTGAGCGCCAGCGTGGCGACCGCGTGACCATCACCTGCCGCGCAGCCAG AGCCTGGTGACAGCAACGGCAACACCTACCTGCACTGGTACAGCAGAAG CCAGGCAAGGCCCAAGTTCTTGATCTACAAGGTGAGCAACCGCTTACAGC GGCGTGCCAAAGCCGCTTACGCGCAGCGGACGCGCACCGACTTCACTCTG ACCATCAGCAGCCTGCAGCCAGAGGACTTCGCCACCTACTACTGCGCAG AGCACCCACGTGCCATTACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG CGCACCGTGGCCGCCCAAGCGTGTTCATCTTCCACCAAGCGACGAGCAG CTGAAGAGCGGCACCGCCAGCGTGGTGTGCTGCTGAACAACCTTCAACCA CAGGAGGCCAAGGTGACGTGGAAGGTGGACACCGCCCTGCAGAGCGGCAAC AGCCAGGAGAGCGTGACCGAGCAGACAGCAAGGACAGCACCTACAGCGCTG

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SEQ ID NO:	Type	Species	Description	Sequence
				AGCAGCACCTGACCTGAGCAAGGCCGACTACGAGAAGCACAGGTGTAC GCCTGCGAGGTGACCCACCAGGGCCTGAGCAGCCAGTGACCAAGAGCTTC AACCGCGCGAGTGCGGCGGCAGCGAGGGCAAGAGCAGCGGCAGCGGCAGC GAGAGCAAGAGCACCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGCAAG AGCACCGCGGCAGCCAGGTGACGTGACGGAGAGCGGCCAGGCCTGGTG AAGCCAAGCGAGACCTGAGCCTGACCTGCACCGTGAGCGGCTACAGCATC ACCAGCGGCTACTTCTGGAAGTGGATCCGCCAGCCACAGGCAAGGGCTG GAGTGGATCGGCTACATCAGTACGACGGCAGCAACAATAACCAAGC CTGAAGAGCCGCGTGACCATCAGCCGCGACACCAGCAAGAACAGTTTACG CTGAAGCTGAGCAGCGTGACCGCGCCGACACCGCGTGTACTACTGCGCC AGCCCAAGCCAGGCACCGGCTACCGCGTGGACTACTGGGGCCAGGGCACC CTGGTGACCGTGAGCAGCGCCAGCACCAGGGCCCAAGCGTGTTCCTACTG GCCCATGACCGCGAGCACAGCGAGAGCACCGCGCCCTGGGCTGCTG GTGAAGGACTACTTCCAGAGCCAGTGACCGTGAGCTGGAACAGCGCGGCC CTGACCAGCGCGGTGCACACCTTCCAGCCGTGCTGCAGAGCAGCGGCTG TACAGCCTGAGCAGCGTGGTGACCGTGCCAAGCAGCAGCCTGGGCAAG ACCTACACCTGCAACGTGGACCACAAGCCAAGCAACCAAGGTGGACAAG CGCGTGGAGAGCAAGTACGGCCCAACCATGCCACCATGCCAGCCAGAG GCGCGCGCGGCCCAAGCGTGTCTGTTCACCAAGCCAAAGCCAAAGCACC CTGATGATCAGCCGACCCAGAGGTGACCTGCGTGGTGGTGGAGTGGAGC CAGGAGGACCCAGAGGTGCAGTTCAACTGGTACGTGGACGGCGTGGAGGTG CACAACGCCAAGACCAAGCCACGCGAGGAGCAGTTCAACAGCACCTACCG GTGGTGAGCGTGTGACCGTGTGCACACGAGTGGCTGAACGGCAAGGAG TACAAGTGCAAGGTGAGCAACAGGGCCCTGCCAAGCAGCATCGAGAAGACC ATCAGCAAGGCCAAGGGCCAGCCACGCGAGCCACAGGTGTACACCTGCCA CCAAGCCAGGAGGAGATGACCAAGAACAGGTGAGCCTGAGCTGCGCCGTG AAGGGCTTCTACCAAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAG CCAGAGAACAACTACAAGACCACCCACCAAGTGTGGACAGCGAGCAGCA TTCTTCTGGTGAGCCGCTGACCGTGAGCAAGAGCCGCTGGCAGGAGGGC AACGTGTTTACGTGACGCGTGTGACAGAGGCCCTGCACAAACCGCTTACAC CAGAAGAGCCTGAGCCTGAGCCTGGGCAAGTGATAG
30	PRT	artificial	I3RB217 half antibody	MAWVWTLFLMAAAQSIQAEIVLTQSPGTLSPGERATLSCRASQSVSSS YLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPED FAVYYCQQDYGFPWTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVV CLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYLSLSTLTLSKA DYEKHKVYACEVTHQGLSPVTKSFNRGECGSGEGKSSGSGSEKSTGKCS SGSGSESKSTGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVR QMPGKGLEWMGIIDPSDSITRYSPSFQGVITADKSI STAYLQWSLKAS DTAMYYCARGDGSTDLDYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSEST AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPS SSLGKTITTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFP PKPKDTLMI SRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQ FNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREP QVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPPV LDSGDSFPLYSRLLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSLGK
31	DNA	artificial	I3RB217 half antibody	ATGGCCTGGGTGTGGACCTGCTGTTCTCTGATGGCCGCCGCCAGAGCATC CAGGCGAGATCGTGCTGACCCAGAGCCAGGCACCTGAGCCTGAGCCCA GGCAGCGCGCCACCTGAGCTGCGCGCCAGCCAGAGCGTGAGCAGCAGC TACCTGGCTGGTACCAGCAGAAGCCAGGCCAGGCCACGCTGCTGATC TACGCGCCAGCAGCGCGCCACCGGCATCCAGACCGCTTACGCGGCAGC GGCAGCGCACCGACTTCACCTGACCATCAGCCGCTGGAGCCAGAGGAC TTCGCCGTGTACTACTGCAGCAGGACTACGGCTTCCCATGGACCTTCGGC CAGGGCACCAAGGTGGAGATCAAGCGCACCGTGGCCGCCCAAGCGTGTTC ATCTTCCCAAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTG TGCCTGCTGAACAATCTTACCCACGCGAGGCCAAGGTGCACTGGAAGGTG GACAACGCCCTGCAGAGCGGCACACGCCAGGAGAGCGTGACCGCAGCAGAC AGCAAGGACAGCACCTACAGCCTGAGCAGCACCTGACCTGAGCAAGGCC GACTACGAGAAGCACAAGGTGTACGCTTGCAGGTTGACCAACAGGGCCTG AGCAGCCCAAGTGACCAAGAGCTTCAACCGCGCGAGTGCggcggcagcgag ggcaagagcagcggcagcggcagcgagagcaagagcaccgagggcagagc agcggcagcggcagcgagagcaagagcaccggcgagcGAGGTGACGTG GTGCAGAGCGCGCCGAGGTGAAGAAGCCAGCGCAGAGCCTGAAGATCAGC TGCAAGGGCAGCGGCTACAGCTTACACGCTACTGGATCAGCTGGGTGCGC CAGATGCCAGGCAAGGGCCTGGAGTGGATGGGCATCATGACCCCAAGCGAC AGCGACACCCGCTACAGCCCAAGCTTCCAGGGCCAGGTGACCATCAGCGCC GACAAGAGCATCAGCACCGCTACCTGCACTGGAGCAGCCTGAAGGCCAGC GACACCGCCATGTACTACTGCGCCGCGGCGACGGCAGCACCGACCTGGAC TACTGGGGCCAGGGCACCTGGTGACCGTGAGCAGCGCCAGCACCAAGGGC CCAAGCGTGTTCCTACTGGCCCCATGCAGCCGCGAGCACCGAGAGCACC GCCGCCCTGGGCTGCCTGGTGAGGACTACTTCCAGAGCCAGTACCGGTG AGCTGGAACAGCGCGCCCTGACAGCGCGGTGCACACCTTCCAGCGGTG

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SEQ ID NO:	Type	Species	Description	Sequence
				CTGCAGAGCAGCGGCTGTACAGCCTGAGCAGCGTGGTGACCGTGCCAAAGC AGCAGCCTGGGCACCAAGACCTACACCTGCAACGTGGACCACAAGCCAAGC AACACCAAGGTGGACAAGCGCGTGGAGAGCAAGTACGGCCACCATGCCCA CCATGCCCAGCCCCAGAGGCCGCCGGCGGCCAAGCGTGTTCCTGTTCCTCA CCAAAGCCAAAGGACACCTGATGATCAGCCGCACCCAGAGGTGACCTGC GTGGTGGTGGACGTGAGCCAGGAGGACCAGAGGTGACGTTCAACTGGTAC GTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCACGCGAGGAGCAG TTCAACAGCACCTACCGCGTGGTGAGCGTGCTGACCGTGCTGCACAGGAC TGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGAGCAACAAGGGCTGCCA AGCAGCATCGAGAAGACCATCAGCAAGGCCAAGGGCAGCCACGCGAGGCCA CAGGTGTACACCTGCCACCAAGCCAGGAGGAGATGACCAAGAACAGGTG AGCCTGTGGTGCTGGTGAAGGGCTTCTACCAAGCGACATCGCGTGGAG TGGGAGAGCAACGGCCAGCCAGAGAACAACCTACAGACCAACCCACAGTG CTGGACAGCGACGGCAGCTTCTTCTGTACAGCCGCCTGACCGTGGACAAG AGCCCGTGGCAGGAGGGCAACGTGTTGAGCTGCAGCGTGATGCACGAGGCC CTGCACAACCACTACACCCAGAAGAGCCTGAGCCTGAGCCTGGGCAAG
32	PRT	artificial	B23B49 half antibody	MAWVWTLFLMAAAQSIQAEIVLTQSPGTLTSLSPGERATLSCRASQSVSSS YLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPED FAVYYCQQDYGFPWTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVV CLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYLSLSTLTLSKA DYKHKVYACEVTHQGLSPVTKSFNRGECGSGEGKSGSGSGSEKSTEGKS SGSGSEKSTGGSEVQLVQSGAEVKKPGESLKISCKGSGYSPTS YWISWVR QMPGKGLEWMMGII DPSDS DTRYSPSFQGVITISADKSI STAYLQWSL KAS DTMYYCARGDGS TDL DYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSEST AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS SSLGKTIT YTCNV DHKPSNTKVDKRVESKYGPCCPAPAEAGGSPVFLFP PKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVDGVEVHNAKTKPREEQ FNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREP QVYTLPPSQEEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPPV LDSGSGFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSLGK
33	DNA	artificial	B23B49 half antibody	ATGGCCTGGGTGTGGACCTGCTGTTCTCTGATGGCCGCCGCCAGAGCATC CAGGCGGACATCGTGATGACCCAGAGCCAGACAGCCTGGCCGTGAGCTG GCGGAGCGCGCCACCATCAACTGCCCGGCCAGCCAGAGCGTGGACTACAAC GGCATCAGCTACATGCATGGTACAGCAGAAGCCAGGCCAGCCACCAAG CTGCTGATCTACGCCGCCAGCAACCCAGAGAGCGGCGTGCCAGACCGCTT AGCGGCAGCGGCAGCGGCACCGACTTCACCTGACCATCAGCAGCCTGCAG GCCAGGACGTGGCCGTGTACTACTGCCAGCAGATCATCGAGGACCATGG ACCTTCGGCCAGGGCACCAAGGTGGAGATCAAGCGCACCGTGGCCGCCCA AGCGTGTTCATCTTCCACCAAGCGACGAGCAGCTGAAGAGCGGCACCGCC AGCGTGGTGTGCTGCTGAACAACCTTCTACCCAGCGAGGCCAAGGTGAC TGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTGACC GAGCAGGACAGCAAGGACAGCACCTACAGCCTGAGCAGCACCTGACCTG AGCAAGGCCGACTACGAGAAGCACAGGTGTACGCCTGCGAGGTGACCCAC CAGGCGCTGAGCAGCCAGTGACCAAGAGCTTCAACCGCGGCGAGTGGCGG GGCAGCGAGGGCAAGAGCAGCGGCAGCGGCAGCGAGGCAAGAGCACCGAG GGCAAGAGCAGCGGCAGCGGCAGCGAGAGCAAGAGCACCGGCGGAGCCAG ATCACCTTGAAGGAGAGCGGCCAACCTGGTGAAGCCAACCCAGACCTG ACCCTGACCTGCACCTTCAGCGGCTTCAGCCTGAGCACCCAGCGCATGGGC GTGAGCTGGATCCGCCAGCCACAGGCAAGGCCCTGGAGTGGCTGGCCAC ATCTACTGGGACGACGACAAGCGCTACAACCCAGCCTGAAGAGCGGCCTG ACCATCACCAAGGACACCAGCAAGAACCAGGTGGTGGTGTGACCATGACCAAC ATGGACCCAGTGGACACCGCCACCTACTACTGCGCCCGCCTGTACGGCTTC ACCTACGGCTTCGCCCTACTGGGGCCAGGGCACCTGGTGACCGTGAGCAGC GCCAGCACCAAGGGCCCAAGCGTGTTCCTACTGGCCCCATGCAGCCGACG ACCAGCGAGAGCACCGCCCGCTGGGCTGCTGGTGAAGGACTACTTCCCA GAGCCAGTGACCGTGAGCTGGAAACAGCGCGCTGACCAAGCGCGCTGCAC ACCTTCCAGCCGTGCTGCAGAGCAGCGGCTGTACAGCCTGAGCAGCGTG GTGACCGTGCCAAAGCAGAGCCTGGGCACCAAGACCTACACCTGCAACGTG GACCAACAGCCAAGCAACACCAAGGTGGACAAGCGCTGAGAGCAAGTAC GGCCCAACATGCCACCATGCCCCAGCCCCAGAGGCCGCCGGCGGCCAAGC GTGTTCTTGTTCACCAAGGCCAAAGGACACCTGATGATCAGCCGACCC CCAGAGGTGACCTGCGTGGTGGTGGACGTGAGCCAGGAGGCCAGAGGTG CAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAG CCACGCGAGGAGCAGTTCAACAGCACCTACCGCGTGGTGGCGTGCTGACC GTGCTGCACCAAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGAGC AACCAAGGGCTGCCAAGCAGCATCGAGAAGACCATCAGCAAGGCCAGGGGC CAGCCACGCGAGGCCACAGGTGTACACCTGCCACCAAGCCAGGAGGAGATG ACCAAGAACCAGGTGAGCCTGTGGTGCTGGTGAAGGGCTTCTACCCAAGC GACATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCAGAGAACAACCTACAAG ACCACCCACAGTGCTGGACAGCGACGCGCAGCTTCTTCTGTACAGCCGC CTGACCGTGGAACAGGCCGTGGCAGGAGGGCAACGTGTTGAGCTGCAGC

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SEQ ID NO:	Type	Species	Description	Sequence
				GTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCCTGAGCCTG AGCCTGGGCAAG
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	QQDYGFPPWT
40	PRT	Artificial	HC	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWISWVRQMPGKGLEWMGII DPSDSDTRYSPSFQGGVTISADKSISTAYLQWSSLKASDTAMYCARGDGS TDLDYWGGTLVTVSS
41	PRT	Artificial	LC	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYG ASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQDYGFPPWTFQG TKVEIK
42	PRT	Artificial	IGHJ1*01 HC	WGQGTLLVTVSS
43	PRT	Artificial	IGKJ2*01 LC	FGQGTKLEIK
44	PRT	Artificial	Val0.2_Fc	MAWVWTLFLMAAAQSIQAQLLEQSPQFLSIQEGENLTVYCNSSSVFSSLO WYRQEPGEGPVLLVTVTGGEVKKLKRITFQPGDARKDSSLHITAAQPGDT GLYLCAGAGSQGNLIFGKGTKLSVKPNIQNPDPAVYQLRDSKSSDKSVCLF TDFDSQTNVSQSKSDVYITDKTVLDMRSMDFKSNSAVAWSNKSDFACANA FNNSIIPEDTFFPSEpkscdkthtcppcpapeLLggpsvflfppkpkdtlm isrtpevtcvvvDvshedpevkfnwyvdgvevhnaktkpreeqynstyrvv sytlvthqdwingkeykckvsnkalpapiektiskakgqprepqvvyVYpps reemtknqvsltcclvkgyfypsdiavewesngqpennykttppvldsdgsfA lvskltvdksrwqqgnvfscsvmhealhnhytqkslspsg

SEQUENCE LISTING

Sequence total quantity: 44

SEQ ID NO: 1 moltype = AA length = 11

FEATURE Location/Qualifiers

REGION 1..11

note = B17B01 HCDR1

source 1..11

mol_type = protein

organism = synthetic construct

SEQUENCE: 1

GYSITSGYFW N

11

SEQ ID NO: 2 moltype = AA length = 9

FEATURE Location/Qualifiers

REGION 1..9

note = B17B01 HCDR2

source 1..9

mol_type = protein

organism = synthetic construct

SEQUENCE: 2

YISYDGSNN

9

SEQ ID NO: 3 moltype = AA length = 11

FEATURE Location/Qualifiers

REGION 1..11

note = B17B01 HCDR3

source 1..11

mol_type = protein

organism = synthetic construct

-continued

SEQUENCE: 3
PSPGTGYAVD Y 11

SEQ ID NO: 4 moltype = AA length = 16
FEATURE Location/Qualifiers
REGION 1..16
note = B17B01 LCDR1
source 1..16
mol_type = protein
organism = synthetic construct

SEQUENCE: 4
RSSQLVHSN GNTYLH 16

SEQ ID NO: 5 moltype = AA length = 7
FEATURE Location/Qualifiers
REGION 1..7
note = B17B01 LCDR2
source 1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 5
KVSNRFS 7

SEQ ID NO: 6 moltype = AA length = 9
FEATURE Location/Qualifiers
REGION 1..9
note = B17B01 LCDR3
source 1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 6
SQSTHVPFT 9

SEQ ID NO: 7 moltype = AA length = 444
FEATURE Location/Qualifiers
REGION 1..444
note = B17B01 Heavy Chain
source 1..444
mol_type = protein
organism = synthetic construct

SEQUENCE: 7
NVQLQESGPG LVKPSQSLSL TCSVAGYSIT SGYFWNWIRQ FPGNKLEWMG YISYDGSNNY 60
NPSLKNRISI TRDTSKNQFF LKLNSVTED TATYYCASPS PGTGYAVDYW GQGTSTVTSS 120
AKTTPPSVYP LAPGSAQTN SMVTLGCLVK GYFPEPVTVT WNSGSLSSGV HTPPAVLQSD 180
LYTLSSSVTV PSSTWPSQTV TCNVAHPASS TKVDKKIVPR DCGCKPCICT VPEVSSVFIF 240
PPKPKDVLTI TLTPKVTCTV VDISKDDPEV QFSWFVDDVE VHTAQTKPRE EQINSTFRSV 300
SELPIMHQDW LNGKEFKCRV NSAAFPAPIE KTISKTYGRP KAPQVYTIPP PKEQMAKDKV 360
SLTCMITNFF PEDITVEWQW NGQPAENYKN TQPIMDTDGS YFVYSKLNVO KSNWEAGNTF 420
TCSVLHEGLH NHHTEKSLSH SPGK 444

SEQ ID NO: 8 moltype = AA length = 219
FEATURE Location/Qualifiers
REGION 1..219
note = B17B01 Light Chain
source 1..219
mol_type = protein
organism = synthetic construct

SEQUENCE: 8
NVVMTQTPLS LPVSLGDQAS ISCRSSQSLV HSNNGTYLHW YLQKPGQSPK FLIYKVSNNF 60
SGVPDRFSGG GSGTEFTLKI SRVEAEDLGV YFCSQSTHVP FTFGSGTKLE IKRADAAPT 120
SIFPPSSEQL TSGGASVVCF LNNFYPKDIN VKWKIDGSER QNGVLNSWTD QDSKDSYISM 180
SSTLTLTKE YERHNSYTCE ATHKTSTSPI VKSPNRNEC 219

SEQ ID NO: 9 moltype = AA length = 447
FEATURE Location/Qualifiers
REGION 1..447
note = B17B1 Heavy Chain
source 1..447
mol_type = protein
organism = synthetic construct

SEQUENCE: 9
NVQLQESGPG LVKPSQSLSL TCSVAGYSIT SGYFWNWIRQ FPGNKLEWMG YISYDGSNNY 60
NPSLKNRISI TRDTSKNQFF LKLNSVTED TATYYCASPS PGTGYAVDYW GQGTSTVTSS 120
ASTKGPSVFP LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSVG HTPPAVLQSS 180
GLYSLSSVVT VPSSSLGTTK YTCNVDHKPS NTKVDKRVES KYGPPCPPCP APEAAGGPSV 240
FLPPPKPKDT LMISRTPEVT CVVVDVSQED PEVQPNWYVD GVEVHNAKTK PREEQFNSTY 300

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RVVSVLTVLH QDWLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYT LPPSQEEMTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTPPVLDL DGSFLLYSKL TVDKSRWQEG 420
NVFSCSVMEH ALHNHYTQKS LSLSLGK 447

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SEQ ID NO: 10      moltype = AA  length = 219
FEATURE           Location/Qualifiers
REGION            1..219
                  note = B17B1 Light Chain
source            1..219
                  mol_type = protein
                  organism = synthetic construct

```

```

SEQUENCE: 10
NVVMTQTPLS LPVSLGDQAS ISCRSSQSLV HSNNGNTYLHW YLQKPGQSPK FLIYKVSNRF 60
SGVPDRFSGG GSGTEFTLKI SRVEAEDLGV YFCSQSTHVP FTFGSGTKLE IKRADAAPT 120
SIFPPSSEQL TSGGASVVCF LNNFYPKDIN VKWKIDGSER QNGVLNSWTD QDSKSTYSM 180
SSTLTTLTKDE YERHNSYTCE ATHKTSTSPI VKSFNRNEC 219

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SEQ ID NO: 11      moltype = AA  length = 447
FEATURE           Location/Qualifiers
REGION            1..447
                  note = B17B2 Heavy Chain
source            1..447
                  mol_type = protein
                  organism = synthetic construct

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```

SEQUENCE: 11
DVQLKESGPG LVKPSQSLV TCSVTGYSIT SGYYWNWYRQ PPGNKLEWMG YISYDGSNNY 60
NPSLKNRISI TRDTSKNQIL LKLTYYVTED TATYYCTRPS PGTGYAVDYW GQGLVTVSS 120
ASTKGPSVFV LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTKT YTCNVDHKPS NTKVDKRVES KYGPPCPPCP APEAAGGPSV 240
FLFPPPKPKD LMISRTPEVT CVVVDVSDQED PEVQFNWYVD GVEVHNAKTK PREEQFNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYT LPPSQEEMTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTPPVLDL DGSFLLYSKL TVDKSRWQEG 420
NVFSCSVMEH ALHNHYTQKS LSLSLGK 447

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SEQ ID NO: 12      moltype = AA  length = 219
FEATURE           Location/Qualifiers
REGION            1..219
                  note = B17B2 Light Chain
source            1..219
                  mol_type = protein
                  organism = synthetic construct

```

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SEQUENCE: 12
DIVMTQSPDS LAVSLGERAT INCRSSQSLV HSNNGNTYLHW YQKPGQPPK LLIYKVSNRF 60
SGVPDRFSGS GSGDTFTLTI SSLQAEDVAV YYCSQSTHVP FTFGQGTKVE IKRADAAPT 120
SIFPPSSEQL TSGGASVVCF LNNFYPKDIN VKWKIDGSER QNGVLNSWTD QDSKSTYSM 180
SSTLTTLTKDE YERHNSYTCE ATHKTSTSPI VKSFNRNEC 219

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SEQ ID NO: 13      moltype = AA  length = 447
FEATURE           Location/Qualifiers
REGION            1..447
                  note = B17B21 Heavy Chain
source            1..447
                  mol_type = protein
                  organism = synthetic construct

```

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SEQUENCE: 13
QVQLQESGPG LVKPSSETLSL TCTVSGYSIT SGYFWNWIRQ PPGKLEWIG YISYDGSNNY 60
NPSLKSRTVI SRDTSKNQFS LKLSSTVTAAD TAVYYCASPS PGTGYAVDYW GQGLVTVSS 120
ASTKGPSVFV LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTKT YTCNVDHKPS NTKVDKRVES KYGPPCPPCP APEAAGGPSV 240
FLFPPPKPKD LMISRTPEVT CVVVDVSDQED PEVQFNWYVD GVEVHNAKTK PREEQFNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYT LPPSQEEMTK 360
NQVSLSCAVK GFYPSDIAVE WESNGQPENN YKTPPVLDL DGSFLLYSRL TVDKSRWQEG 420
NVFSCSVMEH ALHNRYTQKS LSLSLGK 447

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SEQ ID NO: 14      moltype = AA  length = 219
FEATURE           Location/Qualifiers
REGION            1..219
                  note = B17B21 Light Chain
source            1..219
                  mol_type = protein
                  organism = synthetic construct

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SEQUENCE: 14
DIQMTQSPSS LSASVGRVIT ITCRSSQSLV HSNNGNTYLHW YQKPGKAPK FLIYKVSNRF 60
SGVPSRFSGS GSGDTFTLTI SSLQPEDFAT YYCSQSTHVP FTFGQGTKLE IKRTVAAPSV 120
FIFPPSDEQL KSGTASVVCL LNNFYPREAK VQWKVDNALQ SGNSQESVTE QDSKSTYSL 180
SSTLTLSKAD YEKHKVYACE VTHQGLSSPV TKSFNREGC 219

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SEQ ID NO: 15 moltype = AA length = 445
FEATURE Location/Qualifiers
REGION 1..445
 note = I3RB217 Heavy Chain
source 1..445
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 15
EVQLVQSGAE VKKPGESLKI SCKGSGYSFT SYWISWVRQM PGKGLEWMGI IDPSDSDTRY 60
SPSFQQQVTI SADKSISTAY LQWSSLKASD TAMYYCARGD GSTDLQDYWGQ GTLVTVSSAS 120
TKGPSVFPLA PCSRSTSEST AALGCLVKDY FPEPVTVSWN SGALTSGVHT FPAVLQSSGL 180
YSLSSVVTVP SSSLGTTKTYT CNVDHKPSNT KVDKRVESKY GPPCPPCPAP EAAGGPSVFL 240
FPPKPKDTLM ISRTPEVTCV VVDVVSQEDPE VQFNWYVDGV EVHNAAKTKPR EEQFNSTYRV 300
VSVLTIVLHGD WLNKEYKCK VSNKGLPSSI EKTISKAKGQ PREPQVYTLPSQEEMTKNQ 360
VSLWCLVKGF YPSDIAVEWE SNGQPENNYK TTPPVLDSDG SFFLYSRLTV DKSRWQEGNV 420
FSCSVMEAL HNHYTQKSLSLSLGK 445

SEQ ID NO: 16 moltype = AA length = 215
FEATURE Location/Qualifiers
REGION 1..215
 note = I3RB217 Light Chain
source 1..215
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 16
EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSVLAWYQQK PGQAPRLLIY GASSRATGIP 60
DRFSGSGSGT DFTLTISRLE PEDFAVYVCQ QDYGFPWTFG QGTEKVEIKRT VAAPSVFIFP 120
PSDEQLKSGT ASVVCLLNNF YPREAKVQWK VDNALQSGNS QESVTEQDSK DSTYSLSTSL 180
TLTKADYKHK KVIYACEVTHQ GLSSPVTKSF NRGEK 215

SEQ ID NO: 17 moltype = AA length = 447
FEATURE Location/Qualifiers
REGION 1..447
 note = Null Heavy Chain
source 1..447
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 17
QITLKESGPT LVKPTQTTLT TCTFSGFSLT TSGMGVSWIR QPPGKALEWL AHYWDDEK 60
YNPSLKSRIT ITKDTSKNQV VLTMTNMDPV DTATYYCARL YGFTYGFAYW GQGTIVTVSS 120
ASTKGPSVFP LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSVVT VPSSSLGTTK YTCNVDHKPS NTKVDKRVES KYGPPCPPCP APEAAGGPSV 240
FLFPPKPKDT LMISRTPEVT CVVVDVVSQED PEVQFNWYVD GVEVHNAAKTK PREEQFNSTY 300
RVVSVLTIVL QDWLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYT LPQSQEEMTK 360
NQVSLWCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSRL TVDKSRWQEG 420
NVFSCSVME ALHNHYTQKS LSLSLGK 447

SEQ ID NO: 18 moltype = AA length = 218
FEATURE Location/Qualifiers
REGION 1..218
 note = Null Light Chain
source 1..218
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 18
DIVMTQSPDS LAVSLGERAT INCRASQSVS YNGISYMHY QKPGQPPKL LIYAASNPES 60
GVPDRFSGSG SGTDFTLTIS SLQAEDVAVY YCQIIEDEW TFGQGTKVEI KRTVAAPSVF 120
IFPPSDEQLK SGTASVCLL NNFYPREKAV QWKVDNALQS GNSQESVTEQ DSKDSTYSL 180
STLTLSKADY EKHKVIYACEV THQGLSSPVT KSFNRGEC 218

SEQ ID NO: 19 moltype = AA length = 119
FEATURE Location/Qualifiers
REGION 1..119
 note = B17H3
source 1..119
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 19
EVQLLESQGG LVQPGGSLRL SCAASGYSIT SGYFNNWVRQ APGKGLEWVS YISYDGSNNY 60
ADSVKGRFTI SRDNSKNTLY LQMNLSRAED TAVYYCAKPS PGTGYAVDYW GQGTIVTVS 119

SEQ ID NO: 20 moltype = AA length = 120
FEATURE Location/Qualifiers
REGION 1..120
 note = B17H4

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source                1..120
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 20
EVQLLESGGG LVQPGGSLRL SCAASGYSIT SGYFWNWVRQ APGKGLEWVS YISYDGSNNY 60
ADSVKGRFTI SRDNSKNTLY LQMNLSRAED TAVYYCASPS PGTGYAVDYW GQGT LVTVSS 120

SEQ ID NO: 21          moltype = AA length = 120
FEATURE               Location/Qualifiers
REGION                1..120
                      note = B17H5
source                1..120
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 21
QVQLQESGPG LVKPSETLSL TCTVSGYSIT SGYFWNWIRQ PPGKGLEWIG YISYDGSNNY 60
NPSLKSRVTI SRDTSKNQFS LKLSSVTAAD TAVYYCASPS PGTGYAVDYW GQGT LVTVSS 120

SEQ ID NO: 22          moltype = AA length = 112
FEATURE               Location/Qualifiers
REGION                1..112
                      note = B17L3
source                1..112
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 22
DIQMTQSPSS LSASVGRVIT ITCRSSQSLV HSNNGNTYLHW YQKPKGKAPK LLIYKVSNRF 60
SGVPSRFGSG GSGTDFTLTI SSLQPEDFAT YYCSQSTHVP FTFGQGTKLE IK 112

SEQ ID NO: 23          moltype = AA length = 112
FEATURE               Location/Qualifiers
REGION                1..112
                      note = B17L4
source                1..112
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 23
DIQMTQSPSS LSASVGRVIT ITCRSSQSLV HSNNGNTYLHW YQKPKGKAPK FLIYKVSNRF 60
SGVPSRFGSG GSGTDFTLTI SSLQPEDFAT YYCSQSTHVP FTFGQGTKLE IK 112

SEQ ID NO: 24          moltype = AA length = 112
FEATURE               Location/Qualifiers
REGION                1..112
                      note = B17L5
source                1..112
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 24
DVVMTQSPLS LPVTLGQPAS ISCRSSQSLV HSNNGNTYLHW FQQRPGQSPR FLIYKVSNRF 60
SGVPDRFGSG GSGTDFTLKI SRVEAEDGVV YYCSQSTHVP FTFGQGTKLE IK 112

SEQ ID NO: 25          moltype = AA length = 120
FEATURE               Location/Qualifiers
REGION                1..120
                      note = B17H1
source                1..120
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 25
NVQLQESGPG LVKPSQSLSL TCSVAGYSIT SGYFWNWIRQ FPGNKLEWVG YISYDGSNNY 60
NPSLKNRISI TRDTSKNQFF LKLNSVTTED TATYYCASPS PGTGYAVDYW GQGT SVTVSS 120

SEQ ID NO: 26          moltype = AA length = 112
FEATURE               Location/Qualifiers
REGION                1..112
                      note = B17L1
source                1..112
                      mol_type = protein
                      organism = synthetic construct

SEQUENCE: 26
NVVMTQTPLS LPVSLGDQAS ISCRSSQSLV HSNNGNTYLHW YLQKPGQSPK FLIYKVSNRF 60
SGVPDRFGSG GSGTEFTLKI SRVEAEDLGV YFCSQSTHVP FTFGSGTKLE IK 112

SEQ ID NO: 27          moltype = AA length = 493
FEATURE               Location/Qualifiers
REGION                1..493

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note = TCR-Vbeta17_Fc fusion
source 1..493
mol_type = protein
organism = synthetic construct

SEQUENCE: 27
MAWVWTLFL MAAQSIQAV DGGITQSPKY LFRKEGQNV LSCQNLNHD AMYWYRQDPG 60
QGLRLIYYSQ IVNDFQKGD I AEGYSVSREK KESFPLTVTS AQKNPTAFYL CASSSRSSYE 120
QYFGPGTRLT VTEDLKNVFP PEVAVFEPSE AEISHTQKAT LVCLATGFYP DHVELSWWVN 180
GKEVHSGVST DPQPLKEQPA LNDSTRYSLSS RLRVSATFWQ NPRNHFRQCV QFYGLSENDE 240
WTQDRAKPV TIVSAEAWGR ADEPKSCDKT HTCPPCPAPE LLGGPSVFLF PPKPKDTLMI 300
SRTPEVTCVV VDVSHEDPEV KFNWYVDGVE VHNAKTKPRE EQYNSTYRVV SVLTVLHQDW 360
LNGKEYKCKV SNKALPAPIE KTISKAKGQP REPQVYVLP SREEMTKNQV SLLCLVKGFY 420
PSDIAVEWES NGQPENNYLT WPPVLDSDGS FFLYSLKLTVD KSRWQQGNV SCSVMHEALH 480
NHYTQKSLSL SPG 493

SEQ ID NO: 28 moltype = AA length = 719
FEATURE Location/Qualifiers
REGION 1..719
note = B17B21 half antibody
source 1..719
mol_type = protein
organism = synthetic construct

SEQUENCE: 28
MAWVWTLFL MAAQSIQAD IQMTQSPSSL SASVGDRVTI TCRSSQSLVH SNGNTYLHWY 60
QKQKPKAPKF LIYKVSNRFS GVPSRFSGSG SGTDFTLTIS SLQPEDFATY YCSQSTHVPF 120
TFGQGTKEI KRTVAAPSVF IFPPSDEQLK SGTASVVCLL NNFPYPREAKV QWKVDNALQS 180
GNSQESVTEQ DSKDSTYSLS STLTLSKADY EKHKVYACEV THQGLSSPVT KSFNRGECGG 240
SEGKSSGSGS ESKSTEGKSS GSGSESKSTG GSQVQLQESG PGLVKPSETL SLTCTVSGYS 300
ITSGYFWNWI RQPPGKGLEW IGYISYDGSN NYNPSLKS RV TISRDTSKNQ FSLKLSSTVA 360
ADTAVYYCAS PSPGTGYAVD YWGQGTLLTV SSASTKGPSV FPLAPCSRST SESTAALGCL 420
VKDYFPEPV TSVNWSGALTS GVHTFPAVLQ SGLYSLSSV VTPSSSLGT KTYTCNVNDRH 480
PSNTKVDKRV ESKYGPCCPP CPAPEAAGGP SVFLFPPKPK DTLNISRTPE VTCVVVDVSQ 540
EDPEVQFNWY VDGVEVHNAK TKPREEQFNS TYRVVSVLTV LHQDNLNGKE YKCKVSNKGL 600
PSSIEKTISK AKGQPREPV YTLPPSQEEM TKNQVSLSCA VKGFYPSDIA VEWESNGQPE 660
NNYKTTTPVL DSDGSFFLV S RLTVDKSRWQ EGNVFSQSV M HEALHNRTQ KSLSLSLGK 719

SEQ ID NO: 29 moltype = DNA length = 4320
FEATURE Location/Qualifiers
misc_feature 1..4320
note = B17B21 half antibody
source 1..4320
mol_type = other DNA
organism = synthetic construct

SEQUENCE: 29
atggcctggg tgtggaccct gctgttccctg atggccgcgcg cccagagcat ccaggccgac 60
atccagatga cccagagccc aagcagcctg agcgcagcgcg tggcgagaccg cgtgaccatc 120
acctgccgca gcagccagag cctgggtgcac agcaacggca acacctacct gcaactggta 180
cagcagaagc caggcaaggg cccaaagttc ctgatctaca aggtgagcaa ccgcttcacg 240
ggcgtgcca cccgcttcag cgcgcagcgcg agcggcaccg acttcacct gaccatcagc 300
agcctgcagc cagaggactt cgccacctac tactgcagcc agagcaccga cgtgccattc 360
accttcggcc agggcaccga gctggagatc aagcgcaccg tggccgcccc aagcgtgttc 420
atcttccac caagcgacga cagcctgaag agcggcaccg ccagcgtggt gtgcctgctg 480
aacaacttct acccagcga ggcgaaggtg cagtggaaagg tggacaacgc cctgcagagc 540
ggcaacagcc aggagagcgt gaccgagcag gacagcaagg acagcaccta cagcctgagc 600
agcaccctga cctcgacga ggcgcactac gagaagcaca aggtgtacgc ctgcgaggtg 660
accaccagc gccctgagcag cccagtgacc aagagcttca accgcggcga gtgcggcgcc 720
agcgagggca agagcagcgg cagcggcagc gagagcaaga gcaccgaggg caagagcagc 780
ggcagcgcca gcgagagcaa gacacccggc ggcagccagg tgcagctgca ggagagcgcc 840
ccaggcctgg tgaagccaag cgagaccctg agcctgacct gcaccgtgag cggctacagc 900
atcaccagcg gctacttctg gaactggatc cgccagccac caggcaaggg cctggaggtg 960
atcggtaca tcaagcaga cggcagcaac aactacaacc caagcctgaa gagcccgctg 1020
accatcagcc gcgacaccag caagaaccag ttcagcctga agctgagcag cgtgaccgcc 1080
gccgacaccg ccgtgtacta ctgcgccagc ccaagccagc gcaccggcta cgccgtggac 1140
tactggggcc agggcaccct ggtgaccgtg agcagcgcca gcaccaagg cccaagcgtg 1200
ttccactgg cccatgcag ccgcagcacc agcgagagca ccgcgcctt gggctgcctg 1260
gtgaaggact acttccaga gccagtgacc gtgagctgga acagcgccg cctgaccagc 1320
ggcgtgcaca ccttccagc cgtgctgcag agcagcgccg tgtacagcct gagcagcgtg 1380
gtgaccgtgc caagcagcag cctgggcacc aagacctaca cctgcaacgt ggaccacaag 1440
ccaagcaaca ccaaggtgga caagcgctg gagagcaagt acggccacc atgccacca 1500
tgccagccc cagaggccgc cggcgcccca agcgtgttcc tgttccacc aaagccaaag 1560
gacaccctga tgatcagc caccagag gtgacctgct tgggtggtgga cgtgagccag 1620
gaggaccag aggtgcagtt caactggtac gtggacggcg tggaggtgca caacgccaa 1680
accaagccac gcgaggagca gttcaacagc acctaccgct tgggtgagcgt gctgaccgtg 1740
ctgcaccagg actggctgaa cggcaaggag tacaagtga aggtgagcaa caaggccctg 1800
ccaagcagca tcgagaagac gccaaaggcc agccacgcga gccacaggtg 1860
tacaccctgc caccaagcca ggaggagatg accaagaacc aggtgagcct gagctgcgcc 1920

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gtgaagggt	tctacccaag	cgacatcgcc	gtggagtggg	agagcaacgg	ccagccagag	1980
aacaactaca	agaccacccc	accagtgtctg	gacagcgacg	gcagcttctt	cctgggtgagc	2040
cgctgacccg	tggaacaagag	ccgctggcag	gagggaacag	tggtcagctg	cagcgtgatg	2100
cacgagggccc	tgacaacaaccg	cttaccaccag	aagagcctga	gcctgagcct	gggcaagatg	2160
gcctgggtgt	ggaccctgct	gttcttgatg	gccgcgcccc	agagcatcca	ggccgacatc	2220
cagatgaccc	agagcccaag	cagcctgagc	gccagcgtgg	gcgaccgcgt	gaccatcacc	2280
tgccgcagca	gccagagcct	ggtgcacagc	aacggcaaca	cctacctgca	ctggtaccag	2340
cagaagccag	gcaaggcccc	aaagtctctg	atctacaagg	tgagcaaccg	cttcagcggc	2400
gtgccaagcc	gcttcagcgg	cagcggcagc	ggcaccgact	tcacctgac	catcagcagc	2460
ctgcagccag	aggacttcgc	cacctactac	tgcagccaga	gcacccacgt	gccattcacc	2520
ttcgggcagg	gcaccaagct	ggagatcaa	cgcaccgtgg	ccgccccaa	cgtgttcac	2580
ttcccaccaa	gcgacgagca	gctgaagagc	ggcaccgcca	gcgtggtgtg	cctgctgaac	2640
aaactctacc	cacgcgaggg	caagggtgcag	tggagggtgg	acaacgcctt	gcagagcggc	2700
aacagccag	gcagcggtgac	cgagcaggac	agcaaggaca	gcacctacag	cctgagcagc	2760
accctgaccc	tgagcaaggg	cgactacgag	aagcacaagg	tgtacgcctg	cgaggtgacc	2820
caccagggcc	tgagcagccc	agtgaccaag	agcttcaacc	gcggcgagtg	cgccggcagc	2880
gagggcaaga	gcagcgcgag	cgccagcgag	agcaagagca	ccgagggcaa	gagcagcggc	2940
agcggcagcg	agagcaagag	caccggcggc	agccaggtgc	agctgcagga	gagcggccca	3000
ggcctggtga	agccaagcga	gacctgagc	ctgacctgca	ccgtgagcgg	ctacagcatc	3060
accagcggct	acttctggaa	ctggatccgc	cagccaccag	gcaaggccct	ggagtggatc	3120
ggctacatca	gctacgacgg	cagcaacaac	tacaacccaa	gcctgaagag	ccgctgaccc	3180
atcagccggc	acaccagcaa	gaaccagttc	agcctgaagc	tgagcagcgt	gaccgcccgc	3240
gacaccggcg	tgactactgt	cgccagccca	agcccaggca	ccggtacgc	cgtggactac	3300
tggggccagg	gcaccctggt	gaccgtgagc	agcggcagca	ccaagggccc	aagcgtgttc	3360
ccactggccc	ctgcagccg	cagcaccagc	gagagcaccg	ccgcctggg	ctgcctggtg	3420
aaggactact	tccagagcc	agtgcacgtg	agctggaa	gcggcgccct	gaccagcggc	3480
gtgcacacct	tccagccgt	gctgcagagc	agcggcctgt	acagcctgag	cagcgtggtg	3540
accgtgccaa	gcagcagcct	gggcaccaa	acctacacct	gcaacgtgga	ccacaagcca	3600
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ccagccccag	aggccggcgg	cgccccaagc	gtgttctctg	ttccacccaa	gcccaggac	3720
accctgatga	tcagccgcac	ccagaggtg	acctgcgtgg	tggtggacgt	gagccaggag	3780
gaccagagag	tgcagtctaa	ctggatcgtg	gacggcgtgg	aggtgcacaa	cgccaagacc	3840
aagccacgcg	aggagcagtt	caacagcacc	taccgctgtg	tgagcgtgct	gaccgtgctg	3900
caccaggact	ggctgaacgg	caaggagtac	aagtgcagg	tgagcaacaa	gggctgcca	3960
agcagcatcg	agaagaccat	cagcaaggcc	aagggccagc	cacgcgagcc	acagggtgac	4020
accctgccac	caagccagga	ggagatgacc	aagaaccagg	tgagcctgag	ctgcgccgtg	4080
aagggcttct	acccaagcga	catcgccgtg	gagtgaggga	gcaacggcca	gccagagaac	4140
aactacaaga	ccacccacc	agtgcctggc	agcgacggca	gcttcttctt	ggtgagccgc	4200
ctgaccgtgg	acaagagccg	ctggcaggag	ggcaacgtgt	tcagctgcag	cgtgatgcac	4260
gaggccctgc	acaaccgctt	caccagaga	agcctgagcc	tgagcctggg	caagtgatag	4320

SEQ ID NO: 30 moltype = AA length = 713
 FEATURE Location/Qualifiers
 REGION 1..713
 note = I3RB217 half antibody
 source 1..713
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 30

MAVWVTLFL	MAAAQSIQAE	IVLTQSPGTL	SLSPGERATL	SCRASQSVSS	SYLAWYQQKP	60
GQAPRLLIYG	ASSRATGIPD	RFSGSGSGTD	FTLTISRLEP	EDFAVYYCQQ	DYGFPPWTFGQ	120
GTKVEIKRTV	AAPSVFIIPP	SDEQLKSGTA	SVVCLLNIFY	PREAKVQWKV	DNALQSGNSQ	180
ESVTEQDSKD	STYLSSTLT	LSKADYEKHK	VYACEVTHQG	LSSPVTKSFN	RGECGGSEK	240
SSGSGSESKS	TEGSSSGSGS	ESKSTGGSEV	QLVQSGAEVK	KPGESLKISC	KSGYSFTSY	300
WISWVRQMPG	KGLEWMGIID	PSDSDTRYSP	SFQQQVTISA	DKSISTAYLQ	WSSLKASDTA	360
MYCARGDGS	TDLDYWGQGT	LVTVSSASTK	GPSVFPLAPC	SRSTSESTAA	LGCLVKDYFP	420
EPVTVSWNSG	ALTSQVHTFP	AVLQSSGLYS	LSSVTVPS	SLGKTYTCN	VDHKPSNTKV	480
DKRVESKYGP	PCPPCPAPEA	AGGPSVFLFP	PKPKDTLMIS	RTPEVTCVVV	DVSQEDPEVQ	540
FNWYVDGVEV	HNAKTKPRE	QFNSTYRVVS	VLTVLHQDWL	NGKEYKCKVS	NKGLPSSIEK	600
TISKAKGQPR	EPQVYTLPPS	QEEMTKNQVS	LWCLVKGFYP	SDIAVEWESN	GQPENNYKTT	660
PPVLDSGDSF	FLYSRLTVDK	SRWQEGNVFS	CSVMHEALHN	HYTQKSLSL	LGK	713

SEQ ID NO: 31 moltype = DNA length = 2139
 FEATURE Location/Qualifiers
 misc_feature 1..2139
 note = I3RB217 half antibody
 source 1..2139
 mol_type = other DNA
 organism = synthetic construct

SEQUENCE: 31

atggcctggg	tgtggacct	gctgttctctg	atggccgcgg	cccagagcat	ccaggccgag	60
atcgtgctga	cccagagccc	aggcacccctg	agcctgagcc	caggcgagcg	cgccaccctg	120
agctgcccg	ccagccagag	cgtgagcagc	agctacctgg	cctggtacca	gcagaagcca	180
ggccaggccc	cacgcctgct	gatctacggc	gccagcagcc	gcgccaccgg	catcccagac	240
cgcttcagc	cgagccgag	cgccaccgac	ttcaccctga	ccatcagccg	cctggagcca	300
gaggacttcg	ccgtgtacta	ctgccagcag	gactacggct	ttccatggac	cttcggccag	360

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ggcaccaagg tggagatcaa gcgcaccgtg gccgccccaa gcgtgttcat cttcccacca 420
agcgacgagc agctgaagag cggcacccgc agcgtgggtg gcctgctgaa caacttttac 480
ccacgcgagc ccaaggtgca gtggaagggtg gacaacgccc tgcagagcgg caacagccag 540
gagagcgtga ccgagcagga cagcaaggac agcacctaca gcctgagcag caccctgacc 600
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 660
ctgagcagcc cagtgaacaa gagcttcaac cgcggcgagt gcggcgcgag cgagggcaag 720
agcagcggca gccgcagcga gagcaagagc accgagggca agagcagcgg cagcggcagc 780
gagagcaaga gcacccggcg cagcgagggtg cagctgggtg agagcggcgc cgagggtgaag 840
aagccaggcg agagcctgaa gatcagctgc aagggcagcg gctacagctt caccagctac 900
tggatcagct ggggtgcgca gatgccaggc aagggccttg agtggatggg catcatcgac 960
ccaagcgaca gcgacacccg ctacagccca agcttccagg gccaggtgac catcagcgcc 1020
gacaagagca tcagcaccgc ctacctgcag tggagcagcc tgaaggccag cgacaccgcc 1080
atgtactact gcgcccggcg cgacggcagc accgacctgg actactgggg ccaggggacc 1140
ctgggtgacc tgagcagcgc cagcaccaag ggcccaagcg tgttcccact ggcccctatg 1200
agccgcagca ccagcgagag caccgcccgc ctgggctgcc tgggtgaagga ctacttccca 1260
gagccagtgga ccgtgagctg gaacagcggc gccctgacca gcggcggtgca caccttccca 1320
gccgtgctgc agcagcagcg cctgtacagc ctgagcagcg tggtgacgct gccaaagcagc 1380
agcctgggca ccaagaccata cactgcaaac gtggaccaca agccaagcaa cccaaggtg 1440
gaccaagcgcg tggagagcga gtacggccca ccatgccac catgccagc cccagaggcc 1500
gccggcgggc caagcgtgtt cctgttccca ccaaagccaa aggacacct gatgatcagc 1560
cgacccccag aggtgacctg cgtggtggtg gacgtgagcc agggaggccc agagggtcag 1620
ttcaactggt acgtggacgg cgtggaggtg cacaacgcca agaccaagcc acgcgaggag 1680
cagttcaaca gcacctaccg cgtggtgagc gtgtgacgg tgctgcacca ggactggctg 1740
aacggcaagg agtacaagtg caaggtgagc aacaagggcc tgccaagcag catcgagaag 1800
accatcgaca aggccaaggc ccagccacgc gagccacagg tgtacacct gccaccaagc 1860
caggaggaga tgaccaagaa ccaggtgagc ctggtggtgcc tgggtgaagg cttctaccca 1920
agcgacatcg ccgtggagtg ggagagcaac ggccagccag agaacaacta caagaccacc 1980
ccaccagtcg tggacagcga cggcagcttc ttctgtaca gccgctgac cgtggacaag 2040
agccgctggc aggagggcaa cgtgttcagc tgcacggtga tgacagggc cctgcacaa 2100
cactacaccc agaagagcct gagcctgagc ctgggcaag 2139

```

```

SEQ ID NO: 32      moltype = AA length = 713
FEATURE           Location/Qualifiers
REGION            1..713
                  note = B23B49 half antibody
source            1..713
                  mol_type = protein
                  organism = synthetic construct

```

```

SEQUENCE: 32
MAWVWTLLEFL MAAASQIQAE IVLTQSPGTL SLSPGERATL SCRASQSVSS SYLAWYQQKP 60
GQAPRLLIYG ASSRATGIPD RFGSGSGSTD FTLTISRLEP EDFAVYYCQQ DYGFPTWTFGQ 120
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNIFY PREAKVQWKV DNALQSGNSQ 180
ESVTEQDSKD STYLSSTLT LSKADYEKKH VYACEVTHQG LSSPVTKSFN RGECSGSEK 240
SSGSGSESKS TEGKSSGSGS ESKSTGGSEV QLVQSGAEVK KPGESLKISC KSGSYFTSY 300
WISWVRQMPG KGLEWMIID PSDSDTRYSP SFQGQVTISA DKSISTAYLQ WSSLKASDTA 360
MYYCARGDGS TDLDYWGGGT LVTVSSASTK GPSVFPLAPC SRSTSESTAA LGCLVKDYFP 420
EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVTVTPSS SLGTKTYTCN VDHKPSNTKV 480
DKRVESKYGP PCPPCPAPEA AGGPSVFLFP PKPKDLMIS RTPEVTCVVV DVSQEDPEVQ 540
FNWYVDGVEV HNAKTKPREE QFNSTYRVVS VLTVLHQDWL NGKEYKCKVS NKGLPSSIEK 600
TISKAKGQPR EPQVYTLPPS QEEMTKNQVS LWCLVKGFYP SDIAVEWESN GPENNYKTT 660
PPVLDSDSGS FLYSRLTVDK SRWQEGNVFS CSMHEALHN HYTKSLSLG LGK 713

```

```

SEQ ID NO: 33      moltype = DNA length = 2154
FEATURE           Location/Qualifiers
misc_feature       1..2154
                  note = B23B49 half antibody
source            1..2154
                  mol_type = other DNA
                  organism = synthetic construct

```

```

SEQUENCE: 33
atggcctggg tgtggacctg gctgttccct atggccgccc ccagagcatc ccaggccgac 60
atcgtgatga cccagagccc agacagcctg gccgtgagcc tgggcgagcg cgccaccatc 120
aactgcccg ccagccagag cgtggactac aacggcatca gctacatgca ctggtaccag 180
cagaagccag gccagccacc aaagctgctg atctacgccg ccagcaaccc agagagcggc 240
gtgccagacc gcttcagcgg cagcggcagc ggcacgcact tcacctgac catcagcagc 300
ctgcaggccc aggacgtggc cgtgtactac tgccagcaga tcatcgagga cccatggacc 360
ttcggccagg gcaccaaggt ggagatcaag cgcaccgtgg ccgccccaa cgtgttcac 420
ttcccaccaa gccacgagca gctgaagagc ggcaccgcca gcgtgggtg cctgctgaac 480
aacttctacc cagcggaggg caaggtgcag tggaaaggtg acaacgccc gcagagcggc 540
aacagccagg agagcgtgac cgagcaggac agcaaggaca gcacctacg cctgagcagc 600
accctgacc ccagcaaggc cagctacgag aagcacaagg tgtacgcctg cgagggtgacc 660
caccagggcc tgagcagccc agtgaccaag agcttcaacc gcggcgagtg cggcggcagc 720
gagggcaaga gcagcggcag cggcagcgag agcaagagca ccgagggcaa gagcagcgcc 780
agcggcagcg agagcaagag caccggcggc agccagatca ccctgaagga gagcggccca 840
accctggtga agccaaccca gaccctgacc ctgacctgca ccttcagcgg cttcagcctg 900
agcaccagcg gcatgggcgt gagctggatc cgccagccac caggcaaggc cctggagtgg 960

```

-continued

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ctggcccaca tctactggga cgaagacaag cgetacaacc caagcctgaa gagccgctg 1020
accatcacca aggacaccag caagaaccag gtgggtgctga ccatgaccaa catggaccca 1080
gtgggacaccg ccacctaacta ctgcgcccgc ctgtacggct tcacctacgg ctgcgcctac 1140
tggggccagg gcacctggt gaccgtgagc agcgccagca ccaagggccc aagcgtgttc 1200
ccactggccc catgcagccg cagcaccagc gagagcaccg ccgcctggg ctgcctgggtg 1260
aaggactact tcccagagcc agtgaccgtg agctggaaca gcggcgccct gaccagcggc 1320
gtgcacacct tcccagccgt gctgcagagc agcgccctgt acagcctgag cagcgtgtgtg 1380
accgtgccaa gcagcagcct gggcaccaa acctacacct gcaacgtgga ccacaagcca 1440
agcaacacca aggtggacaa gcgcgtggag agcaagtacg gccaccatg cccaccatgc 1500
ccagccccag agggcgcccg cggcccaagc gtgttcctgt tcccaccaa gccaaaggac 1560
accctgatga tcagccgcac cccagaggtg acctgcgtgg tgggtggacgt gagccaggag 1620
gaccagagg tgcaagtcaa ctggtacgtg gacggcgtgg aggtgcacaa cgccaagacc 1680
aagccacgcg agggagcagtt caacagcacc taccgcgtgg tgagcgtgct gaccgtgtgtg 1740
caccaggact ggctgaagg caaggagtag aagtgcaagg tgagcaacaa gggcctggca 1800
agcagcatcg agaagaccat cagcaaggcc aagggccagc cagcgagcc acaggtgtac 1860
accctgccac caagccagga ggagatgacc aagaaccagg tgagcctgtg gtgcctgggtg 1920
aagggtctct acccaagcga catcgccgtg gagtgggaga gcaacggcca gccagagaac 1980
aactacaaga cccccacc agtgctggac agcgacggca gcttcttct gtacagccgc 2040
ctgaccgtgg acaagagccg ctggcaggag ggcaacgtgt tcagctgcag cgtgatgcac 2100
gaggccctgc acaaccacta caccagaag agcctgagcc tgagcctggg caag 2154

```

```

SEQ ID NO: 34      moltype = AA length = 5
FEATURE           Location/Qualifiers
REGION            1..5
                  note = I3RB217 HCDR1
source            1..5
                  mol_type = protein
                  organism = synthetic construct

```

```

SEQUENCE: 34
SYWIS                                                    5

```

```

SEQ ID NO: 35      moltype = AA length = 17
FEATURE           Location/Qualifiers
REGION            1..17
                  note = I3RB217 HCDR2
source            1..17
                  mol_type = protein
                  organism = synthetic construct

```

```

SEQUENCE: 35
IIDPSDSDTR YSPSFQG                                     17

```

```

SEQ ID NO: 36      moltype = AA length = 9
FEATURE           Location/Qualifiers
REGION            1..9
                  note = I3RB217 HCDR3
source            1..9
                  mol_type = protein
                  organism = synthetic construct

```

```

SEQUENCE: 36
GDGSTDL DY                                              9

```

```

SEQ ID NO: 37      moltype = AA length = 11
FEATURE           Location/Qualifiers
REGION            1..11
                  note = I3RB217 LCDR1
source            1..11
                  mol_type = protein
                  organism = synthetic construct

```

```

SEQUENCE: 37
RASQSVSSSY L                                           11

```

```

SEQ ID NO: 38      moltype = AA length = 7
FEATURE           Location/Qualifiers
REGION            1..7
                  note = I3RB217 LCDR2
source            1..7
                  mol_type = protein
                  organism = synthetic construct

```

```

SEQUENCE: 38
GASSRAT                                                 7

```

```

SEQ ID NO: 39      moltype = AA length = 9
FEATURE           Location/Qualifiers
REGION            1..9
                  note = I3RB217 LCDR3
source            1..9

```


-continued

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mol_type = protein
organism = synthetic construct

SEQUENCE: 39
QQDYGFPPWT 9

SEQ ID NO: 40
FEATURE
REGION
source
moltype = AA length = 118
Location/Qualifiers
1..118
note = I3RB217 HC
1..118
mol_type = protein
organism = synthetic construct

SEQUENCE: 40
EVQLVQSGAE VKKPGESLKI SCKGSGYSFT SYWISWVRQM PGKGLEWMGI IDPSDSDTRY 60
SPSFQGGVTI SADKSISTAY LQWSSLKASD TAMYCCARGD GSTDLDDYWGQ GTLVTVSS 118

SEQ ID NO: 41
FEATURE
REGION
source
moltype = AA length = 108
Location/Qualifiers
1..108
note = I3RB217 LC
1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 41
EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSYLAWYQQK PGQAPRLLIY GASSRATGIP 60
DRFSGSGSGT DFTLTISRLE PEDFAVYVCQ QDYGFPPWTFG QGTKVEIK 108

SEQ ID NO: 42
FEATURE
REGION
source
moltype = AA length = 11
Location/Qualifiers
1..11
note = IGHJ1*01 HC
1..11
mol_type = protein
organism = synthetic construct

SEQUENCE: 42
WGQGTLLVTVS S 11

SEQ ID NO: 43
FEATURE
REGION
source
moltype = AA length = 10
Location/Qualifiers
1..10
note = IGKJ2*01 LC
1..10
mol_type = protein
organism = synthetic construct

SEQUENCE: 43
FGQGTKLEIK 10

SEQ ID NO: 44
FEATURE
REGION
source
moltype = AA length = 449
Location/Qualifiers
1..449
note = Val10.2_Fc fusion
1..449
mol_type = protein
organism = synthetic construct

SEQUENCE: 44
MAVWVTLLEFL MAAQSIQAI LLEQSPQFLS IQEGENLTVY CNSSSVFSSL QWYRQEPGEG 60
PVLLVTVVVG GEVKKLKRLT FQPGDARKDS SLHITAAQPG DTGLYLCAGA GSQGNLIFGK 120
GTKLSVKPNI QNPDPVYQL RDSKSSDKSV CLFTDFDSQT NVSQSKSDV YITDKTVLDM 180
RSMDFKNSA VAWSNKSDFA CANAFNNSII PEDTFFPSEP KSCDKTHTCP PCPAPELLGG 240
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VVYPPPSREE 360
MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTTPV LDSDGSPALV SKLTVDKSRW 420
QQGNVFSCSV MHEALHNHYT QKSLSLSPG 449

```

1.-34. (canceled)

35. A Vb17 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 variable region comprising the amino acid sequences of SEQ ID NO: 25, SEQ ID NO: 19, SEQ ID NO: 20, or SEQ ID NO: 21, and LC1 comprises a light chain variable region comprising the amino acid sequences of SEQ ID NO: 26, SEQ ID NO: 22, SEQ ID NO: 23, or SEQ ID NO: 24.

36. The bispecific antibody of claim **35**, wherein HC1 comprises a heavy chain variable region comprising the amino acid sequences of SEQ ID NO: 25 and LC1 comprises

a light chain variable region comprising the amino acid sequences of SEQ ID NO: 26.

37. The bispecific antibody of claim **35**, wherein the bispecific antibody or antigen-binding fragment thereof is an IgG isotype.

38. The bispecific antibody of claim **35**, wherein HC1 and LC1 are humanized.

39. The bispecific antibody of claim **35**, wherein HC2 and LC2 bind to CD123.

40. The bispecific antibody of claim **39**, 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.

41. The bispecific antibody of claim **35**, 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.

42. A nucleic acid encoding the HC1, LC1, HC2, and LC2 of the Vb17 bispecific antibody or antigen-binding fragment thereof of claim **35**.

43. A vector comprising the isolated nucleic acid of claim **42**.

44. A host cell comprising the vector of claim **43**.

45. A buffered composition comprising the isolated anti-Vb17/anti-CD123 bispecific antibody or antigen-binding fragment thereof of claim **35**.

46. A method of directing a Vb17-expressing CD8+ or CD4+ T cell to a cancer cell, the method comprising contacting a Vb17-expressing CD8+ or CD4+ T cell with the bispecific antibody or antigen-binding fragment thereof of claim **35**, wherein the contacting directs the Vb17-expressing CD8+ or CD4+ T cell to a cancer cell.

47. The method of claim **46**, wherein the cancer cell is a CD123-expressing cancer cell.

48. A method for inhibiting growth or proliferation of cancer cells, the method comprising contacting the cancer cells with the bispecific antibody or antigen-binding fragment thereof of claim **35**, wherein the contacting inhibits the growth or proliferation of the cancer cells.

49. The method of claim **48**, wherein the cancer cell is a CD123-expressing cancer cell.

50. A kit comprising a bispecific antibody or antigen-binding fragment thereof of claim **35** and packaging for the same.

51. A method of producing a bispecific antibody or antigen-binding fragment thereof comprising culturing the host cell of claim **44** to produce the bispecific antibody or antigen-binding fragment thereof, and recovering the bispecific antibody or antigen-binding fragment thereof from the cell or culture.

* * * * *