

T-CELL RECEPTOR (TCR)-BINDING ANTIBODIES AND USES THEREOF

This application claims the benefit of U.S. Provisional Patent Application No. 62/218,990, filed September 15, 2015, the entirety of which is incorporated herein by reference.

INCORPORATION OF SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on September 15, 2016, is named 0100-0021WO1_SL.txt and is 15 kb in size.

BACKGROUND OF THE INVENTION

Field of the Invention

[0001] The present invention relates generally to the field of molecular biology and immunology. More particularly, it concerns monoclonal recombinant antibodies that bind $\alpha\beta$ -TCR (T-cell receptors) and the use of such antibodies in the manipulation of $\alpha\beta$ -TCR⁺ T-cells inside and outside the body.

Description of Related Art

[0002] T-cell based therapies are currently being explored for treatment of a wide range of diseases. However, one of the major hurdles in any T-cell-based therapy is efficient selection (isolation) and numeric expansion of T-cells for use in the therapy. Furthermore, T cells can be altered inside the body for activation and immune suppression. Thus, there remains a need for new methods and compositions that can be used for manipulation of T-cells *in vivo* and *ex vivo*.

SUMMARY

[0003] The disclosure provides an isolated antibody or antigen-binding fragment thereof that specifically binds to an epitope of T-cell receptor alpha (TCR α) polypeptide comprising sequence GSTLRG (SEQ ID NO:1).

[0003a] In one aspect, the present disclosure refers to an isolated antibody or antigen-binding fragment thereof that specifically binds to an epitope of T-cell receptor alpha (TCR α) polypeptide, wherein the antibody or antigen-binding fragment thereof comprises a set of

complementarity determining regions (CDRs) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein (a) HCDR1 has the amino acid sequence of SEQ ID NO: 2; or SEQ ID NO: 15; (b) HCDR2 has the amino acid sequence of SEQ ID NO: 3; or SEQ ID NO: 16; (c) HCDR3 has the amino acid sequence of SEQ ID NO: 21; SEQ ID NO: 23; SEQ ID NO: 22 or SEQ ID NO: 17 (d) LCDR1 has the amino acid sequence of SEQ ID NO: 4; or SEQ ID NO: 9; (e) LCDR2 has the amino acid sequence of SEQ ID NO: 5; and (f) LCDR3 has the amino acid sequence of SEQ ID NO: 6; or SEQ ID NO: 10.

[0003b] In another aspect, the present disclosure refers to an isolated polynucleotide comprising a sequence encoding the antibody or antigen binding fragment thereof according to the present disclosure.

[0003c] In another aspect, the present disclosure refers to a method for selecting a cell comprising a T-cell Receptor α chain (TCR α) comprising: (i) contacting the cell with an antibody or antigen-binding fragment thereof that specifically binds to an epitope of T-cell receptor alpha (TCR α) polypeptide; wherein the antibody or antigen-binding fragment thereof comprises a set of complementarity determining regions (CDRs) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein (a) HCDR1 has the amino acid sequence of SEQ ID NO: 2; or SEQ ID NO: 15; (b) HCDR2 has the amino acid sequence of SEQ ID NO: 3; or SEQ ID NO: 16; (c) HCDR3 has the amino acid sequence of SEQ ID NO: 21; SEQ ID NO: 23; SEQ ID NO: 22 or SEQ ID NO: 17; (d) LCDR1 has the amino acid sequence of SEQ ID NO: 4; or SEQ ID NO: 9; (e) LCDR2 has the amino acid sequence of SEQ ID NO: 5; and (f) LCDR3 has the amino acid sequence of SEQ ID NO: 6; or SEQ ID NO: 10; and (ii) selecting a cell comprising the TCR α chain.

[0003d] In yet another aspect, the present disclosure refers to a method for expanding and/or activating T-cells comprising contacting the T-cells with artificial antigen presenting cells (aAPCs) in the presence of an antibody or antigen-binding fragment thereof that binds to an epitope of T-cell Receptor (TCR), wherein the antibody or antigen-binding fragment thereof comprises a set of complementarity determining regions (CDRs) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein (a) HCDR1 has the amino acid sequence of SEQ ID NO: 2; or SEQ ID NO: 15; (b) HCDR2 has the amino acid sequence of SEQ ID NO: 3; or SEQ ID NO: 16; (c) HCDR3 has the amino acid sequence of SEQ ID NO: 21; SEQ ID NO: 23; SEQ ID NO: 22 or SEQ ID NO: 17; (d) LCDR1 has the amino acid sequence of SEQ

ID NO: 4; or SEQ ID NO: 9; (e) LCDR2 has the amino acid sequence of SEQ ID NO: 5; and (f) LCDR3 has the amino acid sequence of SEQ ID NO: 6; or SEQ ID NO: 10.

[0003e] In yet another aspect, the present disclosure refers to a use of an antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating an autoimmune disease or a T cell leukemia in a subject in need of treatment, wherein the antibody or antigen-binding fragment thereof comprises a set of complementarity determining regions (CDRs) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein (a) HCDR1 has the amino acid sequence of SEQ ID NO: 2; or SEQ ID NO: 15; (b) HCDR2 has the amino acid sequence of SEQ ID NO: 3; or SEQ ID NO: 16; (c) HCDR3 has the amino acid sequence of SEQ ID NO:21; SEQ ID NO:23; SEQ ID NO:22 or SEQ ID NO: 17; (d) LCDR1 has the amino acid sequence of SEQ ID NO: 4; or SEQ ID NO: 9; (e) LCDR2 has the amino acid sequence of SEQ ID NO: 5; and (f) LCDR3 has the amino acid sequence of SEQ ID NO: 6; or SEQ ID NO: 10.

[0003f] In yet another aspect, the present disclosure refers to an isolated host cell comprising one or more polynucleotide molecule(s) encoding an antibody or antigen-binding fragment thereof as disclosed herein.

[0004] In examples, the antibody or antigen binding fragment thereof specifically binds to an epitope of T-cell receptor alpha (TCR α) polypeptide comprising the sequence GSTLRG (SEQ ID NO:1) with an affinity characterized by a dissociation constant (K_D) no

greater than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 8.4×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M. In examples, the K_D is about 5×10^{-9} M to about 6×10^{-9} M. In further examples, the K_D is about 1×10^{-9} M to about 2×10^{-9} M.

[0005] In further examples, the disclosure relates to an antibody or antigen-binding fragment thereof that specifically binds to TCR α polypeptide, comprising (a) HCDR1 at least 80%, 85%, 90% or 95% identical to SEQ ID NO: 2; (b) HCDR2 at least 80%, 85%, 90% or 95% identical to SEQ ID NO: 3; (c) HCDR3 identical to CDYW (SEQ ID NO:21); CAYW (SEQ ID NO:23); or CAYL (SEQ ID NO:22); (d) LCDR1 at least 80%, 85%, 90% or 95% identical to SEQ ID NO: 4 or SEQ ID NO: 9; (e) LCDR2 at least 80%, 85%, 90% or 95% identical to SEQ ID NO: 5; and (f) LCDR3 at least 80%, 85%, 90% or 95% identical to SEQ ID NO: 6 or SEQ ID NO: 10.

[0006] The disclosure further provides an antibody or antigen-binding fragment thereof that specifically binds to TCR α polypeptide comprising (a) HCDR1 at least 80%, 85%, 90% or 95% identical to V_H CDR1 of 79A-15 SEQ ID NO: 2; (b) HCDR2 at least 80%, 85%, 90% or 95% identical to V_H CDR2 of 79A-15 SEQ ID NO: 3; (c) HCDR3 at least 80%, 85%, 90% or 95% identical to V_H CDR3 of 79A-15 (SEQ ID NO:22); (d) LCDR1 at least 80%, 85%, 90% or 95% identical to V_L CDR1 of 79A-15 SEQ ID NO: 9; (e) LCDR2 at least 80%, 85%, 90% or 95% identical to V_L CDR2 of 79A-15 SEQ ID NO: 5; and (f) LCDR3 at least 80%, 85%, 90% or 95% identical to V_L CDR3 of 79A-15 SEQ ID NO: 10.

[0007] In further examples, the disclosure provides an isolated antibody or antigen binding fragment thereof that specifically binds to TCR α polypeptide, comprising (a) HCDR1 at least 80%, 85%, 90% or 95% identical to V_H CDR1 of 79A-13 KASGYTFTDYIMNWV (SEQ ID NO: 2); (b) HCDR2 at least 80%, 85%, 90% or 95% identical to V_H CDR2 of 79A-13 WIGEINPNN (SEQ ID NO: 3); (c) HCDR3 at least 80%, 85%, 90% or 95% identical to V_H CDR3 of 79A-13 CAYL (SEQ ID NO:22); (d) LCDR1 at least 80%, 85%, 90% or 95% identical to V_L CDR1 of 79A-13 NTYLEWY (SEQ ID NO: 4); (e) LCDR2 at least 80%, 85%, 90% or 95% identical to V_L CDR2 of 79A-13 KLLIYKVSNRFS (SEQ ID NO: 5); and (f) LCDR3 at least 80%, 85%, 90% or 95% identical to V_L CDR3 of 79A-13 MQGSHVPW (SEQ ID NO: 10).

[0008] In examples, the disclosure further relates to an antibody or antigen-binding fragment thereof that specifically binds to TCR α polypeptide, comprising (a) HCDR1 at least 80%, 85%, 90% or 95% identical to V_H CDR1 of 79A-11 KASGYTFTDYIMNWV (SEQ ID NO: 2); (b) HCDR2 at least 80%, 85%, 90% or 95% identical to V_H CDR2 of 79A-11 WIGEINPNN (SEQ ID NO: 3); (c) HCDR3 at least 80%, 85%, 90% or 95% identical to V_H CDR3 of 79A-11 CAYW (SEQ ID NO:23); (d) LCDR1 at least 80%, 85%, 90% or 95% identical to V_L CDR1 of 79A-11 NTYLEWF (SEQ ID NO: 9); (e) LCDR2 at least 80%, 85%, 90% or 95% identical to V_L CDR2 of 79A-11 KLLIYKVSNRFS (SEQ ID NO: 5); and (f) LCDR3 at least 80%, 85%, 90% or 95% identical to V_L CDR3 of 79A-11 MQGSHVPW (SEQ ID NO: 10).

[0009] The disclosure also provides an isolated antibody or antigen binding fragment thereof that specifically binds to TCR α polypeptide, comprising (a) HCDR1 at least 80%, 85%, 90% or 95% identical to V_H CDR1 of 79A KASGYTFTDYIMNWV (SEQ ID NO: 2); (b) HCDR2 at least 80%, 85%, 90% or 95% identical to V_H CDR2 of 79A WIGEINPNN (SEQ ID NO: 3); (c) HCDR3 at least 80%, 85%, 90% or 95% identical to V_H CDR3 of 79A CDYW (SEQ ID NO:21); (d) LCDR1 at least 80%, 85%, 90% or 95% identical to V_L CDR1 of 79A NTYLEWY (SEQ ID NO: 4); (e) LCDR2 at least 80%, 85%, 90% or 95% identical to V_L CDR2 of 79A KLLIYKVSNRFS (SEQ ID NO: 5); and (f) LCDR3 at least 80%, 85%, 90% or 95% identical to V_L CDR3 of 79A FQGSHVPW (SEQ ID NO: 6).

[0010] In examples, the disclosure provides an isolated antibody or antigen binding fragment thereof that specifically binds to TCR α polypeptide, comprising (a) HCDR1 at least 80%, 85%, 90% or 95% identical to KASGYTFTGYIMNWV (SEQ ID NO:15); (b) HCDR2 at least 80%, 85%, 90% or 95% identical to WIGGINPNN (SEQ ID NO:16); (c) HCDR3 identical to CRYW (SEQ ID NO:17); (d) LCDR1 at least 80%, 85%, 90% or 95% identical to QSIVHGGGNTY (SEQ ID NO:18); (e) LCDR2 at least 80%, 85%, 90% or 95% identical to KLLIYKVSNRFS (SEQ ID NO: 5); and (f) LCDR3 at least 80%, 85%, 90% or 95% identical to FQGSHVPW (SEQ ID NO: 6).

[0011] In additional examples, the disclosure further provides an isolated polynucleotide comprising a nucleic acid encoding an antibody or antigen binding fragment thereof that specifically binds to a T-cell Receptor α chain (TCR α), said antibody binding to an epitope of TCR α polypeptide comprising the sequence GSTLRG (SEQ ID NO: 1).

[0012] In further examples, the disclosure provides a vector comprising the polynucleotides encoding an antibody or antigen binding fragment thereof that specifically binds to a T-cell Receptor α chain (TCR α), said antibody binding to an epitope of TCR α polypeptide comprising the sequence GSTLRG (SEQ ID NO: 1).

[0013] In still further examples, the disclosure provides a method of manufacturing an antibody or antigen binding fragment thereof comprising: (a) expressing one or more polynucleotide molecule(s) encoding a V_L and V_H chain of an antibody in a cell; and (b) purifying the antibody from the cell, wherein the antibody specifically binds to a T-cell Receptor α chain (TCR α).

[0014] The disclosure further provides a method for selecting a cell comprising a T-cell Receptor α chain (TCR α) comprising: (a) contacting the cell with an antibody or antigen fragment thereof that binds to a TCR α chain, wherein the antibody or fragment binds to T-cells having a plurality of T-cell epitope specificities; and (b) selecting a cell comprising the TCR α chain based on binding of the antibody or fragment.

[0015] In additional examples, the disclosure provides a method for expanding and/or activating T-cells comprising contacting the T-cells with artificial antigen presenting cells (aAPCs) in the presence of an antibody or antigen binding fragment thereof that binds to an epitope of a T-cell Receptor (TCR), wherein said epitope is a polypeptide comprising sequence GSTLRG (SEQ ID NO:1).

[0016] In certain examples, the disclosure provides a method of treating an autoimmune disease or a T cell leukemia in an animal in need of treatment, comprising administering to said animal a host cell comprising a chimeric antigen receptor targeting TCR α polypeptide comprising sequence GSTLRG (SEQ ID NO:1).

[0017] In further examples, the disclosure provides a host cell comprising one or more polynucleotide molecules encoding an antibody or antigen binding fragment thereof that binds to a TCR α chain comprising GSTLRG (SEQ ID NO:1), wherein the antibody or antigen binding fragment thereof selectively binds to T-cells having a plurality of T-cell epitope specificities.

[0018] A further example provides a kit comprising an antibody of the present examples or a host cell comprising one or more polynucleotide molecule(s) encoding an

antibody that binds to a T-Cell Receptor (TCR) wherein the antibody binds to T-cells having a plurality of T-cell epitope specificities and at least a first agent for increasing proliferation of mammalian T-cells. In certain examples, kit additionally comprises an APC.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] The following drawings form part of the present specification and are included to further demonstrate certain aspects of the present invention. The invention may be better understood by reference to one or more of these drawings in combination with the detailed description of specific embodiments presented herein.

[0020] FIGS. 1A-1E(i), 1E(ii). **A)** Binding specificity of monoclonal antibody (Clone 79A). ELISA performed on solid phase coated with linear TCR-invariant chain specific synthetic peptides. Antibody dose curve were run with a concentration range from 1000ng/mL to 7.5ng/mL. Controls include non-specific peptides, secondary antibody control and buffer control in the assay. Assay plate was read at OD450 by VictorTM plate reader. Samples were run in duplicate. **B)** Ala-Scan library confirmed linear epitope specificity of mAb 79A on lyophilized peptides (MimotopeTM Ala-scan peptide library) coated onto solid phase ELISA. Graph shows highest binding intensity of 79A mAb upon substitution with selected AA with Alanine. **C)** Moderate binding of 79A to specific peptides as shown in figure substituted with alanine. **D)** GSTLGR (SEQ ID NO:1) represents junction of TCR Va24 and Ja18 where 79A binding focuses as substitution of these AA by alanine completely abrogates binding. **E(i) and E(ii))** 79A lacks conformational fit to TCR-CDR3 invariant chain. Flow cytometry assay shows that 79A fails to bind either purified iNKT cell (in image) or regular $\alpha\beta^+$ -T cells (shown later) where as iNKT-specific mAb 6B11 detects conformational epitopes on iNKT cells.

[0021] FIG. 2. V-gene amplification of mAb clone 79A. Agarose gel image showing amplification of VH and VL chain of hybridoma clone A79. VH chain (400~bp) shown in image after amplification using a mixture of mouse heavy chain constant region primes (MH-IgG₁) along with mouse heavy chain FR1 region primers (contains a mixture of high and low degeneracy), and VL chain (370~ bp) after amplification using mixture of mouse kappa chain universal degeneracy primers and kappa-chain constant primers. All 5' primer designed both for VL and VH starting at first nucleotide of FR1.

WHAT IS CLAIMED IS:

1. An isolated antibody or antigen-binding fragment thereof that specifically binds to an epitope of T-cell receptor alpha (TCR α) polypeptide, wherein the antibody or antigen-binding fragment thereof comprises a set of complementarity determining regions (CDRs) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein
 - (a) HCDR1 has the amino acid sequence of SEQ ID NO: 2; or SEQ ID NO: 15;
 - (b) HCDR2 has the amino acid sequence of SEQ ID NO: 3; or SEQ ID NO: 16;
 - (c) HCDR3 has the amino acid sequence of SEQ ID NO: 21; SEQ ID NO: 23; SEQ ID NO: 22 or SEQ ID NO: 17
 - (d) LCDR1 has the amino acid sequence of SEQ ID NO: 4; or SEQ ID NO: 9;
 - (e) LCDR2 has the amino acid sequence of SEQ ID NO: 5; and
 - (f) LCDR3 has the amino acid sequence of SEQ ID NO: 6; or SEQ ID NO: 10.
2. The antibody or antigen-binding fragment thereof according to claim 1, wherein the antibody or antigen-binding fragment thereof is human or humanized.
3. The antibody or antigen-binding fragment thereof according to claim 1, wherein the antigen-binding fragment thereof is a Fab, Fab', F(ab')₂, scFv, or disulfide-linked Fv (sdFv).
4. The antibody or antigen-binding fragment thereof according to claim 1, wherein the antibody is an IgG, IgM or IgA antibody.
5. The antibody or antigen-binding fragment thereof according to claim 1, wherein the antibody or antigen-binding fragment thereof is membrane bound.
6. The antibody or antigen-binding fragment thereof according to claim 1, wherein the antibody or antigen-binding fragment thereof is conjugated to a reporter gene.
7. The antibody or antigen-binding fragment thereof according to claim 1, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) having the amino acid sequence of SEQ ID NO:11, and a light chain variable region (VL) having the amino acid sequence of SEQ ID NO:12.

8. The antibody or antigen-binding fragment thereof according to claim 1, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) having the amino acid sequence of SEQ ID NO:11, and a light chain variable region (VL) having the amino acid sequence of SEQ ID NO:14.
9. The antibody or antigen-binding fragment thereof according to claim 1, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) having the amino acid sequence of SEQ ID NO: 13, and a light chain variable region (VL) having the amino acid sequence of SEQ ID NO: 12.
10. The antibody or antigen-binding fragment thereof according to claim 1, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) having the amino acid sequence of SEQ ID NO:19, and a light chain variable region (VL) having the amino acid sequence of SEQ ID NO:20.
11. An isolated polynucleotide comprising a sequence encoding the antibody or antigen-binding fragment thereof according to any one of claims 7-10.
12. A method for selecting a cell comprising a T-cell Receptor α chain (TCR α) comprising:
 - (i) contacting the cell with an antibody or antigen-binding fragment thereof that specifically binds to an epitope of T-cell receptor alpha (TCR α) polypeptide; wherein the antibody or antigen-binding fragment thereof comprises a set of complementarity determining regions (CDRs) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein
 - (a) HCDR1 has the amino acid sequence of SEQ ID NO: 2; or SEQ ID NO: 15;
 - (b) HCDR2 has the amino acid sequence of SEQ ID NO: 3; or SEQ ID NO: 16;
 - (c) HCDR3 has the amino acid sequence of SEQ ID NO:21; SEQ ID NO:23; SEQ ID NO:22 or SEQ ID NO: 17;
 - (d) LCDR1 has the amino acid sequence of SEQ ID NO: 4; or SEQ ID NO: 9;

- (e) LCDR2 has the amino acid sequence of SEQ ID NO: 5; and
 - (f) LCDR3 has the amino acid sequence of SEQ ID NO: 6; or SEQ ID NO: 10; and
 - (ii) selecting a cell comprising the TCR α chain.
13. The method of claim 12, wherein the antibody or antigen-binding fragment thereof is conjugated to a reporter gene.
14. A method for expanding and/or activating T-cells comprising contacting the T-cells with artificial antigen presenting cells (aAPCs) in the presence of an antibody or antigen-binding fragment thereof that binds to an epitope of T-cell Receptor (TCR), wherein the antibody or antigen-binding fragment thereof comprises a set of complementarity determining regions (CDRs) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein
- (a) HCDR1 has the amino acid sequence of SEQ ID NO: 2; or SEQ ID NO: 15;
 - (b) HCDR2 has the amino acid sequence of SEQ ID NO: 3; or SEQ ID NO: 16;
 - (c) HCDR3 has the amino acid sequence of SEQ ID NO: 21; SEQ ID NO:23; SEQ ID NO:22 or SEQ ID NO: 17;
 - (d) LCDR1 has the amino acid sequence of SEQ ID NO: 4; or SEQ ID NO: 9;
 - (e) LCDR2 has the amino acid sequence of SEQ ID NO: 5; and
 - (f) LCDR3 has the amino acid sequence of SEQ ID NO: 6; or SEQ ID NO: 10.
15. The method of claim 14, wherein the antibody or antigen-binding fragment thereof further comprises a transmembrane domain.
16. Use of an antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating an autoimmune disease or a T cell leukemia in a subject in need of treatment, wherein the antibody or antigen-binding fragment thereof comprises a set of complementarity determining regions (CDRs) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein
- (a) HCDR1 has the amino acid sequence of SEQ ID NO: 2; or SEQ ID NO: 15;
 - (b) HCDR2 has the amino acid sequence of SEQ ID NO: 3; or SEQ ID NO: 16;
 - (c) HCDR3 has the amino acid sequence of SEQ ID NO:21; SEQ ID NO:23; SEQ ID NO:22 or SEQ ID NO: 17;

- (d) LCDR1 has the amino acid sequence of SEQ ID NO: 4; or SEQ ID NO: 9;
 - (e) LCDR2 has the amino acid sequence of SEQ ID NO: 5; and
 - (f) LCDR3 has the amino acid sequence of SEQ ID NO: 6; or SEQ ID NO: 10.
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- 17. An isolated host cell comprising one or more polynucleotide molecule(s) encoding an antibody or antigen-binding fragment thereof of claim 1.
 - 18. The antibody or antigen-binding fragment thereof according to claim 1, wherein the epitope of T-cell receptor alpha (TCR α) polypeptide comprises GSTLRG (SEQ ID NO: 1).
 - 19. The method of claim 12, wherein the epitope of T-cell receptor alpha (TCR α) polypeptide comprises GSTLRG (SEQ ID NO: 1).
 - 20. The method of claim 14, wherein the epitope of T-cell receptor alpha (TCR α) polypeptide comprises GSTLRG (SEQ ID NO: 1).