

Several ongoing clinical trials rely on the generation of cytotoxic T lymphocyte (CTL) responses upon vaccination with WT1 peptides. However, despite the recognition that WT1 is useful for immunotherapy, a small number of WT1 epitopes, which are restricted to a limited number of HLA alleles, are presently used for vaccination purposes (Di Stasi, A. et al. Front. Immunol. (2015)). One such epitope is the WT1 126-134 epitope (RMFPNAPYL; SEQ ID NO: 255), which is presented by MHC encoded by the HLA-A*0201 allele (i.e. the epitope is HLA-A*0201 restricted).

HLA-A*0201 restricted epitopes and corresponding TCRs are of interest since major histocompatibility complex (MHC) having the HLA-A*0201 haplotype are expressed in the vast majority (60%) of the Caucasian population. Accordingly, TCRs that target HLA-A*0201-restricted WT1 epitopes are particularly advantageous since an immunotherapy making use of such TCRs may be widely applied.

The WT1 126-134 epitope has been widely studied in several trials, alone or in combination with additional tumor antigens. However, recent reports have highlighted a major concern regarding the processing of this particular epitope, which may impair its use for immunotherapy purposes. Notably, the WT1 126-134 epitope is more efficiently processed by the immunoproteasome compared with standard proteasomes (Jaigirdar, A. et al. J Immunother. 39(3):105-16 (2016)), which leads to poor recognition of many HLA-A*0201 tumour cell lines or primary leukemia cells that endogenously express WT1.

Thus, there remains a need for new WT1 epitopes, particularly those presented by MHC with prevalent HLA haplotypes (e.g. HLA-A*0201).

One naturally processed HLA-A*0201 restricted epitope that has been identified is WT1 37-45, which has the amino acid sequence VLDFAPPGA (SEQ ID NO: 157, see e.g. Smithgall et al 2001; Blood 98 (11 Part 1): 121a). However, few TCR amino acid sequences, particularly CDR sequences, specific for this peptide sequence have been reported (Schmitt, T.M. et al. (2017) Nat Biotechnol 35: 1188-1195).

Accordingly, there remains a need for new WT1 epitopes, particularly those restricted to common HLA alleles and a need for new TCRs capable of binding to WT1 epitopes.

SUMMARY

We have identified novel TCRs that bind to WT1 peptides when presented by an MHC. Further, we have determined the amino acid sequences of the TCRs, including the amino acid sequences of their CDR regions, which are responsible for binding specificity for WT1. Moreover, we have demonstrated that T-cells expressing TCRs according to the present

invention specifically target and kill cells that overexpress the WT1 protein. In addition, it has been shown that the TCRs of the present invention are restricted to MHC encoded by HLA class 1 and 2 alleles common in the Caucasian population, such as HLA-A*0201 and HLA-B*3501 or HLA-B*3502.

5 Accordingly, in a first aspect, the present disclosure provides a T-cell receptor (TCR), which binds to a Wilms tumour 1 protein (WT1) peptide when presented by a major histocompatibility complex (MHC), wherein the TCR:

10 (i) comprises a CDR3 α comprising the amino acid sequence of CGTAWINDYKLSF (SEQ ID NO: 3) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASRKTGGYSNQPQHF (SEQ ID NO: 8) or a variant thereof having up to three amino acid substitutions, additions or deletions;

15 (ii) comprises a CDR3 α comprising the amino acid sequence of CVVNLLSNQGGKLIF (SEQ ID NO: 36) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSQDYLVSNKLFF (SEQ ID NO: 41) or a variant thereof having up to three amino acid substitutions, additions or deletions;

20 (iii) comprises a CDR3 α comprising the amino acid sequence of CAVRLSGSARQLTF (SEQ ID NO: 14) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSLLGDEQYF (SEQ ID NO: 24) or a variant thereof having up to three amino acid substitutions, additions or deletions;

25 (iv) comprises a CDR3 α comprising the amino acid sequence of CAVRLSGSARQLTF (SEQ ID NO: 14) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSLVALQGAGEQYF (SEQ ID NO: 30) or a variant thereof having up to three amino acid substitutions, additions or deletions;

30 (v) comprises a CDR3 α comprising the amino acid sequence of CAYRSLKYGNKLVF (SEQ ID NO: 19) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSLLGDEQYF (SEQ ID NO: 24) or a variant thereof having up to three amino acid substitutions, additions or deletions;

acid sequence of CASSLGLSISQETQYF (SEQ ID NO: 288) or a variant thereof having up to three amino acid substitutions, additions or deletions;

5 (xxxix) comprises a CDR3 α comprising the amino acid sequence of CAVRTSYDKVIF (SEQ ID NO: 113) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSLGLSISQETQYF (SEQ ID NO: 288) or a variant thereof having up to three amino acid substitutions, additions or deletions;

10 (xxxx) comprises a CDR3 α comprising the amino acid sequence of CAERLNTDKLIF (SEQ ID NO: 103) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSARDVLTGDYGYTF (SEQ ID NO: 282) or a variant thereof having up to three amino acid substitutions, additions or deletions;

15 (xxxxi) comprises a CDR3 α comprising the amino acid sequence of CAVEATDSWGKLQF (SEQ ID NO: 108) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSARDVLTGDYGYTF (SEQ ID NO: 282) or a variant thereof having up to three amino acid substitutions, additions or deletions; or

20 (xxxixii) comprises a CDR3 α comprising the amino acid sequence of CAVRTSYDKVIF (SEQ ID NO: 113) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSARDVLTGDYGYTF (SEQ ID NO: 282) or a variant thereof having up to three amino acid substitutions, additions or deletions.

25 In another aspect, the present disclosure refers to a T-cell receptor (TCR), which binds to a Wilms tumour 1 protein (WT1) peptide when presented by a major histocompatibility complex (MHC), wherein the WT1 peptide comprises an amino acid sequence selected from the group consisting of EPASQHTLRSG (SEQ ID NO: 123), YESDNHTTPIL (SEQ ID NO: 126), NHTTPILCGAQYRIH (SEQ ID NO: 127), QCLSAFTVHFSGQFT (SEQ ID NO: 118), EDPMGQQGSLGEQQY (SEQ ID NO: 119), SQLECMTWNQMNLGA (SEQ ID NO: 120), APVLDFAPPGA (SEQ ID NO: 117), NQMNLGATLKG (SEQ ID NO: 250),
30 DPGGIWAKLGAAEAS (SEQ ID NO: 251), NHTTPILCGAQYRIH (SEQ ID NO: 252), KRHRQRRTGVKPFQC (SEQ ID NO: 253) PSCQKKFARSDLVLR (SEQ ID NO: 254) and variants thereof each having up to three amino acid substitutions, additions or deletions

In another aspect, the present disclosure refers to a TCR according to: a. (i), (ii), (xv), (xvi), (xxix), (xxx)-(xxxiii), (xxxv) or (xxxx) of any one of claims 1-4, which is restricted to HLA-A*0201; b. (vii) of any one of claims 1-4, which is restricted to HLA-B*3502; or c. any of (xiii)-(xiv) of any one of claims 1-4, which is restricted to HLA-B*3501

- 5 In yet another aspect, the present disclosure refers to an isolated polynucleotide encoding the α chain of a T-cell receptor (TCR) of the present disclosure, and/or the β chain of a TCR of the present disclosure.

In yet another aspect, the present disclosure refers to a vector comprising a polynucleotide as disclosed herein.

- 10 In a further aspect, the present disclosure refers to a cell comprising a TCR as disclosed herein, a polynucleotide as disclosed herein, or a vector as disclosed herein, optionally wherein the cell further comprises a vector which encodes one or more CD3 chains, CD8, a suicide gene and/or a selectable marker.

- In still another aspect, the present disclosure refers to a method of preparing a cell, which
15 comprises the step of introducing a vector as disclosed herein into a cell *in vitro*, *ex vivo* or *in vivo*, e.g. by transfection or transduction.

- In yet another aspect, the present disclosure refers to a chimeric molecule comprising a TCR of the present disclosure, or a portion thereof, conjugated to a non-cellular substrate, a toxin and/or an antibody, optionally wherein the non-cellular substrate is selected from the group
20 consisting of nanoparticles, exosomes and other non-cellular substrates.

- In yet another aspect, the present disclosure refers to the use of the TCR as disclosed herein, an isolated polynucleotide as disclosed herein, a vector as disclosed herein, a cell as disclosed herein, a cell prepared by the method as disclosed herein, or a chimeric molecule according to claim in the manufacture of a medicament for treating and/or preventing a
25 disease associated with expression of WT1, optionally wherein the disease associated with expression of WT1 is a proliferative disorder, preferably wherein the proliferative disorder is a hematological malignancy or a solid tumor, preferably wherein the hematological malignancy is selected from the group consisting of acute myeloid leukemia (AML), chronic myeloid leukemia (CML), lymphoblastic leukemia, myelodysplastic syndromes, lymphoma,
30 multiple myeloma, non Hodgkin lymphoma, and Hodgkin lymphoma; or preferably wherein the solid tumor is selected from the group consisting of lung cancer, breast cancer, oesophageal cancer, gastric cancer, colon cancer, cholangiocarcinoma, pancreatic cancer, ovarian cancer, head and neck cancers, synovial sarcoma, angiosarcoma, osteosarcoma,

thyroid cancer, endometrial cancer, neuroblastoma, rhabdomyosarcoma, liver cancer, melanoma, prostate cancer, renal cancer, soft tissue sarcoma, urothelial cancer, biliary cancer, glioblastoma, mesothelioma, cervical cancer, and colorectal cancer.

5 In yet another example, the present disclosure refers to the use of a TCR as disclosed herein, an isolated polynucleotide as disclosed herein, a vector as disclosed herein, a cell as disclosed herein, a cell prepared by the method as disclosed herein, or a chimeric molecule as disclosed herein in the manufacture of a medicament for treating and/or preventing a disease associated with expression of WT1 in a subject in need thereof, wherein the use comprises that the medicament is to be administered to the subject.

10 In yet another example, the present disclosure refers to an isolated immunogenic WT1 peptide comprising an amino acid sequence selected from the group consisting of EPASQHTLRSG (SEQ ID NO: 123) YESDNHTTPIL (SEQ ID NO: 126), NHTTPILCGAQYRIH (SEQ ID NO: 127), QCLSAFTVHFSGQFT (SEQ ID NO: 118), EDPMGQQGSLGEQQY (SEQ ID NO: 119), SQLECMTWNQMNLGA (SEQ ID NO: 120),
15 APVLDFAPPGA (SEQ ID NO: 117), NQMNLGATLKG (SEQ ID NO: 250), DPGGIWAKLGAAEAS (SEQ ID NO: 251), NHTTPILCGAQYRIH (SEQ ID NO: 252), KRHQRRHTGVKPFQC (SEQ ID NO: 253), PSCQKKFARSDLVLR (SEQ ID NO: 254) and variants thereof each having up to three amino acid substitutions, additions or deletions.

20 In one example, the present disclosure provides a TCR of the present disclosure comprising the following CDR sequences:

(i) CDR1 α - KALYS (SEQ ID NO: 1),
CDR2 α - LLKGGEQ (SEQ ID NO: 2),
CDR3 α - CGTAWINDYKLSF (SEQ ID NO: 3),
CDR1 β - SGHDY (SEQ ID NO: 6),
25 CDR2 β - FNNNVP (SEQ ID NO: 7), and
CDR3 β - CASRKTGGYSNQPQHF (SEQ ID NO: 8),
or variants thereof each having up to three amino acid substitutions, additions or deletions;

- (xxxxi) CDR1 α - DSVNN (SEQ ID NO: 106),
 CDR2 α – IPSGT (SEQ ID NO: 107),
 CDR3 α - CAVEATDSWGKLQF (SEQ ID NO: 108),
 CDR1 β – DFQATT (SEQ ID NO: 280),
 5 CDR2 β – SNEGSKA (SEQ ID NO: 281), and
 CDR3 β – CSARDVLTGDYGYTF (SEQ ID NO: 282),
 or variants thereof each having up to three amino acid substitutions, additions or
 deletions; or
- (xxxxii) CDR1 α - DSASNY (SEQ ID NO: 111),
 10 CDR2 α – IRSNVGE (SEQ ID NO: 112),
 CDR3 α - CAVRTSYDKVIF (SEQ ID NO: 113),
 CDR1 β – DFQATT (SEQ ID NO: 280),
 CDR2 β – SNEGSKA (SEQ ID NO: 281), and
 CDR3 β – CSARDVLTGDYGYTF (SEQ ID NO: 282),
 15 or variants thereof each having up to three amino acid substitutions, additions or
 deletions.

In one example, the present disclosure provides a TCR of the present disclosure comprising:

- (i) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 4 or
 a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at
 20 at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at
 least 75%, sequence identity thereto; and a β chain variable domain comprising the
 amino acid sequence of SEQ ID NO: 9 or a variant thereof having at least 75%, at
 least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at
 least 98%, or at least 99%, preferably at least 75%, sequence identity thereto;
- 25 (ii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 37
 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at
 least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at
 least 75%, sequence identity thereto; and a β chain variable domain comprising the
 amino acid sequence of SEQ ID NO: 42 or a variant thereof having at least 75%, at
 30 at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at
 least 98%, or at least 99%, preferably at least 75%, sequence identity thereto;
- (iii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 15
 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at
 least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at

least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto.

In one example, the present disclosure provides a TCR of the present disclosure comprising:

- 5 (i) an α chain comprising the amino acid sequence of SEQ ID NO: 5 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 10, SEQ ID NO: 11 and variants of SEQ ID NOs: 10 and 11 having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto;
- 10 (ii) an α chain comprising the amino acid sequence of SEQ ID NO: 38 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 43, SEQ ID NO: 44 and variants of SEQ ID NOs: 43 and 44 having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto;
- 15 (iii) an α chain comprising the amino acid sequence of SEQ ID NO: 16 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 26, SEQ ID NO: 27 and variants of SEQ ID NOs: 26 and 27 having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto;
- 20 (iv) an α chain comprising the amino acid sequence of SEQ ID NO: 16 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33 and variants of SEQ ID NOs: 32 and 33 having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto;
- 25 (v) an α chain comprising the amino acid sequence of SEQ ID NO: 16 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33 and variants of SEQ ID NOs: 32 and 33 having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto;
- 30 (vi) an α chain comprising the amino acid sequence of SEQ ID NO: 16 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33 and variants of SEQ ID NOs: 32 and 33 having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto;

- sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 290, SEQ ID NO: 291 and variants of SEQ ID NOs: 290 and 291 having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto;
- (xxxx) an α chain comprising the amino acid sequence of SEQ ID NO: 105 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 284, SEQ ID NO: 285 and variants of SEQ ID NOs: 284 and 285 having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto;
- (xxxxi) an α chain comprising the amino acid sequence of SEQ ID NO: 110 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 284, SEQ ID NO: 285 and variants of SEQ ID NOs: 284 and 285 having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; or
- (xxxixii) an α chain comprising the amino acid sequence of SEQ ID NO: 160 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 284, SEQ ID NO: 285 and variants of SEQ ID NOs: 284 and 285 having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto.
- In one example, the present disclosure provides a TCR of the present disclosure comprising an α chain comprising the amino acid sequence of SEQ ID NO: 257 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; and a β chain comprising an amino acid sequence of SEQ ID NO: 259 or a variant thereof

having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto.

In one example, the present disclosure provides a TCR of the present disclosure comprising an α chain comprising the amino acid sequence of SEQ ID NO: 261 or a variant thereof
5 having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto; and a β chain comprising an amino acid sequence of SEQ ID NO: 263 or a variant thereof having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, preferably at least 75%, sequence identity thereto.

10 A TCR of the present disclosure may bind to a WT1 peptide comprising an amino acid sequence selected from the group consisting of EPASQHTLRSG (SEQ ID NO: 123), YESDNHTTPIL (SEQ ID NO: 126), NHTTPILCGAQYRIH (SEQ ID NO: 127), QCLSAFTVHFSGQFT (SEQ ID NO: 118), EDPMGQQGSLGEQQY (SEQ ID NO: 119), SQLECMTWNQMNLGA (SEQ ID NO: 120), APVLDFAPPGA (SEQ ID NO: 117)
15 NQMNLGATLKG (SEQ ID NO: 250), DPGGIWAKLGAAEAS (SEQ ID NO: 251), NHTTPILCGAQYRIH (SEQ ID NO: 252), KRHQRRHTGVKPFQC (SEQ ID NO: 253), PSCQKKFARSDELVR (SEQ ID NO: 254) and variants thereof each having up to three amino acid substitutions, additions or deletions.

In another example, the present disclosure provides a T-cell receptor (TCR), which binds to
20 a Wilms tumour 1 protein (WT1) peptide when presented by a major histocompatibility complex (MHC), wherein the WT1 peptide comprises an amino acid sequence selected from the group consisting of EPASQHTLRSG (SEQ ID NO: 123), YESDNHTTPIL (SEQ ID NO: 126), NHTTPILCGAQYRIH (SEQ ID NO: 127), QCLSAFTVHFSGQFT (SEQ ID NO: 118), EDPMGQQGSLGEQQY (SEQ ID NO: 119), SQLECMTWNQMNLGA (SEQ ID NO: 120), APVLDFAPPGA (SEQ ID NO: 117), NQMNLGATLKG (SEQ ID NO: 250),
25 DPGGIWAKLGAAEAS (SEQ ID NO: 251), NHTTPILCGAQYRIH (SEQ ID NO: 252), KRHQRRHTGVKPFQC (SEQ ID NO: 253), PSCQKKFARSDELVR (SEQ ID NO: 254) and variants thereof each having up to three amino acid substitutions, additions or deletions.

In one example, a TCR of the present disclosure binds to an MHC I and/or MHC II peptide
30 complex.

In one example, a TCR of the present disclosure is restricted to a human leukocyte antigen (HLA) allele. In one example, a TCR of the present disclosure is restricted to a HLA-A or a HLA-B allele. In one example, a TCR of the present disclosure is restricted to a HLA-A allele selected from the group consisting of HLA-A*0201, HLA-A*0101, HLA-A*2402 and HLA-

A*0301 or a HLA-B allele selected from the group consisting of HLA-B*0702, HLA-B*3501 and HLA-B*3502.

In one example, a TCR of the present disclosure is restricted to HLA-A*0201.

In one example, a TCR of the present disclosure is restricted to HLA-B*3502.

- 5 In one example, a TCR of the present disclosure is restricted to HLA-B*3501.

In one example, a TCR of the present disclosure is restricted to a HLA-C allele. In one example, a TCR of the present disclosure is restricted to a HLA-C allele selected from the group consisting of HLA-C*07:01, HLA-C*03:04, HLA-C*04:01, HLA-C*05:01, HLA-C*06:02 and HLA-C*07:02.

- 10 In one example, a TCR of the present disclosure comprises one or more mutations at the α chain/ β chain interface, such that when the α chain and the β chain are expressed in a T-cell, the frequency of mispairing between said chains and endogenous TCR α and β chains is reduced.

- 15 In one example, a TCR of the present disclosure comprises one or more mutations at the α chain/ β chain interface, such that when the α chain and the β chain are expressed in a T-cell, the level of expression of the TCR α and β chains is increased.

In one example, the one or more mutations introduce a cysteine residue into the constant region domain of each of the α chain and the β chain, wherein the cysteine residues are capable of forming a disulphide bond between the α chain and the β chain.

- 20 A TCR of the present disclosure may comprise a murinized constant region.

In one example, the TCR of the disclosure is a soluble TCR.

In another example, the present disclosure provides an isolated polynucleotide encoding the α chain of a T-cell receptor (TCR) of the present disclosure, and/or the β chain of a TCR of the present disclosure.

- 25 In another example, the present disclosure provides an isolated polynucleotide comprising a nucleotide sequence of SEQ ID NO: 256 and/or a nucleotide sequence of SEQ ID NO: 258, or variants thereof having at least 40%, at least 50%, at least 60%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity thereto.

In another example, the present disclosure provides an isolated polynucleotide comprising a nucleotide sequence of SEQ ID NO: 260 and/or a nucleotide sequence of SEQ ID NO: 262, or variants thereof having at least 40%, at least 50%, at least 60%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity thereto.

In one example, the isolated polynucleotide encodes the α chain linked to the β chain. In one example, the isolated polynucleotide encodes one or more short interfering RNA (siRNA) sequences and/or one or more other agents capable of reducing or preventing expression of one or more endogenous TCR genes.

In another example, the present disclosure provides a vector comprising a polynucleotide of the present disclosure. In one example, the vector comprises a polynucleotide which encodes one or more CD3 chains, CD8, a suicide gene, and/or a selectable marker.

In another example, the present disclosure provides a cell comprising a TCR of the present disclosure, a polynucleotide of the present disclosure, or a vector of the present disclosure.

In one example, the cell further comprises a vector which encodes one or more CD3 chains, CD8, a suicide gene and/or a selectable marker.

In one example, the cell is a T-cell, a lymphocyte or a stem cell, such as hematopoietic stem cells or induced pluripotent stem cells (iPS). The T-cell, the lymphocyte, or the stem cell may be selected from the group consisting of CD4 cells, CD8 cells, Th0 cells, Tc0 cells, Th1 cells, Tc1 cells, Th2 cells, Tc2 cells, Th17 cells, Th22 cells, gamma/delta T-cells, natural killer (NK) cells, natural killer T (NKT) cells, double negative T-cells, naive T-cells, memory stem T-cells, central memory T-cells, effector memory T-cells, effector T cells, hematopoietic stem cells and pluripotent stem cells.

In one example, the cell is a T-cell which has been isolated from a subject.

In one example, an endogenous gene encoding a TCR α chain and/or an endogenous gene encoding a TCR β chain in the cell is disrupted, preferably such that the endogenous gene encoding a TCR α chain and/or the endogenous gene encoding a TCR β chain is not expressed. In one example, the endogenous gene encoding a TCR α chain and/or the endogenous gene encoding a TCR β chain is disrupted by insertion of an expression cassette comprising a polynucleotide sequence encoding a TCR of the present disclosure. In one example, one or more endogenous genes encoding an MHC in the cell is disrupted, preferably wherein the cell is a non-alloreactive universal T-cell. In one example, an endogenous gene involved in persistence, expansion, activity, resistance to

exhaustion/senescence/inhibitory signals, homing capacity, or other T-cell functions in the cell is disrupted, preferably wherein the endogenous gene involved in persistence, expansion, activity, resistance to exhaustion/senescence/inhibitory signals, homing capacity, or other T-cell functions is selected from the group consisting of *PD1*, *TIM3*, *LAG3*, *2B4*,
5 *KLRG1*, *TGFbR*, *CD160* and *CTLA4*. In one example, the endogenous gene involved in persistence, expansion, activity, resistance to exhaustion/senescence/inhibitory signals, homing capacity, or other T-cell functions is disrupted by integration of an expression cassette, wherein the expression cassette comprises a polynucleotide sequence encoding a TCR of the present disclosure.

10 In another example, the present disclosure provides a method of preparing a cell, which comprises the step of introducing a vector of the disclosure into a cell *in vitro*, *ex vivo* or *in vivo*, for example by transfection or transduction.

In another example, the present disclosure provides a method of preparing a cell, which comprises the step of transducing a cell *in vitro*, *ex vivo* or *in vivo* with one or more vectors
15 of the present disclosure.

In one example, the cell to be transduced with the one or more vectors is selected from the group consisting of T-cells, lymphocytes or stem cells, such as hematopoietic stem cells or induced pluripotent stem cells (iPS), optionally the T-cell, the lymphocyte or the stem cell may be selected from the group consisting of CD4 cells, CD8 cells, Th0 cells, Tc0 cells, Th1
20 cells, Tc1 cells, Th2 cells, Tc2 cells, Th17 cells, Th22 cells, gamma/delta T-cells, natural killer (NK) cells, natural killer T (NKT) cells, double negative T-cells, naive T-cells, memory stem T-cells, central memory T-cells, effector memory T-cells, effector T cells, hematopoeitic stem cells and pluripotent stem cells.

In one example, the method comprises the step of T-cell editing, which comprises disrupting
25 an endogenous gene, for example an endogenous gene encoding a TCR α chain and/or an endogenous gene encoding a TCR β chain with an artificial nuclease, preferably wherein the artificial nuclease is selected from the group consisting of zinc finger nucleases (ZFN), transcription activator-like effector nucleases (TALEN) and CRISPR/Cas system.

In one example, the method comprises the step of T-cell editing, which comprises disrupting
30 an endogenous gene encoding a TCR α chain and/or an endogenous gene encoding a TCR β chain with an artificial nuclease, preferably wherein the artificial nuclease is selected from the group consisting of zinc finger nucleases (ZFN), transcription activator-like effector nucleases (TALEN) and CRISPR/Cas system.

In one example, the method comprises the step of targeted integration of an expression cassette into the endogenous gene encoding the TCR α chain gene and/or the endogenous gene encoding the TCR β chain disrupted by the artificial nuclease, wherein the expression cassette comprises a polynucleotide encoding a TCR of the present disclosure or a polynucleotide sequence of the present disclosure.

In one example, the method comprises the step of disrupting one or more endogenous genes encoding an MHC, preferably wherein the cell prepared by the method is a non-alloreactive universal T-cell.

In one example, the method comprises the step of disrupting one or more endogenous MHC genes, preferably wherein the cell prepared by the method is a non-alloreactive universal T-cell.

In one example, the method comprises the step of disrupting one or more endogenous genes to modify the persistence, expansion, activity, resistance to exhaustion/senescence/inhibitory signals, homing capacity, or other T-cell functions, preferably wherein the method comprises the step of targeted integration of an expression cassette into an endogenous gene involved in persistence, expansion, activity, resistance to exhaustion/senescence/inhibitory signals, homing capacity, or other T-cell functions disrupted by an artificial nuclease, wherein the expression cassette comprises a polynucleotide sequence encoding a TCR of the present disclosure, preferably wherein the endogenous gene is selected from the group consisting of *PD1*, *TIM3*, *LAG3*, *2B4*, *KLRG1*, *TGFbR*, *CD160* and *CTLA4*.

In another example, the present disclosure provides a cell of the present disclosure or a cell prepared by a method of the present disclosure for use in adoptive cell transfer, preferably adoptive T-cell transfer, optionally the adoptive T-cell transfer may be allogenic adoptive T-cell transfer, universal non-alloreactive T-cell transfer, or autologous adoptive T-cell transfer.

In another example, the present disclosure provides a TCR of the present disclosure, an isolated polynucleotide of the present disclosure, a vector of the present disclosure, a cell of the present disclosure, a cell prepared by a method of the present disclosure, or a chimeric molecule of the present disclosure for use in therapy.

In another example, the present disclosure provides a TCR of the present disclosure, an isolated polynucleotide of the present disclosure, a vector of the present disclosure, a cell of the present disclosure, a cell prepared by a method the present disclosure for use in treating and/or preventing a disease associated with expression of WT1.

In another example, the present disclosure provides a T-cell genetically engineered (genetically edited) to modify the persistence, expansion, activity, resistance to exhaustion/senescence/inhibitory signals, homing capacity, or other T cell functions, wherein the T-cell expresses a TCR α chain of the present disclosure and/or a TCR β chain of the present disclosure.

In another example, the present disclosure provides a T cell genetically engineered (genetically edited) by a protocol which comprises the step of targeted integration of an expression cassette into an endogenous gene involved in persistence, expansion, activity, resistance to exhaustion/senescence/inhibitory signals, homing capacity, or other T-cell functions disrupted by an artificial nuclease, wherein the expression cassette comprises a polynucleotide sequence encoding TCR α chain of the present disclosure and/or a TCR β chain of the present disclosure.

In another example, the present disclosure provides a method for treating and/or preventing a disease associated with expression of WT1, which comprises the step of administering a TCR of the present disclosure, an isolated polynucleotide of the present disclosure, a vector of the present disclosure, a cell of the present disclosure, a cell prepared by a method of the present disclosure, or a chimeric molecule of the present disclosure to a subject in need thereof.

The disease associated with expression of WT1 may be a proliferative disorder. Preferably the proliferative disorder may be selected from the group consisting of hematological malignancies, such as acute myeloid leukemia (AML), chronic myeloid leukemia (CML), lymphoblastic leukemia, myelodysplastic syndromes, multiple myeloma, non Hodgkin lymphoma, Hodgkin lymphoma. The proliferative disorder may be selected from the group of solid tumors, such as lung cancer, breast cancer, oesophageal cancer, gastric cancer, colon cancer, cholangiocarcinoma, pancreatic cancer, ovarian cancer, head and neck cancers, synovial sarcoma, angiosarcoma, osteosarcoma, thyroid cancer, endometrial cancer, neuroblastoma, rhabdomyosarcoma, liver cancer, melanoma, prostate cancer, renal cancer, soft tissue sarcoma, urothelial cancer, biliary cancer, glioblastoma, mesothelioma, cervical cancer, and colorectal cancer.

In a preferred example, the disease associated with expression of WT1 is acute myeloid leukemia (AML).

In another preferred example, the disease associated with expression of WT1 is chronic myeloid leukemia (CML).

In another example, the present disclosure provides an isolated immunogenic WT1 peptide comprising an amino acid sequence selected from the group consisting of EPASQHTLRSG (SEQ ID NO: 123), YESDNHTTPIL (SEQ ID NO: 126), NHTTPILCGAQYRIH (SEQ ID NO: 127), QCLSAFTVHFSGQFT (SEQ ID NO: 118), EDPMGQQGSLGEQQY (SEQ ID NO: 119), SQLECMTWNQMNLGA (SEQ ID NO: 120), APVLDFAPPGA (SEQ ID NO: 117), NQMNLGATLKG (SEQ ID NO: 250), DPGGIWAKLGAAEAS (SEQ ID NO: 251), NHTTPILCGAQYRIH (SEQ ID NO: 252), KRHQRRHTGVKPFQC (SEQ ID NO: 253), PSCQKKFARSDLVLR (SEQ ID NO: 254) and variants thereof each having up to three amino acid substitutions, additions or deletions.

10 DESCRIPTION OF THE DRAWINGS

Figure 1. Plots showing the results of *in vitro* expansion of functional WT-1 specific T-cells from peripheral blood of ten healthy donors

Peripheral blood mononuclear cells of ten healthy donors (HD) were stimulated with pooled, overlapping WT1 15-mer peptides for 26-30 hours, enriched for CD137⁺ cells, and expanded for 9-19 days. Expanded T-cells were re-stimulated for 6 hours with autologous antigen presenting cells (APCs) loaded with an unrelated peptide pool or WT1 peptide pool. Additionally, negative (T-cells unstimulated) and positive (T-cells cultured in the presence of PMA and Ionomycin) controls were included in the experimental setting (not shown). Dot plots indicate the results of the intracellular staining for IFN γ production and CD107a exposure on cell surface. After several re-stimulations with autologous APCs loaded with WT1 peptide pool, T-cells specificity was tested by intracellular staining as previously described. Results showed an enrichment of WT1-specific T-cells in the CD8 T cell compartment for HD1 (a), HD3 (c), HD4 (d), HD5 (e), HD6 (f), HD7 (g), and HD10 (j) and in the CD4 T cell compartment for HD2 (b), HD8 (h) and HD9 (i). WT1, Wilms Tumor 1; PMA, Phorbol 12-myristate 13-acetate; IFN γ , interferon- γ ; S, stimulation.

Figure 2. Grid and plots showing the identification of WT1-immunogenic peptides by a mapping grid strategy

Epitopes recognized by T-cells sensitized *in vitro* by repeated stimulations with the pool of overlapping WT1 peptides were identified by intracellular staining. In particular, the percentage of specific T-cells responding to the mapping grid of subpools of WT1 pentadecapeptides loaded on APCs was assessed. Additionally, negative (T-cells unstimulated and T-cells co-cultured with APCs loaded with an unrelated peptide pool) and positive (T-cells cultured in the presence of PMA and Ionomycin) controls were included in the experimental setting (T-cells unstimulated and PMA/Iono conditions are not shown).

CLAIMS

1. A T-cell receptor (TCR), which binds to a Wilms tumour 1 protein (WT1) peptide when presented by a major histocompatibility complex (MHC), wherein the TCR:
- 5 (i) comprises a CDR3 α comprising the amino acid sequence of CGTAWINDYKLSF (SEQ ID NO: 3) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASRKTGGYSNQPQHF (SEQ ID NO: 8) or a variant thereof having up to three amino acid substitutions, additions or deletions;
 - 10 (ii) comprises a CDR3 α comprising the amino acid sequence of CVVNLLSNQGGKLIF (SEQ ID NO: 36) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSQDYLVSNKLFF (SEQ ID NO: 41) or a variant thereof having up to three amino acid substitutions, additions or deletions;
 - 15 (iii) comprises a CDR3 α comprising the amino acid sequence of CAVRLSGSARQLTF (SEQ ID NO: 14) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSLLGDEQYF (SEQ ID NO: 24) or a variant thereof having up to three amino acid substitutions, additions or deletions;
 - 20 (iv) comprises a CDR3 α comprising the amino acid sequence of CAVRLSGSARQLTF (SEQ ID NO: 14) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSLVALQGAGEQYF (SEQ ID NO: 30) or a variant thereof having up to three amino acid substitutions, additions or deletions;
 - 25 (v) comprises a CDR3 α comprising the amino acid sequence of CAYRSLKYGNKLVF (SEQ ID NO: 19) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSLLGDEQYF (SEQ ID NO: 24) or a variant thereof having up to three amino acid substitutions, additions or deletions;
 - 30 (vi) comprises a CDR3 α comprising the amino acid sequence of CAYRSLKYGNKLVF (SEQ ID NO: 19) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSLVALQGAGEQYF (SEQ ID NO: 30) or a variant thereof having up to three amino acid substitutions, additions or deletions;

- 5 (vii) comprises a CDR3 α comprising the amino acid sequence of CATDAYSGNTPLVF (SEQ ID NO: 47) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASRAAGLDTEAFF (SEQ ID NO: 57) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 10 (viii) comprises a CDR3 α comprising the amino acid sequence of CATDAYSGNTPLVF (SEQ ID NO: 47) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASTQTPYEQYF (SEQ ID NO: 63) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 15 (ix) comprises a CDR3 α comprising the amino acid sequence of CATDAYSGNTPLVF (SEQ ID NO: 47) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSTVGGEDYGYTF (SEQ ID NO: 69) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 20 (x) comprises a CDR3 α comprising the amino acid sequence of CAVRAEIYNQGGKLIF (SEQ ID NO: 52) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASRAAGLDTEAFF (SEQ ID NO: 57) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 25 (xi) comprises a CDR3 α comprising the amino acid sequence of CAVRAEIYNQGGKLIF (SEQ ID NO: 52) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASTQTPYEQYF (SEQ ID NO: 63) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 30 (xii) comprises a CDR3 α comprising the amino acid sequence of CAVRAEIYNQGGKLIF (SEQ ID NO: 52) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSTVGGEDYGYTF (SEQ ID NO: 69) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- (xiii) comprises a CDR3 α comprising the amino acid sequence of CAASMAGAGSYQLTF (SEQ ID NO: 75) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of

CAISVGQGALYEQYF (SEQ ID NO: 80) or a variant thereof having up to three amino acid substitutions, additions or deletions;

- 5 (xiv) comprises a CDR3 α comprising the amino acid sequence of CAASMAGAGSYQLTF (SEQ ID NO: 75) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSVARDRRNYGYTF (SEQ ID NO: 86) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 10 (xv) comprises a CDR3 α comprising the amino acid sequence of CAANNARLMF (SEQ ID NO: 92) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSDTRAREQFF (SEQ ID NO: 97) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 15 (xvi) comprises a CDR3 α comprising the amino acid sequence of CAERLNTDKLIF (SEQ ID NO: 103) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSARDSVSGNTIYF (SEQ ID NO: 163) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 20 (xvii) comprises a CDR3 α comprising the amino acid sequence of CAERLNTDKLIF (SEQ ID NO: 103) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSVGGSGSYNEQFF (SEQ ID NO: 169) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 25 (xviii) comprises a CDR3 α comprising the amino acid sequence of CAVEATDSWGKLQF (SEQ ID NO: 108) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSARDSVSGNTIYF (SEQ ID NO: 163) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 30 (xix) comprises a CDR3 α comprising the amino acid sequence of CAVEATDSWGKLQF (SEQ ID NO: 108) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSVGGSGSYNEQFF (SEQ ID NO: 169) or a variant thereof having up to three amino acid substitutions, additions or deletions;

- 5 (xx) comprises a CDR3 α comprising the amino acid sequence of CAVRTSYDKVIF (SEQ ID NO: 113) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSARDSVSGNTIYF (SEQ ID NO: 163) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 10 (xxi) comprises a CDR3 α comprising the amino acid sequence of CAVRTSYDKVIF (SEQ ID NO: 113) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSVGGSGSYNEQFF (SEQ ID NO: 169) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 15 (xxii) comprises a CDR3 α comprising the amino acid sequence of CAVTVGNKLVF (SEQ ID NO: 175) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASRGWREQFF (SEQ ID NO: 180) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 20 (xxiii) comprises a CDR3 α comprising the amino acid sequence of CAARSYNTDKLIF (SEQ ID NO: 186) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSWGYQETQYF (SEQ ID NO: 196) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 25 (xxiv) comprises a CDR3 α comprising the amino acid sequence of CAARSYNTDKLIF (SEQ ID NO: 186) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSPTGGEYYGYTF (SEQ ID NO: 202) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 30 (xxv) comprises a CDR3 α comprising the amino acid sequence of CAARSYNTDKLIF (SEQ ID NO: 186) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSYPLRTGRYNSYNSPLHF (SEQ ID NO: 208) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- (xxvi) comprises a CDR3 α comprising the amino acid sequence of CAASYNARLMF (SEQ ID NO: 191) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of

CASSWGYQETQYF (SEQ ID NO: 196) or a variant thereof having up to three amino acid substitutions, additions or deletions;

5 (xxvii) comprises a CDR3 α comprising the amino acid sequence of CAASYNNARLMF (SEQ ID NO: 191) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSPTGGEYYGYTF (SEQ ID NO: 202) or a variant thereof having up to three amino acid substitutions, additions or deletions;

10 (xxviii) comprises a CDR3 α comprising the amino acid sequence of CAASYNNARLMF (SEQ ID NO: 191) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSYPLRTGRYNSYNSPLHF (SEQ ID NO: 208) or a variant thereof having up to three amino acid substitutions, additions or deletions;

15 (xxix) comprises a CDR3 α comprising the amino acid sequence of CAASGGRDDKIIF (SEQ ID NO: 214) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSYSRTESTDTQYF (SEQ ID NO: 219) or a variant thereof having up to three amino acid substitutions, additions or deletions;

20 (xxx) comprises a CDR3 α comprising the amino acid sequence of CAANNARLMF (SEQ ID NO: 92) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSPGQHGELEFF (SEQ ID NO: 271) or a variant thereof having up to three amino acid substitutions, additions or deletions;

25 (xxxi) comprises a CDR3 α comprising the amino acid sequence of CAASATGNQFYF (SEQ ID NO: 266) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSDTRAREQFF (SEQ ID NO: 97) or a variant thereof having up to three amino acid substitutions, additions or deletions;

30 (xxxii) comprises a CDR3 α comprising the amino acid sequence of CAASATGNQFYF (SEQ ID NO: 266) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSPGQHGELEFF (SEQ ID NO: 271) or a variant thereof having up to three amino acid substitutions, additions or deletions;

- 5 (xxxiii) comprises a CDR3 α comprising the amino acid sequence of CATDGDSSYKLIF (SEQ ID NO: 277) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSARDSVSGNTIYF (SEQ ID NO: 163) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 10 (xxxiv) comprises a CDR3 α comprising the amino acid sequence of CATDGDSSYKLIF (SEQ ID NO: 277) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSVGGSGSYNEQFF (SEQ ID NO: 169) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 15 (xxxv) comprises a CDR3 α comprising the amino acid sequence of CATDGDSSYKLIF (SEQ ID NO: 277) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSARDVLTGDYGYTF (SEQ ID NO: 282) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 20 (xxxvi) comprises a CDR3 α comprising the amino acid sequence of CATDGDSSYKLIF (SEQ ID NO: 277) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSLGLSISQETQYF (SEQ ID NO: 288) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 25 (xxxvii) comprises a CDR3 α comprising the amino acid sequence of CAERLNTDKLIF (SEQ ID NO: 103) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSLGLSISQETQYF (SEQ ID NO: 288) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- 30 (xxxviii) comprises a CDR3 α comprising the amino acid sequence of CAVEATDSWGKLQF (SEQ ID NO: 108) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CASSLGLSISQETQYF (SEQ ID NO: 288) or a variant thereof having up to three amino acid substitutions, additions or deletions;
- (xxxix) comprises a CDR3 α comprising the amino acid sequence of CAVRTSYDKVIF (SEQ ID NO: 113) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of

CASSLGLSISQETQYF (SEQ ID NO: 288) or a variant thereof having up to three amino acid substitutions, additions or deletions.

5 (xxxx) comprises a CDR3 α comprising the amino acid sequence of CAERLNTDKLIF (SEQ ID NO: 103) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSARDVLTGDYGYTF (SEQ ID NO: 282) or a variant thereof having up to three amino acid substitutions, additions or deletions;

10 (xxxxi) comprises a CDR3 α comprising the amino acid sequence of CAVEATDSWGKLQF (SEQ ID NO: 108) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSARDVLTGDYGYTF (SEQ ID NO: 282) or a variant thereof having up to three amino acid substitutions, additions or deletions; or

15 (xxxixii) comprises a CDR3 α comprising the amino acid sequence of CAVRTSYDKVIF (SEQ ID NO: 113) or a variant thereof having up to three amino acid substitutions, additions or deletions, and a CDR3 β comprising the amino acid sequence of CSARDVLTGDYGYTF (SEQ ID NO: 282) or a variant thereof having up to three amino acid substitutions, additions or deletions.

2. A TCR according to claim 1 comprising the following CDR sequences:

20 (i) CDR1 α - KALYS (SEQ ID NO: 1),
CDR2 α - LLKGGEQ (SEQ ID NO: 2),
CDR3 α - CGTAWINDYKLSF (SEQ ID NO: 3),
CDR1 β - SGHDY (SEQ ID NO: 6),
CDR2 β - FNNNVP (SEQ ID NO: 7), and
CDR3 β - CASRKTGGYSNQPQHF (SEQ ID NO: 8),
25 or variants thereof each having up to three amino acid substitutions, additions or deletions;

30 (ii) CDR1 α - NSASQS (SEQ ID NO: 34),
CDR2 α - VYSSGN (SEQ ID NO: 35),
CDR3 α - CVVNLLSNQGGKLIF (SEQ ID NO: 36),
CDR1 β - LGHNA (SEQ ID NO: 39),
CDR2 β - YSLEER (SEQ ID NO: 40), and
CDR3 β - CASSQDYLVSNKLFF (SEQ ID NO: 41),

or variants thereof each having up to three amino acid substitutions, additions or deletions;

- 5 (iii) CDR1 α - SSVPPY (SEQ ID NO: 12),
CDR2 α - Y TSAATLV (SEQ ID NO: 13),
CDR3 α - CAVRLSGSARQLTF (SEQ ID NO: 14),
CDR1 β - SGHAT (SEQ ID NO: 22),
CDR2 β - FQNNGV (SEQ ID NO: 23), and
CDR3 β - CASSLLGDEQYF (SEQ ID NO: 24),
or variants thereof each having up to three amino acid substitutions, additions or
10 deletions;
- (iv) CDR1 α - SSVPPY (SEQ ID NO: 12),
CDR2 α - Y TSAATLV (SEQ ID NO: 13),
CDR3 α - CAVRLSGSARQLTF (SEQ ID NO: 14),
CDR1 β - SGHTA (SEQ ID NO: 28),
15 CDR2 β - FQGNSA (SEQ ID NO: 29), and
CDR3 β - CASSLVALQGAGEQYF (SEQ ID NO: 30),
or variants thereof each having up to three amino acid substitutions, additions or
deletions;
- 20 (v) CDR1 α - TSEDYY (SEQ ID NO: 17),
CDR2 α - QEAYKQQN (SEQ ID NO: 18),
CDR3 α - CAYRSLKYGNKLVF (SEQ ID NO: 19),
CDR1 β - SGHAT (SEQ ID NO: 22),
CDR2 β - FQNNGV (SEQ ID NO: 23), and
CDR3 β - CASSLLGDEQYF (SEQ ID NO: 24),
25 or variants thereof each having up to three amino acid substitutions, additions or
deletions;
- 30 (vi) CDR1 α - TSEDYY (SEQ ID NO: 17),
CDR2 α - QEAYKQQN (SEQ ID NO: 18),
CDR3 α - CAYRSLKYGNKLVF (SEQ ID NO: 19),
CDR1 β - SGHTA (SEQ ID NO: 28),
CDR2 β - FQGNSA (SEQ ID NO: 29), and
CDR3 β - CASSLVALQGAGEQYF (SEQ ID NO: 30),
or variants thereof each having up to three amino acid substitutions, additions or
deletions;

- (vii) CDR1 α – TSINN (SEQ ID NO: 45),
 CDR2 α - IRSNERE (SEQ ID NO: 46),
 CDR3 α – CATDAYSGNTPLVF (SEQ ID NO: 47),
 CDR1 β - MNHNS (SEQ ID NO: 55),
 5 CDR2 β - SASEGT (SEQ ID NO: 56), and
 CDR3 β - CASRAAGLDTEAFF (SEQ ID NO: 57),
 or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (viii) CDR1 α – TSINN (SEQ ID NO: 45),
 10 CDR2 α - IRSNERE (SEQ ID NO: 46),
 CDR3 α – CATDAYSGNTPLVF (SEQ ID NO: 47),
 CDR1 β – MNHNY (SEQ ID NO: 61),
 CDR2 β - SVGAGI (SEQ ID NO: 62), and
 CDR3 β - CASTQTPYEQYF (SEQ ID NO: 63),
 15 or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (ix) CDR1 α – TSINN (SEQ ID NO: 45),
 CDR2 α - IRSNERE (SEQ ID NO: 46),
 CDR3 α – CATDAYSGNTPLVF (SEQ ID NO: 47),
 20 CDR1 β – SGHNS (SEQ ID NO: 67),
 CDR2 β - FNNNVP (SEQ ID NO: 68), and
 CDR3 β – CASSTVGGEDYGYTF (SEQ ID NO: 69),
 or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (x) CDR1 α - DSAIYN (SEQ ID NO: 50),
 25 CDR2 α – IQSSQRE (SEQ ID NO: 51),
 CDR3 α - CAVRAEIYNQGGKLIF (SEQ ID NO: 52),
 CDR1 β - MNHNS (SEQ ID NO: 55),
 CDR2 β - SASEGT (SEQ ID NO: 56), and
 30 CDR3 β - CASRAAGLDTEAFF (SEQ ID NO: 57),
 or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (xi) CDR1 α - DSAIYN (SEQ ID NO: 50),
 CDR2 α – IQSSQRE (SEQ ID NO: 51),
 35 CDR3 α - CAVRAEIYNQGGKLIF (SEQ ID NO: 52),

- CDR1 β – MNHNY (SEQ ID NO: 61),
 CDR2 β - SVGAGI (SEQ ID NO: 62), and
 CDR3 β - CASTQTPYEQYF (SEQ ID NO: 63),
 or variants thereof each having up to three amino acid substitutions, additions or
 deletions;
- (xii) CDR1 α - DSAIYN (SEQ ID NO: 50),
 CDR2 α – IQSSQRE (SEQ ID NO: 51),
 CDR3 α - CAVRAEIYNQGGKLIF (SEQ ID NO: 52),
 CDR1 β – SGHNS (SEQ ID NO: 67),
 CDR2 β - FNNNVP (SEQ ID NO: 68), and
 CDR3 β – CASSTVGGEDYGYTF (SEQ ID NO: 69),
 or variants thereof each having up to three amino acid substitutions, additions or
 deletions;
- (xiii) CDR1 α - DSASNY (SEQ ID NO: 73),
 CDR2 α – IRSNVGE (SEQ ID NO: 74),
 CDR3 α - CAASMAGAGSYQLTF (SEQ ID NO: 75),
 CDR1 β - ENHRY (SEQ ID NO: 78),
 CDR2 β – SYGVKD (SEQ ID NO: 79), and
 CDR3 β - CAISVGQGALYEQYF (SEQ ID NO: 80),
 or variants thereof each having up to three amino acid substitutions, additions or
 deletions;
- (xiv) CDR1 α - DSASNY (SEQ ID NO: 73),
 CDR2 α – IRSNVGE (SEQ ID NO: 74),
 CDR3 α - CAASMAGAGSYQLTF (SEQ ID NO: 75),
 CDR1 β – SGDLS (SEQ ID NO: 84),
 CDR2 β – YYNGEE (SEQ ID NO: 85), and
 CDR3 β – CASSVARDRRNYGYTF (SEQ ID NO: 86),
 or variants thereof each having up to three amino acid substitutions, additions or
 deletions;
- (xv) CDR1 α - NSMFDY (SEQ ID NO: 90),
 CDR2 α – ISSIKDK (SEQ ID NO: 91),
 CDR3 α - CAANNARLMF (SEQ ID NO: 92),
 CDR1 β – SGHNS (SEQ ID NO: 95),
 CDR2 β – FNNNVP (SEQ ID NO: 96), and
 CDR3 β – CASSDTRAREQFF (SEQ ID NO: 97),

or variants thereof each having up to three amino acid substitutions, additions or deletions;

(xvi) CDR1 α - DSSSTY (SEQ ID NO: 101),
CDR2 α – IFSNMDM (SEQ ID NO: 102),
5 CDR3 α - CAERLNTDKLIF (SEQ ID NO: 103),
CDR1 β – DFQATT (SEQ ID NO: 161),
CDR2 β – SNEGSKA (SEQ ID NO: 162), and
CDR3 β – CSARDSVSGNTIYF (SEQ ID NO: 163),
or variants thereof each having up to three amino acid substitutions, additions or
10 deletions;

(xvii) CDR1 α - DSSSTY (SEQ ID NO: 101),
CDR2 α – IFSNMDM (SEQ ID NO: 102),
CDR3 α - CAERLNTDKLIF (SEQ ID NO: 103),
CDR1 β – SQVTM (SEQ ID NO: 167),
15 CDR2 β – ANQGSEA (SEQ ID NO: 168), and
CDR3 β – CSVGGSGSYNEQFF (SEQ ID NO: 169),
or variants thereof each having up to three amino acid substitutions, additions or
deletions;

(xviii) CDR1 α - DSVNN (SEQ ID NO:106),
20 CDR2 α – IPSGT (SEQ ID NO: 107),
CDR3 α - CAVEATDSWGKLQF (SEQ ID NO: 108),
CDR1 β – DFQATT (SEQ ID NO: 161),
CDR2 β – SNEGSKA (SEQ ID NO: 162), and
CDR3 β – CSARDSVSGNTIYF (SEQ ID NO: 163),
25 or variants thereof each having up to three amino acid substitutions, additions or
deletions;

(xix) CDR1 α - DSVNN (SEQ ID NO:106),
CDR2 α – IPSGT (SEQ ID NO: 107),
CDR3 α - CAVEATDSWGKLQF (SEQ ID NO: 108),
30 CDR1 β – SQVTM (SEQ ID NO: 167),
CDR2 β – ANQGSEA (SEQ ID NO: 168), and
CDR3 β – CSVGGSGSYNEQFF (SEQ ID NO: 169),
or variants thereof each having up to three amino acid substitutions, additions or
deletions;

- (xx) CDR1 α - DSASNY (SEQ ID NO: 111),
 CDR2 α – IRSNVGE (SEQ ID NO: 112),
 CDR3 α - CAVRTSYDKVIF (SEQ ID NO: 113),
 CDR1 β – DFQATT (SEQ ID NO: 161),
 5 CDR2 β – SNEGSKA (SEQ ID NO: 162), and
 CDR3 β – CSARDSVSGNTIYF (SEQ ID NO: 163),
 or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (xxi) CDR1 α - DSASNY (SEQ ID NO: 111),
 10 CDR2 α – IRSNVGE (SEQ ID NO: 112),
 CDR3 α - CAVRTSYDKVIF (SEQ ID NO: 113),
 CDR1 β – SQVTM (SEQ ID NO: 167),
 CDR2 β – ANQGSEA (SEQ ID NO: 168), and
 CDR3 β – CSVGGSGSYNEQFF (SEQ ID NO: 169),
 15 or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (xxii) CDR1 α - VGISA (SEQ ID NO: 173),
 CDR2 α – LSSGK (SEQ ID NO: 174),
 CDR3 α - CAVTVGNKLVF (SEQ ID NO: 175),
 20 CDR1 β – MNHNS (SEQ ID NO: 178),
 CDR2 β – SASEGT (SEQ ID NO: 179), and
 CDR3 β – CASRGWREQFF (SEQ ID NO: 180),
 or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (xxiii) CDR1 α - VGISA (SEQ ID NO: 184),
 25 CDR2 α – LSSGK (SEQ ID NO: 185),
 CDR3 α - CAARSYNTDKLIF (SEQ ID NO: 186),
 CDR1 β – SGHTS (SEQ ID NO: 194),
 CDR2 β – YDEGEE (SEQ ID NO: 195), and
 30 CDR3 β – CASSWGYQETQYF (SEQ ID NO: 196),
 or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (xxiv) CDR1 α - VGISA (SEQ ID NO: 184),
 CDR2 α – LSSGK (SEQ ID NO: 185),
 35 CDR3 α - CAARSYNTDKLIF (SEQ ID NO: 186),

- CDR1 β – KGHSH (SEQ ID NO: 200),
 CDR2 β – LQKENI (SEQ ID NO: 201), and
 CDR3 β – CASSPTGGGEYYGYTF (SEQ ID NO: 202),
 or variants thereof each having up to three amino acid substitutions, additions or
 deletions;
- (xxv) CDR1 α - VGISA (SEQ ID NO: 184),
 CDR2 α – LSSGK (SEQ ID NO: 185),
 CDR3 α - CAARSYNTDKLIF (SEQ ID NO: 186),
 CDR1 β – MNHEY (SEQ ID NO: 206),
 CDR2 β – SVGAGI (SEQ ID NO: 207), and
 CDR3 β – CASSYPLRTGRYNSYNSPLHF (SEQ ID NO: 208),
 or variants thereof each having up to three amino acid substitutions, additions or
 deletions;
- (xxvi) CDR1 α - NSMFDY (SEQ ID NO: 189),
 CDR2 α – ISSIKDK (SEQ ID NO: 190),
 CDR3 α - CAASYNNARLMF (SEQ ID NO: 191),
 CDR1 β – SGHTS (SEQ ID NO: 194),
 CDR2 β – YDEGEE (SEQ ID NO: 195), and
 CDR3 β – CASSWGYQETQYF (SEQ ID NO: 196),
 or variants thereof each having up to three amino acid substitutions, additions or
 deletions;
- (xxvii) CDR1 α - NSMFDY (SEQ ID NO: 189),
 CDR2 α – ISSIKDK (SEQ ID NO: 190),
 CDR3 α - CAASYNNARLMF (SEQ ID NO: 191),
 CDR1 β – KGHSH (SEQ ID NO: 200),
 CDR2 β – LQKENI (SEQ ID NO: 201), and
 CDR3 β – CASSPTGGGEYYGYTF (SEQ ID NO: 202),
 or variants thereof each having up to three amino acid substitutions, additions or
 deletions;
- (xxviii) CDR1 α - NSMFDY (SEQ ID NO: 189),
 CDR2 α – ISSIKDK (SEQ ID NO: 190),
 CDR3 α - CAASYNNARLMF (SEQ ID NO: 191),
 CDR1 β – MNHEY (SEQ ID NO: 206),
 CDR2 β – SVGAGI (SEQ ID NO: 207), and

CDR3 β – CASSSYPLRTGRYNSYNSPLHF (SEQ ID NO: 208),
or variants thereof each having up to three amino acid substitutions, additions or
deletions;

5 (xxix) CDR1 α - NSMFDY (SEQ ID NO: 212),
CDR2 α – ISSIKDK (SEQ ID NO: 213),
CDR3 α - CAASGGRDDKIIF (SEQ ID NO: 214),
CDR1 β – MNHEY (SEQ ID NO: 217),
CDR2 β – SVGAGI (SEQ ID NO: 218), and
CDR3 β – CASSYSRTESTDTQYF (SEQ ID NO: 219),
10 or variants thereof each having up to three amino acid substitutions, additions or
deletions;

(xxx) CDR1 α - NSMFDY (SEQ ID NO: 90),
CDR2 α – ISSIKDK (SEQ ID NO: 91),
CDR3 α - CAANNARLMF (SEQ ID NO: 92),
15 CDR1 β – SGHRS (SEQ ID NO: 269),
CDR2 β – YFSETQ (SEQ ID NO: 270), and
CDR3 β – CASSPGQHGEFF (SEQ ID NO: 271),
or variants thereof each having up to three amino acid substitutions, additions or
deletions;

20 (xxxi) CDR1 α - NSMFDY (SEQ ID NO: 264),
CDR2 α – ISSIKDK (SEQ ID NO: 265),
CDR3 α - CAASATGNQFYF (SEQ ID NO: 266),
CDR1 β – SGHNS (SEQ ID NO: 95),
CDR2 β – FNNNVP (SEQ ID NO: 96), and
25 CDR3 β – CASSDTRAREQFF (SEQ ID NO: 97),
or variants thereof each having up to three amino acid substitutions, additions or
deletions;

(xxxii) CDR1 α - NSMFDY (SEQ ID NO: 264),
CDR2 α – ISSIKDK (SEQ ID NO: 265),
30 CDR3 α - CAASATGNQFYF (SEQ ID NO: 266),
CDR1 β – SGHRS (SEQ ID NO: 269),
CDR2 β – YFSETQ (SEQ ID NO: 270), and
CDR3 β – CASSPGQHGEFF (SEQ ID NO: 271),
or variants thereof each having up to three amino acid substitutions, additions or
35 deletions;

- (xxxiii) CDR1 α - TSINN (SEQ ID NO: 275),
CDR2 α – IRSNERE (SEQ ID NO: 276),
CDR3 α - CATDGDSSYKLIF (SEQ ID NO: 277),
CDR1 β – DFQATT (SEQ ID NO: 161),
5 CDR2 β – SNEGSKA (SEQ ID NO: 162), and
CDR3 β – CSARDSVSGNTIYF (SEQ ID NO: 163),
or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (xxxiv) CDR1 α - TSINN (SEQ ID NO: 275),
10 CDR2 α – IRSNERE (SEQ ID NO: 276),
CDR3 α - CATDGDSSYKLIF (SEQ ID NO: 277),
CDR1 β – SQVTM (SEQ ID NO: 167),
CDR2 β – ANQGSEA (SEQ ID NO: 168), and
CDR3 β – CSVGGSGSYNEQFF (SEQ ID NO: 169),
15 or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (xxxv) CDR1 α - TSINN (SEQ ID NO: 275),
CDR2 α – IRSNERE (SEQ ID NO: 276),
CDR3 α - CATDGDSSYKLIF (SEQ ID NO: 277),
20 CDR1 β – DFQATT (SEQ ID NO: 280),
CDR2 β – SNEGSKA (SEQ ID NO: 281), and
CDR3 β – CSARDVLTGDYGYTF (SEQ ID NO: 282),
or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (xxxvi) CDR1 α - TSINN (SEQ ID NO: 275),
25 CDR2 α – IRSNERE (SEQ ID NO: 276),
CDR3 α - CATDGDSSYKLIF (SEQ ID NO: 277),
CDR1 β – SGHDY (SEQ ID NO: 286),
CDR2 β – FNNNVP (SEQ ID NO: 287), and
30 CDR3 β – CASSLGLSISQETQYF (SEQ ID NO: 288),
or variants thereof each having up to three amino acid substitutions, additions or deletions;
- (xxxvii) CDR1 α - DSSSTY (SEQ ID NO: 101),
CDR2 α – IFSNMDM (SEQ ID NO: 102),
35 CDR3 α - CAERLNTDKLIF (SEQ ID NO: 103),

CDR1 β – SGHDY (SEQ ID NO: 286),
 CDR2 β – FNNNVP (SEQ ID NO: 287), and
 CDR3 β – CASSLGLSISQETQYF (SEQ ID NO: 288),
 or variants thereof each having up to three amino acid substitutions, additions or
 5 deletions;

(xxxviii) CDR1 α - DSVNN (SEQ ID NO: 106),
 CDR2 α – IPSGT (SEQ ID NO: 107),
 CDR3 α - CAVEATDSWGKLQF (SEQ ID NO: 108),
 CDR1 β – SGHDY (SEQ ID NO: 286),
 10 CDR2 β – FNNNVP (SEQ ID NO: 287), and
 CDR3 β – CASSLGLSISQETQYF (SEQ ID NO: 288),
 or variants thereof each having up to three amino acid substitutions, additions or
 deletions;

(xxxix) CDR1 α - DSASNY (SEQ ID NO: 111),
 15 CDR2 α – IRSNVGE (SEQ ID NO: 112),
 CDR3 α - CAVRTSYDKVIF (SEQ ID NO: 113),
 CDR1 β – SGHDY (SEQ ID NO: 286),
 CDR2 β – FNNNVP (SEQ ID NO: 287), and
 CDR3 β – CASSLGLSISQETQYF (SEQ ID NO: 288),
 20 or variants thereof each having up to three amino acid substitutions, additions or
 deletions;

(xxxx) CDR1 α - DSSSTY (SEQ ID NO: 101),
 CDR2 α – IFSNMDM (SEQ ID NO: 102),
 CDR3 α - CAERLNTDKLIF (SEQ ID NO: 103),
 25 CDR1 β – DFQATT (SEQ ID NO: 280),
 CDR2 β – SNEGSKA (SEQ ID NO: 281), and
 CDR3 β – CSARDVLTGDYGYTF (SEQ ID NO: 282),
 or variants thereof each having up to three amino acid substitutions, additions or
 deletions;

30 (xxxxi) CDR1 α - DSVNN (SEQ ID NO: 106),
 CDR2 α – IPSGT (SEQ ID NO: 107),
 CDR3 α - CAVEATDSWGKLQF (SEQ ID NO: 108),
 CDR1 β – DFQATT (SEQ ID NO: 280),
 CDR2 β – SNEGSKA (SEQ ID NO: 281), and
 35 CDR3 β – CSARDVLTGDYGYTF (SEQ ID NO: 282),

or variants thereof each having up to three amino acid substitutions, additions or deletions; or

(xxxixii) CDR1 α - DSASNY (SEQ ID NO: 111),

CDR2 α – IRSNVGE (SEQ ID NO: 112),

5 CDR3 α - CAVRTSYDKVIF (SEQ ID NO: 113),

CDR1 β – DFQATT (SEQ ID NO: 280),

CDR2 β – SNEGSKA (SEQ ID NO: 281), and

CDR3 β – CSARDVLTGDYGYTF (SEQ ID NO: 282),

10 or variants thereof each having up to three amino acid substitutions, additions or deletions.

3. A TCR according to claim 1 or 2 comprising:

(i) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 4 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 9 or a variant thereof having at least 75% sequence identity thereto;

15

(ii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 37 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 42 or a variant thereof having at least 75% sequence identity thereto;

20 (iii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 15 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 25 or a variant thereof having at least 75% sequence identity thereto;

25 (iv) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 15 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 31 or a variant thereof having at least 75% sequence identity thereto;

30 (v) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 20 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 25 or a variant thereof having at least 75% sequence identity thereto;

- (vi) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 20 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 31 or variants thereof having at least 75% sequence identity thereto;
- 5 (vii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 48 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 58 or a variant thereof having at least 75% sequence identity thereto;
- 10 (viii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 48 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or a variant thereof having at least 75% sequence identity thereto;
- 15 (ix) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 48 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 70 or a variant thereof having at least 75% sequence identity thereto;
- 20 (x) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 53 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 58 or a variant thereof having at least 75% sequence identity thereto;
- (xi) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 53 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or a variant thereof having at least 75% sequence identity thereto;
- 25 (xii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 53 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 70 or a variant thereof having at least 75% sequence identity thereto;
- 30 (xiii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 76 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 81 or a variant thereof having at least 75% sequence identity thereto;

- (xiv) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 76 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 87 or a variant thereof having at least 75% sequence identity thereto;
- 5 (xv) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 93 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 98 or a variant thereof having at least 75% sequence identity thereto;
- 10 (xvi) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 104 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 164 or a variant thereof having at least 75% sequence identity thereto;
- 15 (xvii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 104 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 170 or a variant thereof having at least 75% sequence identity thereto;
- 20 (xviii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 109 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 164 or a variant thereof having at least 75% sequence identity thereto;
- (xix) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 109 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 170 or a variant thereof having at least 75% sequence identity thereto;
- 25 (xx) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 114 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 164 or a variant thereof having at least 75% sequence identity thereto;
- 30 (xxi) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 114 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 170 or a variant thereof having at least 75% sequence identity thereto;

- (xxii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 176 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 181 or a variant thereof having at least 75% sequence identity thereto;
- 5 (xxiii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 187 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 197 or a variant thereof having at least 75% sequence identity thereto;
- 10 (xxiv) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 187 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 203 or a variant thereof having at least 75% sequence identity thereto;
- 15 (xxv) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 187 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 209 or a variant thereof having at least 75% sequence identity thereto;
- 20 (xxvi) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 192 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 197 or a variant thereof having at least 75% sequence identity thereto;
- (xxvii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 192 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 203 or a variant thereof having at least 75% sequence identity thereto;
- 25 (xxviii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 192 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 209 or a variant thereof having at least 75% sequence identity thereto;
- 30 (xxix) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 215 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 220 or a variant thereof having at least 75% sequence identity thereto;

- (xxx) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 93 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 272 or a variant thereof having at least 75% sequence identity thereto;
- 5 (xxxi) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 267 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 98 or a variant thereof having at least 75% sequence identity thereto;
- 10 (xxxii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 267 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 272 or a variant thereof having at least 75% sequence identity thereto;
- 15 (xxxiii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 278 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 164 or a variant thereof having at least 75% sequence identity thereto;
- 20 (xxxiv) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 278 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 170 or a variant thereof having at least 75% sequence identity thereto;
- (xxxv) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 278 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 283 or a variant thereof having at least 75% sequence identity thereto;
- 25 (xxxvi) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 278 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 289 or a variant thereof having at least 75% sequence identity thereto;
- 30 (xxxvii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 104 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 289 or a variant thereof having at least 75% sequence identity thereto;

- (xxxviii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 109 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 289 or a variant thereof having at least 75% sequence identity thereto;
- 5 (xxxix) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 114 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 289 or a variant thereof having at least 75% sequence identity thereto;
- 10 (xxxx) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 104 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 283 or a variant thereof having at least 75% sequence identity thereto;
- 15 (xxxxi) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 109 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 283 or a variant thereof having at least 75% sequence identity thereto; or
- 20 (xxxxii) an α chain variable domain comprising the amino acid sequence of SEQ ID NO: 114 or a variant thereof having at least 75% sequence identity thereto; and a β chain variable domain comprising the amino acid sequence of SEQ ID NO: 283 or a variant thereof having at least 75% sequence identity thereto.
4. A TCR according to any preceding claim comprising:
- 25 (i) an α chain comprising the amino acid sequence of SEQ ID NO: 5 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 10, SEQ ID NO: 11 and variants of SEQ ID NOs: 10 and 11 having at least 75% sequence identity thereto;
- 30 (ii) an α chain comprising the amino acid sequence of SEQ ID NO: 38 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 43, SEQ ID NO: 44 and variants of SEQ ID NOs: 43 and 44 having at least 75% sequence identity thereto;

- 5 (iii) an α chain comprising the amino acid sequence of SEQ ID NO: 16 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 26, SEQ ID NO: 27 and variants of SEQ ID NOs: 26 and 27 having at least 75% sequence identity thereto;
- 10 (iv) an α chain comprising the amino acid sequence of SEQ ID NO: 16 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33 and variants of SEQ ID NOs: 32 and 33 having at least 75% sequence identity thereto;
- 15 (v) an α chain comprising the amino acid sequence of SEQ ID NO: 21 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 26, SEQ ID NO: 27 and variants of SEQ ID NOs: 26 and 27 having at least 75% sequence identity thereto;
- 20 (vi) an α chain comprising the amino acid sequence of SEQ ID NO: 21 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33 and variants of SEQ ID NOs: 32 and 33 having at least 75% sequence identity thereto;
- 25 (vii) an α chain comprising the amino acid sequence of SEQ ID NO: 49 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 59, SEQ ID NO: 60 and variants of SEQ ID NOs: 59 and 60 having at least 75% sequence identity thereto;
- 30 (viii) an α chain comprising the amino acid sequence of SEQ ID NO: 49 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 65, SEQ ID NO: 66 and variants of SEQ ID NOs: 65 and 66 having at least 75% sequence identity thereto;
- (ix) an α chain comprising the amino acid sequence of SEQ ID NO: 49 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 71, SEQ ID

NO: 72 and variants of SEQ ID NOs: 71 and 72 having at least 75% sequence identity thereto;

- 5 (x) an α chain comprising the amino acid sequence of SEQ ID NO: 54 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 59, SEQ ID NO: 60 and variants of SEQ ID NOs: 59 and 60 having at least 75% sequence identity thereto;
- 10 (xi) an α chain comprising the amino acid sequence of SEQ ID NO: 54 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 65, SEQ ID NO: 66 and variants of SEQ ID NOs: 65 and 66 having at least 75% sequence identity thereto;
- 15 (xii) an α chain comprising the amino acid sequence of SEQ ID NO: 54 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 71, SEQ ID NO: 72 and variants of SEQ ID NOs: 71 and 72 having at least 75% sequence identity thereto;
- 20 (xiii) an α chain comprising the amino acid sequence of SEQ ID NO: 77 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 82, SEQ ID NO: 83 and variants of SEQ ID NOs: 82 and 83 having at least 75% sequence identity thereto;
- 25 (xiv) an α chain comprising the amino acid sequence of SEQ ID NO: 77 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 88, SEQ ID NO: 89 and variants of SEQ ID NOs: 88 and 89 having at least 75% sequence identity thereto;
- 30 (xv) an α chain comprising the amino acid sequence of SEQ ID NO: 94 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 99, SEQ ID NO: 100 and variants of SEQ ID NO: 99, SEQ ID NO: 100 having at least 75% sequence identity thereto;

- 5 (xvi) an α chain comprising the amino acid sequence of SEQ ID NO: 105 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 165, SEQ ID NO: 166 and variants of SEQ ID NOs: 165 and 166 having at least 75% sequence identity thereto;
- 10 (xvii) an α chain comprising the amino acid sequence of SEQ ID NO: 105 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 171, SEQ ID NO: 172 and variants of SEQ ID NOs: 171 and 172 having at least 75% sequence identity thereto;
- 15 (xviii) an α chain comprising the amino acid sequence of SEQ ID NO: 110 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 165, SEQ ID NO: 166 and variants of SEQ ID NOs: 165 and 166 having at least 75% sequence identity thereto;
- 20 (xix) an α chain comprising the amino acid sequence of SEQ ID NO: 110 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 171, SEQ ID NO: 172 and variants of SEQ ID NOs: 171 and 172 having at least 75% sequence identity thereto;
- 25 (xx) an α chain comprising the amino acid sequence of SEQ ID NO: 160 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 165, SEQ ID NO: 166 and variants of SEQ ID NOs: 165 and 166 having at least 75% sequence identity thereto;
- 30 (xxi) an α chain comprising the amino acid sequence of SEQ ID NO: 160 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 171, SEQ ID NO: 172 and variants of SEQ ID NOs: 171 and 172 having at least 75% sequence identity thereto;
- (xxii) an α chain comprising the amino acid sequence of SEQ ID NO: 177 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 182, SEQ ID

NO: 183 and variants of SEQ ID NOs: 182 and 183 having at least 75% sequence identity thereto;

- 5 (xxiii) an α chain comprising the amino acid sequence of SEQ ID NO: 188 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 198, SEQ ID NO: 199 and variants of SEQ ID NOs: 198 and 199 having at least 75% sequence identity thereto;
- 10 (xxiv) an α chain comprising the amino acid sequence of SEQ ID NO: 188 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 204, SEQ ID NO: 205 and variants of SEQ ID NOs: 204 and 205 having at least 75% sequence identity thereto;
- 15 (xxv) an α chain comprising the amino acid sequence of SEQ ID NO: 188 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 210, SEQ ID NO: 211 and variants of SEQ ID NOs: 210 and 211 having at least 75% sequence identity thereto;
- 20 (xxvi) an α chain comprising the amino acid sequence of SEQ ID NO: 193 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 198, SEQ ID NO: 199 and variants of SEQ ID NOs: 198 and 199 having at least 75% sequence identity thereto;
- 25 (xxvii) an α chain comprising the amino acid sequence of SEQ ID NO: 193 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 204, SEQ ID NO: 205 and variants of SEQ ID NOs: 204 and 205 having at least 75% sequence identity thereto;
- 30 (xxviii) an α chain comprising the amino acid sequence of SEQ ID NO: 193 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 210, SEQ ID NO: 211 and variants of SEQ ID NOs: 210 and 211 having at least 75% sequence identity thereto;

- 5 (xxix) an α chain comprising the amino acid sequence of SEQ ID NO: 216 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 221, SEQ ID NO: 222 and variants of SEQ ID NOs: 221 and 222 having at least 75% sequence identity thereto;
- 10 (xxx) an α chain comprising the amino acid sequence of SEQ ID NO: 94 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 273, SEQ ID NO: 274 and variants of SEQ ID NOs: 273 and 274 having at least 75% sequence identity thereto;
- 15 (xxxi) an α chain comprising the amino acid sequence of SEQ ID NO: 268 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 99, SEQ ID NO: 100 and variants of SEQ ID NOs: 99 and 100 having at least 75% sequence identity thereto;
- 20 (xxxii) an α chain comprising the amino acid sequence of SEQ ID NO: 268 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 273, SEQ ID NO: 274 and variants of SEQ ID NOs: 273 and 274 having at least 75% sequence identity thereto;
- 25 (xxxiii) an α chain comprising the amino acid sequence of SEQ ID NO: 279 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 165, SEQ ID NO: 166 and variants of SEQ ID NOs: 165 and 166 having at least 75% sequence identity thereto;
- 30 (xxxiv) an α chain comprising the amino acid sequence of SEQ ID NO: 279 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 171, SEQ ID NO: 172 and variants of SEQ ID NOs: 171 and 172 having at least 75% sequence identity thereto;
- (xxxv) an α chain comprising the amino acid sequence of SEQ ID NO: 279 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 284, SEQ ID

NO: 285 and variants of SEQ ID NOs: 284 and 285 having at least 75% sequence identity thereto;

5 (xxxvi) an α chain comprising the amino acid sequence of SEQ ID NO: 279 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 290, SEQ ID NO: 291 and variants of SEQ ID NOs: 290 and 291 having at least 75% sequence identity thereto;

10 (xxxvii) an α chain comprising the amino acid sequence of SEQ ID NO: 105 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 290, SEQ ID NO: 291 and variants of SEQ ID NOs: 290 and 291 having at least 75% sequence identity thereto;

15 (xxxviii) an α chain comprising the amino acid sequence of SEQ ID NO: 110 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 290, SEQ ID NO: 291 and variants of SEQ ID NOs: 290 and 291 having at least 75% sequence identity thereto;

20 (xxxix) an α chain comprising the amino acid sequence of SEQ ID NO: 160 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 290, SEQ ID NO: 291 and variants of SEQ ID NOs: 290 and 291 having at least 75% sequence identity thereto;

25 (xxxx) an α chain comprising the amino acid sequence of SEQ ID NO: 105 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 284, SEQ ID NO: 285 and variants of SEQ ID NOs: 284 and 285 having at least 75% sequence identity thereto;

30 (xxxxi) an α chain comprising the amino acid sequence of SEQ ID NO: 110 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 284, SEQ ID NO: 285 and variants of SEQ ID NOs: 284 and 285 having at least 75% sequence identity thereto; or

- (xxxxii) an α chain comprising the amino acid sequence of SEQ ID NO: 160 or a variant thereof having at least 75% sequence identity thereto; and a β chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 284, SEQ ID NO: 285 and variants of SEQ ID NOs: 284 and 285 having at least 75% sequence identity thereto.
- 5
5. A T-cell receptor (TCR), which binds to a Wilms tumour 1 protein (WT1) peptide when presented by a major histocompatibility complex (MHC), wherein the WT1 peptide comprises an amino acid sequence selected from the group consisting of EPASQHTLRSG (SEQ ID NO: 123), YESDNHTTPIL (SEQ ID NO: 126), NHTTPILCGAQYRIH (SEQ ID NO: 127), QCLSAFTVHFSGQFT (SEQ ID NO: 118), EDPMGQQGSLGEQQY (SEQ ID NO: 119), SQLECMTWNQMNLGA (SEQ ID NO: 120), APVLDFAPPGA (SEQ ID NO: 117), NQMNLGATLKG (SEQ ID NO: 250), DPGGIWAKLGAAEAS (SEQ ID NO: 251), NHTTPILCGAQYRIH (SEQ ID NO: 252), KRHQRRHTGVKPFQC (SEQ ID NO: 253) PSCQKKFARSDLVLR (SEQ ID NO: 254) and variants thereof each having up to three amino acid substitutions, additions or deletions.
- 10
6. A TCR according to any preceding claim which binds to an MHC I and/or MHC II peptide complex.
7. A TCR according to any preceding claim, which is restricted to a human leukocyte antigen (HLA) allele, preferably wherein the TCR is restricted to a HLA-A or a HLA-B allele, more preferably wherein the TCR is restricted to a HLA-A allele selected from the group consisting of HLA-A*0201, HLA-A*0101, HLA-A*2402 and HLA-A*0301 or wherein the TCR is restricted to a HLA-B allele selected from the group consisting of HLA-B*0702, HLA-B*3501 and HLA-B*3502.
- 20
8. A TCR according to:
- 25
- a. (i), (ii), (xv), (xvi), (xxix), (xxx)-(xxxiii), (xxxv) or (xxxx) of any one of claims 1-4, which is restricted to HLA-A*0201;
- b. (vii) of any one of claims 1-4, which is restricted to HLA-B*3502; or
- c. any of (xiii)-(xiv) of any one of claims 1-4, which is restricted to HLA-B*3501.
9. A TCR according to any preceding claim comprising one or more mutations at the α chain/ β chain interface, such that when the α chain and the β chain are expressed in a T-cell, the frequency of mispairing between said chains and endogenous TCR α and β chains is reduced.
- 30

- 10.** A TCR according to claim 9, wherein the one or more mutations introduce a cysteine residue into the constant region domain of each of the α chain and the β chain, wherein the cysteine residues are capable of forming a disulphide bond between the α chain and the β chain.
- 5 **11.** A TCR according to any preceding claim, which comprises a murinized constant region.
- 12.** A TCR according to any preceding claim, wherein the TCR is a soluble TCR.
- 13.** An isolated polynucleotide encoding the α chain of a T-cell receptor (TCR) according to any preceding claim, and/or the β chain of a TCR according to any preceding claim.
- 10 **14.** An isolated polynucleotide according to claim 13, wherein the polynucleotide encodes the α chain linked to the β chain.
- 15.** An isolated polynucleotide according to claim 13 or 14, which encodes one or more short interfering RNA (siRNA) or other agents capable of reducing or preventing expression of one or more endogenous TCR gene.
- 15 **16.** A vector comprising a polynucleotide according to any one of claims 13-15.
- 17.** A vector according to claim 16 comprising a polynucleotide, which encodes one or more CD3 chains, CD8, a suicide gene, and/or a selectable marker.
- 18.** A cell comprising a TCR according to any one of claims 1-11, a polynucleotide according to any one of claims 13-15 or a vector according to claim 16 or 17,
- 20 optionally wherein the cell further comprises a vector which encodes one or more CD3 chains, CD8, a suicide gene and/or a selectable marker.
- 19.** A cell according to claim 18, wherein the cell is a T-cell, a lymphocyte, or a stem cell, optionally wherein the T-cell, the lymphocyte, or the stem cell is selected from the group consisting of CD4 cells, CD8 cells, naive T-cells, memory stem T-cells, central memory T-cells, double negative T-cells, effector memory T-cells, effector T-cells, Th0 cells, Tc0 cells, Th1 cells, Tc1 cells, Th2 cells, Tc2 cells, Th17 cells, Th22 cells, gamma/delta T-cells, natural killer (NK) cells, natural killer T (NKT) cells, hematopoietic stem cells and pluripotent stem cells.
- 25 **20.** A cell according to claim 19, wherein the cell is a T-cell which has been isolated from
- 30 a subject.

- 21.** A cell according to any one of claims 18-20, wherein an endogenous gene encoding a TCR α chain and/or an endogenous gene encoding a TCR β chain is disrupted, preferably such that the endogenous gene encoding a TCR α chain and/or the endogenous gene encoding a TCR β chain is not expressed,
- 5 optionally wherein the endogenous gene encoding a TCR α chain and/or the endogenous gene encoding a TCR β chain is disrupted by insertion of an expression cassette comprising a polynucleotide sequence encoding a TCR of any one of claims 1-11,
- further optionally wherein one or more endogenous genes encoding an MHC is disrupted,
- further optionally wherein an endogenous gene involved in persistence, expansion, activity,
 10 resistance to exhaustion/senescence/inhibitory signals, homing capacity, or other T-cell functions is disrupted, preferably wherein the endogenous gene involved in persistence, expansion, activity, resistance to exhaustion/senescence/inhibitory signals, homing capacity, or other T-cell functions is selected from the group consisting of *PD1*, *TIM3*, *LAG3*, *2B4*, *KLRG1*, *TGF β R*, *CD160* and *CTLA4*.
- 15 **22.** A method of preparing a cell, which comprises the step of introducing a vector according to claim 16 and/or 17 into a cell *in vitro*, *ex vivo* or *in vivo*, e.g. by transfection or transduction.
- 23.** A method of preparing a cell according to claim 22, which comprises the step of T-cell editing, which comprises disrupting an endogenous gene encoding a TCR α chain
 20 and/or an endogenous gene encoding a TCR β chain with an artificial nuclease, preferably wherein the artificial nuclease is selected from the group consisting of zinc finger nucleases (ZFN), transcription activator-like effector nucleases (TALEN) and CRISPR/Cas systems.
- 24.** A method of preparing a cell according to claim 23, which comprises the step of targeted integration of an expression cassette into the endogenous gene encoding the TCR
 25 α chain and/or the endogenous gene encoding the TCR β chain disrupted by the artificial nuclease, wherein the expression cassette comprises a polynucleotide sequence encoding a TCR of any one of claims 1-11.
- 25.** A method of preparing a cell according to any one of claims 22-24, which comprises the step of disrupting one or more endogenous genes encoding an MHC, preferably wherein
 30 the cell prepared by the method is a non-alloreactive universal T-cell.
- 26.** A method of preparing a cell according to any one of claims 22-25, which comprises the step of disrupting one or more endogenous genes to modify the persistence, expansion,

activity, resistance to exhaustion/senescence/inhibitory signals, homing capacity, or other T-cell functions, preferably wherein the method comprises the step of targeted integration of an expression cassette into an endogenous gene involved in persistence, expansion, activity, resistance to exhaustion/senescence/inhibitory signals, homing capacity, or other T-cell functions disrupted by an artificial nuclease, wherein the expression cassette comprises a polynucleotide sequence encoding a TCR of any one of claims 1-11, preferably wherein the endogenous gene is selected from the group consisting of *PD1*, *TIM3*, *LAG3*, *2B4*, *KLRG1*, *TGFbR*, *CD160* and *CTLA4*.

27. A cell according to any one of claims 18-21 or a cell prepared by the method of any one of claims 22-26 for use in adoptive cell transfer, preferably adoptive T-cell transfer, optionally wherein the adoptive T-cell transfer is allogenic adoptive T-cell transfer, autologous adoptive T-cell transfer, or universal non-alloreactive adoptive T-cell transfer.

28. A chimeric molecule comprising a TCR of any one of claims 1-11, or a portion thereof, conjugated to a non-cellular substrate, a toxin and/or an antibody, optionally wherein the non-cellular substrate is selected from the group consisting of nanoparticles, exosomes and other non-cellular substrates.

29. A TCR according to any one of claims 1-11, an isolated polynucleotide according to any one of claims 13-15, a vector according to claim 16 or 17, a cell according to any one of claims 18-21, a cell prepared by the method of any one of claims 22-26, or a chimeric molecule according to claim 28 for use in therapy.

30. Use of the TCR according to any one of claims 1-11, an isolated polynucleotide according to any one of claims 13-15, a vector according to claim 16 or 17, a cell according to any one of claims 18-21, a cell prepared by the method of any one of claims 22-26, or a chimeric molecule according to claim 28 in the manufacture of a medicament for treating and/or preventing a disease associated with expression of WT1, optionally wherein the disease associated with expression of WT1 is a proliferative disorder, preferably wherein the proliferative disorder is a hematological malignancy or a solid tumor, preferably wherein the hematological malignancy is selected from the group consisting of acute myeloid leukemia (AML), chronic myeloid leukemia (CML), lymphoblastic leukemia, myelodysplastic syndromes, lymphoma, multiple myeloma, non Hodgkin lymphoma, and Hodgkin lymphoma; or preferably wherein the solid tumor is selected from the group consisting of lung cancer, breast cancer, oesophageal cancer, gastric cancer, colon cancer, cholangiocarcinoma, pancreatic cancer, ovarian cancer, head and neck cancers, synovial sarcoma, angiosarcoma, osteosarcoma, thyroid cancer, endometrial cancer, neuroblastoma, rhabdomyosarcoma, liver

cancer, melanoma, prostate cancer, renal cancer, soft tissue sarcoma, urothelial cancer, biliary cancer, glioblastoma, mesothelioma, cervical cancer, and colorectal cancer.

5 **31.** Use of a TCR according to any one of claims 1-11, an isolated polynucleotide according to any one of claims 13-15, a vector according to claim 16 or 17, a cell according to any one of claims 18-21, a cell prepared by the method of any one of claims 22-26, or a chimeric molecule according to claim 28 in the manufacture of a medicament for treating and/or preventing a disease associated with expression of WT1 in a subject in need thereof, wherein the use comprises that the medicament is to be administered to the subject.

10 **32.** The use of claim 31, wherein the disease associated with expression of WT1 is a proliferative disorder, preferably wherein the proliferative disorder is a hematological malignancy or a solid tumor, preferably wherein the hematological malignancy is selected from the group consisting of acute myeloid leukemia (AML), chronic myeloid leukemia (CML), lymphoblastic leukemia, myelodysplastic syndromes, lymphoma, multiple myeloma, non Hodgkin lymphoma, and Hodgkin lymphoma; or preferably wherein the solid tumor is
15 selected from the group consisting of lung cancer, breast cancer, oesophageal cancer, gastric cancer, colon cancer, cholangiocarcinoma, pancreatic cancer, ovarian cancer, head and neck cancers, synovial sarcoma, angiosarcoma, osteosarcoma, thyroid cancer, endometrial cancer, neuroblastoma, rhabdomyosarcoma, liver cancer, melanoma, prostate cancer, renal cancer, soft tissue sarcoma, urothelial cancer, biliary cancer, glioblastoma,
20 cervical cancer, mesothelioma and colorectal cancer.

25 **33.** An isolated immunogenic WT1 peptide comprising an amino acid sequence selected from the group consisting of EPASQHTRLRSG (SEQ ID NO: 123) YESDNHTTPIL (SEQ ID NO: 126), NHTTPILCGAQYRIH (SEQ ID NO: 127), QCLSAFTVHFSGQFT (SEQ ID NO: 118), EDPMGQQGSLGEQQY (SEQ ID NO: 119), SQLECMTWNQMNLGA (SEQ ID NO: 120), APVLDFAPPGA (SEQ ID NO: 117), NQMNLGATLKG (SEQ ID NO: 250), DPGGIWAKLGAAEAS (SEQ ID NO: 251), NHTTPILCGAQYRIH (SEQ ID NO: 252), KRHRRRHTGVKPFQC (SEQ ID NO: 253), PSCQKKFARSDELVR (SEQ ID NO: 254) and variants thereof each having up to three amino acid substitutions, additions or deletions.