CLAIMS

What is claimed is:

1. An antigen-binding protein specific for a WT1 peptide/HLAcomplex, wherein the antigen binding protein is a full length antibody, a Fab fragment, a Fab' fragment or a $F(ab)_2$ fragment.

2. An antigen-binding protein specific for a WT1 peptide/HLA complex, wherein the antigen binding protein comprises:

(A) (i) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 38, 39 and 40; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences selected from SEQ ID NOS: 44, 45 and 46;

(ii) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 2, 3, and 4; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 8, 9 and 10;

(iii) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 20, 21and 22; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 26, 27 and 28;

(iv) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 56, 57 and 58; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 62, 63 and 64;

(v) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 74, 75 and 76; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 80, 81 and 82; or

(vi) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 92, 93 and 94; and a

light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 98, 99 and 100; or

(B) a V_H and V_L comprising first and second amino acid sequences, respectively, selected from SEQ ID NOS: 50 and 52; 14 and 16; 32 and 34; 68 and 70; 86 and 88; and 104 and 106; or

(C) an amino acid sequence selected from SEQ ID NOS: 54, 18, 36, 72, 90, and 108.

3. The antigen-binding protein of claim 2, wherein the antigen-binding protein is a full-length antibody or is an antigen-binding fragment of said antibody selected from the group consisting of Fab, Fab', $F(ab')_2$, Fv and single chain Fv (scFv) or is a chimeric antigen receptor.

~~1. An isolated antibody, or antigen-binding fragment thereof, comprising one of:~~

~~(A) (i) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 2, 3, and 4; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 8, 9 and 10;~~

~~(ii) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 20, 21and 22; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 26, 27 and 28;~~

~~(iii) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 38, 39 and 40; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences selected from SEQ ID NOS: 44, 45 and 46;~~

~~(iv) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 56, 57 and 58; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 62, 63 and 64;~~

~~(v) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 74, 75 and~~

~~76; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 80, 81 and 82; or~~

~~(vi) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 92, 93 and 94; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 98, 99 and 100; or~~

~~(B) a V_H and V_L comprising first and second amino acid sequences, respectively, selected from SEQ ID NOS: 14 and 16; 32 and 34; 50 and 52; 68 and 70; 86 and 88; and 104 and 106; or~~

~~(C) an amino acid sequence selected from SEQ ID NOS: 18, 36, 54, 72, 90, and108.~~

~~2. An isolated antibody, or antigen-binding fragment thereof, comprising:~~

~~(A) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences selected from SEQ ID NOS: (i) 2, 3, and 4; (ii) 20, 21and 22; (iii) 38, 39 and 40; (iv) 56, 57 and 58; (v) 74, 75 and 76 ; and (vi) 92, 93 and 94; and~~

~~(B) a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences selected from SEQ ID NOS: (i) 8, 9 and 10; (ii) 26, 27 and 28; (iii) 44, 45 and 46; (iv) 62, 63 and 64; (v) 80, 81 and 82; and (vi) 98, 99 and 100.~~

~~3. An isolated antibody, or antigen-binding fragment thereof, comprising:~~

~~a V_H and V_L comprising first and second amino acid sequences, respectively, selected from SEQ ID NOS: (i) 14 and 16; (ii) 32 and 34; (iii) 50 and 52; (iv) 68 and 70; (v) 86 and 88; and (vi) 104 and 106.~~

~~4. An isolated antibody, or antigen-binding fragment thereof, comprising an amino acid sequence selected from SEQ ID NOS: 18, 36, 54, 72, 90, and108.~~

4.~~5.~~ The antigen-binding protein~~antibody~~ of any one of claims ~~1 to 4~~1 to 3, wherein the antigen-binding protein~~antibody~~ comprises a human variable region framework region.

5.~~6.~~ The antigen-binding protein~~antibody~~ of any one of claims ~~1 to 4~~1 to 3, wherein the antigen-binding protein~~antibody~~ is fully human.

~~7. The antibody of any of claims 1 to 4, wherein said antibody specifically binds to an WT1 peptide bound to HLA-A2.~~

6.~~8.~~ The antigen-binding protein~~antibody~~ of any preceding claim~~claim 7~~, wherein said WT1 peptide has the amino acid sequence RMFPNAPYL.

7.~~9.~~ The antigen-binding protein~~antibody~~ of any preceding claim~~claim 7~~, wherein said HLA-A2 is HLA-A0201.

~~10. The antibody of any of claims 1 to 9, wherein the antigen-binding fragment of said antibody is an Fab, Fab', $F(ab')_2$, Fv or single chain Fv (scFv).~~

8.~~11.~~ The antigen-binding protein~~antibody~~ of any one of claims ~~1 to 9~~1 to 7 conjugated to a therapeutic agent.

9.~~12.~~ The antigen-binding protein~~antibody~~ of claim ~~11~~8, wherein said therapeutic agent is a drug, toxin, radioisotope, protein, or peptide.

10.~~13.~~ An isolated nucleic acid that encodes an antigen-binding protein~~antibody~~ of any one of claims ~~1 to 4~~1 to 7.

11.~~14.~~ An isolated nucleic acid comprising:

(A) (i) first, second and third nucleotide sequences selected from the group consisting of SEQ ID NOS: 41, 42 and 43; 5, 6 and 7; 23, 24 and 25; ~~41, 42 and 43;~~ 58, 59 and 60; 77, 78 and 79; and 95, 96 and 97; and

(ii) fourth, fifth and sixth nucleotide sequences selected from the group consisting of SEQ ID NOS: 47, 48 and 49; 11, 12 and 13; 29, 30 and 31; ~~47, 48 and 49;~~ 65, 66 and 67; 83, 84 and 85; and 101, 102 and 103; or

(B) first and second nucleotide sequences selected from the group consisting of SEQ ID NOS: 51 and 53; 15 and 17; 33 and 35; ~~51 and 53;~~ 69 and 71; 87 and 89 and 105 and 107; or

(C) a nucleotide sequence selected from the group consisting of SEQ ID NOS: 55, 19, 37, ~~55,~~ 73, 91 and 109.

~~15. An isolated nucleic acid comprising:~~

~~(A) first, second and third nucleotide sequences selected from the group consisting of SEQ ID NOS: (i) 5, 6 and 7; (ii) 23, 24 and 25; (iii) 41, 42 and 43; (iv) 58, 59 and 60; (v) 77, 78 and 79; and (vi) 95, 96 and 97; and~~

~~(B) fourth, fifth and sixth nucleotide sequences selected from the group consisting of SEQ ID NOS: (vii) 11, 12 and 13; (viii) 29, 30 and 31; (ix) 47, 48 and 49; (x) 65, 66 and 67; (xi) 83, 84 and 85; and (xii) 101, 102 and 103.~~

~~16. The nucleic acid of claim 15, wherein said first, second and third nucleotide sequences encode HC-CDR1, HC-CDR2 and HC-CDR3, respectively of an antibody and said fourth, fifth and sixth nucleotide sequences encodes LC-CDR1, LC-CDR2 and LC-CDR3, respectively of said antibody.~~

~~17. An isolated nucleic acid comprising first and second nucleotide sequences respectively, selected from the group consisting of SEQ ID NOS: (i) 15 and 17; (ii) 33 and 35; (iii) 51 and 53; (iv) 69 and 71; (v) 87 and 89 and (vi)105 and 107.~~

~~18. The nucleic acid of claim 17, wherein said first nucleotide sequence encodes a V_H, and said second nucleotide sequence encodes a V_L of an antibody.~~

~~19. An isolated nucleic acid, comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS: 19, 37, 55, 73, 91 and 109.~~

~~20. The nucleic acid of claim 19, wherein said nucleic acid encodes an scFv.~~

12.~~21.~~ A vector comprising a nucleic acid of ~~any one of claims 13 to 20~~claim 10 or claim 11.

13.~~22.~~ A cell comprising a nucleic acid of ~~any one of claims 13 to 20~~claim 10 or claim 11.

14.~~23.~~ The cell of claim ~~22~~13, wherein said cell expresses on its surface an antigen-binding protein~~antibody~~ of any one claims ~~1 to 4~~1 to 3.

15.~~24.~~ ~~A~~An *in vitro* method for detecting WT1 in a whole cell or tissue, said method comprising:

(A) contacting a cell or tissue with an antibody or antigen-binding fragment thereof that specifically binds to a WT1_peptide that is bound to HLA-A2, wherein said antibody comprises a detectable label;

(B) determining the amount of antibody bound to said cell or tissue by measuring the amount of detectable label associated with said cell or tissue, wherein the amount of bound antibody indicates the mount of WT1 in said cell or tissue.

16.~~25.~~ The method of claim ~~24~~15, wherein the antibody specifically binds to a WT1 peptide with the amino acid sequence RMFPNAPYL (SEQ ID NO: 1), bound to HLA-A2.

17.~~26.~~ The method of claim ~~25~~16, wherein the WT1 peptide is bound to HLA-A0201.

18. The method of claim 15, wherein the antibody is a full length antibody, a Fab fragment, a Fab' fragment or a $F(ab)_2$ fragment.

19.~~27.~~ The method of claim ~~24~~15, wherein the antibody is an isolated antibody or antigen-binding fragment thereof comprising one of:

(A) (i) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 38, 39 and 40; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences selected from SEQ ID NOS: 44, 45 and 46;

(ii) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 2, 3~~,~~ and 4; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 8, 9 and 10;

(iii) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 20, 21 and 22; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 26, 27 and 28;

~~(iii) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 38, 39 and 40; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences selected from SEQ ID NOS: 44, 45 and 46;~~

(iv) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 56, 57 and 58; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 62, 63 and 64;

(v) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 74, 75 and 76; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 80, 81 and 82; or

(vi) a heavy chain (HC) variable region comprising HC-CDR1, HC-CDR2 and HC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 92, 93 and 94; and a light chain (LC) variable region comprising LC-CDR1, LC-CDR2 and LC-CDR3 respectively, comprising amino acid sequences SEQ ID NOS: 98, 99 and 100; or

(B) a V_H and V_L comprising first and second amino acid sequences, respectively, selected from SEQ ID NOS: 50 and 52; 14 and 16; 32 and 34; ~~50 and 52;~~ 68 and 70; 86 and 88; and 104 and 106; or

(C) an amino acid sequence selected from SEQ ID NOS: 54, 18, 36, ~~54,~~ 72, 90, and 108.

20. The method of claim 19, wherein the antigen binding protein is a full-length antibody or is an antigen-binding fragment of said antibody selected from the group consisting of Fab, Fab', $F(ab')_2$, Fv and single chain Fv (scFv) or is a chimeric antigen receptor.

21.~~28.~~ A kit comprising an antigen-binding protein~~antibody~~ of any one of claims ~~1 to 4~~1 to 9.

~~29. Use of an antibody of any of claims 1 to 4 for the treatment of a WT1 positive disease.~~

22.~~30.~~ A pharmaceutical composition comprising an antigen-binding protein~~antibody~~ of any one of claims ~~1 to 4~~1 to 9 and a pharmaceutically acceptable carrier.

23.~~31.~~ An antigen-binding protein of any of claims 1 to 9 for use in a ~~A~~ method for treatment of a subject having a WT1-positive disease, ~~comprising administering to the subject a therapeutically effective amount of an antibody or antigen binding fragment thereof of any of claims 1 to 4.~~

~~32. The method of claim 31,~~ wherein the WT1-positive disease is a chronic leukemia or acute leukemia or $WT1^+$ cancer; or~~.~~

~~33. The method of claim 31, wherein~~ the WT1-positive disease is selected from the group consisting of chronic myelocytic leukemia, multiple myeloma (MM), acute lymphoblastic leukemia (ALL), acute myeloid/myelogenous leukemia (AML), myelodysplastic syndrome (MDS), mesothelioma, ovarian cancer, gastrointestinal cancers, breast cancer, prostate cancer and glioblastoma.

24.~~34.~~ The antigen-binding protein for use according to~~method of claim 34~~ claim 22, wherein said antibody is a conjugate having a cytotoxic moiety linked thereto.

~~35. A method for treatment of a subject having a WT1-positive disease, comprising administering to the subject a therapeutically effective amount of a nucleic acid of any of claims 13 to 20.~~

25.~~36.~~ A nucleic acid of claim 10 or claim 11 for use in a method for treatment of a subject having a WT1-positive disease, ~~The method of claim 35,~~ wherein the WT1-positive disease is a chronic leukemia, acute leukemia or WT^+ cancer~~.~~;

~~37. The method of claim 35, wherein~~or the WT1-positive disease is selected from the group consisting of chronic myelocytic leukemia, multiple myeloma, acute lymphoblastic leukemia (ALL), acute myeloid/myelogenous leukemia (AML), myelodysplastic syndrome (MDS), mesothelioma, ovarian cancer, gastrointestinal cancers, breast cancer, prostate cancer and glioblastoma.

~~38. Use of a nucleic acid of any of claims 13 to 20 for the treatment of a WT1 positive disease.~~

26.~~39.~~ A pharmaceutical composition comprising a nucleic acid of ~~any of claims 13 to 20~~claim 10 or claim 11.

27.~~40.~~ ~~A~~An *in vitro* method for killing a $WT1^+$ cell, said method comprising~~:~~
contacting the cell with an antigen-binding protein of any one of claims 1 to 9.~~antibody or antigen-binding fragment thereof that specifically binds to a WT1peptide that is bound to HLA-A2.~~

28.~~41.~~ The method of claim ~~40~~27, wherein said antibody or antigen-binding fragment thereof has a cytotoxic moiety linked thereto.