

## CLAIMS

1. ~~1. An antigen binding protein which specifically binds to a MAGE-A antigenic peptide comprising or consisting of the amino acid sequence 'KVLEHVVRV' of SEQ ID NO: 1, wherein said antigenic peptide is in a complex with a major histocompatibility complex (MHC) protein, the antigen binding protein comprising~~

a) ~~a first polypeptide chain comprising a first variable domain comprising three complementary determining regions (CDRs) CDRa1, CDRa2 and CDRa3, wherein~~

~~the CDRa1 comprises or consists of the amino acid sequence 'X<sub>1</sub>SSSTY' SEQ ID NO: 72, wherein X<sub>1</sub> is any amino acid, or an amino acid sequence differing from SEQ ID NO: 72 by at least one amino acid substitution,~~

~~the CDRa2 comprises or consists of the amino acid sequence 'IX<sub>1</sub>SX<sub>2</sub>X<sub>3</sub>DX<sub>4</sub>' SEQ ID NO: 73, wherein X<sub>1</sub> to X<sub>4</sub> is any amino acid,~~

~~the CDRa3 comprises or consists of the amino acid sequence 'CAEX<sub>1</sub>X<sub>2</sub>SX<sub>3</sub>SKIIF' SEQ ID NO: 77, wherein X<sub>1</sub> to X<sub>3</sub> is any amino acid, with the proviso that the CDRa3 does not comprise or consist of the amino acid sequence 'CAEYSSASKIIF' (SEQ ID NO: 7) if CDRa1 comprises or consists of the amino acid sequence SEQ ID NO: 5 and CDRa2 comprises or consists of the amino acid sequence SEQ ID NO: 6, preferably with the proviso that the CDRa3 does not comprise or consist of the amino acid sequence 'CAEYSSASKIIF' (SEQ ID NO: 7),~~

(b) ~~a second polypeptide chain comprising a second variable domain comprising three CDRs CDRb1, CDRb2 and CDRb3, wherein~~that together form two antigen binding sites,

~~the CDRb1~~wherein the first polypeptide chain comprises or consists of a structure represented by the formula:

$$\underline{V_3-L_1-V_4[I]}$$

wherein V<sub>3</sub> is an antibody variable light chain domain; V<sub>4</sub> is a T cell receptor (TCR) beta variable domain comprising a complementary determining region (CDR)1 comprising the amino acid sequence 'X<sub>1</sub>GHDY' of SEQ ID NO: 78 wherein X<sub>1</sub> is any amino acid, or an amino acid sequence differing from SEQ ID NO: 78 by at least one amino acid substitution, 71; and; L<sub>1</sub> is a linker; and wherein the second polypeptide chain comprises a structure represented by the formula:

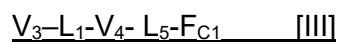
$$\underline{V_5-L_3-V_6[III]}$$

wherein V<sub>5</sub> is a TCR alpha variable domain comprising a CDR1 comprising the amino acid sequence of SEQ ID NO: 5, a CDR2 comprising the amino acid sequence of SEQ ID NO: 56, and a CDR3 comprising the amino acid sequence of SEQ ID NO: 35; V<sub>6</sub> is an antibody variable heavy chain domain; and L<sub>3</sub> is a linker; and wherein the antibody

variable light chain domain (V3) and the antibody variable heavy chain domain (V6) form together one antigen binding site that binds specifically to the human TCR-CD3 complex, and wherein the TCR beta variable domain (V4) and the TCR alpha variable domain (V5) form together one antigen binding site that binds specifically to a MAGE-A antigenic peptide consisting of the amino acid sequence KVLEHVVRV according to SEQ ID NO: 1 in a complex with a human major histocompatibility complex (MHC) protein.

2. The antigen binding protein according to claim 1, \_\_\_\_\_

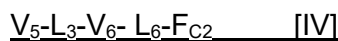
wherein the CDRb2 first polypeptide chain comprises or consists of a structure represented by the amino acid sequence 'FX<sub>1</sub>X<sub>2</sub>X<sub>3</sub>X<sub>4</sub>P' SEQ ID NO: 79, wherein X<sub>1</sub> to X<sub>4</sub> is any amino acid, formula :



and the second polypeptide chain comprises a structure represented by the formula :

\_\_\_\_\_ the CDRb3 comprises or consists of the amino acid sequence 'CASRAX<sub>4</sub>TGELFF' SEQ ID NO: 82, wherein X<sub>4</sub> is any amino acid or an amino acid sequence differing from SEQ ID NO: 82 by at least one amino acid substitution.

2. The antigen binding protein according to claim 1, wherein said antigen binding protein specifically binds to the amino acid sequence 'KVLEHVVRV' of SEQ ID NO: 1 of said antigenic peptide and wherein said antigenic peptide is in a complex with a MHC protein, and wherein, preferably, the MHC protein is a human leukocyte antigen (HLA) protein, preferably HLA-A\*02.



wherein V<sub>3</sub>, L<sub>1</sub>, V<sub>4</sub>, V<sub>5</sub>, L<sub>3</sub> and V<sub>6</sub>, are as defined in claim 1 and wherein L<sub>5</sub> and L<sub>6</sub> are linkers and present or absent and F<sub>C1</sub>, and F<sub>C2</sub> are Fc-domains and wherein F<sub>C1</sub> and F<sub>C2</sub> are the same or different.

3. The antigen binding protein according to claim 1 or 2, wherein said antigen binding protein specifically binds to an epitope comprising or consisting of at least three amino acid positions of the MAGE-A antigenic peptide of SEQ ID NO: 1, preferably, at least three amino acid positions selected from the group of amino acid positions consisting of the amino acid positions 1, 5, 7 and 8 or 1, 3, 5 and 7 of the amino acid sequence of SEQ ID NO: 1.

4. ~~An antigen binding protein according to any of claims 1 to 3, wherein said antigen binding protein binds to a complex of said MAGE-A antigenic peptide comprising or consisting of the amino acid sequence of SEQ ID NO: 1 and HLA-A\*02, with a  $K_D$  which is  $\leq 100 \mu\text{M}$ ,  $\leq 50 \mu\text{M}$ ,  $\leq 30 \mu\text{M}$ ,  $\leq 25 \mu\text{M}$ ,  $\leq 1 \mu\text{M}$ ,  $\leq 500\text{nM}$ ,  $\leq 100\text{nM}$ ,  $\leq 50\text{nM}$ ,  $\leq 10\text{nM}$ , preferably  $50\text{pM}$  to  $100\mu\text{M}$ ,  $50\text{pM}$  to  $10\mu\text{M}$ ,  $50\text{pM}$  to  $1\mu\text{M}$ , more preferably,  $50\text{pM}$  to  $500\text{nM}$ ,  $50\text{pM}$  to  $400\text{nM}$ ,  $50\text{pM}$  to  $50\text{nM}$  and  $50\text{pM}$  to  $10\text{nM}$ .~~

5. ~~An antigen binding protein according to any of claims 1 to 4, wherein said antigen binding protein has an  $\text{EC}_{50}$  value for MAGE-A/MHC complex presenting cells which is less than  $400\text{nM}$ , less than  $50\text{nM}$ , less than  $10\text{nM}$ , less than  $900\text{pM}$ , less than  $500\text{pM}$ , less than  $300\text{pM}$ , less than  $200\text{pM}$ , less than  $150\text{pM}$ , less than  $100\text{pM}$ , less than  $50\text{pM}$ , less than  $20\text{pM}$ , less than  $10\text{pM}$ , such as between  $0.1\text{nM}$  and  $20\text{nM}$ , such as  $0.5\text{nM}$  and  $15\text{nM}$ ,  $0.8\text{nM}$  and  $12\text{nM}$ ,  $0.8\text{nM}$  and  $10\text{nM}$ ,  $0.8\text{nM}$  and  $10\text{nM}$ ,  $0.8\text{nM}$  and  $10\text{nM}$  or such as between  $1\text{pM}$  and  $150\text{pM}$ ,  $1\text{pM}$  and  $100\text{pM}$ ,  $1\text{pM}$  and  $50\text{pM}$ ,  $1\text{pM}$   $V_3$  and  $20\text{pM}$ ,  $1\text{pM}$  and  $20\text{pM}$   $V_6$  are humanized.~~

64. ~~The antigen binding protein according to any one of claimclaims 1 to 5-3, wherein the antigen binding proteins does not significantly bind to the peptides selected from the list consisting of RABGAP1L-001, AXIN1-001, ANO5-001, TPX2-001, SYNE3-001, MIA3-001, HERC4-001, PSME2-001, HEATR5A-001, CNOT1-003, TEP1-003, PITPNM3-001, INTS4-002, SAMH-001, PPP1CA-006, RPL-007, SETD1A-001, NOMAP-1-0320, NOMAP-1-1223 and ODC-001, preferably HEATR5A-001 and CNOT1-003, when said peptide is in a complex with a human MHC protein, preferably in complex with is HLA-A\*02.~~

75. ~~The antigen binding protein according to any one of claim 1 to 6, wherein the antigen binding protein is an antibody or a fragment thereof, or a bispecific antibody or fragment thereof, or a T cell receptor (TCR) or a fragment thereof, or a bispecific T cell receptor (TCR) or fragment thereof. claims 1-4, wherein~~

$V_3$  comprises complementarity determining regions (CDRs) CDR1, CDR2 and CDR3 of SEQ ID NO: 159; and

$V_6$  comprises CDR1, CDR2 and CDR3 of SEQ ID NO: 160.

6. The antigen binding protein according to any one of claims 1-5, wherein

$V_3$  comprises the amino acid sequence of SEQ ID NO: 159 or an amino acid sequence at least 95% identical thereto; and

V<sub>6</sub> comprises the amino acid sequence of SEQ ID NO: 160 or an amino acid sequence at least 95% identical thereto.

7. The antigen binding protein according to claim 6, wherein

V<sub>3</sub> comprises the amino acid sequence of SEQ ID NO: 159; and

V<sub>6</sub> comprises the amino acid sequence of SEQ ID NO: 160.

8. ~~The antigen binding protein according to any one of claims 1 to 7, wherein the first polypeptide and the second polypeptide are covalently or non-covalently linked together.~~ 7, wherein

9. ~~The antigen binding protein according to claim 8, wherein said antigen binding protein is a single chain TCR (scTCR) or a single chain bispecific antibody.~~

10. ~~The antigen binding protein according to any one of claims 1 to 9, wherein said first variable domain further~~ V<sub>5</sub> comprises one or more framework regions selected from the group consisting of FR1-a, FR2-a, FR3-a and FR4-a, wherein

-- FR1-a comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 83 or an amino acid sequence at least 85%, ~~at least 90% or at least 95%~~ identical to SEQ ID NO: 83 thereto,

- FR2-a comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 84 or an amino acid sequence at least 85%, ~~at least 90% or at least 95%~~ identical to SEQ ID NO: 84 thereto,

-- FR3-a comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 85 or an amino acid sequence at least 85%, ~~at least 90% or at least 95%~~ identical to SEQ ID NO: 85, thereto, and/or

-- FR4-a comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 86 or an amino acid sequence at least 85%, ~~at least 90% or at least 95%~~ identical to SEQ ID NO: 86 thereto, and

~~said second variable domain further~~ V<sub>4</sub> comprises one or more framework regions selected from the group consisting of FR1-b, FR2-b, FR3-b and FR4-b, and wherein

- FR1-b comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 87 or an amino acid sequence at least 85%, ~~at least 90% or at least 95%~~ identical to SEQ ID NO: 87 thereto,

- FR2-b comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 88 or an amino acid sequence at least 85%, ~~at least 90% or at least 95%~~ identical to SEQ ID NO: 88 thereto,

- FR3-b comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 89 or an amino acid sequence at least ~~85%, at least 90% or at least 95%~~ identical to ~~SEQ ID NO: 89, thereto, and/or~~
- FR4-b comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 90 or an amino acid sequence at least ~~85%, at least 90% or at least 95%~~ identical to ~~SEQ ID NO: 90 thereto.~~

149. The antigen binding protein according to ~~claim 10~~ any one of claims 1-8, wherein the framework region(s) comprise(s) at least one amino acid substitution selected from the group of amino acid substitutions comprising:

- an amino acid substitution at position 19 in FR1-a, wherein ~~said~~ the amino acid substitution is ~~preferably~~ optionally S19A, S19V, ~~more preferably S19V,~~
  - an amino acid substitution at position 48 and/or 50 in FR2-a, wherein ~~said~~ the amino acid substitution at position 48 is ~~preferably~~ optionally A48K and ~~said~~ the amino acid substitution at position 50 is ~~preferably~~ optionally L50P,
  - an amino acid substitution at position 46, 47 and/or 54 in FR2-b, wherein ~~said~~ the amino acid substitution at position 46, 47 and 54 is ~~preferably~~ optionally M46P, M47G and I54F, respectively, ~~wherein preferably said amino acid at position 54 is I54F when the CDRb3 amino acid sequence as defined above comprises at position 109 the amino acid 109D,~~
  - an amino acid substitution at position 66 in FR3-b, wherein ~~said~~ the amino acid substitution at position 66 is ~~preferably~~ optionally I66C, ~~and wherein preferably said amino acid at position 66 is 66C when the CDRb2 amino acid sequence as defined above comprises at position 57 the amino acid 57C,~~
- and wherein the positions of the substitutions are given according to the IMGT nomenclature.

1210. The antigen binding protein according to ~~claim 11~~ any one of claims 1-9,

wherein ~~said first variable domain further~~ V<sub>5</sub> comprises one or more framework regions selected from the group consisting of FR1-a, FR2-a, FR3-a and FR4-a, wherein

- FR1-a comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 91 or an amino acid sequence at least ~~85~~ 95% identical to SEQ ID NO: 91, wherein ~~preferably said~~ optionally the amino acid sequence at least ~~85~~ 95% identical to SEQ ID NO: 91 comprises the amino acid 19V,
- FR2-a comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 92 or an amino acid sequence at least ~~85~~ 95% identical to SEQ ID NO: 92, wherein ~~preferably said~~ optionally the amino acid sequence at least ~~85~~ 95% identical to

SEQ ID NO: 92 comprises the amino acid 48K and optionally an amino acid substitution at position 50, ~~preferably~~optionally L50P,

-- FR3-a comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 85 or an amino acid sequence at least ~~85~~95% identical to SEQ ID NO: 85, and/or

- FR4-a comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 86 or an amino acid sequence at least ~~85~~95% identical to SEQ ID NO: 86, and ~~said second variable domain further~~V<sub>4</sub> comprises one or more framework regions, ~~preferably framework regions~~, selected from the group consisting of FR1-b, FR2-b, FR3-b and FR4-b, and wherein

-- FR1-b comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 87 or an amino acid sequence at least ~~85~~95% identical to SEQ ID NO: 87,

- FR2-b comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 93 or an amino acid sequence at least ~~85~~95% identical to SEQ ID NO: 93, wherein ~~preferably said~~optionally the amino acid sequence at least ~~85~~95% identical to SEQ ID NO: 93 comprises ~~preferably~~optionally the amino acid 54F, and optionally an amino acid substitution at position 46 and/or 47, wherein ~~said the~~ amino acid substitution at position 46 and/or 47 is ~~preferably~~optionally M46P and/or M47G, respectively,

-- FR3-b comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 89 or an amino acid sequence at least ~~85~~95% identical to SEQ ID NO: 89, or of the amino acid sequence of SEQ ID NO: 94 or an amino acid sequence at least ~~85~~95% identical to SEQ ID NO: 94, wherein ~~preferably said~~optionally the amino acid sequence at least ~~85~~95% identical to SEQ ID NO: 94 comprises the amino acid 66C, and ~~wherein FR3-b preferably comprises /or consists of an amino acid sequence at least 85% identical to SEQ ID NO: 94 comprising the amino acid 66C, when the CDRb2 amino acid sequence as defined above comprises at position 57 the amino acid 57C,~~

- FR4-b comprises ~~or consists of~~ the amino acid sequence of SEQ ID NO: 90 or an amino acid sequence at least ~~85~~95% identical to SEQ ID NO: 90.

~~43~~11. The antigen binding protein according to any one of claims 1 ~~to 42~~10, wherein ~~said first variable domain is part of~~

V<sub>5</sub> comprises one or more framework regions selected from the group consisting of FR1-a-TCR  $\alpha$  or  $\gamma$  chain, FR2-a, FR3-a and/or FR4-a, wherein ~~said second variable domain is part of a TCR  $\beta$~~

FR1-a comprises the amino acid sequence of SEQ ID NO: 91,

FR2-a comprises the amino acid sequence of SEQ ID NO: 92,

FR3-a comprises the amino acid sequence of SEQ ID NO: 85, and/or

FR4-a comprises the amino acid sequence of SEQ ID NO: 86; and

V<sub>4</sub> comprises one or more framework regions selected from the group consisting of FR1-b, FR2-b, FR3-b and FR4-b, and wherein

FR1-b comprises the amino acid sequence of SEQ ID NO: 87,

FR2-b comprises the amino acid sequence of SEQ ID NO: 93,

FR3-b comprises the amino acid sequence of SEQ ID NO: 94, and/or  $\delta$ -chain.

FR4-b comprises the amino acid sequence of SEQ ID NO: 90.

12. The antigen binding protein according to any one of claims 1 to 13, ~~further comprising one or more of the following: 10, wherein~~

~~(i) — one or more further antigen binding sites;~~

~~(ii) — a transmembrane region, optionally including a cytoplasmic signaling region;~~

~~(iii) — a diagnostic agent;~~

~~(iv) — a therapeutic agent; or~~

~~(v) — PK modifying moiety~~ V<sub>5</sub> comprises framework regions FR1-a, FR2-a, FR3-a and FR4-a, wherein

FR1-a comprises the amino acid sequence of SEQ ID NO: 91,

FR2-a comprises the amino acid sequence of SEQ ID NO: 92,

FR3-a comprises the amino acid sequence of SEQ ID NO: 85, and

FR4-a comprises the amino acid sequence of SEQ ID NO: 86; and

V<sub>4</sub> comprises framework regions FR1-b, FR2-b, FR3-b and FR4-b, and wherein

FR1-b comprises the amino acid sequence of SEQ ID NO: 87,

FR2-b comprises the amino acid sequence of SEQ ID NO: 93,

FR3-b comprises the amino acid sequence of SEQ ID NO: 94, and

FR4-b comprises the amino acid sequence of SEQ ID NO: 90.

13=

45. The antigen binding protein according to any one of claims 1-12, wherein

V<sub>3</sub> comprises the amino acid sequence of SEQ ID NO: 159 or an amino acid sequence at least 95% identical thereto;

V<sub>4</sub> comprises the amino acid sequence of SEQ ID NO: 150 or an amino acid sequence at least 95% identical thereto;

V<sub>5</sub> comprises the amino acid sequence of SEQ ID NO: 151 or an amino acid sequence at least 95% identical thereto; and

V<sub>6</sub> comprises the amino acid sequence of SEQ ID NO: 160 or an amino acid sequence at least 95% identical thereto.

14. The antigen binding protein according to claim 13, wherein

V<sub>3</sub> comprises the amino acid sequence of SEQ ID NO: 159;

V<sub>4</sub> comprises the amino acid sequence of SEQ ID NO: 150;

V<sub>5</sub> comprises the amino acid sequence of SEQ ID NO: 151; and

V<sub>6</sub> comprises the amino acid sequence of SEQ ID NO: 160.

15. The antigen binding protein according to any one of claims 1-14, wherein L<sub>1</sub> and L<sub>3</sub> each separately comprises the amino acid sequence of GGGSGGGG (SEQ ID NO: 96).

16. The antigen binding protein according to any one of claims 1-15, wherein F<sub>C1</sub> comprises the amino acid sequence of SEQ ID NO: 112 and F<sub>C2</sub> comprises the amino acid sequence of SEQ ID NO: 113.

17. The antigen binding protein according to any one of claims 1-16, wherein

the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 136 or an amino acid sequence at least 95% identical thereto, and

the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 137 or an amino acid sequence at least 95% identical thereto.

18. The antigen binding protein according to any one of claims 1-17, wherein

the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 136, and

the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 137.

~~19 to 7 and 10 to 13.~~ The antigen binding protein of claim 18, wherein

the first polypeptide chain consists of the amino acid sequence of SEQ ID NO: 136, and

the second polypeptide chain consists of the amino acid sequence of SEQ ID NO: 137.

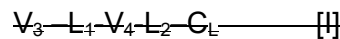
20. The antigen binding protein according to any one of claims 1-19, wherein the first polypeptide and the second polypeptide are covalently bonded by a disulfide bond.

21. An antigen binding protein comprising a first polypeptide chain and a second polypeptide chain that together form two antigen binding sites, wherein

the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 136, and

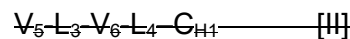
the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 137, wherein one antigen binding site binds specifically to the human TCR-CD3 complex and another antigen binding site binds specifically to an antigenic peptide consisting of the amino acid sequence KVLEHVVRV (SEQ ID NO: 1) in a complex with human major histocompatibility complex (MHC) protein HLA-A\*02.

22. An antigen binding protein comprising two a first polypeptide chain and a second polypeptide chain that together form two antigen binding sites, wherein a first polypeptide chain has a structure represented by the formula:



~~wherein  $V_3$  is a third variable domain;  $V_4$  is a fourth variable domain;  $L_1$  and  $L_2$  are linkers;  $L_2$  may be present or absent;  $C_L$  is a light chain constant domain or a portion thereof and present or absent;~~

~~and wherein a second polypeptide chain has a structure represented by the formula:~~



~~wherein  $V_5$  is a fifth variable domain;  $V_6$  is a sixth variable domain;  $L_3$  and  $L_4$  are linkers;  $L_4$  may be present or absent;  $C_{H1}$  is a heavy chain constant domain 1 or a portion thereof and is present or absent; and wherein~~

~~$V_3$  or  $V_4$  is a first variable domain as defined in claim 1 and  $V_5$  or  $V_6$  is a second variable domain as defined in claim 1, or~~

~~$V_5$  or  $V_6$  is a first variable domain as defined in claim 1 and  $V_3$  or  $V_4$  is a second variable domain as defined in claim 1, and wherein~~

~~$V_3$  is polypeptide chain consists of the first variable domain and  $V_5$  is the second variable domain in claim 1, and  $V_4$  is a light chain variable domain and  $V_6$  is a heavy chain variable domain or  $V_4$  is a heavy chain variable domain and  $V_6$  is a light chain variable domain, or, amino acid sequence of SEQ ID NO: 136, and~~

~~$V_3$  is the second variable domain and  $V_5$  is the first variable domain in claim 1, and  $V_4$  is a light chain variable domain and  $V_6$  is a heavy chain variable domain or  $V_4$  is a heavy chain variable domain and  $V_6$  is a light chain variable domain, or,~~

~~$V_3$  is the first variable domain and  $V_6$  is the second variable domain in claim 1, and  $V_4$  is a light~~  
the second polypeptide chain consists of the amino acid sequence of SEQ ID NO: 137, wherein one antigen binding site binds specifically to the human TCR-CD3 complex and another antigen binding site binds specifically to an antigenic peptide consisting of the amino acid sequence KVLEHVVRV (SEQ ID NO: 1) in a complex with human major histocompatibility complex (MHC) protein HLA-A\*02.

23. An antigen binding protein consisting of a first polypeptide chain variable domain and V<sub>5</sub> is a heavy chain variable domain or V<sub>4</sub> is a heavy chain variable domain and V<sub>5</sub> is a light chain variable domain, or

V<sub>3</sub> is the second variable domain and V<sub>6</sub> is the first variable domain in claim 1, and V<sub>4</sub> is a light chain variable domain and V<sub>5</sub> is a heavy chain variable domain or V<sub>4</sub> is a heavy chain variable domain and V<sub>5</sub> is a light chain variable domain,

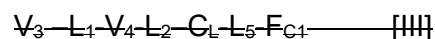
V<sub>4</sub> is the first variable domain and V<sub>5</sub> is the and a second variable domain in claim 1, and V<sub>3</sub> is a light chain variable domain and V<sub>6</sub> is a heavy chain variable domain or V<sub>3</sub> is a heavy chain variable domain and V<sub>6</sub> is a light chain variable domain, or

V<sub>4</sub> is the second variable domain and V<sub>5</sub> is the first variable domain in claim 1, and V<sub>3</sub> is a light chain variable domain and V<sub>6</sub> is a heavy chain variable domain or V<sub>3</sub> is a heavy chain variable domain and V<sub>6</sub> is a light chain variable domain,

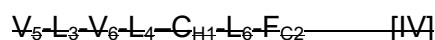
and wherein the light chain variable domain and the heavy chain variable domain form together one antigen binding site, and wherein the first and second variable domain form together one antigen binding site.

46. The antigen binding protein according to claim 15, wherein said heavy chain variable domain and said light chain variable domain bind to an antigen selected from the group consisting of CD3 (such as the CD3γ, CD3δ, and CD3ε chains), CD4, CD7, CD8, CD10, CD11b, CD11c, CD14, CD16, CD18, CD22, CD25, CD28, CD32a, CD32b, CD33, CD41, CD41b, CD42a, CD42b, CD44, CD45RA, CD49, CD55, CD56, CD61, CD64, CD68, CD94, CD90, CD117, CD123, CD125, CD134, CD137, CD152, CD163, CD193, CD203c, CD235a, CD278, CD279, CD287, Nkp46, NKG2D, GITR, FcεRI, TCRα/β and TCRγ/δ, HLA-DR and/or bind to an effector cell.

47. The antigen binding protein according to claim 15 or 16, comprising two polypeptide chainschain that together form two antigen binding sites, wherein wherein onethe first polypeptide chain has a structure represented by the formula [III]:



comprises the amino acid sequence of SEQ ID NO: 136, and one polypeptide chain has a structure represented by the formula [IV]:



wherein V<sub>3</sub>, L<sub>1</sub>, V<sub>4</sub>, L<sub>2</sub>, C<sub>L</sub>, V<sub>5</sub>, L<sub>3</sub>, V<sub>6</sub>, L<sub>4</sub> and C<sub>H4</sub>, are as defined in the preceding claims and wherein L<sub>5</sub> and L<sub>6</sub> are linkers and present or absent and F<sub>C1</sub>, and F<sub>C2</sub> are Fc domains and wherein F<sub>C1</sub> and F<sub>C2</sub> are the same or different.

18. ~~The antigen binding protein according to claim 17, wherein V<sub>3</sub> is the first variable domain and V<sub>6</sub> is the second variable domain as defined in the preceding claims, and V<sub>4</sub> is a light chain variable domain and V<sub>5</sub> is a heavy chain variable domain, or~~

V<sub>3</sub> is the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 137, wherein one antigen binding site binds specifically to the human TCR-CD3 complex and the other antigen binding site binds specifically to an antigenic peptide consisting of the amino acid sequence KVLEHVVRV (SEQ ID NO: 1) in a complex with human major histocompatibility complex (MHC) protein HLA-A\*02.

24. An antigen binding protein consisting of a first polypeptide chain and a second polypeptide chain that together form two antigen binding sites, wherein

~~the first variable domain and V<sub>6</sub> is the second variable domain as defined in the preceding claims, and V<sub>4</sub> is a heavy polypeptide chain variable domain and V<sub>5</sub> is a light chain variable domain, and wherein L<sub>1</sub> and L<sub>2</sub> comprise or consist of the amino acid sequence 'GGGSGGGG' of SEQ ID NO: 96, and wherein L<sub>3</sub>, L<sub>5</sub>, L<sub>4</sub> and L<sub>6</sub> are absent, and wherein F<sub>C1</sub> comprises or consists of the amino acid sequence of SEQ ID NO: 113, when V<sub>4</sub> is a heavy~~  
136, and

~~the second polypeptide chain variable domain and F<sub>C2</sub> comprises or consists of the amino acid sequence SEQ ID NO: 112 when V<sub>5</sub> is a light chain variable domain, or of SEQ ID NO: 137, wherein one antigen binding site binds specifically to the human TCR-CD3 complex and the other antigen binding site binds specifically to an antigenic peptide consisting of the amino acid sequence KVLEHVVRV (SEQ ID NO: 1) in a complex with human major histocompatibility complex (MHC) protein HLA-A\*02.~~

~~F<sub>C1</sub> comprises or consists of the amino acid sequence SEQ ID NO: 112, when V<sub>4</sub> is a light chain variable domain and, F<sub>C2</sub> comprises or consist of the amino acid sequence SEQ ID NO: 113 when V<sub>5</sub> is a heavy chain variable domain~~  
25.

49. An isolated nucleic acid or isolated nucleic acids comprising a sequence encoding for an antigen binding protein according to any one of claims 1 to 48, or a nucleic acid vector comprising said isolated nucleic acid or isolated nucleic acids.

2026. A recombinant host cell comprising an antigen binding protein according to any one of claims 1 to 48, or a nucleic acid, isolated nucleic acids or a vector according to claim 49, wherein said host cell preferably is

a) a lymphocyte, such as preferably a T lymphocyte or T lymphocyte progenitor cell, for example a CD4 or CD8 positive T cell or b) or

b) a cell for recombinant expression, such as preferably a Chinese Hamster Ovary (CHO) cell.

2427. The recombinant host cell according to claim 26, wherein the T lymphocyte is a CD4 or CD8 positive T cell.

28. A composition comprising the antigen binding protein of according to any one of claims 1 to 24, or the isolated nucleic acid or the isolated nucleic acids of claim 25.

29. A pharmaceutical composition comprising the antigen binding protein according to any one of claims 1 to 4824, the isolated nucleic acid, isolated nucleic acids or vector according to claim 4925, or the host cell according to claim 2026 or 27, and a pharmaceutically acceptable carrier, diluent stabilizer, and/or excipient.

2230. A method of producing the antigen binding protein according to any one of claims 1 to 4824, comprising

- a. providing a suitable host cell,
- b. providing a genetic construct comprising a coding sequence encoding the antigen binding protein according to any of claims 1 to 4824,
- c. introducing said genetic construct into said suitable host cell, and
- d. expressing said genetic construct by said suitable host cell.

2331. The method according to claim 2230, further comprising the isolation and purification of the antigen binding protein from the suitable host cell and, optionally, reconstitution of the antigen binding protein in a T cell.

2432. The antigen binding protein according to any one of claims 1 to 4824, the nucleic acid or vector according to claim 4925, the host cell according to claim 2026 or 27 or the pharmaceutical composition according to claim 2429 for use in medicine.

2533. The antigen binding protein according to any one of claims 1 to 4824, the isolated nucleic acid, isolated nucleic acids or vector according to claim 4925, the host cell according to claim 2026 or 27, or the pharmaceutical composition according to claim 2429 for use in the diagnosis, ~~prevention, and/or treatment~~ of a proliferative disease, ~~such as preferably~~ cancer, ~~such as more preferably~~ a MAGEA4 and/or MAGEA8 positive cancer.

26. The antigen binding protein according to claim 2534. The antigen binding protein, the isolated nucleic acid, isolated nucleic acids or vector, the host cell, or the pharmaceutical composition for use according to claim 33, wherein said cancer is selected from the group consisting of lung cancer, liver cancer, head and neck cancer, skin cancer, renal cell cancer, brain cancer, gastric cancer, colorectal cancer, pancreatic cancer, prostate cancer, leukemia, breast cancer, Merkel cell carcinoma, ovarian cancer, urinary bladder cancer, uterine cancer, gallbladder cancer, bile duct cancer, osteosarcoma cancer, and esophageal cancer.

35. The antigen binding protein, the isolated nucleic acid, isolated nucleic acids or vector, the host cell; or the pharmaceutical composition for use according to claim 34, wherein  
 (i) lung cancer is non-small cell lung cancer (NSCLC), preferably non-small cell lung cancer adenocarcinoma or squamous cell non-small cell lung cancer (SNSCLC); or small cell lung cancer (SCLC);  
 (ii) skin cancer is melanoma;  
 (iii) head and neck cancer is head and neck squamous cell carcinoma (HNSCC);  
 (iv) liver cancer is hepatocellular cancer (HCC);  
 (v) esophageal cancer is gastroesophageal junction cancer.

36. Use of the antigen binding protein according to any one of claims 1 to 24, the isolated nucleic acid, isolated nucleic acids or vector according to claim 25, the host cell according to claim 26 or 27, or the pharmaceutical composition according to claim 29 in the manufacture of a medicament for the treatment of a proliferative disease, wherein the medicament is for the diagnosis of the proliferative disease, and wherein the proliferative disease is preferably cancer, more preferably a MAGEA4 and/or MAGEA8 positive cancer.

37. Use of the antigen binding protein according to any one of claims 1 to 24, the isolated nucleic acid, isolated nucleic acids or vector according to claim 25, the host cell according to claim 26 or 27, or the pharmaceutical composition according to claim 29 in the manufacture of a medicament for the prevention, and/or treatment of a proliferative disease, preferably cancer, more preferably a MAGEA4 and/or MAGEA8 positive cancer.

38. Use of the antigen binding protein, the isolated nucleic acid, isolated nucleic acids or vector, the host cell, or the pharmaceutical composition according to claim 36 or 37, wherein said cancer is selected from the group consisting of lung cancer, liver cancer, head and neck cancer, skin cancer, renal cell cancer, brain cancer, gastric cancer,

colorectal cancer, pancreatic cancer, prostate cancer, leukemia, breast cancer, Merkel cell carcinoma, ovarian cancer, urinary bladder cancer, uterine cancer, gallbladder cancer, bile duct cancer, osteosarcoma cancer, and esophageal cancer.

5 ~~27.~~ 39. Use of the antigen binding protein, the isolated nucleic acid, isolated nucleic acids or vector, the host cell; or the pharmaceutical composition according to claim ~~26~~38, wherein

- (i) lung cancer is non-small cell lung cancer (NSCLC), preferably non-small cell lung cancer adenocarcinoma or squamous cell non-small cell lung cancer (SNSCLC);
- 10 or small cell lung cancer (SCLC);
- (ii) skin cancer is melanoma;
- (iii) head and neck cancer is head and neck squamous cell carcinoma (HNSCC);
- (iv) liver cancer is hepatocellular cancer (HCC);
- 15 (v) esophageal cancer is gastroesophageal junction cancer.