

CLAIMS

1. A humanized anti-HLA-A2 antibody, or an antigen-binding fragment thereof that exhibits reduced binding to one or more HLA-A subtype selected from the group comprising A03, A11, A23, A25, A26, A29, A30, A31, A33, A34 and any combination thereof as compared to the antibody BB7.2 (ATCC Deposit No. HB-82) or to an antibody comprising the VH and VL of the BB7.2 antibody, wherein
 - a) the variable region of the heavy chain (VH) comprises the following CDRs:
 - i. **VH-CDR1**: SEQ ID NO: 1 or SEQ ID NO: 4
 - ii. **VH-CDR2**: SEQ ID NO: 2 or SEQ ID NO: 5
 - iii. **VH-CDR3**: SEQ ID NO: 3, and
 - b) the variable region of the light chain (VL) comprises the following CDRs:
 - i. **VL-CDR1**: SEQ ID NO: 6
 - ii. **VL-CDR2**: SEQ ID NO: 7
 - iii. **VL-CDR3**: SEQ ID NO: 8.
2. The humanized anti-HLA-A2 antibody or antigen-binding fragment according to claim 1, wherein the variable region of the heavy chain comprises the following CDRs:
 - a) SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3; or
 - b) SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 3.
3. The humanized anti-HLA-A2 antibody or antigen-binding fragment according to claim 1 or claim 2, wherein the amino acid sequence of the heavy chain variable region comprises SEQ ID NO: 9 or any amino acid sequence that shares at least 90% identity with said SEQ ID NO: 9.

4. The humanized anti-HLA-A2 antibody or antigen-binding fragment according to any one of claims **1** to **3**, wherein the amino acid sequence of the light chain variable region comprises SEQ ID NO: 10, or any amino acid sequence that shares at least 90% identity with said SEQ ID NO: 10, wherein X₁ is V or I, X₂ is T or S, X₃ is L or S or A, X₄ is S or T, X₅ is P or S, X₆ is T or S, X₇ is L or P, X₈ is E or D, X₉ is P or R, X₁₀ is A or V, X₁₁ is S or T, X₁₂ is L or Q, X₁₃ is S or A, X₁₄ is V or I, X₁₅ is K or T, X₁₆ is V or L, X₁₇ is A or P, X₁₈ is L or F and X₁₉ is G or A.
5. The humanized anti-HLA-A2 antibody or antigen-binding fragment according to any one of claims **1** to **4**, wherein the amino acid sequence of the light chain variable region comprises a sequence selected from the group comprising SEQ ID NO: 11, SEQ ID NO: 12 and SEQ ID NO: 13 or any amino acid sequence that shares at least 90% identity with said SEQ ID NO: 11-13.
6. The humanized anti-HLA-A2 antibody or antigen-binding fragment according to any one of claims **1** to **5**,

wherein the amino acid sequence of the heavy chain variable region comprises SEQ ID NO: 9, and

wherein the amino acid sequence of the light chain variable region comprises SEQ ID NO: 10 wherein X₁ is V or I, X₂ is T or S, X₃ is L or S or A, X₄ is S or T, X₅ is P or S, X₆ is T or S, X₇ is L or P, X₈ is E or D, X₉ is P or R, X₁₀ is A or V, X₁₁ is S or T, X₁₂ is L or Q, X₁₃ is S or A, X₁₄ is V or I, X₁₅ is K or T, X₁₆ is V or L, X₁₇ is A or P, X₁₈ is L or F and X₁₉ is G or A.
7. The humanized anti-HLA-A2 antibody or antigen-binding fragment according to any one of claims **1** to **6**,

wherein the amino acid sequence of the heavy chain variable region comprises SEQ ID NO: 9, and

wherein the amino acid sequence of the light chain variable region comprises a sequence selected from the group comprising SEQ ID NO: 11, SEQ ID NO: 12 and SEQ ID NO: 13.

8. The humanized anti-HLA-A2 antibody or antigen-binding fragment according to any one of claims 1 to 7,

wherein the amino acid sequence of the heavy chain variable region comprises SEQ ID NO: 9, and

5 wherein the amino acid sequence of the light chain variable region comprises SEQ ID NO: 13.
9. The humanized anti-HLA-A2 antibody or antigen-binding fragment according to any one of claims 1 to 8, wherein said antibody or antigen-binding fragment is a whole antibody, a single chain antibody, a dimeric single chain antibody, a Fv, a
10 scFv, a Fab, a F(ab)₂, a defucosylated antibody, a bi-specific antibody, a diabody, a triabody, a tetrabody, an antibody fragment selected from the group consisting of a unibody, a domain antibody, and a nanobody or an antibody mimetic selected from the group consisting of an affibody, an alphabody, an armadillo repeat protein based scaffold, a knottin, a kunitz domain peptide, an affilin, an affitin, an adnectin,
15 an atrimer, an evasin, a DARPin, an anticalin, an avimer, a fynomer, a versabody or a duocalin.
10. The humanized anti-HLA-A2 antibody or antigen-binding fragment according to any one of claims 1 to 9, wherein said antibody or antigen-binding fragment is a scFv.
- 20 11. The humanized anti-HLA-A2 antibody or antigen-binding fragment according to any one of claims 1 to 10, wherein said antibody or antigen-binding fragment is a scFv comprising the sequence SEQ ID NO: 69 or SEQ ID NO: 73, wherein X₁ is V or I, X₂ is T or S, X₃ is L or S or A, X₄ is S or T, X₅ is P or S, X₆ is T or S, X₇ is L or P, X₈ is E or D, X₉ is P or R, X₁₀ is A or V, X₁₁ is S or T, X₁₂ is L or Q, X₁₃ is S
25 or A, X₁₄ is V or I, X₁₅ is K or T, X₁₆ is V or L, X₁₇ is A or P, X₁₈ is L or F, and X₁₉ is G or A.

12. The humanized anti-HLA-A2 antibody or antigen-binding fragment according to any one of claims **1** to **11**, wherein said antibody or antigen-binding fragment is a scFv comprising the sequence SEQ ID NO: 70-72 or 74-76.
13. A chimeric antigen receptor (CAR) comprising:
 - 5 a) an extracellular domain comprising the humanized anti-HLA-A2 antibody or antigen-binding fragment according to any one of claims **1** to **12**,
 - b) a transmembrane domain, and
 - c) a cytoplasmic domain comprising an intracellular signaling domain.
14. The CAR according to claim **13**, wherein the humanized anti-HLA-A2 antibody or antigen-binding fragment is an scFv comprising the amino acid sequence of SEQ ID NO: 72.
15. The CAR according to claim **13** or claim **14**, wherein the CAR specifically binds to HLA-A*02:01.
16. The CAR according to any one of claims **13** to **15**, wherein the transmembrane domain is a CD8 transmembrane domain and the intracellular signaling domain comprises a 4-1BB costimulatory domain and a CD3 zeta primary signaling domain
17. A nucleic acid molecule encoding the CAR according to any one of claims **13** to **16**.
18. An immune cell comprising the CAR according to any one of claims **13** to **16** or the nucleic acid molecule according to claim **17**.
19. The immune cell according to claim **18**, wherein said immune cell is a regulatory T cell.
20. A pharmaceutical composition comprising immune cells according to claim **18** or claim **19** and a pharmaceutically acceptable excipient.

- 21.** Use of the immune cell according to claim **18** or claim **19** for the manufacture of a medicament for inducing immune tolerance and/or for treating organ or tissue transplant rejection or graft versus host disease (GVHD) in a subject in need thereof.
- 5 **22.** Use of the immune cell according to claim **18** or claim **19** in combination with at least one immunosuppressive agent for the manufacture of a medicament for inducing immune tolerance and/or for treating organ or tissue transplant rejection or graft versus host disease (GVHD) in a subject in need thereof.
- 10 **23.** A kit of part comprising, in a first part, an immune cell according to claim **18** or claim **19** or a pharmaceutical composition according to claim **20** and in a second part at least one immunosuppressive agent.