

CLAIMS

1. A chimeric antigen receptor (CAR) specific for human CD45RC, wherein said CAR comprises:
 - (a) at least one extracellular binding domain, wherein said binding domain binds to said human CD45RC,
 - (b) at least one transmembrane domain, and
 - (c) at least one intracellular signaling domain, wherein the intracellular domain comprises at least one T cell primary signaling domain
 wherein the extracellular binding domain comprises at least one antigen-binding fragment that binds to human CD45RC comprising:
 - (a) a HCVR which comprises the following three CDRs:
 - (i) V_H-CDR1 of sequence SEQ ID NO: 1;
 - (ii) V_H-CDR2 with a sequence selected from the group comprising sequences SEQ ID NOs: 4, 5, 6, 8, 100, 116, 117, 118 and 119; and
 - (iii) V_H-CDR3 of sequence SEQ ID NO: 3; and
 - (b) a LCVR which comprises the following three CDRs:
 - (i) V_L-CDR1 with a sequence selected from the group comprising sequences SEQ ID NO: 15 (SASSSVS-X₁₂-YMH) and 18 (RASSSVS-X₁₂-YMH), wherein X₁₂ is absent or is selected from Asn (N), Ser (S) and Gly (G);
 - (ii) V_L-CDR2 with a sequence selected from the group comprising sequences SEQ ID NO: 16, 111, and 120; and
 - (iii) V_L-CDR3 of sequence SEQ ID NO: 17.

2. The CAR according to claim 1, further comprising at least one extracellular hinge domain; and/or wherein the intracellular domain further comprises at least one T cell costimulatory signaling domain.

3. The CAR according to claim 1 or 2, wherein the extracellular binding domain comprises at least one antigen-binding fragment that binds to human CD45RC comprising:
 - (a) a HCVR which comprises the following three CDRs:
 - (i) V_H-CDR1 of sequence SEQ ID NO: 1;
 - (ii) V_H-CDR2 with a sequence selected from the group comprising sequences SEQ ID NO: 4; and

- (iii) V_H-CDR3 of sequence SEQ ID NO: 3; and
 - (b) a LCVR which comprises the following three CDRs:
 - (i) V_L-CDR1 of sequence SEQ ID NO: 15, wherein X₁₂ is absent;
 - (ii) V_L-CDR2 of sequence SEQ ID NO: 16; and
 - (iii) V_L-CDR3 of sequence SEQ ID NO: 17.
4. The CAR according to claim 1 or 2, wherein the extracellular binding domain comprises at least one antigen-binding fragment that binds to human CD45RC comprising:
- (a) a HCVR which comprises the following three CDRs:
 - (i) V_H-CDR1 of sequence SEQ ID NO: 1;
 - (ii) V_H-CDR2 of sequence 5; and
 - (iii) V_H-CDR3 of sequence SEQ ID NO: 3; and
 - (b) a LCVR which comprises the following three CDRs:
 - (i) V_L-CDR1 of sequence SEQ ID NO: 15, wherein X₁₂ is absent;
 - (ii) V_L-CDR2 of sequence SEQ ID NO: 16; and
 - (iii) V_L-CDR3 of sequence SEQ ID NO: 17.
5. The CAR according to claim 1 or 2, wherein the extracellular binding domain comprises at least one antigen-binding fragment that binds to human CD45RC comprising:
- (a) a HCVR which comprises the following three CDRs:
 - (i) V_H-CDR1 of sequence SEQ ID NO: 1;
 - (ii) V_H-CDR2 with a sequence selected from the group comprising sequences SEQ ID NOs: 4, 6, 8, and 100; and
 - (iii) V_H-CDR3 of sequence SEQ ID NO: 3; and
 - (b) a LCVR which comprises the following three CDRs:
 - (i) V_L-CDR1 of sequence SEQ ID NO: 18, wherein X₁₂ is absent;
 - (ii) V_L-CDR2 with a sequence selected from the group comprising sequences SEQ ID NO: 16; and
 - (iii) V_L-CDR3 of sequence SEQ ID NO: 17.
6. The CAR according to claim 1 or 2, wherein the extracellular binding domain comprises at least one antigen-binding fragment that binds to human CD45RC comprising:
- (a) a HCVR which comprises the following three CDRs:
 - (i) V_H-CDR1 of sequence SEQ ID NO: 1;
 - (ii) V_H-CDR2 of sequence SEQ ID NO: 4; and

- (iii) V_H-CDR3 of sequence SEQ ID NO: 3; and
 - (b) a LCVR which comprises the following three CDRs:
 - (i) V_L-CDR1 of sequence SEQ ID NO: 15, wherein X₁₂ is absent;
 - (ii) V_L-CDR2 of sequence SEQ ID NO: 120; and
 - (iii) V_L-CDR3 of sequence SEQ ID NO: 17.
7. The CAR according to claim 1 or 2, wherein the extracellular binding domain comprises at least one antigen-binding fragment that binds to human CD45RC comprising:
- (a) a HCVR which comprises the following three CDRs:
 - (i) V_H-CDR1 of sequence SEQ ID NO: 1;
 - (ii) V_H-CDR2 of sequence SEQ ID NO: 118; and
 - (iii) V_H-CDR3 of sequence SEQ ID NO: 3; and
 - (b) a LCVR which comprises the following three CDRs:
 - (i) V_L-CDR1 of sequence SEQ ID NO: 15, wherein X₁₂ is absent;
 - (ii) V_L-CDR2 of sequence SEQ ID NO: 120; and
 - (iii) V_L-CDR3 of sequence SEQ ID NO: 17.
8. The CAR according to claim 1 or 2, wherein the extracellular binding domain comprises at least one antigen-binding fragment that binds to human CD45RC comprising:
- 1) a HCVR of sequence SEQ ID NO: 61 and a LCVR of sequence SEQ ID NO: 81;
 - 2) a HCVR of sequence SEQ ID NO: 62 and a LCVR of sequence SEQ ID NO: 82;
 - 3) a HCVR of sequence SEQ ID NO: 62 and a LCVR of sequence SEQ ID NO: 83;
 - 4) a HCVR of sequence SEQ ID NO: 62 and a LCVR of sequence SEQ ID NO: 84;
 - 5) a HCVR of sequence SEQ ID NO: 63 and a LCVR of sequence SEQ ID NO: 82;
 - 6) a HCVR of sequence SEQ ID NO: 63 and a LCVR of sequence SEQ ID NO: 83;
 - 7) a HCVR of sequence SEQ ID NO: 63 and a LCVR of sequence SEQ ID NO: 84;
 - 8) a HCVR of sequence SEQ ID NO: 64 and a LCVR of sequence SEQ ID NO: 82;

- 9) a HCVR of sequence SEQ ID NO: 64 and a LCVR of sequence SEQ ID NO: 83;
- 10) a HCVR of sequence SEQ ID NO: 64 and a LCVR of sequence SEQ ID NO: 84;
- 11) a HCVR of sequence SEQ ID NO: 101 and a LCVR of sequence SEQ ID NO: 85;
- 12) a HCVR of sequence SEQ ID NO: 101 and a LCVR of sequence SEQ ID NO: 103;
- 13) a HCVR of sequence SEQ ID NO: 65 and a LCVR of sequence SEQ ID NO: 85;
- 14) a HCVR of sequence SEQ ID NO: 65 and a LCVR of sequence SEQ ID NO: 103;
- 15) a HCVR of sequence SEQ ID NO: 62 and a LCVR of sequence SEQ ID NO: 85;
- 16) a HCVR of sequence SEQ ID NO: 101 and a LCVR of sequence SEQ ID NO: 82;
- 17) a HCVR of sequence SEQ ID NO: 121 and a LCVR of sequence SEQ ID NO: 85;
- 18) a HCVR of sequence SEQ ID NO: 122 and a LCVR of sequence SEQ ID NO: 85;
- 19) a HCVR of sequence SEQ ID NO: 123 and a LCVR of sequence SEQ ID NO: 85;
- 20) a HCVR of sequence SEQ ID NO: 124 and a LCVR of sequence SEQ ID NO: 85;
- 21) a HCVR of sequence SEQ ID NO: 63 and a LCVR of sequence SEQ ID NO: 85;
- 22) a HCVR of sequence SEQ ID NO: 67 and a LCVR of sequence SEQ ID NO: 85;
- 23) a HCVR of sequence SEQ ID NO: 67 and a LCVR of sequence SEQ ID NO: 103;
- 24) a HCVR of sequence SEQ ID NO: 61 and a LCVR of sequence SEQ ID NO: 113;
- 25) a HCVR of sequence SEQ ID NO: 61 and a LCVR of sequence SEQ ID NO: 126; or

- 26) a HCVR and a LCVR comprising a sequence of the non-CDR regions sharing at least 70% of identity with the sequence of the non-CDR regions of the HCVR and LCVR according to 1) to 25), or
 - 27) a HCVR of sequence SEQ ID NO: 62 or a HCVR of sequence SEQ ID NO: 123.
9. The CAR according to any one of claims 1 to 8, wherein the amino acid residue at Kabat position L71 of the LCVR is Phe (F).
 10. The CAR according to any one of claims 1 to 9, comprising:
 - (i) an anti-human CD45RC scFv,
 - (ii) a hinge domain derived from CD8 α ,
 - (iii) a human CD8 α transmembrane domain, and
 - (iv) an intracellular signaling domain comprising a human CD28 signaling domain, and a human CD3 zeta signaling domain.
 11. The CAR according to claim 10, wherein:
 - the anti-human CD45RC scFv of (i) comprises a HCVR having the sequence of SEQ ID NO: 61 and/or a LCVR having the sequence of SEQ ID NO: 81;
 - the anti-human CD45RC scFv of (i) comprises a HCVR and a LCVR linked by a linker having the sequence of SEQ ID NO: 134;
 - the hinge domain derived from CD8 α of (ii) has the sequence of SEQ ID NO: 145;
 - the human CD8 α transmembrane domain of (iii) has the sequence of SEQ ID NO: 153;
 - the intracellular signaling domain of (iv) has the sequence of SEQ ID NO: 167; and/or
 - the human CD3 zeta signaling domain of (iv) has the sequence of SEQ ID NO: 157.
 12. An isolated nucleic acid encoding the CAR according to any one of claims 1 to 11.
 13. An expression vector comprising the isolated nucleic acid according to claim 12.
 14. An isolated immune cell population, engineered to express at the cell surface the CAR according to any one of claims 1 to 11.

15. The immune cell population according to claim **14**, wherein said immune cell population is a regulatory T cell population.
16. The immune cell population according to claim **15**, wherein said regulatory T cell population is selected from the group consisting of CD4⁺CD25⁺Foxp3⁺ Treg, Tr1 cells, TGF- β secreting Th3 cells, regulatory NKT cells, regulatory $\gamma\delta$ T cells, regulatory CD8⁺ T cells, and double negative regulatory T cells.
17. A composition comprising at least one immune cell population engineered to express at the cell surface the CAR according to any one of claims **1** to **11**.
18. A pharmaceutical composition comprising at least one immune cell population engineered to express at the cell surface the CAR according to any one of claims **1** to **11**, and at least one pharmaceutically acceptable excipient or carrier.
19. Use of the immune cell population according to any one of claims **14** to **16**, or the composition according to claim **17** or **18**, wherein the immune cell population is a T cell, an NK cell, and/or a regulatory immune cells, in the manufacture of a medicament for inducing immune tolerance, for preventing or reducing transplant rejection, or for preventing or treating graft-versus-host disease (GVHD), or for reducing and/or treating a CD45RC^{high}-related condition selected from the group consisting of an autoimmune disease, an undesired immune response, a monogenic disease, lymphoma and cancer in a subject in need thereof.