

CLAIMS

1. A chimeric antigen receptor (CAR) comprising an extracellular binding domain, a transmembrane domain, and an intracellular domain, wherein
 - (i) the transmembrane domain comprises a human tumor necrosis factor receptor 2 (TNFR2) transmembrane domain or a fragment or variant thereof, or
 - (ii) the intracellular domain comprises a human TNFR2 costimulatory intracellular signaling domain or a fragment or variant thereof, or
 - (iii) both (i) and (ii).

2. The CAR according to claim 1, further comprising an extracellular hinge domain preferably wherein the hinge domain comprises a hinge region of human CD8 or CD28, and
 more preferably wherein the hinge domain comprises the sequence of SEQ ID NO: 14 or a sequence having at least about 70% identity with SEQ ID NO: 14.

3. The CAR according to claim 1 or claim 2, wherein the intracellular domain comprises an immune cell primary intracellular signaling domain
 preferably a T cell primary intracellular signaling domain of human CD3 zeta,
 more preferably comprising the sequence of SEQ ID NO: 28, 29, 30 or 31 or a sequence having at least about 70% identity with SEQ ID NO: 28, 29, 30 or 31.

4. The CAR according to any one of claims 1 to 3, wherein the CAR comprises:
 - an extracellular binding domain, and
 - an extracellular hinge domain comprising a hinge region of human CD8 or CD28, and
 - (i) a transmembrane domain comprising a human TNFR2 transmembrane domain or a fragment or variant thereof, and an intracellular domain comprising a primary intracellular signaling domain of human CD3 zeta or

- (ii) a transmembrane domain, and an intracellular domain comprising a human TNFR2 costimulatory intracellular signaling domain or a fragment or variant thereof, and a primary intracellular signaling domain of human CD3 zeta, or
- 5 (iii) a transmembrane domain comprising a human TNFR2 transmembrane domain or a fragment or variant thereof, and an intracellular domain comprising a human TNFR2 costimulatory intracellular signaling domain or a fragment or variant thereof, and a primary intracellular signaling domain of human CD3 zeta.
- 10 5. The CAR according to any one of claims 1 to 4, wherein the transmembrane domain comprises at least eight contiguous amino acids of SEQ ID NO: 22 or of a sequence having at least about 70% identity with SEQ ID NO: 22,
- optionally in combination with amino acid residues from a transmembrane domain of a protein that is not TNFR2.
- 15 6. The CAR according to any one of claims 1 to 5, wherein the transmembrane domain comprises the amino acid sequence of VNCVIMTQV (SEQ ID NO: 63).
7. The CAR according to any one of claims 1 to 6, wherein the intracellular domain comprises at least 30 contiguous amino acid residues of SEQ ID NO: 34 or of a sequence having at least about 70% identity with SEQ ID NO: 34,
- 20 optionally in combination with amino acid residues from a costimulatory intracellular signaling domain of a protein that is not TNFR2.
8. The CAR according to any one of claims 1 to 7, wherein said intracellular domain comprises residues 1-70, 1-115, or 1-156 of SEQ ID NO: 34.
9. The CAR according to claims 1 to 8, comprising:
- 25 an extracellular binding domain,
- an extracellular hinge domain comprising a CD8 hinge region of SEQ ID NO: 14,

a transmembrane domain comprising a TNFR2 transmembrane domain of SEQ ID NO: 22, and

an intracellular domain comprising:

5 a) a TNFR2 costimulatory intracellular signaling domain of SEQ ID NO: 34, and

 b) a primary human CD3 zeta intracellular signaling domain of SEQ ID NO: 28, 29, 30, or 31.

10 **10.** The CAR according to any one of claims **1** to **9**, wherein the extracellular binding domain is an antibody or an antigen-binding fragment thereof, preferably a single chain variable fragment (scFv).

11. A nucleic acid sequence encoding the CAR according to any one of claims **1** to **10**.

12. A population of immune cells expressing the CAR according to any one of claims **1** to **10**, or the nucleic acid sequence according to claim **11**.

15 **13.** The immune cell population according to claim **12**, wherein the immune cells are selected from the group consisting of T cells, natural killer (NK) cells, $\alpha\beta$ T cells, $\gamma\delta$ T cells, double negative (DN) cells, regulatory immune cells, regulatory T (Treg) cells, effector immune cells, effector T cells, B cells, and myeloid-derived cells, and any combination thereof, wherein the immune cells are optionally human cells, preferably

20 wherein the population comprises Treg cells, wherein the Treg cells are optionally human cells.

14. Use of an immune cell population according to claim **12** or **13**, for the manufacture of a medicament.

25 **15.** Use of an immune cell population according to claim **12** or **13**, for the manufacture of a medicament for the treatment of a disease or disorder in a human subject in need thereof, preferably

wherein the disease or disorder is selected from the group consisting of an inflammatory disease, an autoimmune disease, an allergic disease, an organ transplantation condition, a cancer, and an infectious disease.

- 5 **16.** The use according to claim **15**, wherein the immune cell population is a Treg cell population and wherein the human subject is in need of immunosuppression.