

## CLAIMS

We claim:

- 1.** A chimeric antigen receptor (CAR) comprising an antigen-binding domain, a hinge domain, a transmembrane domain, one or more co-stimulatory domains, and an intracellular signaling domain, wherein the antigen binding domain specifically binds to three or more different citrullinated proteins or citrullinated fragments thereof, and comprises complementarity-determining regions (CDRs) from VH and VL domains of SEQ ID NO:1 and SEQ ID NO:4.
- 2.** The CAR of Claim **1**, wherein the antigen-binding domain binds to all three of (i) citrullinated vimentin, (ii) citrullinated filaggrin, and (iii) citrullinated fibrinogen, or citrullinated peptides fragments thereof.
- 3.** The CAR of Claim **1** or Claim **2**, wherein the antigen-binding domain comprises a VH domain and a VL domain, wherein:
  - (i) the VH domain comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:32, a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:34, and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:36, and
  - (ii) the VL domain comprises a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:39, a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:41, and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:43.
- 4.** The CAR of any one of Claims **1-3**, wherein the intracellular signaling domain is derived from CD3-zeta.
- 5.** The CAR of any one of Claims **1-4**, wherein the one or more co-stimulatory domains comprises a domain of the group consisting of FcεR1g, Fcγ, CD28, CD134 (OX40), CD137 (4-1BB), CTLA-4, CTLA-4/CD-28 hybrid, DAP10, CD27, 2B4, and combinations thereof.
- 6.** The CAR of any one of Claims **1-5**, wherein the antigen-binding domain comprises an antibody, an antibody fragment, a camelid nanobody, a heavy chain only antibody or an aptamer.
- 7.** The CAR of any one of Claims **1-6**, wherein the transmembrane domain is a CD8 transmembrane domain or a CD28 transmembrane domain.

**8.** The CAR of any one of Claims **1-7**, wherein the hinge domain is a CD8 hinge domain or a CD28 hinge domain.

**9.** The CAR of any one of Claims **1-8**, wherein the antigen-binding domain comprises a single chain fragment.

**10.** The CAR of Claim **9**, wherein the single chain fragment comprises a single chain variable fragment (scFv).

**11.** The CAR of Claim **10**, wherein the scFv fragment comprises:

(a) a VH domain comprising the amino acid sequence having at least 95% identity to SEQ ID NO:1; and

(b) a VL domain comprising the amino acid sequence having at least 95% identity to SEQ ID NO:4.

**12.** The CAR of Claim **10**, wherein the scFv fragment comprises:

(a) a VH domain comprising the amino acid sequence of SEQ ID NO:1; and

(b) a VL domain comprising the amino acid sequence of SEQ ID NO:4.

**13.** The CAR of Claim **12**, wherein the VH domain and the VL domain are joined by a linker comprising the amino acid sequence of SEQ ID NO:20, SEQ ID NO:21, or SEQ ID NO:22.

**14.** The CAR of Claim **13**, wherein the scFv comprises the amino acid sequence of SEQ ID NO:5.

**15.** A nucleic acid encoding the CAR of any one of Claims **1-14**.

**16.** The nucleic acid of Claim **15**, wherein the VH domain is encoded by the nucleic acid sequence comprising SEQ ID NO:8; and the VL domain is encoded by the nucleic acid sequence comprising SEQ ID NO:11.

**17.** The nucleic acid of Claim **16**, wherein the VH and VL fragments are joined by a linker and comprise the nucleic acid sequence of SEQ ID NO:12, or (ii) SEQ ID NO:13, or (iii) SEQ ID NO:14.

**18.** An expression vector comprising an expression control sequence operatively linked to the nucleic acid sequence of any one of Claims 15-17.

**19.** A modified T cell that has been modified to express the chimeric antigen receptor (CAR) of any one of Claims **1-14**.

**20.** The modified T cell of Claim **19**, wherein the T cell is a T regulatory (Treg) cell.

**21.** The modified T cell of Claim **20**, wherein the T cell is a human T cell.

**22.** The modified T cell of Claim **21**, wherein the T cell is a primary T-cell.

**23.** The modified T cell of Claim **22**, wherein the T cell is CD4+, CD25+ and CD127lo.

**24.** A pharmaceutical composition comprising a plurality of the modified T cells of any one of Claims **19-23**, and a pharmaceutically acceptable carrier.

**25.** Use of the pharmaceutical composition of Claim **24** for the manufacture of a medicament for treating rheumatoid arthritis.

**26.** The use of Claim **25**, wherein the pharmaceutical composition is formulated for administration into a synovium of a subject.

**27.** The use of Claim **25**, wherein the pharmaceutical composition is formulated for intravenous administration to a subject.

**28.** A method comprising:

- (a) enriching T cells from a biological sample for T regulatory (Treg) cells;
- (b) transfecting the enriched Treg cells with an expression vector encoding the CAR of any one of Claims **1-14**; and
- (c) expanding the transfected Treg cells.

**29.** The method of Claim **28**, wherein the expansion comprises using anti-CD3/CD28 coated beads.

**30.** The method of Claim **28**, wherein the expansion does not comprise using anti-CD3/CD28 coated beads.