

CLAIMS

1. A chimeric antigen receptor (CAR) which binds B cell maturation antigen (BCMA), in which the CAR comprises a Fab antigen binding domain comprising:

(a) a heavy chain variable region (VH) having complementarity determining regions (CDRs) with the following sequences:

CDR1 - GFIFSDYN (SEQ ID NO: 79)

CDR2 - IIYDGSST (SEQ ID NO: 80)

CDR3 - ATRPGPFAY (SEQ ID NO: 81); and

(b) a light chain variable region (VL) having complementarity determining regions (CDRs) with the following sequences:

CDR1 - QSLHSHNGNTY (SEQ ID NO: 82)

CDR2 - LVS (SEQ ID NO: 83)

CDR3 - VHGTHAWT (SEQ ID NO: 84).

2. A CAR according to Claim 1, in which the Fab antigen-binding domain comprises a VH domain having the sequence shown as SEQ ID NO: 29; and a VL domain having the sequence shown as SEQ ID NO: 30.

3. A nucleic acid sequence which encodes a CAR according to Claim 1 or 2.

4. A nucleic acid construct which encodes a CAR according to Claim 1 or 2 and has one of the following general structures:

VH-CH-spacer-TM-endo-coexpr-VL-CL;

VL-CL-coexpr-VH-CH-spacer-TM-endo;

VL-CL-spacer-TM-endo-coexpr-VH-CH; or

VH-CH-coexpr-VL-CL-spacer-TM-endo;

in which:

VH is a nucleic acid sequence encoding a heavy chain variable region;

CH is a nucleic acid sequence encoding a heavy chain constant region

spacer is a nucleic acid encoding a spacer;

TM is a nucleic acid sequence encoding a transmembrane domain;

endo is a nucleic acid sequence encoding an endodomain;

coexpr is a nucleic acid sequence enabling co-expression of the first and second polypeptides;

VL is a nucleic acid sequence encoding a light chain variable region; and

CL is a nucleic acid sequence encoding a light chain constant region.

5. A nucleic acid construct according to Claim 4, which encodes a first CAR according to Claim 1, and which also encodes a second chimeric antigen receptor which binds CD19.

10 6. A vector which comprises a nucleic acid sequence according to Claim 3 or a nucleic acid construct according to Claim 4 or 5.

7. A T-cell or natural killer (NK) cell which expresses a CAR according to Claim 1 or 2.

8. A T-cell or natural killer (NK) cell which expresses a first CAR, in which the first CAR is a CAR according to Claim 1 or 2, and a second chimeric antigen receptor which binds
15 CD19.

9. A method for making a T-cell or natural killer (NK) cell according to Claim 7 or 8, which comprises the step of introducing a nucleic acid sequence according to Claim 3; a nucleic acid construct according to Claim 4 or 5; or a vector according to Claim 6 into a T-cell or natural killer (NK) cell *ex vivo*.

20 10. A pharmaceutical composition which comprises a plurality of T-cells or natural killer (NK) cells according to Claim 7 or 8, together with a pharmaceutically acceptable carrier, diluent or excipient.

11. A pharmaceutical composition according to Claim 10 for use in treating cancer.

12. A pharmaceutical composition for use according to Claim 11, in which the cancer is
25 multiple myeloma.

13. A pharmaceutical composition according to Claim 10 for use in treating amyloidosis.