CLAIMS

1. A chimeric antigen receptor (CAR) comprising:
(i) a B cell maturation antigen (BCMA)-binding domain which comprises at least part of a proliferation-inducing ligand (APRIL);
(ii) a spacer domain; and
(ii) a transmembrane domain; and
(iii) an intracellular T cell signaling domain.

2. A CAR according to claim 1, wherein the BCMA-binding domain comprises a truncated APRIL which comprises the BCMA binding site but lacks the amino terminal portion of APRIL responsible for proteoglycan binding.

3. A CAR according to claim 2, which comprises the sequence shown as SEQ ID No. 14 or a variant thereof having at least 80% sequence identity which binds BCMA.

4. A CAR according to any preceding claim, wherein the transmembrane and intracellular T-cell signalling domain comprise the sequence shown as SEQ ID No. 7 or a variant thereof having at least 80% sequence identity.

5. A CAR according to any preceding claim, wherein the spacer comprises one of the following: a human IgG1 spacer; an IgG1 hinge; or a CD8 stalk.

6. A CAR according to claim 5, wherein the spacer comprises a CD8 stalk.

7. A CAR according to any preceding claim, which comprises the sequence shown as SEQ ID No. 1, 2, 3, 4, 5 or 6 or a variant thereof which has at least 80% sequence identity but retains the capacity to i) bind BCMA and ii) induce T cell signalling.

8. A nucleic acid sequence which encodes a CAR according to any preceding claim.

9. A nucleic acid sequence according to claim 8 which comprises the sequence shown as SEQ ID No 15, 16, 17, 18, 19 or 20 or a variant thereof having at least 80% sequence identity.

10. A vector which comprises a nucleic acid sequence according to claim 8 or 9.

11. A T cell or NK cell which expresses a CAR according to any of claims 1 to 7.

12. A method for making a T cell or NK cell according to claim 11, which comprises the step of introducing a nucleic acid according to claim 8 or 9 into a T cell or NK cell.

13. A pharmaceutical composition which comprises a vector according to claim 10 or T cell/NK cell according to claim 11, together with a pharmaceutically acceptable carrier, diluent or excipient.

14. A method for treating a plasma cell disorder which comprises the step of administering a vector according to claim 10 or T cell/NK cell according to claim 11 to a subject.

15. A method according to claim 14, wherein the plasma cell disorder is selected from plasmacytoma, plasma cell leukemia, multiple myeloma, macroglobulinemia, amyloidosis, Waldenstrom's macroglobulinemia, solitary bone plasmacytoma, extramedullary plasmacytoma, osteosclerotic myeloma, heavy chain diseases, monoclonal gammopathy of undetermined significance and smoldering multiple myeloma.

16. A method according to claim 15, wherein the plasma cell disorder is multiple myeloma.

17. A vector according to claim 10 or T cell/NK cell according to claim 11 for use in treating a plasma cell disorder.

18. The use of a vector according to claim 10 or T cell/NK cell according to claim 11 in the manufacture of a medicament for treating a plasma cell disorder.

CLAIMS

1. A chimeric antigen receptor (CAR) which binds the B-cell maturation antigen (BCMA) and comprises:

(i) a BCMA-binding domain which comprises at least part of a proliferation-inducing ligand (APRIL);

(ii) a spacer domain;

(iii) a transmembrane domain; and

(iv) an intracellular T cell signaling domain.

2. A CAR according to Claim 1, in which the BCMA-binding domain comprises a truncated APRIL which comprises the BCMA binding site but lacks the amino terminal portion of APRIL responsible for proteoglycan binding.

3. A CAR according to Claim 2, which comprises the sequence shown as SEQ ID No. 14 or a variant thereof having at least 80% sequence identity which binds BCMA.

4. A CAR according to any preceding claim, in which the transmembrane and intracellular T-cell signalling domain comprise the sequence shown as SEQ ID No. 7 or a variant thereof having at least 80% sequence identity.

5. A CAR according to any preceding claim, in which the spacer comprises one of the following: a human IgG1 spacer; an IgG1 hinge; or a CD8 stalk.

6. A CAR according to Claim 5, in which the spacer comprises a CD8 stalk.

7. A CAR according to any preceding claim, which comprises the sequence shown as SEQ ID No. 1, 2, 3, 4, 5 or 6 or a variant thereof which has at least 80% sequence identity but retains the capacity to i) bind BCMA and ii) induce T cell signalling.

8. A nucleic acid sequence which encodes a CAR according to any preceding claim.

9. A nucleic acid sequence according to Claim 8 which comprises the sequence shown as SEQ ID No 15, 16, 17, 18, 19 or 20 or a variant thereof having at least 80% sequence identity.

10. A vector which comprises a nucleic acid sequence according to Claim 8 or 9.

11. A T cell or NK cell which expresses a CAR according to any of Claim 1 to 7.

12. A method for making a T cell or NK cell according to Claim 11, which comprises the step of introducing a nucleic acid according to Claim 8 or 9 into a T cell or NK cell.

13. A pharmaceutical composition which comprises a vector according to Claim 10 or T cell/NK cell according to Claim 11, together with a pharmaceutically acceptable carrier, diluent or excipient.

14. A method for treating a plasma cell disorder which comprises the step of administering a vector according to Claim 10 or T cell/NK cell according to Claim 11 to a subject.

15. A method according to Claim 14, in which the plasma cell disorder is selected from plasmacytoma, plasma cell leukemia, multiple myeloma, macroglobulinemia, amyloidosis, Waldenstrom's macroglobulinemia, solitary bone plasmacytoma, extramedullary plasmacytoma, osteosclerotic myeloma, heavy chain diseases, monoclonal gammopathy of undetermined significance and smoldering multiple myeloma.

16. A method according to Claim 15, in which the plasma cell disorder is multiple myeloma.

17. A vector according to Claim 10 or T cell/NK cell according to Claim 11 for use in treating a plasma cell disorder.

18. The use of a vector according to Claim 10 or T cell/NK cell according to Claim 11 in the manufacture of a medicament for treating a plasma cell disorder.