CLAIMS

1. A chimeric antigen receptor including:
an antigen-recognition domain that recognises a dysfunctional $P2X_7$ receptor;
a transmembrane domain; and
a signalling domain, wherein the antigen-recognition domain recognises a dysfunctional $P2X_7$ receptor.

2. The chimeric antigen receptor according to claim 1, wherein the antigen-recognition domain includes a portion having sequence identity to: an antigen-binding site of an antibody; or an antigen-binding site of a fragment of an antibody.

3. The chimeric antigen receptor according to claim 1, wherein the antigen-recognition domain includes a portion having sequence identity to at least the complementarity-determining region 1(CDR1), CDR2 and CDR3 from the heavy chain of an antibody or the light chain of an antibody.

4. The chimeric antigen receptor according to claim 1, wherein the antigen-recognition domain includes amino acid sequences at least 80%, or at least 90% or at least 94% identical to:

the CDR regions spanning positions 30 to 35, 50 to 67 or 98 to 108 of SEQ ID NO: 10; or

the CDR regions spanning positions 30 to 35, 50 to 67 or 98 to 108 of SEQ ID NO: 32; or

the CDR regions spanning positions 30 to 35, 50 to 67 or 98 to 108 of SEQ ID NO: 33; or

the CDR regions spanning positions 30 to 35, 50 to 67 or 98 to 108 of SEQ ID NO: 34.

5. The chimeric antigen receptor according to any one of claims 1 to 3, wherein the antigen-recognition domain recognises an epitope associated with an adenosine triphosphate (ATP)-binding site of the dysfunctional $P2X_7$ receptor.

6. The chimeric antigen receptor according to any one of claims 1 to 4, wherein the dysfunctional $P2X_7$ receptor has a reduced capacity to bind ATP compared to an ATP-binding capacity of a wild-type (functional) $P2X_7$ receptor.

7. The chimeric antigen receptor according to any one of claims 1 to 5, wherein the dysfunctional $P2X_7$ receptor has a conformational change that renders the receptor dysfunctional.

8. The chimeric antigen receptor according to claim 6, wherein the conformational change that renders the receptor dysfunctional is a trans-conformation to a cis-conformation change of proline at amino acid position 210 of the dysfunctional $P2X_7$ receptor.

9. The chimeric antigen receptor according to any one of claim 1 to 8, wherein the antigen-recognition domain recognises an epitope that includes proline at amino acid position 210 of the dysfunctional $P2X_7$ receptor.

10. The chimeric antigen receptor according to any one of claims 1 to 9, wherein the signalling domain includes a portion derived from an activation receptor and/or a co-stimulatory receptor.

11. The chimeric antigen receptor according to claim 10, wherein the activation receptor is a member of the CD3 co-receptor complex and/or an Fc receptor.

12. The chimeric antigen receptor according claim 11, wherein the portion derived from the CD3 co-receptor complex is CD3-ζ.

13. The chimeric antigen receptor according claim 11, wherein the portion derived from the Fc receptor is FcεRI or FcγRI.

14. The chimeric antigen receptor according to any one of claims 1 to 12, wherein the co-stimulatory receptor is selected from the group consisting of CD27, CD28, CD30, CD40, DAP10, OX40, 4-1BB (CD137) and ICOS.

15. A nucleic acid molecule including a nucleotide sequence encoding the chimeric antigen receptor according to claim 1 to 14.

16. A nucleic acid construct including a nucleic acid molecule according to claim 15.

17. A viral vector including a nucleic acid according to claim 15 or the nucleic acid construct according to claim 16, for viral transduction of a host cell.

18. An ex vivo genetically modified cell, the cell including the chimeric antigen receptor according to of any one of claim 1 to 13, a nucleic acid molecule according to claim 14, or a nucleic acid construct according to claim 15.

19. The ex vivo genetically modified cell according claim 18, wherein the cell is a leukocyte, a Peripheral Blood Mononuclear Cell (PBMC), a lymphocyte, a T cell, a CD4+ T cell, a CD8+ T cell, a natural killer cell or a natural killer T cell.

20. A pharmaceutical composition including a genetically modified cell according to claim 16 or 17 and a pharmaceutically acceptable carrier.