CLAIMS

1. A chimeric antigen receptor including:
- an antigen-recognition domain that recognises a dysfunctional $P2X_7$ receptor but not a functional $P2X_7$ receptor,
- a transmembrane domain; and
- a signalling domain including an intracellular signalling portion of an activation receptor and/or an intracellular signalling portion of a co-stimulatory receptor,

wherein the dysfunctional $P2X_7$ receptor has a reduced capacity to bind ATP compared to of a wild-type (functional) $P2X_7$ receptor, wherein the dysfunctional $P2X_7$ receptor has a conformational change that renders the receptor dysfunctional, the conformational change being a trans-conformation to a cis-conformation change of proline at amino acid position 210 of the 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 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.

5. The chimeric antigen receptor according to any one of claims 1 to 4, wherein the antigen-recognition domain recognises an epitope that includes amino acids 200 to 210 of the dysfunctional $P2X_7$ receptor.

6. The chimeric antigen receptor according to any one of claims 1 to 5, wherein the activation receptor is a member of the CD3 co-receptor complex and/or an Fc receptor.

7. The chimeric antigen receptor according to claim 6, wherein the portion derived from the CD3 co-receptor complex is CD3-ζ.

8. The chimeric antigen receptor according to claim 6, wherein the portion derived from the Fc receptor is FCεRI or FCγRI.

9. The chimeric antigen receptor according to any one of claims 1 to 8, wherein the co-stimulatory receptor is selected from the group consisting of CD27, CD28, CD30, CD40, DAP10, OX40, 4-1BB (CD137) and ICOS.

10. The chimeric antigen receptor according to any one of claims 1 to 9, wherein the antigen-recognition domain comprises:

a CDR1 comprising the amino acid sequence of residues 30 to 35 of SEQ ID NO: 10, a CDR2 comprising the amino acid sequence of residues 50 to 67 of SEQ ID NO: 10 and a CDR3 comprising the amino acid sequence of residues or 98 to 108 of SEQ ID NO: 10; or

a CDR1 comprising the amino acid sequence of residues 30 to 35 of SEQ ID NO: 32, a CDR2 comprising the amino acid sequence of residues 50 to 67 of SEQ ID NO: 32 and a CDR3 comprising the amino acid sequence of residues or 98 to 108 of SEQ ID NO: 32; or

a CDR1 comprising the amino acid sequence of residues 30 to 35 of SEQ ID NO: 33, a CDR2 comprising the amino acid sequence of residues 50 to 67 of SEQ ID NO: 33 and a CDR3 comprising the amino acid sequence of residues or 98 to 108 of SEQ ID NO: 33; or

a CDR1 comprising the amino acid sequence of residues 30 to 35 of SEQ ID NO: 34, a CDR2 comprising the amino acid sequence of residues 50 to 67 of SEQ ID NO: 34 and a CDR3 comprising the amino acid sequence of residues or 98 to 108 of SEQ ID NO: 34.

11. The chimeric antigen receptor according to any one of claims 1 to 10, wherein the chimeric antigen receptor comprises the amino acid sequence of any one of SEQ ID NOs: 26, 27, 52, 53 or 54.

12. A nucleic acid molecule including a nucleotide sequence encoding the chimeric antigen receptor according to claim 1 to 11.

13. A nucleic acid vector including a nucleic acid molecule according to claim 12.

14. A viral vector including a nucleic acid according to claim 13 or the nucleic acid construct according to claim 13, for viral transduction of a host cell.

15. An *ex vivo* genetically modified cell, the cell including the chimeric antigen receptor according to of any one of claim 1 to 11, or a nucleic acid molecule according to claim 12, or a nucleic vector according to claim 13.

16. The *ex vivo* genetically modified cell according to claim 15, 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.

17. Use of a genetically modified cell according to claim 14 or 15, in the manufacture of a medicament for the treatment of cancer or for killing a cell expressing a dysfunctional $P2X_7$ receptor.

18. The use according to claim 17, wherein cancer or the cell expressing a dysfunctional $P2X_7$ receptor is a cancer cell, selected from one or more of; brain cancer, oesophageal cancer, mouth cancer, tongue cancer, thyroid cancer, lung cancer, stomach cancer, pancreatic cancer, kidney cancer, colon cancer, rectal cancer, prostate cancer, bladder cancer, cervical cancer, epithelial cell cancers, skin cancer, leukaemia, lymphoma, myeloma, breast cancer, ovarian cancer, endometrial cancer and testicular cancer, preferably wherein the cancer cell is selected from one or more of; lung cancer, oesophageal cancer, stomach cancer, colon cancer, prostate cancer, bladder cancer, cervical cancer, vaginal cancers, epithelial cell cancers, skin cancer, blood-related cancers, breast cancer, endometrial cancer, uterine cancer and testicular cancer.

19. A pharmaceutical composition including a genetically modified cell according to claim 14 or 15 and a pharmaceutically acceptable carrier.