The claims defining the invention are as follows:

1. A chimeric antigen receptor including:

an extracellular domain including a binding domain which recognises Lgr5;

a transmembrane domain; and

an intracellular signalling domain that activates a cellular function.

~~2. The chimeric antigen receptor of claim 1, wherein the binding domain recognises an epitope on the convex surface of Lgr5.~~

~~3. The chimeric antigen receptor of claim 1 or claim 2, wherein the binding domain recognises an epitope within leucine rich repeats 6 to 9 of Lgr5.~~

2~~4~~. The chimeric antigen receptor ~~of any one of~~ claim~~s~~ 1 ~~to 3~~, wherein the binding domain includes the variable heavy chain of an antibody that binds to Lgr5, or a functional variant of the variable heavy chain, or ~~.~~

~~5. The chimeric antigen receptor of any one of claims 1 to 4, wherein the binding domain~~ includes the variable light chain of an antibody that binds to Lgr5, or a functional variant of the variable light chain.

~~6. The chimeric antigen receptor of any one of claims 1 to 5, wherein the binding domain includes a binding portion of the antibody 18G7.1, 18G7H6A1 or 18G7H6A3, or a functional variant thereof.~~

3~~7~~. The chimeric antigen receptor of ~~any one of~~ claim~~s~~ 1 or claim 2 ~~to 6~~, wherein the binding domain includes:

a heavy chain CDR1 having an amino acid sequence as set forth in SEQ ID No. 37 or having an amino acid sequence as set forth in SEQ ID No. 37 with up to 2 amino acid modifications,

a heavy chain CDR2 having an amino acid sequence as set forth in SEQ ID No. 38, or having an amino acid sequence as set forth in SEQ ID No. 38 with up to 2 amino acid modifications, and

a heavy chain CDR3 having an amino acid sequence as set forth in SEQ ID No. 39, or having an amino acid sequence as set forth in SEQ ID No. 39 with up to 2 amino acid modifications;. and/or

8. The chimeric antigen receptor of any one of claims 1 to 7, wherein the binding domain includes:

a light chain CDR1 having an amino acid sequence set forth in SEQ ID No. 40 or having an amino acid sequence as set forth in SEQ ID No. 40 with up to 2 amino acid modifications,

a light chain CDR2 having an amino acid sequence set forth in SEQ ID No. 41 or having an amino acid sequence as set forth in SEQ ID No. 41 with up to 2 amino acid modifications, and

a light chain CDR3 having an amino acid sequence set forth in SEQ ID No. 42 or having an amino acid sequence as set forth in SEQ ID No. 42 with up to 2 amino acid modifications.

9. The chimeric antigen receptor of any one of claims 1 to 8, wherein the binding domain includes a sequence identical to a single-domain antibody (sdAb) including a sequence identical to a VH or VL chain of an antibody that binds to Lgr5, or includes a sequence identical to a fragment antigen binding (Fab) derived from an antibody that binds to Lgr5, or includes a sequence identical to a single-chain variable fragment (scFv) comprising the VH and VL regions of an antibody that binds to Lgr5.

410. The chimeric antigen receptor of any one of claims 1 to 3 to 6, wherein the binding domain includes the C-terminus of a variable heavy (VH) chain linked to the N-terminus of a variable light (VL) chain, or

wherein the VH chain includes; a CDR1 having the sequence of SEQ ID No. 37, a CDR2 having the sequence of SEQ ID No. 38, and a CDR3 having the sequence of SEQ ID No. 39, and

the VL chain includes; a CDR1 having the sequence of SEQ ID No. 40, a CDR2 having the sequence of SEQ ID No. 41, and a CDR3 having the sequence of SEQ ID No. 42, and

wherein each CDR can have up to 2 amino acid modifications.

~~11. The chimeric antigen receptor of any one of claims 1 to 6,~~ wherein the single-chain variable fragment includes the C-terminus of the variable light (VL) chain linked to the N-terminus of the variable light (VH) chain.~~,~~

~~wherein the VL chain includes; a CDR1 having the sequence of SEQ ID No. 40, a CDR2 having the sequence of SEQ ID No. 41, and a CDR3 having the sequence of SEQ ID No. 42, and~~

~~the VH chain includes; a CDR1 having the sequence of SEQ ID No. 37, a CDR2 having the sequence of SEQ ID No. 38, and a CDR3 having the sequence of SEQ ID No. 39, and~~

~~wherein each CDR can have up to 2 amino acid modifications.~~

5~~12~~. The chimeric antigen receptor of any one of claims 1 to 3, wherein the binding domain includes SEQ ID No. 49 and/or SEQ ID No. 50, or variants thereof having at least 90% sequence identity to SEQ ID No. 49 or 50 or~~.~~

~~13. The chimeric antigen receptor of any one of claims 1 to 3,~~ wherein the binding domain includes SEQ ID No. 53 or SEQ ID No. 54 or variants thereof having at least 90% sequence identity to SEQ ID No. 53 or 54.

6~~14~~. The chimeric antigen receptor of any one of claims 1 to 5~~ to 13~~, wherein the extracellular domain includes a linker domain which links the binding domain to the transmembrane domain.

7~~15~~. The chimeric antigen receptor of claim 6~~14~~, wherein the linker domain is at least 12 amino acids in length, or is at least about 12 amino acids in length, or~~.~~

~~16. The chimeric antigen receptor of claim 14, wherein the linker domain~~ is at least 119 amino acids in length, or is at least about 119 amino acids in length, or~~.~~

~~17. The chimeric antigen receptor of claim 14, wherein the linker domain~~ is at least 229 amino acids in length, or is at least about 229 amino acids in length.

8~~18~~. The chimeric antigen receptor of claim 6~~15~~, wherein the linker domain is up to 119 amino acids in length, or up to about 119 amino acids in length, or~~.~~

~~19. The chimeric antigen receptor of claim 16, wherein the linker domain~~ is up to 229 amino acids in length, or up to about 229 amino acids in length.

~~20. The chimeric antigen receptor of claim 14 to 19, wherein the linker domain includes an amino acid sequence identical to the sequence of the IgG4 hinge or includes a sequence identical to a modified version of the IgG4 hinge, having up to 2 amino acid modifications.~~

9~~21~~. The chimeric antigen receptor of claim 6~~14~~, wherein the linker domain includes, or consists of, a sequence selected from SEQ ID No. 55, SEQ ID No. 56 or SEQ ID No. 57, or functional variants thereof.

~~22. The chimeric antigen receptor of claim 11, wherein the extracellular domain includes a linker greater than 12 amino acids in length, at least 119 amino acids in length, greater than 119 amino acids in length, or at least 229 amino acids in length, and which links the binding domain to the transmembrane domain, and wherein the linker domain is linked to the C-terminus of the VH domain.~~

~~23. The chimeric antigen receptor of any one of claims 1 to 22, wherein the intracellular signalling domain includes a portion having an amino acid sequence identical to a signalling portion of an activation receptor, or functional variants thereof.~~

~~24. The chimeric antigen receptor of claim 23, wherein the activation receptor is a member of the CD3 co-receptor complex.~~

~~25. The chimeric antigen receptor of claim 23, wherein the activation receptor is CD3-ζ (CD3 zeta).~~

~~26. The chimeric antigen receptor of any one of claims 1 to 25, wherein the signalling domain includes a portion having an amino acid sequence identical to a signalling portion of a co-stimulatory receptor.~~

~~27. The chimeric antigen receptor of claim 26, wherein the co-stimulatory receptor is selected from the group consisting of: CD27, CD28, CD30, CD40, DAP10, OX40, 4-1BB (CD137) and ICOS.~~

~~28. The chimeric antigen receptor of claim 26, wherein the co-stimulatory receptor is 4-1BB (CD137).~~

~~29. A chimeric antigen receptor according to any one of claims 1 to 28, wherein the intracellular domain includes an amino acid sequence identical to at least a signalling portion of CD3-ζ (CD3 zeta) and an amino acid sequence identical to a signalling portion of 4-1BB.~~

10~~30~~. The~~A~~ chimeric antigen receptor of~~according to~~ any one of claims 1 to 9~~ to 22~~, wherein the intracellular domain includes SEQ ID No. 58 and/or SEQ ID No. 59.

11~~31~~. A chimeric antigen receptor comprising, or consisting of, an amino acid sequence selected from the group consisting of: SEQ ID No. 60, 61, 62, 63, 64 and 65, or functional variants thereof.

~~32. A chimeric antigen receptor comprising, or consisting of, an amino acid sequence selected from the group consisting of: SEQ ID No. 62, 63, 64, and 65, or functional variants thereof.~~

12~~33~~. A nucleic acid molecule including a nucleotide sequence encoding the chimeric antigen receptor of any one of claims 1 to 11~~ to 32~~.

~~34. A nucleic acid construct including a nucleic acid molecule of claim 33 and a promoter.~~

~~35. A nucleic acid construct according to claim 34 wherein the promoter is selected from the group consisting of: Simian virus 40 (SV40), cytomegalovirus (CMV), P-actin, Ubiquitin C (UBC), elongation factor-1 alpha (EF1A), phosphoglycerate kinase (PGK) and CMV early enhancer/chicken β actin (CAGG).~~

~~36. A nucleic acid construct according to claim 34 wherein the promoter is the CMV promoter.~~

~~37. The nucleic acid construct of any one of claims 34 to claim 36, wherein the nucleic acid construct is a vector.~~

~~38. The nucleic acid molecule of claim 33 or the nucleic acid construct of any one of claims 34 to 37 for use in preparing a genetically modified cell.~~

~~39. Use of the nucleic acid molecule of claim 33 or the nucleic acid construct of any one of claims 34 to 37 in the preparation of a genetically modified cell.~~

13~~40~~. A viral vector including the nucleic acid molecule of claim 12~~33 or the nucleic acid construct of any one of claims 34 to 37~~.

~~41. The viral vector of claim 40, wherein viral vector is a lentivirus.~~

~~42. The viral vector of claim 40 or claim 41, for use in a method of preparing a genetically modified cell.~~

14~~43~~. Use of the viral vector of claim 13~~40 or claim 41~~ in a method of preparing a genetically modified cell.

~~44. The viral vector of claim 40 or claim 41 for use in the preparation of a medicament for the treatment of cancer associated with Lgr5 expression or for the killing of a cell expressing, or aberrantly-expressing, Lgr5.~~

~~45. Use of the viral vector of claim 40 or claim 41 in the preparation of a medicament for the treatment of cancer associated with Lgr5 expression or for the killing of a cell expressing or aberrantly-expressing Lgr5.~~

~~46. A cell including the chimeric antigen receptor of any one of claims 1 to 32.~~

15~~47~~. A genetically modified cell, the cell including the nucleic acid molecule of claim 12~~33~~, ~~or the nucleic acid construct of any one of claims 34 to 37,~~ or a genomically integrated form of the nucleic acid molecule~~ or construct~~.

16~~48~~. The ~~cell of claim 46 or the~~ genetically modified cell of claim 15~~47~~, wherein the cell is a leukocyte, a peripheral blood mononuclear cell (PBMC), a lymphocyte, a T cell, a natural killer cell or a natural killer T cell.

~~49. The cell or genetically modified cell of claim 48, wherein the T cell is a CD4+ T cell.~~

~~50. The cell or genetically modified cell of claim 48, wherein the T cell is a CD8+ T cell.~~

17~~51~~. Use of a cell including a chimeric antigen receptor of any one of claims 1 to 11 in the manufacture of a medicament for killing a target cell expressing or aberrantly-expressing Lgr5~~A method of killing a target cell expressing or~~

~~aberrantly-expressing Lgr5, the method including exposing the target cell to a cell or genetically modified cell expressing a chimeric antigen receptor, wherein the chimeric antigen receptor targets Lgr5.~~

~~52. The method of claim 51, wherein the cell or genetically modified cell includes a chimeric antigen receptor according to any one of claims 1 to 32~~.

~~53. The method of claim 51, wherein the cell or the genetically modified cell is the cell or genetically modified cell of any one of claims 46 to 50.~~

~~54. The method of any one of claims 51 to 53, wherein the cell or genetically modified cell is autologous to the target cell.~~

~~55. The method of any one of claims 51 to 53, wherein the cell or genetically modified cell is allogeneic to the target cell.~~

~~56. The method of any one of claims 51 to 55, wherein the target cell is within the body of a subject.~~

18~~57~~. The use of ~~method of any one of~~ claim~~s~~ 17~~51 to 56~~, wherein the target cell is a cancer cell.

19. Use of a cell expressing a chimeric antigen receptor of any one of claims 1 to 11 in the manufacture of a medicament for preventing or treating cancer associated with Lgr5 expression in a patient.

20~~58~~. The use of ~~method of~~ claim 18~~57~~ or claim 19, wherein the cancer ~~cell~~ is selected from one or more of; breast, pancreatic, prostate, colon, colorectal, gastrointestinal, lung (NSCLC), lymphoma, ovarian or B-cell lymphoma.

~~59. The method of claim 57, wherein the cancer cell is selected from: colorectal cancer, colon cancer or a gastrointestinal cancer.~~

~~60. The method of any one of claims 51 to 59, further including analysing the surface expression of Lgr5 on the target cells prior to exposing the target cell to the cell or genetically modified cell expressing a chimeric antigen receptor.~~

~~61. The method of claim 60, wherein the target cell is a cancer cell, the surface expression of Lgr5 on the target cells is compared to a comparable non-cancerous cell to identify aberrant expression.~~

~~62. A method of preventing or treating a patient having cancer associated with Lgr5 expression, the method including exposing the patient to a cell expressing a chimeric antigen receptor, wherein the chimeric antigen receptor targets Lgr5.~~

~~63. The method of claim 62, wherein the patient is administered a chimeric antigen receptor according to any one of claims 1 to 32.~~

~~64. The method of claim 63, wherein the patient is administered a cell or genetically modified cell of any one of claims 46 to 50.~~

~~65. The method of claim 64, wherein the cell or genetically modified cell is autologous to the patient.~~

~~66. The method of claim 64, wherein the cell or genetically modified cell is allogeneic to the patient.~~

~~67. The method of any one of claims 62 to 66 further including identifying the presence of cancer stem cells in a patient prior to exposing the patient to a cell expressing a chimeric antigen receptor.~~

~~68. The method of any one of claims 62 to 67, wherein the cancer is metastatic or is recurrent cancer.~~

21~~69~~. A pharmaceutical composition including a nucleic acid molecule according to claim 12~~33, a nucleic acid construct according to any one of claims 34 to 37~~, a viral vector of ~~according to any one of~~ claim~~s~~ 13~~40 to 42~~ or the ~~cell or~~ genetically modified cell of ~~any one of~~ claim~~s~~ 15 or claim 16~~46 to 50~~ and further including a pharmaceutically acceptable carrier, excipient or diluent.

~~70. The pharmaceutical composition of claim 69, further comprising a cytokine.~~