Claims

1. An isolated polypeptide comprising a sequence selected from:
   (a) the sequence of SEQ ID NO. 2; and
   (b) an immunogenic variant of the sequence of (a) which is at least 80% identical to SEQ ID NO. 2; and
   (c) an immunogenic fragment of the sequence of (a) comprising at least 9 contiguous amino acids of SEQ ID NO. 2.
2. The isolated polypeptide according to claim 1 comprising or consisting of the sequence selected from SEQ ID NOs. 2 and 11 to 14.
3. A fusion protein comprising the isolated polypeptide according to claim 1 or claim 2 fused to a second or further polypeptide selected from (i) one or more other polypeptides selected from (x) polypeptides having the sequences of SEQ ID NOs. 1 and 3-8 and immunogenic variants of the polypeptides of (x) which are at least 80% identical thereto and immunogenic fragments of the polypeptides of (x) which comprise at least 9 contiguous amino acids of the sequence of the said polypeptide and (y) polypeptides having the sequences of SEQ ID NOs. 9, 10, 15-22 and 39 (ii) other polypeptides which are melanoma associated antigens (iii) polypeptide sequences which are capable of enhancing an immune response and (iv) polypeptide sequences which are capable of providing strong CD4+ help to increase CD8+ T cell responses to antigen epitopes.
4. An isolated nucleic acid encoding the polypeptide or fusion protein according to any one of claims 1 to 3.
5. The nucleic acid according to claim 4 which is a DNA.
6. The nucleic acid according to claim 5 comprising or consisting of a sequence selected from any one of SEQ ID NOs. 24 and 32.
7. The nucleic acid according to claim 6 which is codon optimised for expression in a human host cell.
8. The nucleic acid according to claim 4 which is an RNA.
9. The nucleic acid according to any one of claims 4, 5, 7 or 8 which is an artificial nucleic acid sequence.
10. A vector comprising the nucleic acid according to any one of claims 4 to 9.

~~11.~~10. ~~The~~, preferably wherein the vector ~~according to claim 10 which~~ comprises DNA encoding regulatory elements suitable for permitting transcription of a translationally active RNA molecule in a human host cell.

~~12.~~ The vector according to claim 10 ~~or claim 11~~ which is a viral vector~~.~~

~~13.~~11. ~~The~~, preferably wherein the vector ~~according to claim 12 which is~~is selected from an adenoviral vector, an adeno-associated virus (AAV), alphavirus, herpes virus, arena virus, measles virus, poxvirus, paramyxovirus, lentivirus or rhabdovirus vector.

~~14.~~12. An immunogenic pharmaceutical composition comprising a polypeptide, nucleic acid, fusion protein or vector according to any one of claims 1 to ~~13~~11 together with a pharmaceutically acceptable carrier.

~~15.~~13. A vaccine composition comprising a polypeptide, nucleic acid or vector according to any one of claims 1 to ~~13~~11 together with a pharmaceutically acceptable carrier.

~~16.~~ The composition according to claim ~~14~~12 or claim ~~15~~13 which comprises one or more immunostimulants~~.~~

~~17.~~14. ~~The composition according to claim 16~~, preferably wherein the immunostimulants are selected from aluminium salts, saponins, immunostimulatory oligonucleotides, oil-in-water emulsions, aminoalkyl glucosaminide 4-phosphates, lipopolysaccharides and derivatives thereof and other TLR4 ligands, TLR7 ligands, TLR8 ligands, TLR9 ligands, IL-12 and interferons.

~~18.~~15. The composition according to any one of claims ~~14~~12 to ~~17~~14 which is a sterile composition suitable for parenteral administration.

~~19.~~16. A polypeptide, nucleic acid, fusion protein, vector or composition according to any one of claims 1 to ~~18~~15 for use in medicine.

~~20. A method~~Use of ~~raising an immune response in a human which comprises administering to said human the~~a polypeptide, nucleic acid, vector or composition according to any one of claims 1 to ~~18.~~

~~21. The method according to claim 20~~15 in the manufacture of a medicament for the treatment of cancer, wherein the ~~immune response~~medicament is ~~raised against a cancerous tumor expressing a sequence selected from SEQ ID NO. 2, an immunogenic variant of SEQ ID NO. 2 which is at least 80%~~

identical to SEQ ID NO. 2, and an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2.

22. A polypeptide, nucleic acid, vector or composition according to any one of claims 1 to 18 for use in raising an immune response in a human.

23.17. The polypeptide, nucleic acid, vector or composition according to claim 22, preferably wherein the immune response is raised against a cancerous tumor expressing a sequence selected from: the sequence of SEQ ID NO. 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2.

24.18. A methodUse of treatinga polypeptide, nucleic acid, fusion protein, vector or composition according to any one of claims 1 to 15 in the manufacture of a medicament for the treatment or prevention of cancer in a human patient suffering from cancer, wherein the cells of the cancer express a sequence selected from SEQ ID NO. 2, an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2, and an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2, or of preventing a human from suffering from cancer which cancer would express a sequence selected from SEQ ID NO. 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2, which method comprises administering to said human a polypeptide, nucleic acid encoding said polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 182.

25.19. AUse of a polypeptide, nucleic acid, fusion protein, vector or composition according to any one of claims 1 to 18 for use in treating or preventing cancer in a human, wherein the cells of the cancer express a sequence selected from SEQ ID NO. 2, an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2, and an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 215 in the manufacture of a medicament for the treatment of cancer, wherein T-cells derived from a human suffering from cancer are to

be *ex vivo* stimulated and/or amplified, and wherein said stimulated and/or amplified T cells are to be subsequently reintroduced into the said human for the treatment of the said cancer in the said human.

~~26. A polypeptide, nucleic acid, fusion protein, vector or composition according to any one of claims 1-18 for use in the *ex vivo* stimulation and/or amplification of T-cells derived from a human suffering from cancer, for subsequent reintroduction of said stimulated and/or amplified T cells into the said human for the treatment of the said cancer in the said human.~~

~~27. A method of treatment of cancer in a human, wherein the cells of the cancer express a sequence selected from SEQ ID NO. 2, an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2, and an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, which comprises taking from said human a population of white blood cells comprising at least T-cells optionally with antigen-presenting cells, stimulating and/or amplifying said T-cells in the presence of a polypeptide, nucleic acid encoding said polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 18, and reintroducing some or all of said white blood cells at least stimulated and/or amplified T cells T-cells into the human.~~

~~28. A method or a polypeptide, nucleic acid, fusion protein, vector or composition for use according to any one of claims 21 and 23 to 27 wherein the cancer is melanoma e.g. cutaneous melanoma.~~

~~29.~~20. A process for preparing a T-cell population which is cytotoxic for cancer cells which express a sequence selected from SEQ ID NO. 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2 which comprises (a) obtaining T-cells optionally with antigen-presenting cells from a cancer patient and (ii) stimulating and amplifying the T-cell population *ex vivo* with a polypeptide, nucleic acid, fusion protein, vector or composition according to any one of claims 1 to ~~18~~15.

~~30.~~21. A T-cell population obtainable by a process~~-~~ which comprises (a) obtaining T-cells optionally with antigen-presenting cells from a cancer patient and (b) stimulating and amplifying the T-cell population *ex vivo* with a

polypeptide having the sequence of SEQ ID NO. 2 or an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2.

~~31.~~22. A T-cell which has been stimulated with a polypeptide having the sequence of SEQ ID NO. 2 or an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2.

~~32.~~23. An antigen presenting cell modified by *ex vivo* loading with the polypeptide, nucleic acid, fusion protein, vector or composition according to any one of claims 1 to ~~18~~15 or genetically engineered to express the polypeptide according to any one of claims 1 to 3, preferably wherein the antigen presenting cell is a dendritic cell.

~~33. The antigen presenting cell of claim 32 which is a dendritic cell.~~

~~34.~~24. An exosome loaded with a polypeptide, nucleic acid, fusion protein, vector or composition according to any one of claims 1 to ~~18~~15 or genetically engineered to express the polypeptide according to any one of claims 1 to 3.

~~35.~~25. A pharmaceutical composition comprising the T-cell population, the T-cell, antigen presenting cell or exosome according to any one of claims ~~30~~21 to ~~34~~24 together with a pharmaceutically acceptable carrier.

~~36.~~26. A T-cell population, T-cell, antigen presenting cell or exosome according to any one of claims ~~30~~21 to ~~34~~24 for use in medicine.

~~37. A method~~Use of ~~treating~~ a ~~human suffering from cancer wherein the cells of the cancer express a sequence selected from SEQ ID NO. 2, an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2, and an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, or of preventing a human from suffering from cancer wherein the cells of the cancer would express a sequence selected from SEQ ID NO. 2 an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2, and an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, which comprises administering to said human the~~ T-cell population, ~~the~~ T-cell, antigen presenting cell, exosome or composition according to any one of claims ~~30~~21 to ~~35.~~

~~38.~~27. ~~A T-cell population, T-cell, antigen presenting cell, exosome or composition according to any one~~25 in the manufacture of ~~claims 30 to 35~~a

medicament for ~~use in treating~~the treatment or ~~preventing~~prevention of cancer in a human, wherein the cells of the cancer express a sequence selected from SEQ ID NO. 2 and immunogenic fragments of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2.

~~39. A process, a method or a T-cell population, T-cell, antigen presenting cell, exosome or composition for use according to any one of claims 29, 37 and 38 wherein the cancer is melanoma e.g. cutaneous melanoma.~~

~~40.~~28. An isolated antigen-binding polypeptide which is immunospecific a polypeptide having the sequence of SEQ ID NO. 2 or an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2.

~~41.~~29. The antigen-binding polypeptide according to claim ~~40~~28 which is a monoclonal antibody or a fragment thereof.

~~42.~~30. The antigen-binding polypeptide according to claim ~~40~~28 or claim ~~41~~29 which is coupled to a cytotoxic moiety.

~~43.~~31. An antigen-binding polypeptide according to any one of claims ~~40~~28 to ~~42~~30 for use in medicine.

~~44.~~32. A pharmaceutical composition comprising the antigen-binding polypeptide according to any one of claims ~~40~~28 to ~~42~~30 together with a pharmaceutically acceptable carrier.

~~45. A method~~Use of ~~treating a human suffering from cancer wherein the cells of the cancer express a sequence selected from SEQ ID NO. 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2 , or of preventing a human from suffering from cancer wherein the cells of the cancer would express a sequence selected from SEQ ID NO. 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2, which comprises administering to said human the~~an antigen-binding polypeptide or a composition according to any one of claims ~~40~~28 to ~~42~~30 and ~~44.~~

~~46. An antigen-binding polypeptide or a composition according to any one~~32 in the manufacture of ~~claims 40 to 42 and 44~~a medicament for ~~use in treating~~the treatment or ~~preventing~~prevention of cancer in a human, wherein

the cells of the cancer express a sequence selected from SEQ ID NO. 2 and immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2~~.~~

~~47.~~33. ~~A method, antigen-binding polypeptide or composition according to claim 45 or claim 46 wherein the cancer is melanoma e.g. cutaneous melanoma~~.

~~48.~~34. An isolated antigen-binding polypeptide which is immunospecific for an HLA-bound polypeptide that is or is part of the polypeptide having a sequence selected from the sequence of SEQ ID NO. 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. ~~2.~~2, preferably wherein the antigen binding polypeptide is a T-cell receptor or a fragment thereof.

~~49. The antigen-binding polypeptide according to claim 48 which is a T-cell receptor or a fragment thereof.~~

~~50.~~35. ~~The antigen-binding polypeptide according to claim 48 or claim 49~~34 which is coupled to another polypeptide that is capable of binding to cytotoxic cells or other immune components in a subject.

~~51.~~36. A cytotoxic cell that has been engineered to express the antigen-binding polypeptide of ~~any one of claims 48 to 50~~claim 34 or claim 35 on its surface~~.~~, preferably wherein the cytotoxic cell is a T-cell.

~~52. The cytotoxic cell according to claim 51 which is a T-cell.~~

~~53.~~37. A cytotoxic cell according to claim ~~51 or claim 52~~36 for use in medicine.

~~54.~~38. A pharmaceutical composition comprising the cell according to claim ~~51 or claim 52~~36.

~~55. A method~~Use of ~~treating a human patient suffering from cancer wherein~~ a cytotoxic cell according to claim 36 in the ~~cells~~manufacture of ~~the cancer express a sequence selected from SEQ ID NO. 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2, or of preventing a human from suffering from cancer which cancer would express a sequence selected from SEQ ID NO. 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9~~

~~contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2, which method comprises administering to said human a cell according to claim 51 or claim 52.~~

~~56.~~39. ~~A cytotoxic cell according to claim 51 or claim 52~~a medicament for ~~use in treating~~the treatment or ~~preventing~~prevention of cancer in a human, wherein the cells of the cancer express a sequence selected from SEQ ID NO. 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2.

~~57.~~40. A method of diagnosing a human as suffering from cancer, comprising the steps of:

determining if the cells of said cancer express a polypeptide sequence selected from SEQ ID NO. 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2, or a nucleic acid encoding said polypeptide sequence, and diagnosing said human as suffering from cancer if said polypeptide or corresponding nucleic acid is overexpressed in said cancer cells.

~~58.~~41. A method of diagnosing that a human suffering from cancer which is cutaneous melanoma or uveal melanoma, comprising the steps of:

determining if the cells of said cancer express a polypeptide sequence selected from SEQ ID NO. ~~2,an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO.~~ 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2; or a nucleic acid encoding said polypeptide sequence, and diagnosing said human as suffering from cancer which is cutaneous melanoma or uveal melanoma if said polypeptide or corresponding nucleic acid is overexpressed in said cancer cells.

~~59. A method of treating a human suffering from cancer, comprising the steps of:~~

~~(a) determining if the cells of said cancer express a polypeptide sequence selected from SEQ ID NO. 2, an immunogenic fragment of SEQ ID NO. 2 comprising at least 9 contiguous amino acids of SEQ ID NO. 2, and an immunogenic variant of SEQ ID NO. 2 which is at least 80% identical to SEQ ID NO. 2 or a nucleic acid encoding said polypeptide (e.g. selected from the sequences of SEQ ID NOs. 24 and 32); and if so~~

~~(b) administering to said human a polypeptide, nucleic acid, fusion protein, vector, composition, T-cell population, T-cell, antigen presenting cell, exosome, antigen-binding polypeptide or cytotoxic cell according to any one of claims 1 to 18, 30 to 35, 40 to 42, 44, 50, 51 and 53.~~

~~60.~~42. ~~Use of a~~A polypeptide comprising a sequence selected from:

(a) the sequence of SEQ ID NO. 2; or

(b) an immunogenic variant of the sequences of (a) which is at least 80% identical to SEQ ID NO. 2; and

(c) an immunogenic fragment of the sequence of (a) comprising at least 9 contiguous amino acids of SEQ ID NO. 2;

isolated from the tumor of a human suffering from cancer, or ~~use of~~ a nucleic acid encoding said polypeptide, for use as a biomarker for the determination of whether said human would be suitable for treatment by a vaccine comprising a polypeptide, nucleic acid, fusion protein, vector, composition, T-cell population, T-cell, antigen presenting cell, exosome, antigen-binding polypeptide or cytotoxic cell according to any one of claims 1 to ~~18, 30~~15, 21 to ~~35, 40~~25, 28 to ~~42, 44, 51, 52~~30, 32, 36, and ~~54~~38.

~~61.~~43. The ~~method or use~~use according to any one of claims 17 to 19, 27 and 33, the process according to claim ~~59 or~~ 20, or the polypeptide for use according to claim ~~60~~42, wherein the cancer is melanoma e.g. cutaneous melanoma.

~~62.~~44. ~~A method~~The use according to any one of claims 17 to 19, 27 and 33, the process according to claim 20, or ~~a~~the polypeptide~~, nucleic acid, vector or composition~~ for use according to ~~any one of claims 21 and 23 to 27~~ claim 42, wherein the cancer is uveal melanoma.

45. A pharmaceutical composition comprising the T-cell population, the T-cell, antigen presenting cell or exosome according to any one of claims 21 to 24

together with a pharmaceutically acceptable carrier for use in treating or preventing cancer in a human.

63. A ~~method according to claim 45 or an~~pharmaceutical composition comprising the antigen-binding polypeptide ~~or composition for use according to claim 46 wherein the cancer is uveal melanoma.~~

64. 46. ~~A process, a method or a T-cell population, T-cell, antigen presenting cell, exosome or composition for use~~ according to any one of claims ~~29, 37 and 38 wherein the~~28 to 30 together with a pharmaceutically acceptable carrier for use in treating or preventing cancer ~~is uveal melanoma~~in a human.

65. ~~The method or use according to claims 59 or 60 wherein the cancer is uveal melanoma.~~