Claims

1. Use of:

(i) a~~A~~n isolated polypeptide comprising a sequence selected from:

(a) the sequence of SEQ ID NO. 1; and

(b) an immunogenic variant of the sequence of (a) which is at least ~~80~~90% identical to SEQ ID NO: 1 and elicits a specific immune response to SEQ ID NO: 1; and

(c) an immunogenic fragment of the sequence of (a) comprising at least 9 contiguous amino acids of SEQ ID NO: 1 and elicits a specific immune response to SEQ ID NO: 1,

(ii) a vector comprising an isolated nucleic acid encoding the polypeptide of (i),

(iii) 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 of (i),

(iv) a T-cell which has been stimulated with a polypeptide of (i),

(v) an antigen presenting cell modified by *ex vivo* loading with the polypeptide of (i) or vector of (ii) or genetically engineered to express the polypeptide of (i),

(vi) an exosome loaded with a polypeptide of part (i),

(vii) an isolated antigen-binding polypeptide which is immunospecific for a polypeptide of (i),

(viii) an isolated antigen-binding polypeptide which is immunospecific for an HLA-bound polypeptide having a sequence of (i).

(ix) a cytotoxic cell engineered to express the antigen-binding polypeptide of (viii) on its surface, or

(x) an immunogenic pharmaceutical composition comprising a polypeptide of (i), a vector of (ii), a T-cell population of (iii), a T-cell of (iv), an antigen presenting cell of (v), exosome of (vi), antigen-binding polypeptide of (vii) or cytotoxic cell of (ix) together with a pharmaceutically acceptable carrier;

in the manufacture of a medicament for the treatment or prevention of cancer in a human, wherein the cells of the cancer express a corresponding sequence selected from SEQ ID NO. 1, an immunogenic variant of SEQ ID NO: 1 which is at least 90% identical to SEQ ID NO: 1 and elicits a specific immune response to SEQ ID NO: 1, and an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1 and elicits a specific immune response to SEQ ID NO: 1.

2. The use according to claim 1 wherein the polypeptide according to (i) is used in the manufacture of the medicament.

~~2~~3. The use according to claim 2 wherein the ~~An~~ isolated polypeptide ~~according to claim 1 comprising~~ comprises or ~~consisting~~ consists of the sequence selected from any one of SEQ ID NOs. 1, 11-14, 55-57 and 73-74.

~~3. A fusion polypeptide 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: 2-10 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 continuous amino acids of the sequence of the said polypeptide and (y) polypeptides having the sequences of SEQ ID NOs: 15-32, 51-54, 58-72 and 75-78 (ii) other polypeptides which are melanoma associated antigens (iii) polypeptide sequences which are capable of enhancing an immune response (i.e. immunostimulant sequences) and (iv) polypeptide sequences, e.g. comprising universal CD4 helper epitopes, which are capable of providing strong CD4+ help to increase CD8+ T-cell responses to antigen epitopes.~~

~~4. An isolated nucleic acid encoding the fusion polypeptide according to claim 3.~~

~~5. A vector comprising an isolated nucleic acid encoding the polypeptide according to any one of claims 1 to 3 or comprising the nucleic acid according to claim 4.~~

4. The use according to claim 1 wherein the vector according to (ii) is used in the manufacture of the medicament.

~~6~~5. The ~~nucleic acid according to claim 4 or the vector~~use according to claim ~~5~~ 4 wherein the nucleic acid of (ii) is a DNA.

~~7~~6. The ~~nucleic acid or vector~~use according to claim ~~6~~ 5 wherein the nucleic acid comprises a sequence selected from any one of SEQ ID NOs. 33 and 41.

~~8~~7. The ~~nucleic acid or vector~~use according to claim ~~7~~ 6 wherein the nucleic acid is codon optimised for expression in a human host cell.

~~9~~8. The ~~nucleic acid according to claim 4 or the vector~~use according to claim ~~5~~ 4 wherein the nucleic acid of (ii) is an RNA.

~~10~~9. The ~~nucleic acid or vector~~use according to any one of claims ~~4, 5, 6, 8 and 9~~4 to 8 wherein the nucleic acid of (ii)is an artificial nucleic acid sequence.

~~11~~10. The use according to any one of claims 4 to 9 wherein the vector of (ii) ~~according to any one of claims 5 to 10 which~~ comprises DNA encoding regulatory elements suitable for permitting transcription of a translationally active RNA molecule in a human host cell.

~~12~~11. The use according to any one of claims 4 to 10 wherein the vector of (ii) ~~according to any one of claims 5 to 11 which~~is a viral vector.

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

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

13. The use according to claim 1 wherein the immunogenic pharmaceutical composition according to (x) is used in the manufacture of the medicament.

~~15~~14. The use according to claim 13 wherein the composition of (x) ~~according to claim 14 which~~ comprises one or more immunostimulants.

~~16~~15. The ~~composition~~ use according to claim ~~15~~ 14 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.

~~17~~16. The use according to any one of claims 13 to 15 wherein the composition of (x) ~~according to any one of claims 14 to 16 which~~ is a sterile composition suitable for parenteral administration.

~~18. Use of a polypeptide, nucleic acid encoding said polypeptide, fusion polypeptide, nucleic acid, vector or composition according to any one of claims 1 to 17 for the manufacture of a medicament for use in medicine.~~

~~19. Use of the polypeptide, nucleic acid encoding said polypeptide, vector or composition according to any one of claims 1 to 17 for the manufacture of a medicament for use in raising an immune response in a human.~~

~~20. The use according to claim 19 wherein the immune response is raised against a cancerous tumor expressing a sequence selected from SEQ ID NO. 1, an immunogenic variant of SEQ ID NO: 1 which is at least 80% identical to SEQ ID NO: 1, and an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1.~~

~~21. Use of a polypeptide, nucleic acid encoding said polypeptide, fusion polypeptide, nucleic acid, vector or composition according to any one of claims 1 to 17 for the manufacture of a medicament for use in treating or preventing cancer in a human, wherein the cells of the cancer express a corresponding sequence selected from SEQ ID NO. 1, an immunogenic variant of SEQ ID NO: 1 which is at least 80% identical to SEQ ID NO: 1, and an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1.~~

~~22. A polypeptide, nucleic acid encoding said polypeptide, fusion polypeptide, nucleic acid, vector or composition according to any one of claims 1-17 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.~~

~~23. The use according to any one of claims 20 to 22 wherein the cancer is melanoma e.g. cutaneous melanoma.~~

~~24. A process for preparing a T-cell population which is cytotoxic for cancer cells which express a sequence selected from SEQ ID NO. 1, an immunogenic variant of SEQ ID NO: 1 which is at least 80% identical to SEQ ID NO: 1, and an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1 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 corresponding polypeptide, nucleic acid encoding said polypeptide, fusion polypeptide, nucleic acid, vector or composition according to any one of claims 1 to 17.~~

~~25. 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: 1 or an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1.~~

~~26. A T-cell which has been stimulated with a polypeptide having the sequence of SEQ ID NO: 1 or an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1.~~

~~27. An antigen presenting cell modified by *ex vivo* loading with the polypeptide, nucleic acid encoding said polypeptide, fusion polypeptide, nucleic acid, vector or composition according to any one of claims 1 to 17 or genetically engineered to express the polypeptide according to any one of claims 1 to 3.~~

~~28~~17. The use according to any one of claim 1 wherein the antigen presenting cell of (v) ~~claim 27 which~~ is a dendritic cell.

~~29. An exosome loaded with a polypeptide prepared from cells loaded with a polypeptide, nucleic acid encoding said polypeptide, fusion polypeptide, nucleic acid, vector or composition according to any one of claims 1 to 17 or genetically engineered to express the polypeptide according to any one of claims 1 to 3.~~

~~30. A pharmaceutical composition comprising the T-cell population, the T-cell, antigen presenting cell or exosome according to any one of claims 25 to 29 together with a pharmaceutically acceptable carrier.~~

~~31. Use of a T-cell population, T-cell, antigen presenting cell or exosome according to any one of claims 25 to 29 for the manufacture of a medicament for use in medicine.~~

~~32. Use of a T-cell population, T-cell, antigen presenting cell, exosome or composition according to any one of claims 25 to 30 for the manufacture of a medicament for use in treating or preventing cancer in a human, wherein the cells of the cancer express a corresponding sequence selected from SEQ ID NO. 1, an immunogenic variant of SEQ ID NO: 1 which is at least 80% identical to SEQ ID NO: 1, and an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1.~~

~~33. The use according to any one of claims 24and 32 wherein the cancer is melanoma e.g. cutaneous melanoma.~~

~~34. An isolated antigen-binding polypeptide which is immunospecific for a polypeptide having the sequence of SEQ ID NO: 1 or an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1.~~

~~35~~18. The use according to claim 1 wherein the antigen-binding polypeptide of (vii) ~~according to claim 34 which~~ is a monoclonal antibody or a fragment thereof.

~~36~~19. The use according to claim 1 or claim 18 wherein the antigen-binding polypeptide of (vii) ~~according to claim 34 or claim 35 which~~ is coupled to a cytotoxic moiety.

~~37. Use of an antigen-binding polypeptide according to any one of claims 34 to 36 for the manufacture of a medicament for use in medicine.~~

~~38. A pharmaceutical composition comprising the antigen-binding polypeptide according to any one of claims 34 to 36 together with a pharmaceutically acceptable carrier.~~

~~39. Use of an antigen-binding polypeptide or a composition according to any one of claims 34 to 36 and 38 for the manufacture of a medicament for use in treating or preventing cancer in a human, wherein the cells of the cancer express a corresponding sequence selected from SEQ ID NO. 1, an immunogenic variant of~~

~~SEQ ID NO: 1 which is at least 80% identical to SEQ ID NO: 1, and an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1.~~

~~40. The use according to claim 39 wherein the cancer is melanoma e.g. cutaneous melanoma.~~

~~41. An isolated antigen-binding polypeptide which is immunospecific for an HLA-bound polypeptide having a sequence selected from SEQ ID NO. 1, an immunogenic variant of SEQ ID NO: 1 which is at least 80% identical to SEQ ID NO: 1, and an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1.~~

~~42~~20. The use according to claim 1 wherein antigen-binding polypeptide ~~according to claim 41 which~~of (viii) is a T-cell receptor or a fragment thereof.

~~43~~21. The use according to claim 1 or claim 20 wherein the antigen-binding polypeptide ~~according to claim 41 or claim 42~~of (viii) ~~which~~ is coupled to another polypeptide that is capable of binding to cytotoxic cells or other immune components in a subject.

~~44. A cytotoxic cell that has been engineered to express the antigen-binding polypeptide of any one of claims 41 to 43 on its surface.~~

~~45~~22. The use according to claim 1 wherein the cytotoxic cell of (ix) ~~according to claim 44 which~~ is a T-cell.

~~46. Use of a cytotoxic cell according to claim 44 or claim 45 for the manufacture of a medicament for use in medicine~~

~~47. A pharmaceutical composition comprising the cell according to claim 44 or claim 45.~~

~~48. Use of a cytotoxic cell according to claim 44 or claim 45 for the manufacture of a medicament for use in treating or preventing cancer in a human, wherein the cells of the cancer express a corresponding sequence selected from SEQ ID NO. 1, an immunogenic variant of SEQ ID NO: 1 which is at least 80% identical to SEQ ID NO:~~

1, and an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1.

49. 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. 1, an immunogenic variant of SEQ ID NO: 1 which is at least 80% identical to SEQ ID NO: 1, and an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1, or a nucleic acid encoding said polypeptide sequence selected from the sequences of SEQ ID NO: 33 and 41, and diagnosing said human as suffering from cancer if said polypeptide or corresponding nucleic acid is overexpressed in said cancer cells.

50. A method of diagnosing that a human is 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. 1, an immunogenic variant of SEQ ID NO: 1 which is at least 80% identical to SEQ ID NO: 1, and an immunogenic fragment of SEQ ID NO: 1 comprising at least 9 contiguous amino acids of SEQ ID NO: 1; 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.

51. Use of a polypeptide comprising a sequence selected from:

(a) the sequence of SEQ ID NO. 1; or

(b) an immunogenic variant of the sequences of (a) which is at least 80% identical to SEQ ID NO: 1; and

(c) an immunogenic fragment of the sequence of (a) comprising at least 9 contiguous amino acids of SEQ ID NO: 1;

isolated from the tumor of a human suffering from cancer, or use of a nucleic acid encoding said polypeptide selected from the sequences of SEQ ID NO: 33 and 41, as a biomarker for the determination of whether said human would be suitable for treatment by a vaccine comprising a corresponding polypeptide, nucleic acid encoding said polypeptide, fusion protein, nucleic acid, 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 17, 25 to 30, 34 to 36, 38, 44, 45 and 47.~~

~~52. The method or use according to claim 50 or claim 51 wherein the cancer is melanoma e.g. cutaneous melanoma~~

23. The use according to any one of claims 1 to 22 wherein the cancer is melanoma e.g. cutaneous melanoma.

~~53~~24. The use according to any one of claims ~~20 to 22~~1 to 22 wherein the cancer is uveal melanoma.~~54. The use according to claim 39 wherein the cancer is uveal melanoma.~~

~~55. The use according to any one of claims 24 and 32 wherein the cancer is uveal melanoma.~~

~~56. The method or use according to claim 50 or claim 51 wherein the cancer is uveal melanoma.~~

~~57. A fusion polypeptide according to claim 3 which comprises (x) a polypeptide comprising a sequence selected from:~~

~~(a) the sequence of SEQ ID NO. 1; and~~

~~(b) an immunogenic variant of the sequence of (a) which is at least 80% identical to SEQ ID NO: 1; and~~

~~(c) an immunogenic fragment of the sequence of (a) comprising at least 9 contiguous amino acids of SEQ ID NO: 1, and~~

~~(y) one or more (e.g. one, two or three) sequences selected from the sequences of SEQ ID NOs. 2, 3 and 4; or, in respect of each of the said sequences of SEQ ID NOs. 2, 3 and 4, a variant of the said sequence which is at least 80% identical to the said sequence or an immunogenic fragment comprising at least 9 contiguous amino acids of the said sequence.~~

~~58. A fusion polypeptide according to claim 57 which comprises:~~

~~(i) a sequence selected from:~~

~~(a) the sequence of SEQ ID NO. 1; and~~

~~(b) an immunogenic variant of the sequence of (a) which is at least 80% identical to SEQ ID NO: 1; and~~

~~(c) an immunogenic fragment of the sequence of (a) comprising at least 9 contiguous amino acids of SEQ ID NO: 1; and~~

(ii) 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; and

(iii) a sequence selected from:

(a) the sequence of SEQ ID NO. 3; and

(b) an immunogenic variant of the sequence of (a) which is at least 80% identical to SEQ ID NO: 3; and

(c) an immunogenic fragment of the sequence of (a) comprising at least 9 contiguous amino acids of SEQ ID NO: 3; and

(iv) a sequence selected from:

(a) the sequence of SEQ ID NO. 4; and

(b) an immunogenic variant of the sequence of (a) which is at least 80% identical to SEQ ID NO: 4; and

(c) an immunogenic fragment of the sequence of (a) comprising at least 9 contiguous amino acids of SEQ ID NO: 4.

59. A fusion polypeptide according to claim 58 which comprises the sequences of SEQ ID NOs. 1, 2, 3 and 4.

60. A fusion polypeptide according to claim 58 which comprises:

(i) a sequence selected from:

(a) the sequence of SEQ ID NO. 1; and

(b) an immunogenic variant of the sequence of (a) which is at least 80% identical to SEQ ID NO: 1; and

(c) an immunogenic fragment of the sequence of (a) comprising at least 9 contiguous amino acids of SEQ ID NO: 1; and

(ii) 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; and

(iii) a sequence selected from:

(a) the sequence of SEQ ID NO. 4; and

(b) an immunogenic variant of the sequence of (a) which is at least 80% identical to SEQ ID NO: 4; and

(c) an immunogenic fragment of the sequence of (a) comprising at least 9 contiguous amino acids of SEQ ID NO: 4.

61. A fusion polypeptide according to claim 60 which comprises the sequences of SEQ ID NOs. 1, 2 and 4.

62. An isolated nucleic acid encoding the fusion polypeptide according to any one of claims 57-61.

63. The nucleic acid according to claim 62 which is a DNA.

64. A vector comprising the nucleic acid according to claim 63.

65. The vector according to claim 63 which comprises DNA encoding regulatory elements suitable for permitting transcription of a translationally active RNA molecule in a human host cell.

66. The vector according to claim 64 or claim 65 which is a viral vector.