

## Claims

1. An isolated polypeptide (A) comprising a sequence selected from:
  - (a) the sequence of SEQ ID NO. 1; and
  - (b) an immunogenic variant of the sequence of SEQ ID NO. 1 which is at least 90% identical to the entire length of SEQ ID NO. 1 and elicits a specific immune response to SEQ ID NO: 1; or (B) consisting of the sequence of any one of SEQ ID NO. 2, SEQ ID NO. 5 and SEQ ID NO. 6.
2. An isolated polypeptide according to claim 1 comprising the sequence of SEQ ID NO. 1.
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 comprising a sequence selected from: (a) the sequence of SEQ ID NO. 1; and (b) an immunogenic variant of the sequence of SEQ ID NO. 1 which is at least 90% identical to the entire length of SEQ ID NO. 1 and elicits a specific immune response to SEQ ID NO: 1; and (c) an immunogenic fragment of the sequence of SEQ ID NO. 1 comprising at least 9 contiguous amino acids of SEQ ID NO. 1 (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. 3 and 4.
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 claim 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. 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. The vector according to claim 12 which is an adenoviral vector, an adeno-associated virus (AAV), alphavirus, herpes virus, arena virus, measles virus, poxvirus, paramyxovirus, lentivirus and rhabdovirus vector.
14. An immunogenic pharmaceutical composition comprising a polypeptide, fusion protein, nucleic acid or vector according to any one of claims 1 to 13 together with a pharmaceutically acceptable carrier.
15. A vaccine composition comprising a polypeptide, fusion protein, nucleic acid or vector according to any one of claims 1 to 13 together with a pharmaceutically acceptable carrier.
16. The composition according to claim 14 or claim 15 which comprises one or more immunostimulants.
17. The composition according to claim 16 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. The composition according to any one of claims 14 to 17 which is a sterile composition suitable for parenteral administration.
19. A polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 18 for use in medicine.
20. ~~A-~~The polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 18 for use in a method of raising an immune response in a human ~~which comprises administering to said human,~~ wherein the polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 18 ~~is to be administered to said human.~~
21. ~~The method~~The polypeptide, fusion protein, nucleic acid, vector or composition for use according to claim 20 wherein the immune response is

raised against a cancerous tumor expressing a sequence selected from SEQ ID NO. 1 and variants of the sequence of SEQ ID NO. 1 which are at least 80% identical to SEQ ID NO. 1 and immunogenic fragments of the sequence of SEQ ID NO. 1 comprising at least 9 contiguous amino acids of SEQ ID NO. 1.

~~22. A use of a polypeptide, fusion protein, 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. The polypeptide, fusion protein, nucleic acid, vector or composition according to claim 22 wherein the immune response is raised against manufacture of a cancerous tumor expressing a sequence selected from SEQ ID NO. 1 and immunogenic variants of medicament for the sequence of SEQ ID NO. 1 which are at least 80% identical to SEQ ID NO. 1 and immunogenic fragments treatment of the sequence of SEQ ID NO. 1 comprising at least 9 contiguous amino acids of SEQ ID NO. 1.~~

~~22. A method of treating a human patient suffering from cancer wherein the cells of the cancer express a sequence selected from SEQ ID NO. 1 and immunogenic variants of the sequence of SEQ ID NO. 1 which are at least 80% identical to SEQ ID NO. 1 and immunogenic fragments of the sequence of SEQ ID NO. 1 comprising at least 9 contiguous amino acids of SEQ ID NO. 1, or of preventing a human from suffering from cancer which cancer would express a sequence selected from SEQ ID NO. 1 and immunogenic variants of the sequence of SEQ ID NO. 1 which are at least 80% identical to SEQ ID NO. 1 and immunogenic fragments of the sequence of SEQ ID NO. 1 comprising at least 9 contiguous amino acids of SEQ ID NO. 1, which method comprises administering to said human1.~~

~~24. Use of a polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 18.~~

~~25-23. A polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 18 for use in treating or preventing in the manufacture of a medicament for the treatment or prevention of cancer in a human, wherein the cells of the cancer express a sequence selected from SEQ ID NO. 1 and immunogenic fragments comprising at least 9 contiguous amino acids of SEQ ID NO. 1.~~

~~26.24.~~ AUse of a polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1-18 ~~for use~~ in the ~~ex vivo stimulation and/or amplification of~~manufacture of a medicament for the treatment of cancer, wherein T-cells derived from a human suffering from cancer, ~~for subsequent reintroduction of~~ 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.

~~27.25.~~ A method of treatment of cancer in a human, wherein the cells of the cancer express a sequence selected from SEQ ID NO. 1 and immunogenic variants of the sequence of SEQ ID NO. 1 which are at least 80% identical to SEQ ID NO. 1 and immunogenic fragments of the sequence of SEQ ID NO. 1 comprising at least 9 contiguous amino acids of SEQ ID NO. 1, which comprises taking from said humanUse of a population of white blood cells comprising at least T-cells optionally with antigen-presenting cells in the manufacture of a medicament for the treatment of cancer wherein the cells of the cancer express a sequence selected from SEQ ID NO. 1 and immunogenic variants of the sequence of SEQ ID NO. 1 which are at least 80% identical to SEQ ID NO. 1 and immunogenic fragments of the sequence of SEQ ID NO. 1 comprising at least 9 contiguous amino acids of SEQ ID NO. 1 and taking from said human the population of white blood cells comprising at least T-cells optionally with antigen-presenting cells, stimulating and/or amplifyingwherein said T-cells are to be stimulated and/or amplified in the presence of a polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 18, and ~~reintroducing~~wherein some or all of said white blood cells at least stimulated and/or amplified T cells T-cells are to be reintroduced into the human.

~~28.26.~~ A method or aThe polypeptide, fusion protein, nucleic acid, vector or composition for use according to claim 21 or the use according to any one of claims ~~21 and 23~~22 to 27~~25~~ wherein the cancer is melanoma e.g. cutaneous melanoma.

~~29.27.~~ A process for preparing a T-cell population which is cytotoxic for cancer cells which express a sequence selected from SEQ ID NO. 1 and immunogenic fragments of the sequence 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 polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 18.

~~30-28.~~ 31-29. A T-cell population obtainable by the process of claim ~~29~~27.

~~31-29.~~ 32-30. A T-cell which has been stimulated with a polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 18.

~~32-30.~~ 33-31. An antigen presenting cell modified by *ex vivo* loading with the polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 18 or genetically engineered to express the polypeptide according to any one of claims 1 to 3.

~~33-31.~~ 34-32. The antigen presenting cell of claim ~~32~~30 which is a dendritic cell.

~~34-32.~~ 35-33. An exosome loaded with a polypeptide prepared from cells loaded with a polypeptide, fusion protein, nucleic acid, vector or composition according to any one of claims 1 to 18 or genetically engineered to express the polypeptide according to any one of claims 1 to 3.

~~35-33.~~ 36-34. A pharmaceutical composition comprising the T-cell population, the T-cell, antigen presenting cell or exosome according to any one of claims ~~30~~28 to ~~34~~32 together with a pharmaceutically acceptable carrier.

~~36-34.~~ 37-35. A T-cell population, T-cell, antigen presenting cell or exosome according to any one of claims ~~30~~28 to ~~34~~32 for use in medicine.

~~37-35.~~ A methodUse of treating a human suffering fromT-cell population, T-cell, antigen presenting cell, exosome or composition according to any one of claims 28 to 33 in the manufacture of a medicament for use in the treatment of cancer wherein wherein the cells of the cancer express a sequence selected from SEQ ID NO. 1 and immunogenic variants of the sequence of SEQ ID NO. 1 which are at least 80% identical to SEQ ID NO. 1 and immunogenic fragments of the sequence of SEQ ID NO. 1 comprising at least 9 contiguous amino acids of SEQ ID NO. 1, or of preventing a human from suffering from cancer wherein the cells of the cancer would express a sequence selected from SEQ ID NO. 1 and immunogenic variants of the sequence of SEQ ID NO. 1 which are at least 80% identical to SEQ ID NO. 1 and immunogenic fragments of the sequence of SEQ ID NO. 1 comprising at

least 9 contiguous amino acids of SEQ ID NO. 1, ~~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 to 35~~.

~~38-36.~~ A Use of a T-cell population, T-cell, antigen presenting cell, exosome or composition according to any one of claims ~~30~~28 to ~~35~~33 in the manufacture of 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. 1 and immunogenic fragments comprising at least 9 contiguous amino acids of SEQ ID NO. 1.

~~39-37.~~ A ~~The process, a method according to claim 27 or a T-cell population, T-cell, antigen presenting cell, exosome or composition for the~~ use according to ~~any one of claims 29, 37 and 38~~claim 35 or 36 wherein the cancer is melanoma e.g. cutaneous melanoma.

~~40-38.~~ 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 and a sequence consisting of SEQ ID NO. 2, SEQ ID NO. 5 or SEQ ID NO. 6, 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.

~~41-39.~~ 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. ~~1 and immunogenic variants of the sequence of SEQ ID NO. 1 which are at least 80% identical to SEQ ID NO. 1~~ and a sequence consisting of SEQ ID NO. 2, SEQ ID NO. 5 or SEQ ID NO. 6; 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.

~~A method~~

~~42. 40.~~ Use of ~~treating a human suffering from~~ a polypeptide, fusion protein, nucleic acid, vector, composition, T-cell population, T-cell, antigen presenting cell or exosome according to any one of claims 1 to 18 and 28 to 33 in the manufacture of a medicament for the treatment of cancer, comprising wherein the steps of:

(a) ~~use comprises the~~ determining if the cells of said cancer express a polypeptide sequence selected from SEQ ID NO. 1 and immunogenic variants of the sequence of SEQ ID NO. 1 which are at least 80% identical to SEQ ID NO. 1 and immunogenic fragments of the sequence of SEQ ID NO. 1 comprising at least 9 contiguous amino acids of SEQ ID NO. 1, or a nucleic acid encoding said polypeptide (e.g. selected from the sequences of SEQ ID NOs. ~~3 and 4~~); ~~and if so~~ 3 and 4); and wherein the polypeptide, fusion protein, nucleic acid, vector, composition, T-cell population, T-cell, antigen presenting cell or exosome is to be administered to said human.

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

~~43. 41.~~ Use of a polypeptide (A) comprising the sequence of SEQ ID NO. 1; or (B) consisting of the sequence of any one of SEQ ID NO. 2, SEQ ID NO. 5 and SEQ ID NO. 6;

isolated from the tumor of a human suffering from cancer, or use of a nucleic acid encoding said polypeptide, as a biomarker for the determination of whether said human would be suitable for treatment by a vaccine comprising a polypeptide, fusion protein, nucleic acid, vector, composition, T-cell population, T-cell, antigen presenting cell or exosome according to any one of claims 1 to 18 and ~~30~~28 to ~~35~~33.

~~44. 42.~~ The ~~method or~~ use according to claim ~~42~~40 or claim ~~43~~41 wherein the cancer is melanoma e.g. cutaneous melanoma.

~~45. 43.~~ ~~A method or a~~ The polypeptide, fusion protein, nucleic acid, vector or composition for use according to ~~any one of claims~~claim 21 ~~and 23 to 27~~ wherein ~~or~~ the use according to any one of claims 22 to 25 wherein the cancer is uveal melanoma.

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~~46.44.~~ AThe process, ~~a method~~ according to claim 27 or the use according to claim 35 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~~36 wherein the cancer is uveal melanoma.

~~47.45.~~ The ~~method or~~ use according to any one of claims ~~42~~40 or ~~43~~41 wherein the cancer is uveal melanoma.