

## CLAIMS

1. A peptide ~~comprising~~ consisting of an amino acid sequence selected from the group consisting of SEQ ID No. 1 and SEQ ID No. 182, ~~SEQ ID No. 2 to 181 and SEQ ID No. 183 to 188~~, or a pharmaceutical acceptable salt thereof, ~~wherein said peptide has an overall length of from 8 to 100, preferably from 8 to 30, and more preferred from 8 to 16 amino acids, and most preferred wherein the peptide consists or consists essentially of an amino acid sequence according to any of SEQ ID No. 1 and SEQ ID No. 182, SEQ ID No. 2 to 181 and SEQ ID No. 183 to 188.~~
2. The peptide or salt thereof according to claim 1, wherein said peptide or salt thereof has the ability to bind to an MHC class-I ~~or~~ II molecule, and wherein said peptide, when bound to said MHC, is capable of being recognized by ~~CD4 and/or~~ CD8 T cells.
3. The peptide or salt thereof according to any of claims 1 to 2, wherein said peptide is ~~modified and/or~~ includes non-peptide bonds.
4. A fusion protein comprising ~~The~~ the peptide according to any of claims 1 to 3, ~~wherein said peptide is part of a fusion protein, in particular comprising N-terminal amino acids of the HLADR antigen-associated invariant chain (Ii).~~
5. An antibody, in particular a soluble or membrane-bound antibody, preferably a monoclonal antibody or fragment thereof, that specifically recognizes the peptide according to any of claims 1 to 4~~3~~, preferably the peptide according to any of claims 1 to 4 when bound to an MHC molecule.
6. A T-cell receptor, preferably soluble or membrane-bound, or a fragment thereof, that is reactive with an HLA ligand, wherein said ligand is the peptide according to any of claims 1 to 4, preferably the peptide according to any of claims 1 to 4~~3~~ when bound to an MHC molecule.
- ~~7. The T-cell receptor according to claim 6, wherein said ligand amino acid sequence is at least 88% identical to any one of SEQ ID No. 1 and SEQ ID No. 182, SEQ ID No. 2 to 181 and SEQ ID No. 183 to 188, or wherein said ligand amino acid sequence consists of any one of SEQ ID No. 1 and SEQ ID No. 182, SEQ ID No. 2 to 181 and SEQ ID No. 183 to 188.~~

87. The T-cell receptor according to claim 6 ~~or 7~~, wherein said T-cell receptor is provided as a soluble molecule and optionally carries a further effector function such as an immune stimulating domain or toxin.
98. A nucleic acid, encoding for a peptide according to any one of claims 1 to 43, an antibody or fragment thereof according to claim 5, a T-cell receptor or fragment thereof according to claim 6 ~~or 7~~, optionally linked to a heterologous promoter sequence, or an expression vector expressing said nucleic acid.
409. A recombinant host cell comprising the peptide according to any one of claims 1 to 43, the antibody or fragment thereof according to claim 5, the T-cell receptor or fragment thereof according to claim 6 ~~or 7~~ or the nucleic acid or the expression vector according to claim 98, wherein said host cell preferably is selected from an antigen presenting cell, such as a dendritic cell, a T cell or an NK cell.
4410. An *in vitro* method for producing activated T lymphocytes, the method comprising contacting *in vitro* T cells with antigen loaded human class I ~~or II~~ MHC molecules expressed on the surface of a suitable antigen-presenting cell or an artificial construct mimicking an antigen-presenting cell for a period of time sufficient to activate said T cells in an antigen specific manner, wherein said antigen is a peptide according to any one of claims 1 to 43.
4211. An activated T lymphocyte, produced by the method according to claim 4410, that selectively recognizes a cell which presents a ~~poly~~peptide comprising an amino acid sequence given in any one of claims 1 to 43.
4312. A pharmaceutical composition comprising at least one active ingredient selected from the group consisting of the peptide or salt thereof according to any one of claims 1 to 43, the fusion protein according to claim 4, the antibody or fragment thereof according to claim 5, the T-cell receptor or fragment thereof according to claim 6 ~~or 7~~, the nucleic acid or the expression vector according to claim 98, the host cell according to claim 409, or the activated T lymphocyte according to claim 4211, or a conjugated or labelled active ingredient, and a pharmaceutically acceptable carrier, and optionally, pharmaceutically acceptable excipients and/or stabilizers.

13. The pharmaceutical composition according to claim 12, wherein (i) the pharmaceutical composition further comprises an adjuvant, and/or (ii) wherein the pharmaceutical composition is a vaccine or a cellular therapeutic agent.

14. The pharmaceutical composition according to claim 13, wherein the adjuvant is an interleukin, including IL-2, IL-15 or a combination thereof.

4415. A method for producing the peptide according to any of claims 1 to 43, the antibody or fragment thereof according to claim 5, or the T-cell receptor or fragment thereof according to claim 6 ~~or 7~~, the method comprising culturing the host cell according to claim 409, and isolating the peptide, the antibody or fragment thereof or the T cell receptor or fragment thereof from said host cell and/or its culture medium.

15. ~~The peptide according to any one of claims 1 to 4, the antibody or fragment thereof according to claim 5, the T-cell receptor or fragment thereof according to claim 6 or 7, the nucleic acid or the expression vector according to claim 9, the host cell according to claim 10, or the activated T lymphocyte according to claim 12 for use in medicine.~~

16. ~~Use of a~~An effective number of activated T lymphocytes as defined in claim 42-11 for use in the manufacture of a medicament for killing target cancer cells in a patient, wherein the target cancer cells present a polypeptide comprising an amino acid sequence given in any one of claims 1 to 43.

17. The peptide or salt thereof according to any one of claims 1 to 43, the fusion protein according to claim 4, the antibody or fragment thereof according to claim 5, the T-cell receptor or fragment thereof according to claim 6 ~~or 7~~, the nucleic acid or the expression vector according to claim 98, the host cell according to claim 409, or the activated T lymphocyte according to claim 42-11 for use in diagnosis and/or treatment of cancer, or for use in the manufacture of a medicament against cancer-, wherein said cancer shows an overpresentation of a peptide selected from any one of SEQ ID No. 1 and SEQ ID No. 182.

18. The peptide, the fusion protein, the antibody, the T-cell receptor, the nucleic acid, the expression vector, the host cell or the activated T lymphocyte for use according to claim 4617, wherein said cancer is selected from the group of AML, bile duct cancer,

brain cancer, breast cancer, chronic lymphocytic leukemia, colon or rectal cancer, esophageal cancer, gallbladder cancer, liver cancer, melanoma, non-hodgkin lymphoma, non-small cell lung cancer, ovarian cancer, pancreatic cancer, prostate cancer, kidney cancer, small cell lung cancer, urinary bladder cancer, uterine cancer, ~~and other tumors that show an overexpression of a protein from which a peptide~~ SEQ ID No. 1 and SEQ ID No. 182, SEQ ID No. 2 to 181 and SEQ ID No. 183 to 188 ~~is derived from.~~

19. A kit comprising:

- a) a container comprising a pharmaceutical composition containing the peptide or salt thereof according to any one of claims 1 to 43, the fusion protein according to claim 4, the antibody or fragment thereof according to claim 5, the T-cell receptor or fragment thereof according to claim 6 ~~or 7~~, the nucleic acid or the expression vector according to claim 98, the host cell according to claim 409, or the activated T lymphocyte according to claim 4211, in solution or in lyophilized form;
- b) optionally, a second container containing a diluent or reconstituting solution for the lyophilized formulation;
- c) optionally, at least one more peptide selected from the group consisting of SEQ ID No. 1 and SEQ ID No. 182, SEQ ID No. 2 to 181 and SEQ ID No. 183 to 198, and
- d) optionally, instructions for (i) use of the solution or (ii) reconstitution and/or use of the lyophilized formulation, and optionally

one or more of (iii) a buffer, (iv) a diluent, (v) a filter, (vi) a needle, ~~or~~ (vii) a syringe, or (viii) an adjuvant.

20. A method for producing a personalized anti-cancer vaccine or a compound-based and/or cellular therapy for an individual patient, said method comprising:

- a) identifying tumor-associated peptides (TUMAPs) presented by a tumor sample from said individual patient;
- b) comparing the peptides as identified in a) with a warehouse of peptides that have been pre-screened for immunogenicity and/or over-presentation in tumors as compared to normal tissues;
- c) selecting at least one peptide from the warehouse that matches a TUMAP identified in the patient; and
- d) manufacturing and/or formulating the personalized vaccine or compound-based or cellular therapy based on step c),

wherein said warehouse comprises the peptides selected from the group consisting of SEQ ID No. 1 and SEQ ID No. 182.

21. The method according to claim 20, wherein said TUMAPs are identified by:

a1) comparing expression data from the tumor sample to expression data from a sample of normal tissue corresponding to the tissue type of the tumor sample to identify proteins that are over-expressed or aberrantly expressed in the tumor sample; and

a2) correlating the expression data with sequences of MHC ligands bound to MHC class I and/or class II molecules in the tumor sample to identify MHC ligands derived from proteins over-expressed or aberrantly expressed by the tumor.

22. The method according to claim 20 or 21 wherein the sequences of MHC ligands are identified by eluting bound peptides from MHC molecules isolated from the tumor sample, and sequencing the eluted ligands.

23. The method according to any of claims 20 to 22, wherein the normal tissue corresponding to the tissue type of the tumor sample is obtained from the same patient.

24. The method according to any of claims 20 to 23, wherein the peptides included in the warehouse are identified based on the following steps:

aa. Performing genome-wide messenger ribonucleic acid (mRNA) expression analysis by highly parallel methods, such as microarrays or sequencing-based expression profiling, comprising identify genes that over-expressed in a malignant tissue, compared with a normal tissue or tissues;

ab. Selecting peptides encoded by selectively expressed or over-expressed genes as detected in step aa, and

ac. Determining an induction of in vivo T-cell responses by the peptides as selected comprising *in vitro* immunogenicity assays using human T cells from healthy donors or said patient; or

ba. Identifying HLA ligands from said tumor sample using mass spectrometry;

bb. Performing genome-wide messenger ribonucleic acid (mRNA) expression analysis by highly parallel methods, such as microarrays or sequencing-based expression profiling, comprising identify genes that over-expressed in a malignant tissue, compared with a normal tissue or tissues;

bc. Comparing the identified HLA ligands to said gene expression data;

bd. Selecting peptides encoded by selectively expressed or over-expressed genes as detected in step bc;

be. Re-detecting of selected TUMAPs from step bd on tumor tissue and lack of or infrequent detection on healthy tissues and confirming the relevance of over-expression at the mRNA level; and

bf. Determining an induction of in vivo T-cell responses by the peptides as selected comprising *in vitro* immunogenicity assays using human T cells from healthy donors or said patient.

25. The method according to any of claims 20 to 24, wherein the immunogenicity of the peptides included in the warehouse is determined by a method comprising in vitro immunogenicity assays, patient immunomonitoring for individual HLA binding, MHC multimer staining, ELISPOT assays and/or intracellular cytokine staining.

26. The method according to any of claims 20 to 25, further comprising identifying at least one mutation that is unique to the tumor sample relative to normal corresponding tissue from the individual patient, and selecting a peptide that correlates with the mutation for inclusion in the vaccine or for the generation of cellular therapies.

27. The method according to claim 26, wherein said at least one mutation is identified by whole genome sequencing.