

CLAIMS

1. A peptide having a length of up to 30 amino acids and comprising an amino acid sequence according to SEQ ID NO 39, wherein said peptide binds to molecule(s) of the major histocompatibility complex (MHC) and/or induces T cells cross-reacting with said peptide, or a pharmaceutically acceptable salt thereof.
2. The peptide or salt thereof according to claim 1, 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 or 2, wherein said peptide or salt thereof has a length of 8 to 16 amino acids.
4. The peptide or salt thereof according to any of claims 1 - 3, wherein said peptide includes non-peptide bonds.
5. An antibody, in particular a soluble or membrane-bound antibody, preferably a monoclonal antibody or fragment thereof, that specifically recognizes the peptide or salt thereof according to any of claims 1 to 4, preferably the peptide or salt thereof 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 or salt thereof according to any of claims 1 to 4, preferably the peptide or salt thereof according to any of claims 1 to 4 when bound to an MHC molecule.
7. The T-cell receptor according to claim 6, wherein said ligand amino acid sequence consists of SEQ ID No. 39.
8. 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 optionally an immune stimulating domain or toxin.

9. A recombinant host cell comprising the peptide according to any one of claims 1 to 4, the antibody or fragment thereof according to claim 5, or the T-cell receptor or fragment thereof according to claim 6-8, wherein said host cell optionally is selected from an antigen presenting cell, optionally a dendritic cell, a T cell or an NK cell.

10. 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 of claims 1 - 4.

11. An activated T lymphocyte, produced by the method according to claim 10, that selectively recognizes a cell which presents a polypeptide comprising an amino acid sequence given in any one of claims 1 to 4.

12. A pharmaceutical composition comprising at least one active ingredient selected from the group consisting of 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 6-8, the host cell according to claim 9, or the activated T lymphocyte according to claim 11, 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, comprising the activated T lymphocyte according to claim 11 and further comprising one or more adjuvants selected from interleukin and immunoadjuvant.

14. The pharmaceutical composition according to claim 13, wherein a) the interleukin is IL-2; and/or b) the immunoadjuvant is IL-15.

15. A method for producing the peptide according to any one of claims 1 to 4, the antibody or fragment thereof according to claim 5, or the T-cell receptor or fragment thereof according to claim 6-8, the method comprising culturing the host cell according to claim 9, 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.

16. Use of the peptide or salt thereof 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 6-8, the host cell according to claim 9, or the activated T lymphocyte according to claim 11 in the manufacture of a medicament for treatment of cancer.

17. The use according to claim 16, wherein said cancer is selected from the group of acute myeloid leukemia, breast cancer, cholangiocellular carcinoma, chronic lymphocytic leukemia, colorectal cancer, gallbladder cancer, glioblastoma, gastric cancer, gastro-esophageal junction cancer, hepatocellular carcinoma, head and neck squamous cell carcinoma, melanoma, non-Hodgkin lymphoma, non-small cell lung cancer, ovarian cancer, esophageal cancer, pancreatic cancer, prostate cancer, renal cell carcinoma, small cell lung cancer, urinary bladder carcinoma, uterine endometrial cancer and other tumors that show an overexpression of a protein from which a peptide SEQ ID No. 39 is derived from.

18. A kit comprising:

- a) a container comprising a pharmaceutical composition containing the peptide or salt thereof 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 6-8, the host cell according to claim 9, or the activated T lymphocyte according to claim 11, in solution or in lyophilized form;
- b) optionally, a second container containing a diluent or reconstituting solution for the lyophilized formulation; and
- c) optionally, at least one more peptides selected from the group consisting of SEQ ID No. 1 to SEQ ID No. 101.

19. The kit according to claim 18, further comprising one or more of (i) a buffer, (ii) a diluent, (iii) a filter, (iv) a needle, (v) a syringe, or (vi) an adjuvant.

20. A method for producing a personalized anti-cancer vaccine or a compound-based and/or cellular therapeutic agent for an individual, 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 individual; and

d) manufacturing and/or formulating the personalized vaccine or compound-based or cellular therapeutic agent based on step c),

wherein said warehouse comprises a peptide comprising the amino acid sequence of SEQ ID No. 39 according to claim 1.

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 individual.

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 individual; 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 individual.

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 and selecting a peptide that correlates with the mutation for inclusion in the vaccine or for the generation of cellular therapeutic agents.

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