CLAIMS

1. AAn isolated peptide comprising consisting of an amino acid sequence selected from the group consisting of of SEQ ID No. 18, SEQ ID No. 1 to SEQ ID No. 17, and SEQ ID No. 19 to SEQ ID No. 32, and variant sequencesor a pharmaceutical acceptable salt thereof.

2. which are at least 88% homologous to SEQ ID No. 18, SEQ ID No. 1 to SEQ ID No. 17, and SEQ ID No. 19 to SEQ ID No. 32, andThe peptide or salt thereof according to claim 1, wherein said variantpeptide or salt thereof binds to molecule(s) of the major histocompatibility complex (MHC) and/or induces T cells cross-reacting with said variant, and/or wherein the peptide; and a pharmaceutical acceptable or salt thereof, has the ability to bind to an MHC class-I molecule, and wherein said peptide, when bound to said MHC, is not a full-length polypeptidecapable of being recognized by CD8 T cells.

2.

3. The peptide or salt thereof according to claim 1 or claim 2, wherein said peptide 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 cellsor salt thereof includes non-peptide bonds.

4.

3. The peptide or variant thereof according to claim 1 or 2, wherein the amino acid sequence thereof comprises a continuous stretch of amino acids according to any one of SEQ ID No. 18, SEQ ID No. 1 to SEQ ID No. 17, and SEQ ID No. 19 to SEQ ID No. 32.

4. The peptide or variantsalt thereof according to any one of claims 1 to 3, wherein said peptide or variantsalt thereof 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. 18, SEQ ID No. 1 to SEQ ID No. 17, and SEQ ID No. 19 to SEQ ID No. 32.~~

~~5. The peptide or variant thereof according to any of Claims 1 to 4, wherein said peptide is modified and/or includes non-peptide bonds.~~

~~6. The peptide or variant thereof according to any of Claims 1 to 5, wherein said peptide~~ is part of a fusion protein, ~~in particular~~or is part of a fusion protein comprising N-terminal amino acids of the HLA-DR antigen-associated invariant chain (Ii).

5.

~~7.~~ An isolated antibody, ~~in particular a~~an isolated soluble ~~or~~antibody, and isolated membrane-bound antibody, ~~preferably a monoclonal antibody~~ or fragment thereof, that specifically recognizes the peptide or ~~variant~~salt thereof according to any one of claims 1 to ~~5, preferably the peptide or variant thereof according to any~~3 which is part of ~~claims 1 to 5 when bound to an~~ a ligand-MHC ~~molecule~~-complex.

6. An antibody according to claim 5, wherein the antibody is a monoclonal antibody, a human antibody, a humanized antibody, a bi-specific antibody and/or a chimeric antibody.

7. ~~8. A~~An isolated T-cell receptor, ~~preferably~~an isolated soluble ~~or~~T-cell receptor , an isolated membrane-bound T-cell receptor, or a fragment thereof, that is reactive with an HLA ligand, wherein said ligand is the peptide or ~~variant~~salt thereof according to any one of claims 1 to ~~5, preferably~~3, or wherein the peptide or ~~variant~~salt thereof according to any one of claims 1 to ~~5 when bound to an~~ 3 which is part of a ligand-MHC ~~molecule~~-complex.

~~9. The T-cell receptor according to claim 8, wherein said ligand amino acid sequence is at least 88% identical to any one of SEQ ID No. 18, SEQ ID No. 1 to SEQ ID No. 17, and SEQ ID No. 19 to SEQ ID No. 54, or wherein said ligand amino acid sequence consists~~

~~of any one of SEQ ID No. 18, SEQ ID No. 1 to SEQ ID No. 17, and SEQ ID No. 19 to SEQ ID No. 54.~~

~~10. The~~ 8. The soluble T-cell receptor according to claim ~~8 or 9~~7, wherein said soluble T-cell receptor ~~is provided as a soluble molecule and optionally~~ carries a further effector function ~~such as~~or comprises an immune stimulating domain or toxin.

~~11~~9. An aptamer that specifically recognizes the peptide or ~~variant~~salt thereof according to any one of claims 1 to 3, or that specifically recognizes the peptide or salt thereof according to any one of claims 1 to ~~5, preferably the peptide or variant thereof according to any of claims 1 to 5 that is bound to an MHC molecule~~3 which is part of a ligand-MHC-complex.

10.

~~12.~~ A nucleic acid~~,~~ linked to a heterologous promoter sequence encoding for a peptide or ~~variant~~salt thereof according to any one of claims 1 to 3, an antibody or fragment thereof according to claim 5 or 6, a T-cell receptor or fragment thereof according to claim 7 or 8.

11. An expression vector expressing the nucleic acid encoding for a peptide or salt thereof according to any one of claims 1 to ~~5~~3, an antibody or fragment thereof according to claim ~~7,~~5 or 6, or a T-cell receptor or fragment thereof according to claim ~~8 or 9, optionally linked to a heterologous promoter sequence, or an expression vector expressing said nucleic acid~~7 or 8.

12.

~~13.~~ A recombinant host cell, a recombinant antigen presenting cell, a recombinant dendritic cell, a recombinant T cell or a recombinant NK cell comprising the peptide according to any one of claims 1 to ~~6~~4, the antibody or fragment thereof according to claim ~~7~~5 or 6, the T-cell receptor or fragment thereof according to claim ~~8~~7 or ~~9 or~~8, the nucleic acid according to claim 10, or the expression vector according to claim ~~12, wherein~~

~~said host cell preferably is selected from an antigen presenting cell, such as a dendritic cell, a T cell or an NK cell~~11.

13.

~~14. 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~~claim 1 ~~to 4~~or claim 2.

~~15~~14. An activated T lymphocyte, produced by the method according to claim ~~14~~13, that selectively recognizes a cell which presents a polypeptide comprising an amino acid sequence ~~given in any one of claims 1 to 4~~of SEQ ID No. 18.

~~16~~15. 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 ~~6~~4, the antibody or fragment thereof according to claim ~~7~~5 or 6, the T-cell receptor or fragment thereof according to claim 7 or 8~~ or 9~~, the aptamer according to claim ~~11~~9, the nucleic acid according to claim 10 or the expression vector according to claim ~~12~~11, the host cell according to claim ~~13~~12, or the activated T lymphocyte according to claim ~~15~~14, or a conjugated or labelled active ingredient, and a pharmaceutically acceptable carrier, and optionally, pharmaceutically acceptable excipients and/or stabilizers.

~~17.~~16. The pharmaceutical composition according to claim 15, wherein

(i) the pharmaceutical composition further comprises one or more adjuvants, and/or

(ii) the pharmaceutical composition is a vaccine or a cellular therapeutic agent.

17. The pharmaceutical composition according to claim 16, wherein the one or more adjuvants are selected from:

a) an interleukin;

b) an immunoadjuvant;

c) IL-2; and/or

d) IL-15.

18. Use of the pharmaceutical composition according to any one of claims 15 to 17 as an anti-cancer vaccine or as a cellular therapeutic agent.

19. A method for producing the peptide or variant thereof according to any of claims 1 to ~~6~~4, the antibody or fragment thereof according to claim ~~7~~5 or 6, or the T-cell receptor or fragment thereof according to claim ~~8~~7 or ~~9~~8, the method comprising culturing the host cell according to claim ~~13~~12, and isolating the peptide or ~~variant~~salt thereof, the antibody or fragment thereof or the T cell receptor or fragment thereof from said host cell and/or its culture medium.

~~18~~20. The peptide according to any one of claims 1 to ~~6~~4, the antibody or fragment thereof according to claim ~~7~~5 or 6, the T-cell receptor or fragment thereof according to claim 7 or 8 ~~or 9~~, the aptamer according to claim ~~11~~9, the nucleic acid according to claim 10 or the expression vector according to claim ~~12~~11, the host cell according to claim ~~13~~12, or the activated T lymphocyte according to claim ~~15~~14 for use in medicine.

~~19~~21. Use of an effective number of activated T cells as defined in claim ~~15~~ 14 in the manufacture of a medicament for killing target cells in a patient, wherein the target cells present a polypeptide comprising an amino acid sequence ~~given in any one of claims 1 to 4~~of SEQ ID No. 18.

22.

~~20. The~~Use of the peptide or salt thereof according to any one of claims 1 to ~~6~~4, the antibody or fragment thereof according to claim ~~7~~5 or 6, the T-cell receptor or fragment thereof according to claim 7 or 8~~ or 9~~, the aptamer according to claim ~~11~~9, the nucleic acid ~~or~~according to claim 10, the expression vector according to claim ~~12~~11, the host cell according to claim ~~13~~12, or the activated T lymphocyte according to claim ~~15 for use~~14 in the diagnosis and/or treatment of cancer~~.~~, or in the manufacture of a medicament for the diagnosis or treatment of cancer, wherein the cancer presents or over-presents a peptide comprising SEQ ID No. 18; or

~~21. Use of~~ the peptide according to any one of claims 1 to 4, the antibody or fragment thereof according to claim 5 or 6, the ~~antibody or fragment thereof according to claim 7, the~~ T-cell receptor or fragment thereof according to claim 7 or 8~~ or 9~~, the aptamer according to claim ~~11~~9, the nucleic acid according to claim 10 or the expression vector according to claim ~~12~~11, the host cell according to claim ~~13~~12, or the activated T lymphocyte according to claim ~~15,~~14 for use in diagnosis and/or treatment of cancer, or for use in the manufacture of a medicament for the diagnosis or treatment of cancer.

~~22.~~

23. The use according to claim 22, or the peptide ~~according to any one of claims 1 to 6~~or salt thereof, the antibody~~ or fragment thereof according to claim 7~~, the T-cell receptor~~ or fragment thereof according to claim 8 or 9~~, the aptamer~~ according to claim 11~~, the nucleic acid~~ or~~, the expression vector~~ according to claim 12~~, the host cell~~ according to claim 13~~, or the activated T lymphocyte ~~according to claim 15, or~~for the use according to claim ~~21~~20, wherein said cancer is selected from the group of gallbladder cancer and cholangiocarcinoma, acute myeloid leukemia, melanoma, small cell lung cancer, non-small cell lung cancer, non-Hodgkin lymphoma, chronic lymphocytic leukemia, pancreatic cancer, liver cancer, ovarian cancer, head and neck cancer, urinary bladder cancer, breast cancer, and kidney cancer and other tumors that ~~show an overexpression of a protein from which~~over-present a peptide comprising SEQ ID No. 18~~, SEQ ID No. 1 to SEQ ID No. 17, and SEQ ID No. 19 to SEQ ID No. 32 is derived from~~.

~~23~~24. A kit comprising:

a) a container comprising a pharmaceutical composition containing the peptide(s) or the variant according to any one of claims 1 to ~~6~~4, the antibody or fragment thereof according to claim ~~7~~5 or 6, the T-cell receptor or fragment thereof according to claim 7 or 8 ~~or 9~~, the aptamer according to claim ~~11~~9, the nucleic acid ~~or~~according to claim 10, the expression vector according to claim ~~12~~11, the host cell according to claim ~~13~~12, or the activated T lymphocyte according to claim ~~15~~14, in solution or in lyophilized form~~;~~.

25. The kit according to claim 24, further comprising one or more of:

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. 18, SEQ ID No. 1 to SEQ ID No. 17, and SEQ ID No. 19 to SEQ ID No. 38, and

d) ~~optionally,~~ instructions for (i) use of the solution or (ii) reconstitution and/or use of the lyophilized formulation~~.~~,

~~24. The kit according to claim 23, further comprising one or more of (iii~~(e) a buffer, ~~(iv~~

(f) a diluent, ~~(v~~

(g) a filter, ~~(vi~~

(h) a needle, ~~or (v~~

(i) a syringe~~.~~, or

~~25~~(j) an adjuvant.

26. 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~~tumor sample from the individual; and

d) manufacturing and/or formulating the personalized vaccine or compound-based or cellular therapy based on step c~~).~~), wherein the warehouse of peptides comprises a peptide according to SEQ ID No. 18.

~~26~~27. The method according to claim ~~25~~26, 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.

~~27~~28. The method according to claim ~~25~~26 or ~~26~~27, 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.

~~28~~29. The method according to any of claims ~~25~~26 to ~~27~~28, wherein the normal tissue corresponding to the tissue type of the tumor sample is obtained from the same ~~patient~~individual.

~~29~~30. The method according to any of claims ~~25~~26 to ~~28~~29, 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~~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 ~~patient~~individual.

~~30~~31. The method according to any of claims ~~25~~26 to ~~29~~30, 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.

~~31~~32. The method according to any of claims ~~25 to 30, wherein said warehouse comprises a plurality of peptides selected from the group consisting of SEQ ID No. 18, SEQ ID No. 1 to SEQ ID No. 17, and SEQ ID No. 19 to SEQ ID No. 32.~~

~~32. The method according to any of claims 25~~26 to 31, 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.

33. The method according to claim 32, wherein said at least one mutation is identified by whole genome sequencing.