

CLAIMS

1. A method for selecting a tumor neoantigenic peptide wherein said method comprises
- a step of identifying, among mRNA sequences from cancer cells of a subject, a fusion transcript sequence comprising a transposable element (TE) sequence and an exonic sequence, and including an open reading frame (ORF), and
 - a step of selecting a tumor neoantigenic peptide of at least 8 amino acids, encoded by a part of said ORF of the fusion transcript sequence,

wherein said ORF overlaps the junction between the TE and the exonic sequence, is pure TE and/or is non-canonical, and

wherein said tumor neoantigenic peptide binds to at least one Major Histocompatibility Complex (MHC) molecule of said subject.

2. A method according to claim 1, wherein said tumor neoantigenic peptide is 8 to 11 amino acids long, and binds to at least one MHC class I molecule of said subject, or wherein said tumor neoantigenic peptide is from 13 to 25 amino acids long, and binds to at least one MHC class II molecule of said subject.

~~3. A tumor neoantigenic peptide comprising at least 8 amino acids, wherein said neoantigenic peptide is encoded by a part of an open reading frame (ORF) from a fusion transcript comprising a transposable element (TE) sequence and an exonic sequence, and wherein said ORF overlaps the junction between the TE and the exonic sequence, is pure TE and/or is non-canonical.~~

~~4. A tumor neoantigenic peptide, according to claim 3 or obtained from the method as defined in any one of claim 1 or 2, wherein the fusion transcript is selected from SEQ ID NO: 118-17492.~~

~~5. A tumor neoantigenic peptide comprising at least 8 amino acids of any of SEQ ID NO: 1-48, 50-117, and 17493-17496.~~

~~6. The isolated tumor neoantigenic peptide according to any one of claims 3 to 5, or obtained according to any one of claim 1 or 2, wherein said neoantigenic peptide —is expressed at higher levels in tumor cells compared to normal healthy cells;~~

~~— is expressed in at least 1 % of subjects from a population of subjects suffering from cancer; and/or~~

~~— binds MHC class I or class II with a Kd binding affinity of less than about 10^{-5} M.~~

5 7. ~~A population of autologous dendritic cells or antigen presenting cells that have been pulsed with one or more of the peptides as defined in any one of claims 3-6 or transfected with a polynucleotide encoding one or more of the peptides as defined in any one of claims 3-6.~~

10 8. ~~A vaccine or immunogenic composition capable of raising a specific T-cell response comprising~~

 a. ~~one or more neoantigenic peptides as defined in any one of claims 3-6, optionally with a physiologically acceptable buffer, carrier, or excipient, and/or optionally with an adjuvant or immunostimulant;~~

15 b. ~~one or more polynucleotides encoding a neoantigenic peptide as defined in any one of claims 3-6, optionally linked to a heterologous regulatory control nucleotide sequence; and/or~~

 c. ~~a population of antigen presenting cells, as defined in claim 7.~~

20 9. ~~An antibody, or an antigen-binding fragment thereof, a T cell receptor (TCR), or a chimeric antigen receptor (CAR) that specifically binds a neoantigenic peptide as defined in any one of claims 3-6, optionally in association with an MHC molecule, with a Kd affinity of about 10^{-6} M or less.~~

25 10. ~~— A method of producing an antibody, TCR or CAR that specifically binds a neoantigenic peptide as defined in any one of claims 3-6, comprising the step of selecting an antibody, TCR or CAR that binds to a tumor neoantigen peptide of any of claims 3-6, optionally in association with an MHC or HLA molecule, with a Kd binding affinity of about 10^{-6} M or less.~~

30 11. ~~— An antibody produced by the method of claim 10.~~

 12. ~~— A T cell receptor according to claim 9, wherein said T cell receptor is made soluble and fused to an antibody fragment directed to a T cell antigen, optionally wherein the targeted antigen is CD3 or CD16.~~

~~13. — An antibody according to any one of claim 9 or 11, wherein said antibody is a multispecific antibody that further targets at least an immune cell antigen, optionally wherein the immune cell is a T cell, a NK cell or a dendritic cell, optionally wherein the targeted antigen is CD3, CD16, CD30 or a TCR.~~

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~~14. — A polynucleotide encoding a neoantigenic peptide as defined in claims 3-6, or an antibody, a CAR or a TCR as defined in any one of claims 9-13, optionally linked to a heterologous regulatory control sequence.~~

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~~15. — A vector comprising the polynucleotide of claim 14.~~

~~16. — An immune cell that specifically binds to one or more neoantigenic peptides as defined in any one of claims 3-6.~~

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~~17. — The immune cell of claim 16, which is an allogenic or autologous cell selected from T cell, NK cell, CD4⁺/CD8⁺, TILs/tumor derived CD8 T cells, central memory CD8⁺ T cells, Treg, MAIT, and Y δ T cell.~~

~~18. — A T cell according to claim 17, which comprises~~

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- ~~— a T cell receptor that specifically binds one or more neoantigenic peptides as defined in any one of claims 3-6, or~~
- ~~— a TCR or a CAR of any one of claims 9,10 or 12.~~

~~19. — The neoantigenic peptide as defined in claims 3-6, the population of dendritic cells according to claim 7, the vaccine or immunogenic composition according to claim 8, the polynucleotide as defined in claim 14 or the vector according to claim 15, for use in inhibiting cancer cell proliferation, or for use in cancer vaccination therapy of a subject, or for treating cancer in a subject.~~

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~~20. — The antibody or the antigen-binding fragment thereof, the multispecific antibody, the TCR, the CAR, the polynucleotide, or the vector as defined in any one of claims 9-15 for use for inhibiting cancer cell proliferation, or for use in the treatment of cancer in a subject in need thereof.~~

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21. — ~~A population of immune cells as defined in any one of claims 16-18, for use in in cell therapy of cancer.~~

22. — ~~The neoantigenic peptide, the population of dendritic cells, the vaccine or immunogenic composition, the polynucleotide or the vector for use according to claim 19, the antibody or the antigen binding fragment thereof, the multispecific antibody, the TCR, the CAR, the polynucleotide, or the vector for use according to claim 20, or the population of immune cells for use according to claim 21, which is administered in combination with at least one further therapeutic agent.~~

23. — ~~The neoantigenic peptide, the population of dendritic cells, the vaccine or immunogenic composition, the polynucleotide, the vector for use according to claim 19, the antibody or the antigen binding fragment thereof, the multispecific antibody, the TCR, the CAR, the polynucleotide, the vector for use according to claim 20, or the population of immune cells for use according to claim 21 wherein said at least one further therapeutic agent is a chemotherapeutic agent, or an immunotherapeutic agent, optionally a checkpoint inhibitor.~~

24. — ~~The neoantigenic peptide, the population of dendritic cells, the vaccine or immunogenic composition, the polynucleotide or the vector for use according to any one of claims 19 or 22-23, the population of immune cell, according to any one of claims 21-23, the antibody or the antigen binding fragment thereof, the multispecific antibody, the TCR, the CAR, the polynucleotide, or the vector for use according to any one of claims 20 or 22-23, wherein the cancer is NSCL and/or wherein the subject is suffering from NSCLC or is at risk of suffering from NSCLC.~~