

CLAIMS

What is claimed is:

1. A method of selecting a neoepitope for immune therapy of a cancer, comprising:
obtaining from a patient omics data from a tumor tissue and a matched normal tissue,
and using the omics data to determine a plurality of expressed missense based
patient- and tumor-specific neoepitopes;
filtering the expressed missense based patient- and tumor-specific neoepitopes by
HLA type of the patient to thereby obtain HLA-matched neoepitopes; and
filtering the HLA-matched neoepitopes by a gene type affected by the HLA-matched
neoepitopes to thereby obtain a cancer driver neoepitope.
2. The method of claim 1 wherein the omics data comprise at least two omics data selected
from the group consisting of whole genome sequencing data, whole exome sequencing
data, RNAseq data, and quantitative proteomics data.
3. The method of any one of the preceding claims wherein the step of determining the
plurality of expressed missense based patient- and tumor-specific neoepitopes comprises
location-guided synchronous alignment of omics data from the tumor tissue and the
matched normal tissue.
4. The method of any one of the preceding claims further comprising a step of filtering the
expressed missense based patient- and tumor-specific neoepitopes by at least one of an *a priori* known molecular variation selected from the group consisting of a single
nucleotide polymorphism, a short deletion and insertion polymorphism, a microsatellite
marker, a short tandem repeat, a heterozygous sequence, a multinucleotide
polymorphism, and a named variant.
5. The method of any one of the preceding claims wherein the tumor tissue is a solid tumor
tissue and wherein the matched normal tissue is blood.
6. The method of any one of the preceding claims wherein the step of filtering the
neoepitopes by HLA type is performed for each of the neoepitopes using a plurality of
distinct individual neoepitope sequences in which a changed amino acid has a distinct
position within the neoepitope sequence.

7. The method of claim 6 wherein the individual neoepitope sequences have a length of between 7 and 20 amino acids.
8. The method of any one of the preceding claims wherein the step of filtering by HLA type comprises determination of the HLA type from the patient omics data.
9. The method of any one of the preceding claims wherein the step of filtering by HLA type is performed to a depth of at least 4 digits.
10. The method of claim 1 wherein the step of filtering by HLA type comprises determination of affinity of the neoepitopes to at least one MHC Class I sub-type and to at least one MHC Class II sub-type of the patient.
11. The method of claim 1 wherein the HLA-matched neoepitopes have an affinity to at least one MHC Class I sub-type or to at least one MHC Class II sub-type of the patient of equal or less than 150 nM.
12. The method of any one of the preceding claims wherein the gene type affected is a cancer driver gene for a cancer selected from the group consisting of ALL, AML, BLCA, BRCA, CLL, CM, COREAD, ESCA, GBM, HC, HNSC, LUAD, LUSC, MB, NB, NSCLC, OV, PRAD, RCCC, SCLC, STAD, THCA, and UCEC.
13. The method of any one of the preceding claims wherein the gene type affected is a cancer driver gene selected from a group consisting of: AURKA, BAP1, BRCA1, BRCA2, CCND2, CCND3, CCNE1, CDK4, CDK6, CDKN1B, CDKN2A, CDKN2B, EGF4, ERBB2, FBXW7, FGFR1, FGFR2, FGFR3, IGF1R, MDM2, MDM4, MET, NF1, PTEN, SMARCA4, SMARCB1, STK11, and TP53.
14. The method of any one of the preceding claims further comprising a step of determining a malfunction in the affected gene type.
15. The method of any one of the preceding claims further comprising a step of generating a recommendation for a non-immune therapeutic drug that targets a protein encoded by the affected gene type.
16. The method of any one of the preceding claims further comprising a step of using the cancer driver neoepitope to prepare an immune therapeutic agent.

17. The method of claim 16 wherein the immune therapeutic agent comprises at least one of a synthetic antibody having binding specificity to the cancer driver neoepitope, a synthetic cancer driver neoepitope, a nucleic acid encoding the cancer driver neoepitope, an immune competent cell carrying a chimeric antigen receptor having binding specificity to the cancer driver neoepitope, and a recombinant virus comprising a nucleic acid encoding the cancer driver neoepitope.
18. The method of claim 1 wherein the step of determining the plurality of expressed missense based patient- and tumor-specific neoepitopes comprises location-guided synchronous alignment of omics data from the tumor tissue and the matched normal tissue.
19. The method of claim 1 further comprising a step of filtering the expressed missense based patient- and tumor-specific neoepitopes by at least one of an *a priori* known molecular variation selected from the group consisting of a single nucleotide polymorphism, a short deletion and insertion polymorphism, a microsatellite marker, a short tandem repeat, a heterozygous sequence, a multinucleotide polymorphism, and a named variant.
20. The method of claim 1 wherein the tumor tissue is a solid tumor tissue and wherein the matched normal tissue is blood.
21. The method of claim 1 wherein the step of filtering the neoepitopes by HLA type is performed for each of the neoepitopes using a plurality of distinct individual neoepitope sequences in which a changed amino acid has a distinct position within the neoepitope sequence.
22. The method of claim 21 wherein the individual neoepitope sequences have a length of between 7 and 20 amino acids.
23. The method of claim 1 wherein the step of filtering by HLA type comprises determination of the HLA type from the patient omics data.
24. The method of claim 1 wherein the step of filtering by HLA type is performed to a depth of at least 4 digits.
25. The method of claim 1 wherein the gene type affected is a cancer driver gene for a cancer selected from the group consisting of ALL, AML, BLCA, BRCA, CLL, CM, COREAD,

ESCA, GBM, HC, HNSC, LUAD, LUSC, MB, NB, NSCLC, OV, PRAD, RCCC, SCLC, STAD, THCA, and UCEC.

26. The method of claim 1 wherein the gene type affected is a cancer driver gene selected from a group consisting of: AURKA, BAP1, BRCA1, BRCA2, CCND2, CCND3, CCNE1, CDK4, CDK6, CDKN1B, CDKN2A, CDKN2B, EGF4, ERBB2, FBXW7, FGFR1, FGFR2, FGFR3, IGF1R, MDM2, MDM4, MET, NF1, PTEN, SMARCA4, SMARCB1, STK11, and TP53.
27. The method of claim 1 further comprising a step of determining a malfunction in the affected gene type.
28. The method of claim 1 further comprising a step of generating a recommendation for a non-immune therapeutic drug that targets a protein encoded by the affected gene type.
29. The method of claim 1 further comprising a step of using the cancer driver neoepitope to prepare an immune therapeutic agent.
30. The method of claim 31 wherein the immune therapeutic agent comprises at least one of a synthetic antibody having binding specificity to the cancer driver neoepitope, a synthetic cancer driver neoepitope, a nucleic acid encoding the cancer driver neoepitope, an immune competent cell carrying a chimeric antigen receptor having binding specificity to the cancer driver neoepitope, and a recombinant virus comprising a nucleic acid encoding the cancer driver neoepitope.
31. An immune therapeutic composition, comprising:
a carrier coupled to (i) a synthetic antibody having binding specificity to a patient specific cancer driver neoepitope, (ii) a synthetic patient specific cancer driver neoepitope, (iii) a nucleic acid encoding the patient specific cancer driver neoepitope, or (iv) a chimeric antigen receptor having binding specificity to the patient specific cancer driver neoepitope.
32. The immune therapeutic composition of claim 31 wherein the carrier comprises a single protein or comprises a pharmaceutically acceptable polymer.
33. The immune therapeutic composition of claim 31 wherein the carrier is an immune competent cell.

34. The immune therapeutic composition of claim 33 wherein the immune competent cell is a CD8⁺ T cell or a NK cell.
35. The immune therapeutic composition of claim 31 wherein the carrier is a recombinant virus.
36. The immune therapeutic composition of claim 31 further comprising a pharmaceutically acceptable carrier suitable for injection or infusion.
37. The immune therapeutic composition of any one of claims 31-36 for use in therapy.
38. The immune therapeutic composition of any one of claims 31-36 for use in the treatment of cancer.
39. Use of an immune therapeutic agent in the preparation of a medicament for the treatment of a cancer, wherein the immune therapeutic agent comprises at least one of a synthetic antibody having binding specificity to a patient specific cancer driver neoepitope, a synthetic patient specific cancer driver neoepitope, a nucleic acid encoding a patient specific cancer driver neoepitope, an immune competent cell carrying a chimeric antigen receptor having binding specificity to a patient specific cancer driver neoepitope, and a recombinant virus comprising a nucleic acid encoding a patient specific cancer driver neoepitope.
40. The use of claim 39 wherein the synthetic antibody is coupled to an NK cell or to a carrier comprising a single protein or comprising a pharmaceutically acceptable polymer.
41. The use of claim 39 wherein the synthetic patient specific cancer driver neoepitope is coupled to a carrier comprising a single protein or comprising a pharmaceutically acceptable polymer.
42. The use of claim 39 wherein the nucleic acid encoding the patient specific cancer driver neoepitope is contained in an immune competent cell or in a virus, or coupled to a carrier comprising a single protein or comprising a pharmaceutically acceptable polymer.
43. A recombinant immune competent cell, comprising a nucleic acid encoding a chimeric antigen receptor having binding specificity to a patient specific cancer driver neoepitope, or encoding the patient specific cancer driver neoepitope.

44. The recombinant immune competent cell of claim 43 wherein the immune competent cell is a CD8⁺ T cell or a NK cell, or an NK92 derivative.