

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,
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, 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 filtering the expressed missense based patient- and tumor-specific neoepitopes by HLA type of the patient comprises constructing a de Bruijn graph and implementing a weighted vote process to determine the HLA type of the patient.
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 (acute lymphocytic leukemia), AML (acute myeloid leukemia), BLCA (bladder cancer), BRCA (breast cancer), CLL (chronic lymphocytic leukemia), CM (cutaneous melanoma), COREAD (colorectal adenocarcinoma), ESCA (esophageal cancer), GBM (glioblastoma multiforme), HC (hepatocarcinoma), HNSC (head and neck squamous cell carcinoma), LUAD (lung adenocarcinoma), LUSC (lung small cell carcinoma), MB (medulloblastoma), NB (neuroblastoma), NSCLC (non-small cell lung cancer), OV (ovarian cancer), PRAD (prostate adenocarcinoma), RCCC (renal clear cell carcinoma), SCLC (small cell lung cancer), STAD (stomach adenocarcinoma), THCA (thyroid cancer), and UCEC (uterine corpus endometrioid cancer).
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 an oncogenic mutation 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.