CLAIMS

1. A computer-implemented method, comprising:

inputting to a trained machine learning classifier genomic information of a non-training subject, the genomic information of the non-training subject comprising features from a tumor profile obtained from the non-training subject, wherein

the trained machine learning classifier trained on genomic information of a plurality of training subjects and a responsiveness of each of the plurality of training subjects to a treatment comprising a checkpoint inhibition, the genomic information of the plurality of training subjects comprising features of tumor profiles obtained from each of the plurality of training subjects, wherein the machine-learning classifier trained to predict responsiveness to the treatment;

generating a checkpoint inhibition responsiveness classification for the non-training subject using the trained machine-learning classifier, the checkpoint inhibition responsiveness classification predictive of the non-training subject responding to the checkpoint inhibition; and

reporting the checkpoint inhibition responsiveness classification of the non-training subject using a graphical user interface, wherein at least some of the features from a tumor profile obtained from the non-training subject or at least some of the features from a tumor profile obtained from one or more of the training subjects comprise:

(A) one or more of (i) total mutational burden consisting of all mutations, (ii) total mutational burden consisting of nonsynonymous mutations, (iii) tumor infiltration by cells expressing cluster of differentiation 8 (CD8), (iv) tumor infiltration by cells expressing cluster of differentiation 4 (CD4), and (v) tumor infiltration by cells expressing cluster of differentiation 19 (CD19); and

(B) expression of one or more of beta 2 microglobulin (B2M), proteasome subunit beta 10 (PSMB10), antigen peptide transmitter 1 (TAP1), antigen peptide transporter 2 (TAP2), human leukocyte antigen A (HLA-A), major histocompatibility complex class I B (HLA-B), major histocompatibility complex class I C (HLA-C), major histocompatibility complex class II DQ alpha 1 (HLA-DQA1), HLA class II histocompatibility antigen DRB1 beta chain (HLA-DRB1), HLA class I histocompatibility antigen alpha chain E (HLA-E), natural killer cell granule protein 7 (NKG7), chemokine like receptor 1 (CMKLR1), granzyme A (GZMA),

perforin-1 (PRF1), lymphocyte-activation gene 3 (LAG3), T cell immunoreceptor with Ig and ITIM domains (TIGIT), cluster of differentiation 276 (CD276), chemokine (C-C motif) ligand 5 (CCL5), CD27, chemokine (C-X-C motif) ligand 9 (CXCL9), C-X-C motif chemokine receptor 6 (CXCR6), indoleamine 2,3-dioxygenase (IDO), signal transducer and activator of transcription 1 (STAT1), 3-fucosyl-N-acetyl-lactosamine (CD15), interleukin-2 receptor alpha chain (CD25), siglec-3 (CD33), cluster of differentiation 39 (CD39), cluster of differentiation (CD118), forkhead box P3 (FOXP3), cytotoxic T-lymphocyte-associated protein 4 (CTLA4), programmed cell death protein 1 (PD1), programmed death-ligand 1 (PDL1), and programmed cell death ligand 2 (PDL2).

2. The method of claim 1, wherein at least some of the training features or at least some of the non-training features comprise gene sets.

3. The method of claim 2 wherein the gene sets were selected using single sample gene set enrichment analysis.

4. The method of claim 1, wherein the machine learning classifier is random forest.

5. The method of claim 4, wherein at least 50,000 trees are used in training the machine learning classifier.

6. The method of claim 1, wherein the checkpoint inhibition responsiveness classification comprises a prediction score and one or more feature identifiers, and the one or more feature identifiers are selected from the group consisting of a feature valence, a feature importance, and a feature weight.

7. The method of claim 6, wherein the graphical user interface reports feature identifiers as aspects of an annulus sector, wherein an angle of the annulus sector reports the feature importance, an outer radius of the annulus sector reports the feature weight, and a color of the annulus sector reports the feature valence.

8. The method of claim 7 wherein feature importance of a feature comprises a Gini index decrease of the feature.

9. The method of claim 8 wherein the graphical user interface reports an identifier of a feature if and only if the feature importance of the feature is above a threshold.

10. The method of claim 9 wherein the feature importance of the feature is not above the threshold if the square of the feature importance of the feature is not above 0.1.

11. The method of claim 9, wherein each of the annulus sectors comprises an inner arc and the inner arcs of the annulus sectors are arranged to form a circle.

12. The method of claim 1, further comprising inputting to the trained machine learning classifier a responsiveness of the non-training subject to the treatment and further training the machine learning classifier, wherein further training comprises training the trained machine learning classifier on features of tumor samples obtained from the non-training subject and a responsiveness of the non-training subject to the treatment.

13. The method of claim 1, further comprising selecting a treatment based upon the generated checkpoint inhibition responsiveness classification.

14. A computer system, comprising:

one or more microprocessors,

one or more memories for storing a trained machine learning classifier and genomic information of a non-training subject, wherein the trained machine learning classifier trained on genomic information of a plurality of training subjects and a responsiveness of each of the plurality of training subjects to a treatment comprising a checkpoint inhibition, the genomic information of the plurality of training subjects comprising features of tumor profiles obtained from each of the plurality of training subjects, and the machine-learning classifier trained to predict responsiveness to the treatment, and the genomic information of the non-training subject comprising features from a tumor profile obtained from the non-training subject, and

the one or more memories storing instructions that, when executed by the one or more microprocessors, cause the computer system to generate a checkpoint inhibition responsiveness classification for the non-training subject using the trained machine-learning classifier and report the checkpoint inhibition responsiveness classification of the non-training subject using a graphical user interface, the checkpoint inhibition responsiveness classification predictive of the non-training subject responding to the checkpoint inhibition, wherein at least some of the features from a tumor profile obtained from the non-training subject or at least some of the features from a tumor profile obtained from one or more of the training subjects comprise:

(A) one or more of (i) total mutational burden consisting of all mutations, (ii) total mutational burden consisting of nonsynonymous mutations, (iii) tumor infiltration by cells expressing cluster of differentiation 8 (CD8), (iv) tumor infiltration by cells expressing cluster of

differentiation 4 (CD4), and (v) tumor infiltration by cells expressing cluster of differentiation 19 (CD19); and

(B) expression of one or more of beta 2 microglobulin (B2M), proteasome subunit beta 10 (PSMB10), antigen peptide transmitter 1 (TAP1), antigen peptide transporter 2 (TAP2), human leukocyte antigen A (HLA-A), major histocompatibility complex class I B (HLA-B), major histocompatibility complex class I C (HLA-C), major histocompatibility complex class II DQ alpha 1 (HLA-DQA1), HLA class II histocompatibility antigen DRB1 beta chain (HLA-DRB1), HLA class I histocompatibility antigen alpha chain E (HLA-E), natural killer cell granule protein 7 (NKG7), chemokine like receptor 1 (CMKLR1), granzyme A (GZMA), perforin-1 (PRF1), lymphocyte-activation gene 3 (LAG3), T cell immunoreceptor with Ig and ITIM domains (TIGIT), cluster of differentiation 276 (CD276), chemokine (C-C motif) ligand 5 (CCL5), CD27, chemokine (C-X-C motif) ligand 9 (CXCL9), C-X-C motif chemokine receptor 6 (CXCR6), indoleamine 2,3-dioxygenase (IDO), signal transducer and activator of transcription 1 (STAT1), 3-fucosyl-N-acetyl-lactosamine (CD15), interleukin-2 receptor alpha chain (CD25), siglec-3 (CD33), cluster of differentiation 39 (CD39), cluster of differentiation (CD118), forkhead box P3 (FOXP3) cytotoxic T-lymphocyte-associated protein 4 (CTLA4), programmed cell death protein 1 (PD1), programmed death-ligand 1 (PDL1), and programmed cell death ligand 2 (PDL2).

15. The system of claim 14, wherein at least some of the training features or at least some of the non-training features comprise gene sets.

16. The system of claim 15 wherein the gene sets were selected using single sample gene set enrichment analysis.

17. The system of claim 14, wherein the machine learning classifier is random forest.

18. The system of claim 17, wherein at least 50,000 trees are used in training the machine learning classifier.

19. The system of claim 14, wherein the checkpoint inhibition responsiveness classification comprises a prediction score and one or more feature identifiers, and the one or more feature identifiers are selected from the group consisting of a feature valence, a feature importance, and a feature weight.

20. The system of claim 19, wherein the instructions, when executed by the one or more microprocessors, cause the graphical user interface to report feature identifiers as aspects of an annulus sector, wherein an angle of the annulus sector reports the feature importance, an outer radius of the annulus sector reports the feature weight, and a color of the annulus sector reports the feature valence.

21. The system of claim 20 wherein feature importance of a feature comprises a Gini index decrease of the feature.

22. The system of claim 21 wherein the instructions, when executed by the one or more microprocessors, cause the graphical user interface to report an identifier of a feature if and only if the feature importance of the feature is above a threshold.

23. The system of claim 22 wherein the feature importance of the feature is not above the threshold if the square of the feature importance of the feature is not above 0.1.

24. The system of claim 22, wherein the instructions, when executed by the one or more microprocessors, cause the graphical user interface to report an inner arc of each of the annulus sectors and a circle comprising the inner arcs of the annulus sectors.

25. The system of claim 14, wherein the instructions, when executed by the one or more microprocessors, cause the computer system to further train the machine learning classifier, wherein further training comprises training the trained machine learning classifier on features of tumor samples obtained from the non-training subject and a responsiveness of the non-training subject to the treatment.

26. A machine learning-based classifier for classification of immune checkpoint responsiveness, the machine learning-based classifier comprising:

instructions for one or more processor on a computer-readable storage medium,

wherein the machine learning-based classifier was trained to predict responsiveness of a non-training subject to an immune checkpoint inhibition treatment by inputting, to the machine-learning based classifier, genomic information of a plurality of training subjects and a responsiveness of each of the plurality of training subjects to the treatment, the genomic information of the plurality of training subjects comprising features of tumor profiles obtained from each of the plurality of training subjects;

an input processor that inputs genomic information of the non-training subject into the machine learning-based classifier, the genomic information of the non-training subject

comprising features from a tumor profile obtained from the non-training subject, wherein the machine-learning classifier is

configured to generate a checkpoint inhibition responsiveness classification for the non-training subject, the checkpoint inhibition responsiveness classification predictive of the subject responding to checkpoint inhibition treatment; and

an output processor that reports checkpoint inhibition responsiveness classification, wherein

at least some of the features from a tumor profile obtained from one or more of the training subjects comprised:

(A) one or more of (i) total mutational burden consisting of all mutations, (ii) total mutational burden consisting of nonsynonymous mutations, (iii) tumor infiltration by cells expressing cluster of differentiation 8 (CD8), (iv) tumor infiltration by cells expressing cluster of differentiation 4 (CD4), and (v) tumor infiltration by cells expressing cluster of differentiation 19 (CD19); and

(B) expression of one or more of beta 2 microglobulin (B2M), proteasome subunit beta 10 (PSMB10), antigen peptide transmitter 1 (TAP1), antigen peptide transporter 2 (TAP2), human leukocyte antigen A (HLA-A), major histocompatibility complex class I B (HLA-B), major histocompatibility complex class I C (HLA-C), major histocompatibility complex class II DQ alpha 1 (HLA-DQA1), HLA class II histocompatibility antigen DRB1 beta chain (HLA-DRB1), HLA class I histocompatibility antigen alpha chain E (HLA-E), natural killer cell granule protein 7 (NKG7), chemokine like receptor 1 (CMKLR1), granzyme A (GZMA), perforin-1 (PRF1) lymphocyte-activation gene 3 (LAG3), T cell immunoreceptor with Ig and ITIM domains (TIGIT), cluster of differentiation 276 (CD276), chemokine (C-C motif) ligand 5 (CCL5), CD27, chemokine (C-X-C motif) ligand 9 (CXCL9), C-X-C motif chemokine receptor 6 (CXCR6), indoleamine 2,3-dioxygenase (IDO), signal transducer and activator of transcription 1 (STAT1), 3-fucosyl-N-acetyl-lactosamine (CD15), interleukin-2 receptor alpha chain (CD25), siglec-3 (CD33), cluster of differentiation 39 (CD39), cluster of differentiation (CD118), forkhead box P3 (FOXP3), cytotoxic T-lymphocyte-associated protein 4 (CTLA4), programmed cell death protein 1 (PD1), programmed death-ligand 1 (PDL1), and programmed cell death ligand 2 (PDL2).

27. The machine learning-based classifier of claim 26, wherein the checkpoint inhibition responsiveness classification comprises a prediction score and a plurality of identifier.

28. The method of any one of claims 1-14, wherein

(A) comprises (i), (ii), (iii), (iv), and (v).

29. The system of any one of claims 14-25, wherein

(A) comprises (i), (ii), (iii), (iv), and (v).

30. The machine learning-based classifier of claim 26 or 27, wherein

(A) comprises (i), (ii), (iii), (iv), and (v).