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Methods and compositions for prognosis and treatment of cancers

Abstract

The invention provides methods of using expression levels of one or more immune cell gene signatures and/or combinations of immune cell gene signatures as selection criteria for selecting a patient having cancer for treatment with an immunotherapy. The invention further provides methods for selecting a patient having cancer who may benefit from a particular immunotherapy, such as an activating immunotherapy or a suppressing immunotherapy and administering to the patient the activating immunotherapy or suppressing immunotherapy to treat the cancer.

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Background/Summary

FIELD OF INVENTION
(1) The present invention is directed to methods for selecting cancer patients for treatment with an immunotherapy.
BACKGROUND OF THE INVENTION
(2) Studies in humans with immune checkpoint inhibitors have demonstrated the promise of harnessing the immune system to control and eradicate tumor growth in difficult to treat indications including melanoma, renal cell carcinoma, lung cancer, breast cancer, ovarian cancer, colorectal

cancer, gastric cancer, liver cancer, and bladder cancer.

(3) Tumors arise from normal cells that accumulate mutations leading to uncontrolled cellular proliferation and survival under conditions of stress. In normal circumstances, the immune system, mainly through cytotoxic CD8 T cells, recognizes these transformed cells and prevents the invasion into normal tissue. In certain circumstances, tumor cells escape immune control and progress to disease. The mechanisms of tumor escape may be the product of one or more of the following mechanisms: inability of tumor cells to present neo-antigens on MHC Class I molecules, down-regulation of MHC Class I molecules on tumor cells, inability of T cells to infiltrate the tumor, increased presence of immunosuppressive regulatory T cells or myeloid suppressor cells, enhanced expression of immune checkpoint inhibitors, or increased Th2 and Th17 mediators. The relative contributions of these various immune cell subsets across cancer types and their affects on tumor progression, treatment response, and clinical outcomes are poorly studied.

(4) Accordingly, there is a need for methods for selecting patients who are likely to respond to immuno-based therapies and to develop alternative strategies for the treatment of cancer.

SUMMARY OF THE INVENTION

(5) In one aspect, the invention features a method of selecting a patient having cancer for treatment with an immunotherapy, the method comprising determining the expression level of an immune cell gene signature in a biological sample obtained from the patient, the immune cell gene signature comprising one or more of the following genes (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 or more of the following genes): CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; NCAM1 or NKP46; KLRC3, KLRK1, KLRC2, or KLRD1; ITGAM, ITGAX, CD1C, or CLEC4C; CD68, CD163, ITGAM, ITGAX, or CD14; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD276, PDL1, PDL2, or IDO1; CD274, PDL2, IDO1, or PVR; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; CD4, IL2RA, or CD69; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; CD40, CD80, CD86, CD70, or GITRL; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, or CD226; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; or FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, or COL8A1, wherein a change in the level of expression of the one or more genes in the immune cell gene signature relative to a median level identifies a patient for treatment with an immunotherapy.

(6) In some embodiments, the method further comprises the step of informing the patient that they have an increased likelihood of being responsive to the immunotherapy. In some embodiments, the method further comprises the step of providing a recommendation to the patient for a particular immunotherapy. In some embodiments, the method further comprises the step of administering an immunotherapy to the patient if it is determined that the patient may benefit from the immunotherapy. In some embodiments, the immunotherapy is an activating immunotherapy or a suppressing immunotherapy.

(7) In some embodiments, the expression level of one or more of CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1 is correlated with the presence of T effector (To) cells in the tumor microenvironment. In some embodiments, an increase in expression level of one or more of CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1 indicates that the patient is likely to benefit from an activating immunotherapy. In some embodiments, the activating immunotherapy comprises a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist.

(8) In some embodiments, the expression level of FOXP3 is correlated to the presence of T regulatory (T.sub.reg) cells in the tumor microenvironment. In some embodiments, an increase in expression level of FOXP3 indicates that the patient is likely to benefit from a suppressing immunotherapy. In some embodiments, the suppressing immunotherapy comprises a CTLA-4, PD-

1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist.

(9) In some embodiments, the expression level of (a) one or more of MS3A1 or CD48 and/or (b) one or more of CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5 is correlated with the presence of B cells in the tumor microenvironment. In some embodiments, the expression level of (a) one or more of NCAM1 or NKP46 and/or (b) KLRC3, KLRK1, KLRC2, or KLRD1 is correlated with the presence of NK cells in the tumor microenvironment. In some embodiments, the expression level of one or more of ITGAM, ITGAX, CD1C, or CLEC4C is correlated with the presence of myeloid cells in the tumor microenvironment. In some embodiments, the expression level of one or more of CD68, CD163, ITGAM, ITGAX, or CD14 is correlated with the presence of macrophage cells in the tumor microenvironment. In some embodiments, the expression level of one or more of LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A is correlated with the presence of M2 macrophage cells in the tumor microenvironment. In some embodiments, the expression level of one or more of IL17A or IL17F is correlated with the presence of Th17 cells in the tumor microenvironment. In some embodiments, the expression level of one or more of CCL2, IL1B, IL8, IL6, or PTGS2 is correlated with the presence of inflammatory cells in the tumor microenvironment. In some embodiments, the expression level of (a) one or more of CTLA4, BTLA, LAG3, HAVCR2, or PDCD1 and/or (b) one or more of CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT is correlated with the presence of T cell immune blockers in the tumor microenvironment. In some embodiments, the expression level of (a) one or more of CD276, PDL1, PDL2, or IDO1 and/or (b) one or more of CD274, PDL2, IDO1, or PVR is correlated to the presence of antigen presenting cell (APC) immune blockers in the tumor microenvironment. In some embodiments, the expression level of one or more of CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22 is correlated to T cell chemotaxis. In some embodiments, the expression level of one or more of CD4, IL2RA, or CD69 is correlated with the presence of activated CD4 T cells in the tumor microenvironment. In some embodiments, the expression level of one or more of TAPBP, TAP1, TAP2, PSMB9, or PSMB8 is correlated with the presence of antigen processing in the tumor microenvironment. In some embodiments, the expression level of one or more of CD40, CD80, CD86, CD70, or GITRL is correlated with the presence of costimulatory ligands in the tumor microenvironment. In some embodiments, the expression level of one or more of CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, or CD226 is correlated with the presence of costimulatory receptors in the tumor microenvironment. In some embodiments, the expression level of one or more of GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7 is correlated with cytolytic activity and/or the presence of cytolytic cells in the tumor microenvironment. In some embodiments, the expression level of one or more of FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, or COL8A1 is correlated with the presence of active fibroblasts in the tumor microenvironment. In some embodiments, the expression level of one or more of CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK is correlated with the presence of T cells in the tumor microenvironment.

(10) In other embodiments of any of the above methods, the expression level is one or more (e.g., 1, 2, 3, 4, 5, or 6) of CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1 is determined. In some embodiments, the expression level of FOXP3 is determined. In some embodiments, the expression level of one or more (e.g., 1 or 2) of MS4A1 or CD48 and/or one or more (e.g., 1, 2, 3, 4, 5, 6, or 7) of CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5 is determined. In some embodiments, the expression level of one or more (e.g., 1 or 2) of NCAM1 and NKP46 and/or one or more (e.g., 1, 2, 3, or 4) of KLRC3, KLRK1, KLRC2, or KLRD1 is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, or 4) of ITGAM, ITGAX, CD1C, or CLEC4C is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, 4, or 5) of CD68, CD163, ITGAM, ITGAX, or CD14 is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14) of LAPTM5,

LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A is determined. In some embodiments, the expression level of one or more (e.g., 1 or 2) of IL17A or IL17B is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, 4, 5, 6, 7, or 8) of CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, 4, or 5) of CCL2, IL1B, IL8, IL6, or PTGS2 is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, 4, or 5) of CTLA4, BTLA, LAG3, HAVCR2, or PDCD1 and/or one or more (e.g., 1, 2, 3, 4, 5, or 6) of CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, or 4) of CD276, PDL1, PDL2, or IDO1 and/or one or more (e.g., 1, 2, 3, or 4) of CD274, PDL2, IDO1, or PVR is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, 4, 5, or 6) of CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22 is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, or 3) of CD4, IL2RA, or CD69 is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, 4, or 5) of TAPBP, TAP1, TAP2, PSMB9, or PSMB8 is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, 4, or 5) of CD40, CD80, CD86, CD70, or GITRL is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, 4, 5, 6, 7, or 8) of CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, or CD226 is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, 4, 5, 6, or 7) of GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7 is determined. In some embodiments, the expression level of one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11) of FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, or COL8A1 is determined.

(11) In some embodiments of any of the above methods, the expression level of one or more of the genes in Table 2 are determined.

(12) In some embodiments of any of the above methods, the expression level of one or more of the genes in Table 3 are determined.

(13) In some embodiments of any of the above methods, the expression level of one or more of the genes in Table 4 are determined.

(14) In some embodiments of any of the above methods, the expression level of one or more of the genes in Table 5 are determined.

(15) In some embodiments of any of the above methods, the expression level of one or more of the genes in Table 6 are determined.

(16) In some embodiments of any of the above methods, the expression level of one or more of the genes in Table 7 are determined.

(17) In some embodiments of any of the above methods, the expression level of one or more of the genes in Table 8 are determined.

(18) In some embodiments of any of the above methods, the expression level of one or more of the genes in Table 9 are determined.

(19) In some embodiments of any of the above methods, the expression level of one or more of the genes from each of the following gene signatures CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; NCAM1 or NKP46; KLRC3, KLRK1, KLRC2, or KLRD1; ITGAM, ITGAX, CD1C, or CLEC4C; CD68, CD163, ITGAM, ITGAX, or CD14; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD276, PDL1, PDL2, or IDO1; CD274, PDL2, IDO1, or PVR; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; CD4, IL2RA, or CD69; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; CD40, CD80, CD86, CD70, or GITRL; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, or CD226; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7;

and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, or COL8A1 are determined.

(20) In some embodiments of any of the above methods, the method further comprises determining the ratio of expression level of one or more of CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1 to the expression level of FOXP3. In some embodiments, if the ratio of expression level of one or more of CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1 to the expression level of FOXP3 is high, the patient will likely benefit from an activating immunotherapy. In some embodiments, wherein if the ratio of expression level of one or more of CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1 to the expression level of FOXP3 is low, the patient will likely benefit from a suppressing immunotherapy.

(21) In some embodiments of any of the above methods, the method further comprises determining the ratio of T.sub.eff to T.sub.reg cells. In some embodiments, if the ratio of T.sub.eff to T.sub.reg is high, the patient will likely benefit from an activating immunotherapy. In some embodiments, if the ratio of T.sub.eff to T.sub.reg is low, the patient will likely benefit from a suppressing immunotherapy. In some embodiments, the activating immunotherapy comprises a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist. In some embodiments, the suppressing immunotherapy comprises a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist.

(22) In some embodiments of any of the above methods, the method is carried out prior to administering an immunotherapy in order to provide a patient with a pre-administration prognosis for response.

(23) In some embodiments of any of the above methods, the cancer is a breast cancer, melanoma, non-small cell lung cancer (NSCLC), bladder cancer, renal cell carcinoma, colorectal cancer, ovarian cancer, gastric cancer, or liver cancer. In some embodiments, the cancer is primary, advanced, refractory, or recurrent. In some embodiments, the breast cancer is hormone receptor+ (HR+), HER2+, or triple negative (TN) breast cancer. In some embodiments, the NSCLC is non-squamous NSCLC or squamous NSCLC.

(24) In some embodiments of any of the above methods, expression of the immune cell gene signature in the biological sample obtained from the patient is detected by measuring mRNA.

(25) In some embodiments of any of the above methods, expression of the immune cell gene signature in the biological sample obtained from the patient is detected by measuring plasma protein levels.

Description

BRIEF DESCRIPTION OF THE DRAWINGS

(1) The application file contains at least one drawing executed in color. Copies of this patent or patent application with color drawings will be provided by the Office upon request and payment of the necessary fee.

(2) FIG. **1**A is a Scattermatrix plot of T cell signature genes.

(3) FIG. **1**B is a Scattermatrix plot of T effector signature genes.

(4) FIG. **1**C is a Scattermatrix plot of activated CD4 T cell signature genes.

(5) FIG. **2**A is a Scattermatrix plot of B cell Signature 1, NK cell Signature 1, and IL17 signature genes.

(6) FIG. **2**B is Scattermatrix plot of B cell Signature 2 genes.

(7) FIG. **2**C is Scattermatrix plot of NK cell Signature 2 genes.

(8) FIG. **3**A is a Scattermatrix plot of myeloid signature genes.

(9) FIG. **3**B is a Scattermatrix plot of macrophage signature genes.

(10) FIG. **3**C is a Scattermatrix plot of M2 macrophage signature genes.

(11) FIG. **4** is a Scattermatrix plot of inflammatory signature genes.

(12) FIG. **5**A is a Scattermatrix plot of T cell immune blocker (IB T cell) Signature 1 genes.

(13) FIG. **5**B is a Scattermatrix plot of IB T cell Signature 2 genes.

(14) FIG. **6**A is a Scattermatrix plot of APC immune blocker (IB APC) Signature 1 genes.

(15) FIG. **6**B is a Scattermatrix plot of IB APC Signature 2 genes.

(16) FIG. **7** is a Scattermatrix plot of antigen processing signature genes.

(17) FIG. **8** is a Scattermatrix plot of costimulatory ligand signature genes.

(18) FIG. **9** is a Scattermatrix plot of costimulatory receptor signature genes.

(19) FIG. **10** is a Scattermatrix plot of cytolytic signature genes.

(20) FIG. **11** is a Scattermatrix plot of active fibroblast signature genes.

(21) FIGS. **12**A-**12**C are plots of Principal Component Analysis of nine gene sets across cancer indications.

(22) FIG. **13** is a plot of gene expression levels of T effector signature genes across indications.

(23) FIG. **14** is a plot of gene expression levels of T regulatory signature genes across indications.

(24) FIG. **15** is a plot of gene expression ratios of T effector vs. T regulatory signature genes across indications.

(25) FIG. **16** is a plot of gene expression levels of B cell signature genes across indications.

(26) FIG. **17** is a plot of gene expression levels of NK cell signature genes across indications.

(27) FIG. **18** is a plot of gene expression levels of myeloid signature genes across indications.

(28) FIG. **19** is a plot of gene expression levels of Th17 (IL17) signature genes across indications.

(29) FIG. **20** shows multiple plots of IL17A/IL17F prevalence by indications. IL17 presence is determined by raw Ct<25. Sq- and Non-Sq Lung are collapsed into one group. HER2+ Breast was not evaluated due to small sample sizes.

(30) FIG. **21** is a plot of gene expression levels of inflammatory signature genes across indications.

(31) FIG. **22** is a plot of gene expression levels of immune blockers on T cells across indications.

(32) FIG. **23** is a plot of gene expression levels of immune blockers on APCs across indications.

(33) FIG. **24** is a plot of gene expression ratios of T effector vs. immune blockers on APC across indications.

(34) FIG. **25** shows multiple plots of gene expression ratios of T effector vs. particular genes in the immune blockers on APC signature genes across indications.

(35) FIG. **26** is a plot showing gene expression levels of particular genes in the immune blockers on T cell signature genes across indications.

(36) FIG. **27** is a plot showing gene expression levels of particular genes in the immune blockers on APC signature genes across indications.

(37) FIG. **28** is a plot showing the hierarchical clustering of immune gene signature expression across indications. Genes were median centered across the samples. Euclidean distance and complete linkage were used to generate the dendrogram. Red and green colors indicate higher and lower expression compared to median, respectively. Black indicates median expression.

(38) FIG. **29** is a Scattermatrix plot of CD8 IHC by regions and CD8 RNA levels. log 2 transformation was performed to normalize the distribution.

(39) FIG. **30** shows Scatterplots of CD8 IHC by regions and by indications. Blue lines are least square regression lines. Shaded areas indicate 95% confidence intervals.

(40) FIG. **31** is a plot showing the empirical distribution function (or Empirical CDF, a cumulative distribution function associated with the empirical measure of a sample) of CD8 IHC by regions. The Y axis is the fraction of samples ≤ that of the associated CD8 IHC percentage indicated by the X axis.

(41) FIG. **32** shows Boxplots of gene set expression in association with primary vs. metastatic status.

(42) FIG. **33** is a Volcano plot for immune gene expression in association with CRC primary vs. metastatic status. Y axis is raw signed-rank Wicoxon p-value, and X axis is log 2 based fold change

between primary and metastatic samples. Genes labeled had Bonferroni adjusted P≤0.05: ARG1, IL17A, VTCN1, IL17F, IL1B, HLA.E, HAVCR2, CD70, FOXP3 and PTGS2.

(43) FIG. **34** shows Boxplots of gene set expression in association with etiology.

(44) FIG. **35** shows Boxplots of immune genes having Kruskal Wallis P≤0.05 for association with etiology.

(45) FIG. **36** is a hierarchical clustering of immune genes having p≤0.1 for etiology differences. Genes were median centered across the samples. Euclidean distance and complete linkage were used to generate the dendrogram. Red and green colors indicate higher and lower expression compared to median, respectively. Black indicates median expression. The following colors differentiate etiologies: black=history of Alcoholism; red=HBV+; green=HCV+; blue=HBV+HCV+.

DETAILED DESCRIPTION OF THE INVENTION

I. Introduction

(46) The tumor immune microenvironment consists of a host of immunosuppressive factors that allow the tumor cells to keep the resident T cells in check and to evade anti-tumor immunity. A study of the factors in the tumor stroma or secreted by the tumor cells to keep the T cells from infiltrating the tumor provides a tool for understanding how to convert aggressive tumors into immunogenic tumors capable of responding to immunotherapy. In the present invention, gene expression was used to evaluate the prevalence of gene signatures that represent immune cell subsets across seven different cancer types. This analysis provides insight into the tumor immune microenvironment of nine different cancer indications and various tumor subtypes to identify the drivers of tumor immune biology that dictate response to immunotherapy.

(47) Accordingly, the invention provides methods for selecting a patient having cancer (e.g., bladder cancer, breast cancer, colorectal cancer, gastric cancer, liver cancer, melanoma, lung cancer (e.g., non-small cell lung carcinoma), ovarian cancer, or renal cell carcinoma) for treatment with an immunotherapy by determining the expression level of one or more immune cell gene signatures, and comparing this level of expression to the median level of expression of the one or more immune cell gene signatures. Detection of increased expression of the one or more immune cell gene signatures relative to a median level (i.e., higher expression of the one or more immune cell gene signatures relative to the median level in the cancer type) identifies the patient for treatment with an immunotherapy. The invention also provides methods for treating a patient having cancer (e.g., bladder cancer, breast cancer, colorectal cancer, gastric cancer, liver cancer, melanoma, lung cancer (e.g., non-small cell lung carcinoma), ovarian cancer, or renal cell carcinoma) who may benefit from immunotherapy by administering an activating immunotherapy or a suppressing immunotherapy alone or in combination with a chemotherapy regimen and/or other anti-cancer therapy regimen by determining the expression level of one or more immune cell gene signatures in the patient.

II. Definitions

(48) Unless defined otherwise, technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Singleton et al., Dictionary of Microbiology and Molecular Biology 2nd ed., J. Wiley & Sons (New York, N.Y. 1994), and March, Advanced Organic Chemistry Reactions, Mechanisms and Structure 4th ed., John Wiley & Sons (New York, N.Y. 1992), provide one skilled in the art with a general guide to many of the terms used in the present application.

(49) For purposes of interpreting this specification, the following definitions will apply and whenever appropriate, terms used in the singular will also include the plural and vice versa. In the event that any definition set forth below conflicts with any document incorporated herein by reference, the definition set forth below shall control.

(50) The term "antagonist" is used in the broadest sense, and includes any molecule that partially or fully blocks, inhibits, interferes, or neutralizes a normal biological activity of a native polypeptide

disclosed herein (e.g., an immune cell receptor or ligand, such as CTLA-4, PD-1, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226), either by decreasing transcription or translation of the nucleic acid encoding the native polypeptide, or by inhibiting or blocking the native polypeptide activity, or both. It will be understood by one of ordinary skill in the art that, in some instances, an antagonist may antagonize one activity of the native polypeptide without affecting another activity of the native polypeptide. It will also be understood by one of ordinary skill in the art that, in some instances, an antagonist may be a therapeutic agent that is considered an activating or suppressing immunotherapy depending on the native polypeptide that it binds, interacts, or associates with. Examples of antagonists include, but are not limited to, antisense polynucleotides, interfering RNAs, catalytic RNAs, RNA-DNA chimeras, native polypeptide-specific aptamers, antibodies, antigen-binding fragments of antibodies, native polypeptide-binding small molecules, native polypeptide-binding peptides, and other peptides that specifically bind the native polypeptide (including, but not limited to native polypeptide-binding fragments of one or more native polypeptide ligands, optionally fused to one or more additional domains), such that the interaction between the antagonist and the native polypeptide results in a reduction or cessation of native polypeptide activity or expression.

(51) In a similar manner, the term "agonist" is used in the broadest sense and includes any molecule that mimics, promotes, stimulates, or enhances a normal biological activity of a native polypeptide disclosed herein (e.g., an immune cell receptor or ligand, such as CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4), by increasing transcription or translation of the nucleic acid encoding the native polypeptide, and/or by inhibiting or blocking activity of a molecule that inhibits the expression or activity of the native polypeptide, and/or by enhancing normal native polypeptide activity (including, but not limited to, enhancing the stability of the native polypeptide, or enhancing binding of the native polypeptide to one or more target ligands). It will be understood by one of ordinary skill in the art that, in some instances, an agonist may agonize one activity of the native polypeptide without affecting another activity of the native polypeptide. It will also be understood by one of ordinary skill in the art that, in some instances, an agonist may be a therapeutic agent that is considered an activating or suppressing immunotherapy depending on the native polypeptide that it binds, interacts, or associates with. The agonist can be selected from an antibody, an antigen-binding fragment, an aptamer, an interfering RNA, a small molecule, a peptide, an antisense molecule, and another binding polypeptide. In another example, the agonist can be a polynucleotide selected from an aptamer, interfering RNA, or antisense molecule that interferes with the transcription and/or translation of a native polypeptide-inhibitory molecule. Methods for identifying agonists or antagonists of a polypeptide may comprise contacting a polypeptide with a candidate agonist or antagonist molecule and measuring a detectable change in one or more biological activities normally associated with the polypeptide.

(52) The term "activating immunotherapy" refers to the use of a therapeutic agent that induces, enhances, or promotes an immune response, including, e.g., a T cell response. The term "suppressing immunotherapy" refers to the use of a therapeutic agent that interferes with, suppresses, or inhibits an immune response, including, e.g., a T cell response.

(53) "Human effector cells" refer to leukocytes that express one or more FcRs and perform effector functions. In certain embodiments, the cells express at least FcγRIII and perform ADCC effector function(s). Examples of human leukocytes which mediate ADCC include peripheral blood mononuclear cells (PBMC), natural killer (NK) cells, monocytes, cytotoxic T cells, and neutrophils. The effector cells may be isolated from a native source, e.g., from blood.

(54) "Regulatory T cells (T.sub.reg)" refer to a subset of helper T cells that play a role in inhibition of self-reactive immune responses and are often found in sites of chronic inflammation such as in tumor tissue. In certain embodiments, T.sub.regs are defined phenotypically by high cell surface expression of CD25, CLTA4, GITR, and neuropilin-1 and are under the control of transcription factor FOXP3. In other embodiments, T.sub.regs perform their suppressive function on activated T

cells through contact-dependent mechanisms and cytokine production. In some embodiments, T.sub.regs also modulate immune responses by direct interaction with ligands on dendritic cells (DC), such as, e.g., CTLA4 interaction with B7 molecules on DC that elicits the induction of indoleamine 2,3-dioxygenase (IDO).

(55) The term "antibody" herein is used in the broadest sense and encompasses various antibody structures, including but not limited to monoclonal antibodies, polyclonal antibodies, multispecific antibodies (e.g., bispecific antibodies), and antibody fragments so long as they exhibit the desired antigen-binding activity. An antibody that binds to a target refers to an antibody that is capable of binding the target with sufficient affinity such that the antibody is useful as a diagnostic and/or therapeutic agent in targeting the target. In one embodiment, the extent of binding of an anti-target antibody to an unrelated, non-target protein is less than about 10% of the binding of the antibody to target as measured, e.g., by a radioimmunoassay (RIA) or biacore assay. In certain embodiments, an antibody that binds to a target has a dissociation constant (Kd) of <1 μM, <100 nM, <10 nM, <1 nM, <0.1 nM, <0.01 nM, or <0.001 nM (e.g. 10.sup.−8 M or less, e.g. from 10.sup.−8 M to 10.sup.−13 M, e.g., from 10.sup.−9 M to 10.sup.−13 M). In certain embodiments, an anti-target antibody binds to an epitope of a target that is conserved among different species.

(56) A "blocking antibody" or an "antagonist antibody" is one that partially or fully blocks, inhibits, interferes, or neutralizes a normal biological activity of the antigen it binds. For example, an antagonist antibody may block signaling through an immune cell receptor (e.g., a T cell receptor) so as to restore a functional response by T cells (e.g., proliferation, cytokine production, target cell killing) from a dysfunctional state to antigen stimulation.

(57) An "agonist antibody" or "activating antibody" is one that mimics, promotes, stimulates, or enhances a normal biological activity of the antigen it binds. Agonist antibodies can also enhance or initiate signaling by the antigen to which it binds. In some embodiments, agonist antibodies cause or activate signaling without the presence of the natural ligand. For example, an agonist antibody may increase memory T cell proliferation, increase cytokine production by memory T cells, inhibit regulatory T cell function, and/or inhibit regulatory T cell suppression of effector T cell function, such as effector T cell proliferation and/or cytokine production.

(58) An "antibody fragment" refers to a molecule other than an intact antibody that comprises a portion of an intact antibody that binds the antigen to which the intact antibody binds. Examples of antibody fragments include but are not limited to Fv, Fab, Fab′, Fab′-SH, F(ab′)2; diabodies; linear antibodies; single-chain antibody molecules (e.g. scFv); and multispecific antibodies formed from antibody fragments.

(59) An "antibody that binds to the same epitope" as a reference antibody refers to an antibody that blocks binding of the reference antibody to its antigen in a competition assay by 50% or more, and conversely, the reference antibody blocks binding of the antibody to its antigen in a competition assay by 50% or more.

(60) The term "benefit" is used in the broadest sense and refers to any desirable effect and specifically includes clinical benefit as defined herein. Clinical benefit can be measured by assessing various endpoints, e.g., inhibition, to some extent, of disease progression, including slowing down and complete arrest; reduction in the number of disease episodes and/or symptoms; reduction in lesion size; inhibition (i.e., reduction, slowing down or complete stopping) of disease cell infiltration into adjacent peripheral organs and/or tissues; inhibition (i.e. reduction, slowing down or complete stopping) of disease spread; decrease of auto-immune response, which may, but does not have to, result in the regression or ablation of the disease lesion; relief, to some extent, of one or more symptoms associated with the disorder; increase in the length of disease-free presentation following treatment, e.g., progression-free survival; increased overall survival; higher response rate; and/or decreased mortality at a given point of time following treatment.

(61) As used herein, the term "binds," "specifically binds to," or is "specific for" refers to measurable and reproducible interactions such as binding between a target and an antibody, which

is determinative of the presence of the target in the presence of a heterogeneous population of molecules including biological molecules. For example, an antibody that specifically binds to a target (which can be an epitope) is an antibody that binds this target with greater affinity, avidity, more readily, and/or with greater duration than it binds to other targets. In one embodiment, the extent of binding of an antibody to an unrelated target is less than about 10% of the binding of the antibody to the target as measured, for example, by a radioimmunoassay (RIA). In certain embodiments, an antibody that specifically binds to a target has a dissociation constant (Kd) of ≤ 1 µM, ≤ 100 nM, ≤ 10 nM, ≤ 1 nM, or ≤ 0.1 nM. In certain embodiments, an antibody specifically binds to an epitope on a protein that is conserved among the protein from different species. In another embodiment, specific binding can include, but does not require exclusive binding.

(62) The term "biological sample" or "sample" as used herein includes, but is not limited to, blood, serum, plasma, sputum, tissue biopsies, tumor tissue, and nasal samples including nasal swabs or nasal polyps.

(63) The terms "cancer" and "cancerous" refer to or describe the physiological condition in mammals that is typically characterized by unregulated cell growth. Included in this definition are benign and malignant cancers. Examples of cancer include but are not limited to, carcinoma, lymphoma, blastoma, sarcoma, and leukemia. More particular examples of such cancers include squamous cell cancer, lung cancer (including small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, and squamous carcinoma of the lung), cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer (including gastrointestinal cancer), pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, liver cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma and various types of head and neck cancer, as well as B-cell lymphoma (including low grade/follicular non-Hodgkin's lymphoma (NHL); small lymphocytic (SL) NHL; intermediate grade/follicular NHL; intermediate grade diffuse NHL; high grade immunoblastic NHL; high grade lymphoblastic NHL; high grade small non-cleaved cell NHL; bulky disease NHL; mantle cell lymphoma; AIDS-related lymphoma; and Waldenstrom's Macroglobulinemia); chronic lymphocytic leukemia (CLL); acute lymphoblastic leukemia (ALL); Hairy cell leukemia; chronic myeloblastic leukemia; and post-transplant lymphoproliferative disorder (PTLD), as well as abnormal vascular proliferation associated with phakomatoses, edema (such as that associated with brain tumors), and Meigs' syndrome.

(64) An "advanced" cancer is one which has spread outside the site or organ of origin, either by local invasion or metastasis.

(65) A "refractory" cancer is one which progresses even though an anti-tumor agent, such as a chemotherapeutic agent, is being administered to the cancer patient. An example of a refractory cancer is one which is platinum refractory.

(66) A "recurrent" cancer is one which has regrown, either at the initial site or at a distant site, after a response to initial therapy.

(67) By "platinum-resistant" cancer is meant cancer in a patient that has progressed while the patient was receiving platinum-based chemotherapy or cancer in a patient that has progressed within, e.g., 12 months (for instance, within 6 months) after the completion of platinum-based chemotherapy. Such a cancer can be said to have or exhibit "platinum-resistance."

(68) By "chemotherapy-resistant" cancer is meant cancer in a patient that has progressed while the patient is receiving a chemotherapy regimen or cancer in a patient that has progressed within, e.g., 12 months (for instance, within 6 months) after the completion of a chemotherapy regimen. Such a cancer can be said to have or exhibit "chemotherapy-resistance."

(69) The term "tumor" refers to all neoplastic cell growth and proliferation, whether malignant or benign, and all pre-cancerous and cancerous cells and tissues. The terms "cancer," "cancerous," "cell proliferative disorder," "proliferative disorder" and "tumor" are not mutually exclusive as

referred to herein.

(70) As used herein, "metastasis" is meant the spread of cancer from its primary site to other places in the body. Cancer cells can break away from a primary tumor, penetrate into lymphatic and blood vessels, circulate through the bloodstream, and grow in a distant focus (metastasize) in normal tissues elsewhere in the body. Metastasis can be local or distant. Metastasis is a sequential process, contingent on tumor cells breaking off from the primary tumor, traveling through the bloodstream, and stopping at a distant site. At the new site, the cells establish a blood supply and can grow to form a life-threatening mass. Both stimulatory and inhibitory molecular pathways within the tumor cell regulate this behavior, and interactions between the tumor cell and host cells in the distant site are also significant.

(71) The term "chimeric" antibody refers to an antibody in which a portion of the heavy and/or light chain is derived from a particular source or species, while the remainder of the heavy and/or light chain is derived from a different source or species.

(72) The "class" of an antibody refers to the type of constant domain or constant region possessed by its heavy chain. There are five major classes of antibodies: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgAI, and IgA2. The heavy chain constant domains that correspond to the different classes of immunoglobulins are called α, δ, ε, γ, and μ, respectively.

(73) A "chemotherapeutic agent" includes chemical compounds useful in the treatment of cancer. Examples of chemotherapeutic agents include erlotinib (TARCEVA®, Genentech/OSI Pharm.), bortezomib (VELCADE®, Millennium Pharm.), disulfiram, epigallocatechin gallate, salinosporamide A, carfilzomib, 17-AAG (geldanamycin), radicicol, lactate dehydrogenase A (LDH-A), fulvestrant (FASLODEX®, AstraZeneca), sunitib (SUTENT®, Pfizer/Sugen), letrozole (FEMARA®, Novartis), imatinib mesylate (GLEEVEC®, Novartis), finasunate (VATALANIB®, Novartis), oxaliplatin (ELOXATIN®, Sanofi), 5-FU (5-fluorouracil), leucovorin, Rapamycin (Sirolimus, RAPAMUNE®, Wyeth), Lapatinib (TYKERB®, GSK572016, Glaxo Smith Kline), Lonafamib (SCH 66336), sorafenib (NEXAVAR®, Bayer Labs), gefitinib (IRESSA®, AstraZeneca), AG1478, alkylating agents such as thiotepa and CYTOXAN® cyclosphosphamide; alkyl sulfonates such as busulfan, improsulfan and piposulfan; aziridines such as benzodopa, carboquone, meturedopa, and uredopa; ethylenimines and methylamelamines including altretamine, triethylenemelamine, triethylenephosphoramide, triethylenethiophosphoramide and trimethylomelamine; acetogenins (especially bullatacin and bullatacinone); a camptothecin (including topotecan and irinotecan); bryostatin; callystatin; CC-1065 (including its adozelesin, carzelesin and bizelesin synthetic analogs); cryptophycins (particularly cryptophycin 1 and cryptophycin 8); adrenocorticosteroids (including prednisone and prednisolone); cyproterone acetate; 5a-reductases including finasteride and dutasteride); vorinostat, romidepsin, panobinostat, valproic acid, mocetinostat dolastatin; aldesleukin, talc duocarmycin (including the synthetic analogs, KW-2189 and CB1-TM1); eleutherobin; pancratistatin; a sarcodictyin; spongistatin; nitrogen mustards such as chlorambucil, chlomaphazine, chlorophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosoureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, and ranimnustine; antibiotics such as the enediyne antibiotics (e.g., calicheamicin, especially calicheamicin γ1I and calicheamicin ω1I (Angew Chem. Intl. Ed. Engl. 1994 33:183-186); dynemicin, including dynemicin A; bisphosphonates, such as clodronate; an esperamicin; as well as neocarzinostatin chromophore and related chromoprotein enediyne antibiotic chromophores), aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, carabicin, caminomycin, carzinophilin, chromomycinis, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, ADRIAMYCIN® (doxorubicin), morpholino-doxorubicin, cyanomorpholino-doxorubicin, 2-pyrrolino-doxorubicin and deoxydoxorubicin), epirubicin, esorubicin, idarubicin, marcellomycin,

mitomycins such as mitomycin C, mycophenolic acid, nogalamycin, olivomycins, peplomycin, porfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites such as methotrexate and 5-fluorouracil (5-FU); folic acid analogs such as denopterin, methotrexate, pteropterin, trimetrexate; purine analogs such as fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimidine analogs such as ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine; androgens such as calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals such as aminoglutethimide, mitotane, trilostane; folic acid replenisher such as frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; eniluracil; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elfomithine; elliptinium acetate; an epothilone; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidainine; maytansinoids such as maytansine and ansamitocins; mitoguazone; mitoxantrone; mopidamnol; nitraerine; pentostatin; phenamet; pirarubicin; losoxantrone; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK® polysaccharide complex (JHS Natural Products, Eugene, Oreg.); razoxane; rhizoxin; sizofuran; spirogermanium; tenuazonic acid; triaziquone; 2,2′,2″-trichlorotriethylamine; trichothecenes (especially T-2 toxin, verracurin A, roridin A and anguidine); urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxoids, e.g., TAXOL (paclitaxel; Bristol-Myers Squibb Oncology, Princeton, N.J.), ABRAXANE® (Cremophor-free), albumin-engineered nanoparticle formulations of paclitaxel (American Pharmaceutical Partners, Schaumberg, Ill.), and TAXOTERE® (docetaxel, doxetaxel; Sanofi-Aventis); chloranmbucil; GEMZAR® (gemcitabine); 6-thioguanine; mercaptopurine; methotrexate; platinum analogs such as cisplatin and carboplatin; vinblastine; etoposide (VP-16); ifosfamide; mitoxantrone; vincristine; NAVELBINE® (vinorelbine); novantrone; teniposide; edatrexate; daunomycin; aminopterin; capecitabine (XELODA®); ibandronate; CPT-11; topoisomerase inhibitor RFS 2000; difluoromethylornithine (DMFO); retinoids such as retinoic acid; and pharmaceutically acceptable salts, acids and derivatives of any of the above.

(74) Chemotherapeutic agent also includes (i) anti-hormonal agents that act to regulate or inhibit hormone action on tumors such as anti-estrogens and selective estrogen receptor modulators (SERMs), including, for example, tamoxifen (including NOLVADEX®; tamoxifen citrate), raloxifene, droloxifene, iodoxyfene, 4-hydroxytamoxifen, trioxifene, keoxifene, LY117018, onapristone, and FARESTON® (toremifine citrate); (ii) aromatase inhibitors that inhibit the enzyme aromatase, which regulates estrogen production in the adrenal glands, such as, for example, 4(5)-imidazoles, aminoglutethimide, MEGASE® (megestrol acetate), AROMASIN® (exemestane; Pfizer), formestanie, fadrozole, RIVISOR® (vorozole), FEMARA® (letrozole; Novartis), and ARIMIDEX® (anastrozole; AstraZeneca); (iii) anti-androgens such as flutamide, nilutamide, bicalutamide, leuprolide and goserelin; buserelin, tripterelin, medroxyprogesterone acetate, diethylstilbestrol, premarin, fluoxymesterone, all transretionic acid, fenretinide, as well as troxacitabine (a 1,3-dioxolane nucleoside cytosine analog); (iv) protein kinase inhibitors; (v) lipid kinase inhibitors; (vi) antisense oligonucleotides, particularly those which inhibit expression of genes in signaling pathways implicated in aberrant cell proliferation, such as, for example, PKC-alpha, Ralf and H-Ras; (vii) ribozymes such as VEGF expression inhibitors (e.g., ANGIOZYME®) and HER2 expression inhibitors; (viii) vaccines such as gene therapy vaccines, for example, ALLOVECTIN®, LEUVECTIN®, and VAXID®; PROLEUKIN®, rIL-2; a topoisomerase 1 inhibitor such as LURTOTECAN®; ABARELIX® rmRH; and (ix) pharmaceutically acceptable salts, acids and derivatives of any of the above.

(75) Chemotherapeutic agent also includes antibodies such as alemtuzumab (Campath), bevacizumab (AVASTIN®, Genentech); cetuximab (ERBITUX®, Imclone); panitumumab (VECTIBIX®, Amgen), rituximab (RITUXAN®, Genentech/Biogen Idec), pertuzumab (OMNITARG®, 2C4, Genentech), trastuzumab (HERCEPTIN®, Genentech), tositumomab

(Bexxar, Corixia), and the antibody drug conjugate, gemtuzumab ozogamicin (MYLOTARG®, Wyeth). Additional humanized monoclonal antibodies with therapeutic potential as agents in combination with the compounds of the invention include: apolizumab, aselizumab, atlizumab, bapineuzumab, bivatuzumab mertansine, cantuzumab mertansine, cedelizumab, certolizumab pegol, cidfusituzumab, cidtuzumab, daclizumab, eculizumab, efalizumab, epratuzumab, erlizumab, felvizumab, fontolizumab, gemtuzumab ozogamicin, inotuzumab ozogamicin, ipilimumab, labetuzumab, lintuzumab, matuzumab, mepolizumab, motavizumab, motovizumab, natalizumab, nimotuzumab, nolovizumab, numavizumab, ocrelizumab, omalizumab, palivizumab, pascolizumab, pecfusituzumab, pectuzumab, pexelizumab, ralivizumab, ranibizumab, reslivizumab, reslizumab, resyvizumab, rovelizumab, ruplizumab, sibrotuzumab, siplizumab, sontuzumab, tacatuzumab tetraxetan, tadocizumab, talizumab, tefibazumab, tocilizumab, toralizumab, tucotuzumab celmoleukin, tucusituzumab, umavizumab, urtoxazumab, ustekinumab, visilizumab, and the anti-interleukin-12 (ABT-874/J695, Wyeth Research and Abbott Laboratories) which is a recombinant exclusively human-sequence, full-length IgG1 A antibody genetically modified to recognize interleukin-12 p40 protein.

(76) Chemotherapeutic agent also includes "EGFR inhibitors," which refers to compounds that bind to or otherwise interact directly with EGFR and prevent or reduce its signaling activity, and is alternatively referred to as an "EGFR antagonist." Examples of such agents include antibodies and small molecules that bind to EGFR. Examples of antibodies which bind to EGFR include MAb 579 (ATCC CRL HB 8506), MAb 455 (ATCC CRL HB8507), MAb 225 (ATCC CRL 8508), MAb 528 (ATCC CRL 8509) (see, U.S. Pat. No. 4,943,533, Mendelsohn et al.) and variants thereof, such as chimerized 225 (C225 or Cetuximab; ERBUTIX®) and reshaped human 225 (H225) (see, WO 96/40210, Imclone Systems Inc.); IMC-11F8, a fully human, EGFR-targeted antibody (Imclone); antibodies that bind type II mutant EGFR (U.S. Pat. No. 5,212,290); humanized and chimeric antibodies that bind EGFR as described in U.S. Pat. No. 5,891,996; and human antibodies that bind EGFR, such as ABX-EGF or Panitumumab (see WO98/50433, Abgenix/Amgen); EMD 55900 (Stragliotto et al. Eur. J. Cancer 32A:636-640 (1996)); EMD7200 (matuzumab) a humanized EGFR antibody directed against EGFR that competes with both EGF and TGF-alpha for EGFR binding (EMD/Merck); human EGFR antibody, HuMax-EGFR (GenMab); fully human antibodies known as E1.1, E2.4, E2.5, E6.2, E6.4, E2.11, E6.3 and E7.6.3 and described in U.S. Pat. No. 6,235,883; MDX-447 (Medarex Inc); and mAb 806 or humanized mAb 806 (Johns et al., J. Biol. Chem. 279(29):30375-30384 (2004)). The anti-EGFR antibody may be conjugated with a cytotoxic agent, thus generating an immunoconjugate (see, e.g., EP659,439A2, Merck Patent GmbH). EGFR antagonists include small molecules such as compounds described in U.S. Pat. Nos. 5,616,582, 5,457,105, 5,475,001, 5,654,307, 5,679,683, 6,084,095, 6,265,410, 6,455,534, 6,521,620, 6,596,726, 6,713,484, 5,770,599, 6,140,332, 5,866,572, 6,399,602, 6,344,459, 6,602,863, 6,391,874, 6,344,455, 5,760,041, 6,002,008, and 5,747,498, as well as the following PCT publications: WO98/14451, WO98/50038, WO99/09016, and WO99/24037. Particular small molecule EGFR antagonists include OSI-774 (CP-358774, erlotinib, TARCEVA® Genentech/OSI Pharmaceuticals); PD 183805 (CI 1033, 2-propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(4-morpholinyl)propoxy]-6-quinazolinyl]-, dihydrochloride, Pfizer Inc.); ZD1839, gefitinib (IRESSA®) 4-(3'-Chloro-4'-fluoroanilino)-7-methoxy-6-(3-morpholinopropoxy)quinazoline, AstraZeneca); ZM 105180 ((6-amino-4-(3-methylphenyl-amino)-quinazoline, Zeneca); BIBX-1382 (N8-(3-chloro-4-fluoro-phenyl)-N2-(1-methyl-piperidin-4-yl)-pyrimido[5,4-d]pyrimidine-2,8-diamine, Boehringer Ingelheim); PKI-166 ((R)-4-[4-[(1-phenylethyl)amino]-1H-pyrrolo[2,3-d]pyrimidin-6-yl]-phenol); (R)-6-(4-hydroxyphenyl)-4-[(1-phenylethyl)amino]-7H-pyrrolo[2,3-d]pyrimidine); CL-387785 (N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-2-butynamide); EKB-569 (N-[4-[(3-chloro-4-fluorophenyl)amino]-3-cyano-7-ethoxy-6-quinolinyl]-4-(dimethylamino)-2-butenamide) (Wyeth); AG1478 (Pfizer); AG1571 (SU 5271; Pfizer); dual EGFR/HER2 tyrosine kinase inhibitors such as lapatinib (TYKERB®, GSK572016 or N-[3-chloro-

4-[(3 fluorophenyl)methoxy]phenyl]-6[5[[[2methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-4-quinazolinamine).

(77) Chemotherapeutic agents also include "tyrosine kinase inhibitors" including the EGFR-targeted drugs noted in the preceding paragraph; small molecule HER2 tyrosine kinase inhibitor such as TAK165 available from Takeda; CP-724,714, an oral selective inhibitor of the ErbB2 receptor tyrosine kinase (Pfizer and OSI); dual-HER inhibitors such as EKB-569 (available from Wyeth) which preferentially binds EGFR but inhibits both HER2 and EGFR-overexpressing cells; lapatinib (GSK572016; available from Glaxo-SmithKline), an oral HER2 and EGFR tyrosine kinase inhibitor; PKI-166 (available from Novartis); pan-HER inhibitors such as canertinib (CI-1033; Pharmacia); Raf-1 inhibitors such as antisense agent ISIS-5132 available from ISIS Pharmaceuticals which inhibit Raf-1 signaling; non-HER targeted TK inhibitors such as imatinib mesylate (GLEEVEC®, available from Glaxo SmithKline); multi-targeted tyrosine kinase inhibitors such as sunitinib (SUTENT®, available from Pfizer); VEGF receptor tyrosine kinase inhibitors such as vatalanib (PTK787/ZK222584, available from Novartis/Schering AG); MAPK extracellular regulated kinase I inhibitor CI-1040 (available from Pharmacia); quinazolines, such as PD 153035,4-(3-chloroanilino) quinazoline; pyridopyrimidines; pyrimidopyrimidines; pyrrolopyrimidines, such as CGP 59326, CGP 60261 and CGP 62706; pyrazolopyrimidines, 4-(phenylamino)-7H-pyrrolo[2,3-d] pyrimidines; curcumin (diferuloyl methane, 4,5-bis (4-fluoroanilino)phthalimide); tyrphostines containing nitrothiophene moieties; PD-0183805 (Warner-Lamber); antisense molecules (e.g. those that bind to HER-encoding nucleic acid); quinoxalines (U.S. Pat. No. 5,804,396); tryphostins (U.S. Pat. No. 5,804,396); ZD6474 (Astra Zeneca); PTK-787 (Novartis/Schering AG); pan-HER inhibitors such as CI-1033 (Pfizer); Affinitac (ISIS 3521; Isis/Lilly); imatinib mesylate (GLEEVEC®); PKI 166 (Novartis); GW2016 (Glaxo SmithKline); CI-1033 (Pfizer); EKB-569 (Wyeth); Semaxinib (Pfizer); ZD6474 (AstraZeneca); PTK-787 (Novartis/Schering AG); INC-1C11 (Imclone), rapamycin (sirolimus, RAPAMUNE®); or as described in any of the following patent publications: U.S. Pat. No. 5,804,396; WO 1999/09016 (American Cyanamid); WO 1998/43960 (American Cyanamid); WO 1997/38983 (Warner Lambert); WO 1999/06378 (Warner Lambert); WO 1999/06396 (Warner Lambert); WO 1996/30347 (Pfizer, Inc); WO 1996/33978 (Zeneca); WO 1996/3397 (Zeneca) and WO 1996/33980 (Zeneca).

(78) Chemotherapeutic agents also include dexamethasone, interferons, colchicine, metoprine, cyclosporine, amphotericin, metronidazole, alemtuzumab, alitretinoin, allopurinol, amifostine, arsenic trioxide, asparaginase, BCG live, bevacuzimab, bexarotene, cladribine, clofarabine, darbepoetin alfa, denileukin, dexrazoxane, epoetin alfa, elotinib, filgrastim, histrelin acetate, ibritumomab, interferon alfa-2a, interferon alfa-2b, lenalidomide, levamisole, mesna, methoxsalen, nandrolone, nelarabine, nofetumomab, oprelvekin, palifermin, pamidronate, pegademase, pegaspargase, pegfilgrastim, pemetrexed disodium, plicamycin, porfimer sodium, quinacrine, rasburicase, sargramostim, temozolomide, VM-26, 6-TG, toremifene, tretinoin, ATRA, valrubicin, zoledronate, and zoledronic acid, and pharmaceutically acceptable salts thereof.

(79) By "platinum-based chemotherapeutic agent" or "platin" is meant an antineoplastic drug that is a coordination complex of platinum. Examples of platinum-based chemotherapeutic agents include carboplatin, cisplatin, satraplatin, picoplatin, nedaplatin, triplatin, lipoplatin, and oxaliplatinum.

(80) By "platinum-based chemotherapy" is meant therapy with one or more platinum-based chemotherapeutic agent, optionally in combination with one or more other chemotherapeutic agents.

(81) By "correlate" or "correlation" is meant comparing, in any way, the performance and/or results of a first analysis or protocol with the performance and/or results of a second analysis or protocol. For example, one may use the results of a first analysis or protocol to determine the outcome or result of a second analysis or protocol. Or one may use the results of a first analysis or protocol to

determine whether a second analysis or protocol should be performed. For example, with respect to the embodiment of gene expression analysis or protocol, one may use the results of the gene expression analysis or protocol to determine whether a specific immune cell type or subset is present.

(82) "Effector functions" refer to those biological activities attributable to the Fc region of an antibody, which vary with the antibody isotype. Examples of antibody effector functions include: Clq binding and complement dependent cytotoxicity (CDC); Fc receptor binding; antibody-dependent cell-mediated cytotoxicity (ADCC); phagocytosis; down regulation of cell surface receptors (e.g. B cell receptor); and B cell activation.

(83) "Enhancing T cell function" means to induce, cause or stimulate an effector or memory T cell to have a renewed, sustained or amplified biological function. Examples of enhancing T cell function include: increased secretion of y-interferon from CD8 effector T cells, increased secretion of y-interferon from CD4+ memory and/or effector T cells, increased proliferation of CD4+ effector and/or memory T cells, increased proliferation of CD8 effector T cells, increased antigen responsiveness (e.g., clearance), relative to such levels before the intervention. In one embodiment, the level of enhancement is at least 50%, alternatively 60%, 70%, 80%, 90%, 100%, 120%, 150%, 200%. The manner of measuring this enhancement is known to one of ordinary skill in the art.

(84) A sample, cell, tumor, or cancer which "expresses" one or more immune cell gene signatures at an increased expression level relative to a median level of expression (e.g., the median level of expression of the one or more immune cell gene signatures in the type of cancer (or in a cancer type, wherein the "cancer type" is meant to include cancerous cells (e.g., tumor cells, tumor tissues) as well as non-cancerous cells (e.g., stromal cells, stromal tissues) that surround the cancerous/tumor environment) is one in which the expression level of one or more immune cell gene signatures is considered to be a "high immune cell gene signature expression level" to a skilled person for that type of cancer. Generally, such a level will be in the range from about 50% up to about 100% or more (e.g., 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 100%, or more) relative to immune cell gene signature levels in a population of samples, cells, tumors, or cancers of the same cancer type. For instance, the population that is used to arrive at the median expression level may be particular cancer samples (e.g., bladder cancer, breast cancer, colorectal cancer, gastric cancer, liver cancer, melanoma, lung cancer (e.g., non-small cell lung carcinoma), ovarian cancer, or renal cell carcinoma) generally, or subgroupings thereof, such as chemotherapy-resistant cancer, platinum-resistant cancer, as well as advanced, refractory, or recurrent cancer samples.

(85) By "determining the expression level" used in reference to a particular biomarker (e.g., one or more immune cell gene signatures), means expression of the biomarker(s) (e.g., one or more immune cell gene signatures) in a cancer-associated biological environment (e.g., expression of the biomarker(s) in the tumor cells), tumor-associated cells (e.g., tumor-associated stromal cells), as determined using a diagnostic test, any of the detection methods described herein, or the similar.

(86) The term "Fc region" herein is used to define a C-terminal region of an immunoglobulin heavy chain that contains at least a portion of the constant region. The term includes native sequence Fc regions and variant Fc regions. In one embodiment, a human IgG heavy chain Fc region extends from Cys226, or from Pro230, to the carboxyl-terminus of the heavy chain. However, the C-terminal lysine (Lys447) of the Fc region may or may not be present. Unless otherwise specified herein, numbering of amino acid residues in the Fc region or constant region is according to the EU numbering system, also called the EU index, as described in Kabat et al, Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md., 1991.

(87) "Framework" or "FR" refers to variable domain residues other than hypervariable region (HVR) residues. The FR of a variable domain generally consists of four FR domains: FR1, FR2, FR3, and FR4. Accordingly, the HVR and FR sequences generally appear in the following

sequence in VH (or VL): FR1-H1(L1)-FR2-H2(L2)-FR3-H3(L3)-FR4.

(88) The terms "full length antibody," "intact antibody," and "whole antibody" are used herein interchangeably to refer to an antibody having a structure substantially similar to a native antibody structure or having heavy chains that contain an Fc region as defined herein.

(89) A "human antibody" is one which possesses an amino acid sequence which corresponds to that of an antibody produced by a human or a human cell or derived from a non-human source that utilizes human antibody repertoires or other human antibody-encoding sequences. This definition of a human antibody specifically excludes a humanized antibody comprising non-human antigen-binding residues.

(90) A "human consensus framework" is a framework which represents the most commonly occurring amino acid residues in a selection of human immunoglobulin VL or VH framework sequences. Generally, the selection of human immunoglobulin VL or VH sequences is from a subgroup of variable domain sequences. Generally, the subgroup of sequences is a subgroup as in Kabat et al, Sequences of Proteins of Immunological Interest, Fifth Edition, NIH Publication 91-3242, Bethesda Md. (1991), vols. 1-3. In one embodiment, for the VL, the subgroup is subgroup kappa I as in Kabat et al, supra. In one embodiment, for the VH, the subgroup is subgroup III as in Kabat et al, supra.

(91) A "humanized" antibody refers to a chimeric antibody comprising amino acid residues from non-human HVRs and amino acid residues from human FRs. In certain embodiments, a humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the HVRs (e.g., CDRs) correspond to those of a non-human antibody, and all or substantially all of the FRs correspond to those of a human antibody. A humanized antibody optionally may comprise at least a portion of an antibody constant region derived from a human antibody. A "humanized form" of an antibody, e.g., a non-human antibody, refers to an antibody that has undergone humanization.

(92) The term "hypervariable region" or "HVR," as used herein, refers to each of the regions of an antibody variable domain which are hypervariable in sequence and/or form structurally defined loops ("hypervariable loops"). Generally, native four-chain antibodies comprise six HVRs; three in the VH (HI, H2, H3), and three in the VL (LI, L2, L3). HVRs generally comprise amino acid residues from the hypervariable loops and/or from the "complementarity determining regions" (CDRs), the latter typically being of highest sequence variability and/or involved in antigen recognition. An HVR region as used herein comprise any number of residues located within positions 24-36 (for HVRL1), 46-56 (for HVRL2), 89-97 (for HVRL3), 26-35B (for HVRH1), 47-65 (for HVRH2), and 93-102 (for HVRH3).

(93) "Tumor immunity" refers to the process in which tumors evade immune recognition and clearance. Thus, as a therapeutic concept, tumor immunity is "treated" when such evasion is attenuated, and the tumors are recognized and attacked by the immune system. Examples of tumor recognition include tumor binding, tumor shrinkage, and tumor clearance. "Immunogenicity" refers to the ability of a particular substance to provoke an immune response. Tumors are immunogenic and enhancing tumor immunogenicity aids in the clearance of the tumor cells by the immune response. Examples of enhancing tumor immunogenicity include but are not limited to treatment with a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist or treatment with a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist.

(94) An "immunoconjugate" is an antibody conjugated to one or more heterologous molecule(s), including but not limited to a cytotoxic agent.

(95) An "individual" or "subject" is a mammal. Mammals include, but are not limited to, domesticated animals (e.g., cows, sheep, cats, dogs, and horses), primates (e.g., humans and non-human primates such as monkeys), rabbits, and rodents (e.g., mice and rats). In certain embodiments, the individual or subject is a human.

(96) An "isolated" antibody is one which has been separated from a component of its natural environment. In some embodiments, an antibody is purified to greater than 95% or 99% purity as determined by, for example, electrophoretic (e.g., SDS-PAGE, isoelectric focusing (IEF), capillary electrophoresis) or chromatographic (e.g., ion exchange or reverse phase HPLC). F or review of methods for assessment of antibody purity, see, e.g., Flatman et al, J. Chromatogr. B 848:79-87 (2007).

(97) An "isolated" nucleic acid refers to a nucleic acid molecule that has been separated from a component of its natural environment. An isolated nucleic acid includes a nucleic acid molecule contained in cells that ordinarily contain the nucleic acid molecule, but the nucleic acid molecule is present extrachromosomally or at a chromosomal location that is different from its natural chromosomal location.

(98) "Isolated nucleic acid encoding an anti-target antibody" refers to one or more nucleic acid molecules encoding antibody heavy and light chains (or fragments thereof), including such nucleic acid molecule(s) in a single vector or separate vectors, and such nucleic acid molecule(s) present at one or more locations in a host cell.

(99) A "loading" dose herein generally comprises an initial dose of a therapeutic agent administered to a patient, and is followed by one or more maintenance dose(s) thereof. Generally, a single loading dose is administered, but multiple loading doses are contemplated herein. Usually, the amount of loading dose(s) administered exceeds the amount of the maintenance dose(s) administered and/or the loading dose(s) are administered more frequently than the maintenance dose(s), so as to achieve the desired steady-state concentration of the therapeutic agent earlier than can be achieved with the maintenance dose(s).

(100) The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical and/or bind the same epitope, except for possible variant antibodies, e.g., containing naturally occurring mutations or arising during production of a monoclonal antibody preparation, such variants generally being present in minor amounts. In contrast to polyclonal antibody preparations, which typically include different antibodies directed against different determinants (epitopes), each monoclonal antibody of a monoclonal antibody preparation is directed against a single determinant on an antigen. Thus, the modifier "monoclonal" indicates the character of the antibody as being obtained from a substantially homogeneous population of antibodies, and is not to be construed as requiring production of the antibody by any particular method. For example, the monoclonal antibodies to be used according to the methods provided herein may be made by a variety of techniques, including but not limited to the hybridoma method, recombinant DNA methods, phage-display methods, and methods utilizing transgenic animals containing all or part of the human immunoglobulin loci, such methods and other exemplary methods for making monoclonal antibodies being described herein.

(101) A "naked antibody" refers to an antibody that is not conjugated to a heterologous moiety (e.g., a cytotoxic moiety) or radiolabel. The naked antibody may be present in a pharmaceutical formulation.

(102) "Native antibodies" refer to naturally occurring immunoglobulin molecules with varying structures. For example, native IgG antibodies are heterotetrameric glycoproteins of about 150,000 daltons, composed of two identical light chains and two identical heavy chains that are disulfide-bonded. From N- to C-terminus, each heavy chain has a variable region (VH), also called a variable heavy domain or a heavy chain variable domain, followed by three constant domains (CHI, CH2, and CH3). Similarly, from N- to C-terminus, each light chain has a variable region (VL), also called a variable light domain or a light chain variable domain, followed by a constant light (CL) domain. The light chain of an antibody may be assigned to one of two types, called kappa (κ) and lambda (λ), based on the amino acid sequence of its constant domain.

(103) "Patient response" or "response" (and grammatical variations thereof) can be assessed using

any endpoint indicating a benefit to the patient, including, without limitation, (1) inhibition, to some extent, of disease progression, including slowing down and complete arrest; (2) reduction in the number of disease episodes and/or symptoms; (3) reduction in lesional size; (4) inhibition (i.e., reduction, slowing down or complete stopping) of disease cell infiltration into adjacent peripheral organs and/or tissues; (5) inhibition (i.e. reduction, slowing down or complete stopping) of disease spread; (6) decrease of auto-immune response, which may, but does not have to, result in the regression or ablation of the disease lesion; (7) relief, to some extent, of one or more symptoms associated with the disorder; (8) increase in the length of disease-free presentation following treatment; and/or (9) decreased mortality at a given point of time following treatment.

(104) By "radiation therapy" is meant the use of directed gamma rays or beta rays to induce sufficient damage to a cell so as to limit its ability to function normally or to destroy the cell altogether. It will be appreciated that there will be many ways known in the art to determine the dosage and duration of treatment. Typical treatments are given as a one-time administration and typical dosages range from 10 to 200 units (Grays) per day.

(105) The term "small molecule" refers to an organic molecule having a molecular weight between 50 Daltons to 2500 Daltons.

(106) The terms "immune cell gene signature" and "immune cell signature" refer to any one or a combination or sub-combination of the 31 genes set forth in Table 1. Such sub-combinations of these 31 genes are sometimes referred to as "gene sets," and exemplary "gene sets" are set forth in Tables 2-8. The gene expression pattern of an immune cell gene signature in a patient correlates with the presence of an immune cell subtype (e.g., T effector cells, T regulatory cells, B cells, NK cells, myeloid cells, Th17 cells, inflammatory cells, T cell immune blockers, and antigen presenting cell (APC) immune blockers). Each individual gene or member of an immune cell gene signature is an "immune cell signature gene." These genes include, without limitation: CD8A, GZMA, GZMB, IFNγ, EOMES, PRF1, FOXP3, MS4A1, CD48, NCAM1, NKP46, ITGAM, ITGAX, CD1C, CLEC4C, IL17A, IL17F, CCL2, IL1B, IL8, IL6, PTGS2, CTLA4, BTLA, LAG3, HAVCR2, PDCD1, CD276, PDL1, PDL2, and IDO1.

(107) The term "PD1-axis antagonist" refers to a molecule that inhibits the interaction of a PD-1 axis binding partner with either one or more of its binding partner, so as to remove T cell dysfunction resulting from signaling on the PD-1 signaling axis—with a result being to restore or enhance T cell function (e.g., proliferation, cytokine production, target cell killing). As used herein, a PD-1 axis antagonist includes a PD-1 binding antagonist, a PD-L1 binding antagonist, and a PD-L2 binding antagonist.

(108) "Survival" refers to the patient remaining alive, and includes overall survival as well as progression free survival.

(109) "Overall survival" refers to the patient remaining alive for a defined period of time, such as 1 year, 5 years, etc. from the time of diagnosis or treatment.

(110) The phrase "progression-free survival" in the context of the present invention refers to the length of time during and after treatment during which, according to the assessment of the treating physician or investigator, a patient's disease does not become worse, i.e., does not progress. As the skilled person will appreciate, a patient's progression-free survival is improved or enhanced if the patient experiences a longer length of time during which the disease does not progress as compared to the average or mean progression free survival time of a control group of similarly situated patients.

(111) By "standard of care" herein is intended the anti-tumor/anti-cancer agent or agents that are routinely used to treat a particular form of cancer.

(112) The terms "therapeutically effective amount" or "effective amount" refer to an amount of a drug effective to treat cancer in the patient. The effective amount of the drug may reduce the number of cancer cells; reduce the tumor size; inhibit (i.e., slow to some extent and preferably stop) cancer cell infiltration into peripheral organs; inhibit (i.e., slow to some extent and preferably stop)

tumor metastasis; inhibit, to some extent, tumor growth; and/or relieve to some extent one or more of the symptoms associated with the cancer. To the extent the drug may prevent growth and/or kill existing cancer cells, it may be cytostatic and/or cytotoxic. The effective amount may extend progression free survival (e.g. as measured by Response Evaluation Criteria for Solid Tumors, RECIST, or CA-125 changes), result in an objective response (including a partial response, PR, or complete response, CR), improve survival (including overall survival and progression free survival) and/or improve one or more symptoms of cancer (e.g. as assessed by FOSI). Most preferably, the therapeutically effective amount of the drug is effective to improve progression free survival (PFS) and/or overall survival (OS).

(113) As used herein, "treatment" refers to clinical intervention in an attempt to alter the natural course of the individual or cell being treated, and can be performed either for prophylaxis or during the course of clinical pathology. Desirable effects of treatment include preventing occurrence or recurrence of disease, alleviation of symptoms, diminishment of any direct or indirect pathological consequences of the disease, decreasing the rate of disease progression, amelioration or palliation of the disease state, and remission or improved prognosis. In some embodiments, methods and compositions of the invention are useful in attempts to delay development of a disease or disorder.

(114) The term "variable region" or "variable domain" refers to the domain of an antibody heavy or light chain that is involved in binding the antibody to antigen. The variable domains of the heavy chain and light chain (VH and VL, respectively) of a native antibody generally have similar structures, with each domain comprising four conserved framework regions (FRs) and three hypervariable regions (HVRs). (See, e.g., Kindt et al. Kuby Immunology, 6th ed., W.H. Freeman and Co., page 91 (2007).) A single VH or VL domain may be sufficient to confer antigen-binding specificity. Furthermore, antibodies that bind a particular antigen may be isolated using a VH or VL domain from an antibody that binds the antigen to screen a library of complementary VL or VH domains, respectively. See, e.g., Portolano et al, J. Immunol. 150:880-887 (1993); Clarkson et al, Nature 352:624-628 (1991).

III. Methods of Prognosis and Detection

(115) The present invention relates to the identification, selection, and use of biomarkers of cancer (e.g., bladder cancer, breast cancer, colorectal cancer, gastric cancer, liver cancer, melanoma, lung cancer (e.g., non-small cell lung carcinoma), ovarian cancer, or renal cell carcinoma) that are correlated with an immune cell subtype (e.g., T effector cells, T regulatory cells, B cells, NK cells, myeloid cells, Th17 cells, inflammatory cells, T cell immune blockers, antigen presenting cell (APC) immune blockers). In this respect, the invention relates to analysis of expression profile(s) in samples from patients with cancer (e.g., bladder cancer, breast cancer, colorectal cancer, gastric cancer, liver cancer, melanoma, lung cancer (e.g., non-small cell lung carcinoma), ovarian cancer, or renal cell carcinoma), to identify biomarkers correlated with an immune cell subtype (e.g., T effector cells, T regulatory cells, B cells, NK cells, myeloid cells, Th17 cells, inflammatory cells, T cell immune blockers, and antigen presenting cell (APC) immune blockers) involved in tumor immunity and the use of these biomarkers in selecting patients for treatment with immunotherapy. The biomarkers of the invention are listed herein, e.g., in Table 1.

(116) TABLE-US-00001 TABLE 1 Gene signature sets and immune cell gene signature set members Gene signature sets Gene signature set members T effector (T.sub.eff) CD8A, GZMA, GZMB, IFNγ, EOMES, PRF1 T regulatory (T.sub.reg) FOXP3 B cell Signature 1 MS4A1, CD48 B cell Signature 2.sup.# CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 NK cell Signature 1 NCAM1, NKP46 NK cell Signature 2.sup.# KLRC3, KLRK1, KLRC2, KLRD1 Myeloid cell ITGAM, ITGAX, CD1C, CLEC4C Macrophage.sup.# CD68, CD163, ITGAM, ITGAX, CD14 M2 Macrophage.sup.# LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A Th17* IL17A, IL17F Inflammatory.sup.# CCL2, IL1B, IL8 (CXCL8), IL6, PTGS2 T cell.sup.# CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK T cell immune blockers CTLA4, BTLA, LAG3, HAVCR2,

PDCD1 (IB T cell) Signature 1 IB T cell Signature 2.sup.# CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT Antigen presenting cell CD276, PDL1, PDL2, IDO1 immune blockers (IB APC) Signature 1 IB APC Signature 2.sup.# CD274, PDL2, IDO1, PVR T cell chemotaxis CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22 Activated CD4 T cell** CD4, IL2RA, CD69 Antigen processing** TAPBP, TAP1, TAP2, PSMB9, PSMB8 Costimulatory ligand.sup.# CD40, CD80, CD86, CD70, GITRL Costimulatory receptor.sup.# CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, CD226 Cytolytic.sup.# GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 Active fibroblast.sup.## FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 All unmarked gene signature sets were derived from analysis of data using a 90-gene PCR based FLUIDIGM ™ panel. *The Th17 gene signature set is also described herein as the IL17 gene set and was derived from analysis of data using a 90-gene PCR based FLUIDIGM ™ panel.. Th17 gene set and IL17 gene set are used interchangeably throughout the application and refer to the same gene set. **Gene signature sets that were derived from analysis of data using an 800-gene custom Nanostring panel (instead of the 90-gene PCR based FLUIDIGM ™ panel) in urothelial bladder cancer (UBC) samples. .sup.#Gene signature sets that were derived from analysis of data using an 800-gene custom Nanostring panel (instead of the 90-gene PCR based FLUIDIGM ™ panel) in non-small cell lung carcinoma (NSCLC) samples. .sup.##Gene signature set that was derived from a targeted RNA-Seq Access in UBC samples.

(117) The invention provides methods for selecting patients with cancer (e.g., bladder cancer, breast cancer, colorectal cancer, gastric cancer, liver cancer, melanoma, lung cancer (e.g., non-small cell lung carcinoma), ovarian cancer, or renal cell carcinoma) for treatment with immunotherapy by determining the expression level of one or more immune cell gene signatures (e.g., one or more of the genes listed in Table 1 or combinations thereof, e.g., as listed in Tables 2-8), and comparing the expression level of the immune cell gene signature to a median level for expression of the immune cell gene signature (e.g., the median level for expression of the immune cell gene signature in the cancer type), where a change in the level of expression of the immune cell gene signature identifies patients for treatment with an immunotherapy. Optionally, the methods include the step of informing the patient that they have an increased likelihood of being responsive to an immunotherapy and/or proving a recommendation to the patient for a particular immunotherapy based on the expression level of one or more immune cell gene signatures (e.g., one or more of the genes listed in Table 1 or combinations thereof, e.g., as listed in Tables 2-8).

(118) In some embodiments, the patient is identified for treatment with an activating immunotherapy or selected as having the likelihood of benefiting from an activating immunotherapy regimen if there is an increase in expression level of one or more immune cell gene signatures in the T.sub.eff gene set (i.e., one or more of CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1) or a decrease in expression level of one or more immune cell gene signatures in the T.sub.reg gene set. In other embodiments, the patient is identified for treatment with a suppressing immunotherapy or selected as having the likelihood of benefiting from a suppressing immunotherapy if there is an increase in expression level of one or more immune cell gene signatures in the T.sub.reg gene set (i.e., FOXP3) or a decrease in expression level of one or more immune cell gene signatures in the T.sub.eff gene set (i.e., one or more of CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1). In other embodiments, in addition to determining the expression levels of one or more immune cell gene signatures in the T.sub.eff and/or T.sub.reg gene sets, expression levels of one or more immune cell gene signatures in combinations of any one of the gene sets as set forth in Tables 2-8 can be determined in order to identify a patient for a particular immunotherapy regimen (e.g., an activating immunotherapy regimen or a suppressing immunotherapy regimen). Optionally, these methods are carried out prior to administering an immunotherapy regimen in order to provide the patient with a pre-administration prognosis for response to immunotherapy.

(119) In certain embodiments, the expression level of one or more of the genes in an immune cell

gene signature in any one particular gene signature set is determined. For example: CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; or FOXP3; or MS4A1 or CD48; or CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; or NCAM1 or NKP46; or KLRC3, KLRK1, KLRC2, or KLRD1; or ITGAM, ITGAX, CD1C, or CLEC4C; or CD68, CD163, ITGAM, ITGAX, or CD14; or LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; or IL17A or IL17F; or CCL2, IL1B, IL8, IL6, or PTGS2; or CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; or CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; or CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; or CD276, PDL1, PDL2, or IDO1; or CD274, PDL2, IDO1, or PVR; or CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; or CD4, IL2RA, or CD69; or TAPBP, TAP1, TAP2, PSMB9, or PSMB8; or CD40, CD80, CD86, CD70, or GITRL; or CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, or CD226; or GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; or FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, or COL8A1 is determined. In another embodiment, the expression levels of one or more of the genes in an immune cell gene signature in two particular gene signature sets are determined. For example, combinations of two particular gene signature sets are set forth in Table 2 below.

(120) TABLE-US-00002 TABLE 2 Combinations of two gene signature sets CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and MS4A1 or CD48. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and NCAM1 or NKP46. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and FOXP3. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and ITGAM, ITGAX, CD1C, or CLEC4C. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and CD276, PDL1, PDL2, or IDO1. FOXP3; and MS4A1 or CD48. FOXP3; and NCAM1 or NKP46. FOXP3; and ITGAM, ITGAX, CD1C, or CLEC4C. FOXP3; and IL17A or IL17F. FOXP3; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; and NCAM1 or NKP46. MS4A1 or CD48; and ITGAM, ITGAX, CD1C, or CLEC4C. MS4A1 or CD48; and IL17A or IL17F. MS4A1 or CD48; and CCL2, IL1B, IL8, IL6, or PTGS2. MS4A1 or CD48; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. MS4A1 or CD48; and CD276, PDL1, PDL2, or IDO1. NCAM1 or NKP46; and ITGAM, ITGAX, CD1C, or CLEC4C. NCAM1 or NKP46; and IL17A or IL17F. NCAM1 or NKP46; and CCL2, IL1B, IL8, IL6, or PTGS2. NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. NCAM1 or NKP46; and CD276, PDL1, PDL2, or IDO1. ITGAM, ITGAX, CD1C, or CLEC4C; and IL17A or IL17F. ITGAM, ITGAX, CD1C, or CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. ITGAM, ITGAX, CD1C, or CLEC4C; and CD276, PDL1, PDL2, or IDO1. IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. NCAM1 or NKP46; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. ITGAM, ITGAX, CD1C, or CLEC4C; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and

CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and KLRC3, KLRK1, KLRC2, KLRD1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and CD68, CD163, ITGAM, ITGAX, CD14 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and CD274, PDL2, IDO1, PVR CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and CD4, IL2RA, CD69 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and CD40, CD80, CD86, CD70, GITRL CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 FOXP3; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 FOXP3; and KLRC3, KLRK1, KLRC2, KLRD1 FOXP3; and CD68, CD163, ITGAM, ITGAX, CD14 FOXP3; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A FOXP3; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK FOXP3; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT FOXP3; and CD274, PDL2, IDO1, PVR FOXP3; and CD4, IL2RA, CD69 FOXP3; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 FOXP3; and CD40, CD80, CD86, CD70, GITRL FOXP3; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 FOXP3; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 FOXP3; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 MS4A1 or CD48; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 MS4A1 or CD48; and KLRC3, KLRK1, KLRC2, KLRD1 MS4A1 or CD48; and CD68, CD163, ITGAM, ITGAX, CD14 MS4A1 or CD48; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A MS4A1 or CD48; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK MS4A1 or CD48; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT MS4A1 or CD48; and CD274, PDL2, IDO1, PVR MS4A1 or CD48; and CD4, IL2RA, CD69 MS4A1 or CD48; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 MS4A1 or CD48; and CD40, CD80, CD86, CD70, GITRL MS4A1 or CD48; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 MS4A1 or CD48; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 MS4A1 or CD48; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 NCAM1 or NKP46; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 NCAM1 or NKP46; and KLRC3, KLRK1, KLRC2, KLRD1 NCAM1 or NKP46; and CD68, CD163, ITGAM, ITGAX, CD14 NCAM1 or NKP46; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A NCAM1 or NKP46; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT NCAM1 or NKP46; and CD274, PDL2, IDO1, PVR NCAM1 or NKP46; and CD4, IL2RA, CD69 NCAM1 or NKP46; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 NCAM1 or NKP46; and CD40, CD80, CD86, CD70, GITRL NCAM1 or NKP46; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 NCAM1 or NKP46; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 NCAM1 or NKP46; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 ITGAM, ITGAX, CD1C, or CLEC4C; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 ITGAM, ITGAX, CD1C, or CLEC4C; and KLRC3, KLRK1, KLRC2, KLRD1 ITGAM, ITGAX, CD1C, or CLEC4C; and CD68, CD163, ITGAM, ITGAX, CD14 ITGAM, ITGAX, CD1C, or CLEC4C; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1,

CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A ITGAM, ITGAX, CD1C, or CLEC4C; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT ITGAM, ITGAX, CD1C, or CLEC4C; and CD274, PDL2, IDO1, PVR ITGAM, ITGAX, CD1C, or CLEC4C; and CD4, IL2RA, CD69 ITGAM, ITGAX, CD1C, or CLEC4C; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 ITGAM, ITGAX, CD1C, or CLEC4C; and CD40, CD80, CD86, CD70, GITRL ITGAM, ITGAX, CD1C, or CLEC4C; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 ITGAM, ITGAX, CD1C, or CLEC4C; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 ITGAM, ITGAX, CD1C, or CLEC4C; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 IL17A or IL17F; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 IL17A or IL17F; and KLRC3, KLRK1, KLRC2, KLRD1 IL17A or IL17F; and CD68, CD163, ITGAM, ITGAX, CD14 IL17A or IL17F; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A IL17A or IL17F; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT IL17A or IL17F; and CD274, PDL2, IDO1, PVR IL17A or IL17F; and CD4, IL2RA, CD69 IL17A or IL17F; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 IL17A or IL17F; and CD40, CD80, CD86, CD70, GITRL IL17A or IL17F; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 IL17A or IL17F; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 IL17A or IL17F; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and KLRC3, KLRK1, KLRC2, KLRD1 CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD68, CD163, ITGAM, ITGAX, CD14 CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD274, PDL2, IDO1, PVR CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD4, IL2RA, CD69 CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD40, CD80, CD86, CD70, GITRL CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and KLRC3, KLRK1, KLRC2, KLRD1 CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD68, CD163, ITGAM, ITGAX, CD14 CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD274, PDL2, IDO1, PVR CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD4, IL2RA, CD69 CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD40, CD80, CD86, CD70, GITRL CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD276, PDL1, PDL2, or IDO1; and CD79A, MS4A1,

CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CD276, PDL1, PDL2, or IDO1; and KLRC3, KLRK1, KLRC2, KLRD1 CD276, PDL1, PDL2, or IDO1; and CD68, CD163, ITGAM, ITGAX, CD14 CD276, PDL1, PDL2, or IDO1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD276, PDL1, PDL2, or IDO1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD276, PDL1, PDL2, or IDO1; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD276, PDL1, PDL2, or IDO1; and CD274, PDL2, IDO1, PVR CD276, PDL1, PDL2, or IDO1; and CD4, IL2RA, CD69 CD276, PDL1, PDL2, or IDO1; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD276, PDL1, PDL2, or IDO1; and CD40, CD80, CD86, CD70, GITRL CD276, PDL1, PDL2, or IDO1; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD276, PDL1, PDL2, or IDO1; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD276, PDL1, PDL2, or IDO1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and KLRC3, KLRK1, KLRC2, KLRD1 CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD68, CD163, ITGAM, ITGAX, CD14 CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD274, PDL2, IDO1, PVR CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD4, IL2RA, CD69 CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD40, CD80, CD86, CD70, GITRL CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and KLRC3, KLRK1, KLRC2, KLRD1 CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and CD68, CD163, ITGAM, ITGAX, CD14 CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and CD274, PDL2, IDO1, PVR CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and CD4, IL2RA, CD69 CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and CD40, CD80, CD86, CD70, GITRL CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 KLRC3, KLRK1, KLRC2, or KLRD1; and CD68, CD163, ITGAM, ITGAX, CD14 KLRC3, KLRK1, KLRC2, or KLRD1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A KLRC3, KLRK1, KLRC2, or KLRD1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK KLRC3, KLRK1, KLRC2, or KLRD1; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT KLRC3, KLRK1, KLRC2, or KLRD1; and CD274, PDL2, IDO1, PVR KLRC3, KLRK1,

KLRC2, or KLRD1; and CD4, IL2RA, CD69 KLRC3, KLRK1, KLRC2, or KLRD1; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 KLRC3, KLRK1, KLRC2, or KLRD1; and CD40, CD80, CD86, CD70, GITRL KLRC3, KLRK1, KLRC2, or KLRD1; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 KLRC3, KLRK1, KLRC2, or KLRD1; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 KLRC3, KLRK1, KLRC2, or KLRD1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD68, CD163, ITGAM, ITGAX, or CD14; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD68, CD163, ITGAM, ITGAX, or CD14; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD68, CD163, ITGAM, ITGAX, or CD14; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD68, CD163, ITGAM, ITGAX, or CD14; and CD274, PDL2, IDO1, PVR CD68, CD163, ITGAM, ITGAX, or CD14; and CD4, IL2RA, CD69 CD68, CD163, ITGAM, ITGAX, or CD14; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD68, CD163, ITGAM, ITGAX, or CD14; and CD40, CD80, CD86, CD70, GITRL CD68, CD163, ITGAM, ITGAX, or CD14; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD68, CD163, ITGAM, ITGAX, or CD14; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD68, CD163, ITGAM, ITGAX, or CD14; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD274, PDL2, IDO1, PVR LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD4, IL2RA, CD69 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD40, CD80, CD86, CD70, GITRL LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD274, PDL2, IDO1, PVR CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD4, IL2RA, CD69 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD40, CD80, CD86, CD70, GITRL CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD274, PDL2, IDO1, PVR CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD4, IL2RA, CD69 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD40, CD80, CD86, CD70, GITRL CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and GNLY, KLRK1, KLRB1, GZMH, GZMA,

KLRD1, NKG7 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD274, PDL2, IDO1, or PVR; and CD4, IL2RA, CD69 CD274, PDL2, IDO1, or PVR; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD274, PDL2, IDO1, or PVR; and CD40, CD80, CD86, CD70, GITRL CD274, PDL2, IDO1, or PVR; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD274, PDL2, IDO1, or PVR; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD274, PDL2, IDO1, or PVR; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD4, IL2RA, or CD69; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD4, IL2RA, or CD69; and CD40, CD80, CD86, CD70, GITRL CD4, IL2RA, or CD69; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD4, IL2RA, or CD69; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD4, IL2RA, or CD69; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD40, CD80, CD86, CD70, GITRL TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD40, CD80, CD86, CD70, or GITRL; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD40, CD80, CD86, CD70, or GITRL; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD40, CD80, CD86, CD70, or GITRL; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1

(121) In another embodiment, the expression levels of one or more of the genes in an immune cell gene signature in three particular gene signature sets are determined. For example, combinations of three particular gene signature sets are set forth in Table 3 below.

(122) TABLE-US-00003 TABLE 3 Combinations of three gene signature sets CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and MS4A1 or CD48. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and NCAM1 or NKP46. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and ITGAM, ITGAX, CD1C, or CLEC4C. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and NCAM1 or NKP46. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and ITGAM, ITGAX, CD1C, or CLEC4C. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and ITGAM, ITGAX, CD1C, or CLEC4C. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA,

GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; and NCAM1 or NKP46. FOXP3; MS4A1 or CD48; and ITGAM, ITGAX, CD1C, or CLEC4C. FOXP3; MS4A1 or CD48; and IL17A or IL17F. FOXP3; MS4A1 or CD48; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; MS4A1 or CD48; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; and ITGAM, ITGAX, CD1C, or CLEC4C. FOXP3; NCAM1 or NKP46; and IL17A or IL17F. FOXP3; NCAM1 or NKP46; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; NCAM1 or NKP46; and CD276, PDL1, PDL2, or IDO1. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and IL17A or IL17F. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CD276, PDL1, PDL2, or IDO1. FOXP3; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. FOXP3; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; NCAM1 or NKP46; and ITGAM, ITGAX, CD1C, or CLEC4C. MS4A1 or CD48; NCAM1 or NKP46; and IL17A or IL17F. MS4A1 or CD48; NCAM1 or NKP46; and CCL2, IL1B, IL8, IL6, or PTGS2. MS4A1 or CD48; NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. MS4A1 or CD48; NCAM1 or NKP46; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and IL17A or IL17F. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. MS4A1 or CD48; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. MS4A1 or CD48; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and IL17A or IL17F. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CD276, PDL1, PDL2, or IDO1. NCAM1 or NKP46; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. NCAM1 or NKP46; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. NCAM1 or NKP46; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. NCAM1 or NKP46; CCL2, IL1B,

IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. NCAM1 or NKP46; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. NCAM1 or NKP46; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21,

CCL22. IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CD276, PDL1, PDL2, or IDO1; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and KLRC3, KLRK1, KLRC2, KLRD1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and KLRC3, KLRK1, KLRC2, KLRD1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and KLRC3, KLRK1, KLRC2, KLRD1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and KLRC3, KLRK1, KLRC2, KLRD1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and KLRC3, KLRK1, KLRC2, KLRD1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and KLRC3, KLRK1, KLRC2, KLRD1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and KLRC3, KLRK1, KLRC2, KLRD1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CD276, PDL1, PDL2, or IDO1; and KLRC3, KLRK1, KLRC2, KLRD1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and KLRC3, KLRK1, KLRC2, KLRD1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and CD68, CD163, ITGAM, ITGAX, CD14 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and CD68, CD163, ITGAM, ITGAX, CD14 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and CD68, CD163, ITGAM, ITGAX, CD14 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and CD68, CD163, ITGAM, ITGAX, CD14 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and CD68, CD163, ITGAM, ITGAX, CD14 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD68, CD163, ITGAM, ITGAX, CD14 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD68, CD163, ITGAM, ITGAX, CD14 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CD276, PDL1, PDL2, or IDO1; and CD68, CD163, ITGAM, ITGAX, CD14 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD68, CD163, ITGAM, ITGAX, CD14 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1;

NCAM1 or NKP46; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CD276, PDL1, PDL2, or IDO1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CD276, PDL1, PDL2, or IDO1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CD276, PDL1, PDL2, or IDO1; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and CD274, PDL2, IDO1, PVR CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and CD274, PDL2, IDO1, PVR CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and CD274, PDL2, IDO1, PVR CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and CD274, PDL2, IDO1, PVR CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and CD274, PDL2, IDO1, PVR CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD274, PDL2, IDO1, PVR CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD274, PDL2, IDO1, PVR CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1;

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CD226 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CD276, PDL1, PDL2, or IDO1; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CD276, PDL1, PDL2, or IDO1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 FOXP3; MS4A1 or CD48; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 FOXP3; NCAM1 or NKP46; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 FOXP3; IL17A or IL17F; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 FOXP3; CD276, PDL1, PDL2, or IDO1; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 FOXP3; MS4A1 or CD48; and KLRC3, KLRK1, KLRC2, KLRD1 FOXP3; NCAM1 or NKP46; and KLRC3, KLRK1, KLRC2, KLRD1 FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and KLRC3, KLRK1, KLRC2, KLRD1 FOXP3; IL17A or IL17F; and KLRC3, KLRK1, KLRC2, KLRD1 FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and KLRC3, KLRK1, KLRC2, KLRD1 FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and KLRC3, KLRK1, KLRC2, KLRD1 FOXP3; CD276, PDL1, PDL2, or IDO1; and KLRC3, KLRK1, KLRC2, KLRD1 FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and KLRC3, KLRK1, KLRC2, KLRD1 FOXP3; MS4A1 or CD48;

and CD68, CD163, ITGAM, ITGAX, CD14 FOXP3; NCAM1 or NKP46; and CD68, CD163, ITGAM, ITGAX, CD14 FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CD68, CD163, ITGAM, ITGAX, CD14 FOXP3; IL17A or IL17F; and CD68, CD163, ITGAM, ITGAX, CD14 FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD68, CD163, ITGAM, ITGAX, CD14 FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD68, CD163, ITGAM, ITGAX, CD14 FOXP3; CD276, PDL1, PDL2, or IDO1; and CD68, CD163, ITGAM, ITGAX, CD14 FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD68, CD163, ITGAM, ITGAX, CD14 FOXP3; MS4A1 or CD48; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A FOXP3; NCAM1 or NKP46; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A FOXP3; IL17A or IL17F; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A FOXP3; CD276, PDL1, PDL2, or IDO1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A FOXP3; MS4A1 or CD48; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK FOXP3; NCAM1 or NKP46; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK FOXP3; IL17A or IL17F; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK FOXP3; CD276, PDL1, PDL2, or IDO1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK FOXP3; MS4A1 or CD48; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT FOXP3; NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT FOXP3; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT FOXP3; CD276, PDL1, PDL2, or IDO1; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT FOXP3; MS4A1 or CD48; and CD274, PDL2, IDO1, PVR FOXP3; NCAM1 or NKP46; and CD274, PDL2, IDO1, PVR FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CD274, PDL2, IDO1, PVR FOXP3; IL17A or IL17F; and CD274, PDL2, IDO1, PVR FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD274, PDL2, IDO1, PVR FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD274, PDL2, IDO1, PVR FOXP3; CD276, PDL1, PDL2, or IDO1; and CD274, PDL2, IDO1, PVR FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD274, PDL2, IDO1, PVR FOXP3; MS4A1 or CD48; and CD4, IL2RA, CD69 FOXP3; NCAM1 or NKP46; and CD4, IL2RA, CD69 FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CD4, IL2RA, CD69 FOXP3; IL17A or IL17F; and CD4, IL2RA, CD69 FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD4, IL2RA, CD69 FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD4, IL2RA, CD69 FOXP3; CD276, PDL1, PDL2, or IDO1; and CD4, IL2RA, CD69 FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD4, IL2RA, CD69

FOXP3; MS4A1 or CD48; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 FOXP3; NCAM1 or NKP46; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 FOXP3; IL17A or IL17F; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 FOXP3; CD276, PDL1, PDL2, or IDO1; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 FOXP3; MS4A1 or CD48; and CD40, CD80, CD86, CD70, GITRL FOXP3; NCAM1 or NKP46; and CD40, CD80, CD86, CD70, GITRL FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CD40, CD80, CD86, CD70, GITRL FOXP3; IL17A or IL17F; and CD40, CD80, CD86, CD70, GITRL FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD40, CD80, CD86, CD70, GITRL FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD40, CD80, CD86, CD70, GITRL FOXP3; CD276, PDL1, PDL2, or IDO1; and CD40, CD80, CD86, CD70, GITRL FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD40, CD80, CD86, CD70, GITRL FOXP3; MS4A1 or CD48; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 FOXP3; NCAM1 or NKP46; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 FOXP3; IL17A or IL17F; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 FOXP3; CD276, PDL1, PDL2, or IDO1; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 FOXP3; MS4A1 or CD48; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 FOXP3; NCAM1 or NKP46; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 FOXP3; IL17A or IL17F; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 FOXP3; CD276, PDL1, PDL2, or IDO1; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 FOXP3; MS4A1 or CD48; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 FOXP3; NCAM1 or NKP46; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 FOXP3; IL17A or IL17F; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 FOXP3; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 FOXP3; CD276, PDL1, PDL2, or IDO1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 FOXP3; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 MS4A1 OR CD48; NCAM1 or NKP46; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 MS4A1 OR CD48; IL17A or

IL17F; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 MS4A1 OR CD48; NCAM1 or NKP46; and KLRC3, KLRK1, KLRC2, KLRD1 MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and KLRC3, KLRK1, KLRC2, KLRD1 MS4A1 OR CD48; IL17A or IL17F; and KLRC3, KLRK1, KLRC2, KLRD1 MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and KLRC3, KLRK1, KLRC2, KLRD1 MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and KLRC3, KLRK1, KLRC2, KLRD1 MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and KLRC3, KLRK1, KLRC2, KLRD1 MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and KLRC3, KLRK1, KLRC2, KLRD1 MS4A1 OR CD48; NCAM1 or NKP46; and CD68, CD163, ITGAM, ITGAX, CD14 MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CD68, CD163, ITGAM, ITGAX, CD14 MS4A1 OR CD48; IL17A or IL17F; and CD68, CD163, ITGAM, ITGAX, CD14 MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD68, CD163, ITGAM, ITGAX, CD14 MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD68, CD163, ITGAM, ITGAX, CD14 MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and CD68, CD163, ITGAM, ITGAX, CD14 MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD68, CD163, ITGAM, ITGAX, CD14 MS4A1 OR CD48; NCAM1 or NKP46; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A MS4A1 OR CD48; IL17A or IL17F; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A MS4A1 OR CD48; NCAM1 or NKP46; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK MS4A1 OR CD48; IL17A or IL17F; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK MS4A1 OR CD48; NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT MS4A1 OR CD48; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT MS4A1

OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT MS4A1 OR CD48; NCAM1 or NKP46; and CD274, PDL2, IDO1, PVR MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CD274, PDL2, IDO1, PVR MS4A1 OR CD48; IL17A or IL17F; and CD274, PDL2, IDO1, PVR MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD274, PDL2, IDO1, PVR MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD274, PDL2, IDO1, PVR MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and CD274, PDL2, IDO1, PVR MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD274, PDL2, IDO1, PVR MS4A1 OR CD48; NCAM1 or NKP46; and CD4, IL2RA, CD69 MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CD4, IL2RA, CD69 MS4A1 OR CD48; IL17A or IL17F; and CD4, IL2RA, CD69 MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD4, IL2RA, CD69 MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD4, IL2RA, CD69 MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and CD4, IL2RA, CD69 MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD4, IL2RA, CD69 MS4A1 OR CD48; NCAM1 or NKP46; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 MS4A1 OR CD48; IL17A or IL17F; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 MS4A1 OR CD48; NCAM1 or NKP46; and CD40, CD80, CD86, CD70, GITRL MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CD40, CD80, CD86, CD70, GITRL MS4A1 OR CD48; IL17A or IL17F; and CD40, CD80, CD86, CD70, GITRL MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD40, CD80, CD86, CD70, GITRL MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD40, CD80, CD86, CD70, GITRL MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and CD40, CD80, CD86, CD70, GITRL MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD40, CD80, CD86, CD70, GITRL MS4A1 OR CD48; NCAM1 or NKP46; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 MS4A1 OR CD48; IL17A or IL17F; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 MS4A1 OR CD48; NCAM1 or NKP46; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 MS4A1 OR CD48; IL17A or IL17F; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 MS4A1 OR CD48; NCAM1 or NKP46; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 MS4A1 OR CD48; ITGAM, ITGAX, CD1C, or

CLEC4C; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 MS4A1 OR CD48; IL17A or IL17F; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 MS4A1 OR CD48; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 MS4A1 OR CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 MS4A1 OR CD48; CD276, PDL1, PDL2, or IDO1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 MS4A1 OR CD48; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 NCAM1 or NKP46; IL17A or IL17F; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 NCAM1 or NKP46; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 NCAM1 or NKP46; CD276, PDL1, PDL2, or IDO1; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 NCAM1 or NKP46; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and KLRC3, KLRK1, KLRC2, KLRD1 NCAM1 or NKP46; IL17A or IL17F; and KLRC3, KLRK1, KLRC2, KLRD1 NCAM1 or NKP46; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and KLRC3, KLRK1, KLRC2, KLRD1 NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and KLRC3, KLRK1, KLRC2, KLRD1 NCAM1 or NKP46; CD276, PDL1, PDL2, or IDO1; and KLRC3, KLRK1, KLRC2, KLRD1 NCAM1 or NKP46; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and KLRC3, KLRK1, KLRC2, KLRD1 NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CD68, CD163, ITGAM, ITGAX, CD14 NCAM1 or NKP46; IL17A or IL17F; and CD68, CD163, ITGAM, ITGAX, CD14 NCAM1 or NKP46; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD68, CD163, ITGAM, ITGAX, CD14 NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD68, CD163, ITGAM, ITGAX, CD14 NCAM1 or NKP46; CD276, PDL1, PDL2, or IDO1; and CD68, CD163, ITGAM, ITGAX, CD14 NCAM1 or NKP46; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD68, CD163, ITGAM, ITGAX, CD14 NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A NCAM1 or NKP46; IL17A or IL17F; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A NCAM1 or NKP46; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A NCAM1 or NKP46; CD276, PDL1, PDL2, or IDO1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A NCAM1 or NKP46; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK NCAM1 or NKP46; IL17A or IL17F; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK NCAM1 or NKP46; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK NCAM1 or NKP46; CD276, PDL1, PDL2, or IDO1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK NCAM1 or NKP46; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK NCAM1 or NKP46; ITGAM,

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COL5A1, COL8A1 NCAM1 or NKP46; IL17A or IL17F; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 NCAM1 or NKP46; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 NCAM1 or NKP46; CD276, PDL1, PDL2, or IDO1; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 NCAM1 or NKP46; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 ITGAM, ITGAX, CD1C, or CLEC4C; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5 ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and KLRC3, KLRK1, KLRC2, KLRD1 ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and KLRC3, KLRK1, KLRC2, KLRD1 ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and KLRC3, KLRK1, KLRC2, KLRD1 ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and KLRC3, KLRK1, KLRC2, KLRD1 ITGAM, ITGAX, CD1C, or CLEC4C; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and KLRC3, KLRK1, KLRC2, KLRD1 ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD68, CD163, ITGAM, ITGAX, CD14 ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD68, CD163, ITGAM, ITGAX, CD14 ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD68, CD163, ITGAM, ITGAX, CD14 ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and CD68, CD163, ITGAM, ITGAX, CD14 ITGAM, ITGAX, CD1C, or CLEC4C; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD68, CD163, ITGAM, ITGAX, CD14 ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A ITGAM, ITGAX, CD1C, or CLEC4C; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK ITGAM, ITGAX, CD1C, or CLEC4C; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8 (CXCL8), IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3,

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STAP1, KIAA0125, POU2AF1, or FCRL5; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 KLRC3, KLRK1, KLRC2, or KLRD1; CD68, CD163, ITGAM, ITGAX, or CD14; and LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A KLRC3, KLRK1, KLRC2, or KLRD1; CD68, CD163, ITGAM, ITGAX, or CD14; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK KLRC3, KLRK1, KLRC2, or KLRD1; CD68, CD163, ITGAM, ITGAX, or CD14; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT KLRC3, KLRK1, KLRC2, or KLRD1; CD68, CD163, ITGAM, ITGAX, or CD14; and CD274, PDL2, IDO1, PVR KLRC3, KLRK1, KLRC2, or KLRD1; CD68, CD163, ITGAM, ITGAX, or CD14; and CD4, IL2RA, CD69 KLRC3, KLRK1, KLRC2, or KLRD1; CD68, CD163, ITGAM, ITGAX, or CD14; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 KLRC3, KLRK1, KLRC2, or KLRD1; CD68, CD163, ITGAM, ITGAX, or CD14; and CD40, CD80, CD86, CD70, GITRL KLRC3, KLRK1, KLRC2, or KLRD1; CD68, CD163, ITGAM, ITGAX, or CD14; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 KLRC3, KLRK1, KLRC2, or KLRD1; CD68, CD163, ITGAM, ITGAX, or CD14; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 KLRC3, KLRK1, KLRC2, or KLRD1; CD68, CD163, ITGAM, ITGAX, or CD14; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 KLRC3, KLRK1, KLRC2, or KLRD1; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK KLRC3, KLRK1, KLRC2, or KLRD1; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT KLRC3, KLRK1, KLRC2, or KLRD1; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD274, PDL2, IDO1, PVR KLRC3, KLRK1, KLRC2, or KLRD1; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD4, IL2RA, CD69 KLRC3, KLRK1, KLRC2, or KLRD1; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 KLRC3, KLRK1, KLRC2, or KLRD1; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD40, CD80, CD86, CD70, GITRL KLRC3, KLRK1, KLRC2, or KLRD1; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 KLRC3, KLRK1, KLRC2, or KLRD1; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 KLRC3, KLRK1, KLRC2, or KLRD1; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 KLRC3, KLRK1, KLRC2, or KLRD1; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT KLRC3, KLRK1, KLRC2, or KLRD1; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD274, PDL2, IDO1, PVR KLRC3, KLRK1, KLRC2, or KLRD1; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD4, IL2RA, CD69 KLRC3, KLRK1, KLRC2, or KLRD1; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 KLRC3, KLRK1, KLRC2, or KLRD1; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD40, CD80, CD86, CD70, GITRL KLRC3, KLRK1, KLRC2, or KLRD1; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226

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CD3G, CD6, TRAT1, CD28, LCK CD68, CD163, ITGAM, ITGAX, or CD14; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD68, CD163, ITGAM, ITGAX, or CD14; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD274, PDL2, IDO1, PVR CD68, CD163, ITGAM, ITGAX, or CD14; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD4, IL2RA, CD69 CD68, CD163, ITGAM, ITGAX, or CD14; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD68, CD163, ITGAM, ITGAX, or CD14; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD40, CD80, CD86, CD70, GITRL CD68, CD163, ITGAM, ITGAX, or CD14; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD68, CD163, ITGAM, ITGAX, or CD14; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD68, CD163, ITGAM, ITGAX, or CD14; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD68, CD163, ITGAM, ITGAX, or CD14; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT CD68, CD163, ITGAM, ITGAX, or CD14; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD274, PDL2, IDO1, PVR CD68, CD163, ITGAM, ITGAX, or CD14; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD4, IL2RA, CD69 CD68, CD163, ITGAM, ITGAX, or CD14; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD68, CD163, ITGAM, ITGAX, or CD14; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD40, CD80, CD86, CD70, GITRL CD68, CD163, ITGAM, ITGAX, or CD14; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD68, CD163, ITGAM, ITGAX, or CD14; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD68, CD163, ITGAM, ITGAX, or CD14; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD68, CD163, ITGAM, ITGAX, or CD14; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD274, PDL2, IDO1, PVR CD68, CD163, ITGAM, ITGAX, or CD14; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD4, IL2RA, CD69 CD68, CD163, ITGAM, ITGAX, or CD14; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD68, CD163, ITGAM, ITGAX, or CD14; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD40, CD80, CD86, CD70, GITRL CD68, CD163, ITGAM, ITGAX, or CD14; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD68, CD163, ITGAM, ITGAX, or CD14; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD68, CD163, ITGAM, ITGAX, or CD14; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD68, CD163, ITGAM, ITGAX, or CD14; CD274, PDL2, IDO1, or PVR; and CD4, IL2RA, CD69 CD68, CD163, ITGAM, ITGAX, or CD14; CD274, PDL2, IDO1, or PVR; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD68, CD163, ITGAM, ITGAX, or CD14; CD274, PDL2, IDO1, or PVR; and CD40, CD80, CD86, CD70, GITRL CD68, CD163, ITGAM, ITGAX, or CD14; CD274, PDL2, IDO1, or PVR; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD68, CD163, ITGAM, ITGAX, or CD14; CD274, PDL2, IDO1, or PVR; and GNLY,

KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD68, CD163, ITGAM, ITGAX, or CD14; CD274, PDL2, IDO1, or PVR; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD68, CD163, ITGAM, ITGAX, or CD14; CD4, IL2RA, or CD69; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD68, CD163, ITGAM, ITGAX, or CD14; CD4, IL2RA, or CD69; and CD40, CD80, CD86, CD70, GITRL CD68, CD163, ITGAM, ITGAX, or CD14; CD4, IL2RA, or CD69; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD68, CD163, ITGAM, ITGAX, or CD14; CD4, IL2RA, or CD69; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD68, CD163, ITGAM, ITGAX, or CD14; CD4, IL2RA, or CD69; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD68, CD163, ITGAM, ITGAX, or CD14; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD40, CD80, CD86, CD70, GITRL CD68, CD163, ITGAM, ITGAX, or CD14; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD68, CD163, ITGAM, ITGAX, or CD14; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD68, CD163, ITGAM, ITGAX, or CD14; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD68, CD163, ITGAM, ITGAX, or CD14; CD40, CD80, CD86, CD70, or GITRL; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD68, CD163, ITGAM, ITGAX, or CD14; CD40, CD80, CD86, CD70, or GITRL; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD68, CD163, ITGAM, ITGAX, or CD14; CD40, CD80, CD86, CD70, or GITRL; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD68, CD163, ITGAM, ITGAX, or CD14; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD68, CD163, ITGAM, ITGAX, or CD14; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD68, CD163, ITGAM, ITGAX, or CD14; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD274, PDL2, IDO1, PVR LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD4, IL2RA, CD69 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD40, CD80, CD86, CD70, GITRL LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD274, PDL2, IDO1,

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MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD40, CD80, CD86, CD70, or GITRL; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD40, CD80, CD86, CD70, or GITRL; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD40, CD80, CD86, CD70, or GITRL; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD274, PDL2, IDO1, PVR CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD4, IL2RA, CD69 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD40, CD80, CD86, CD70, GITRL CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD274, PDL2, IDO1, or PVR; and CD4, IL2RA, CD69 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD274, PDL2, IDO1, or PVR; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD274, PDL2, IDO1, or PVR; and CD40, CD80, CD86, CD70, GITRL CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD274, PDL2, IDO1, or PVR; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD274, PDL2, IDO1, or PVR; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD274, PDL2, IDO1, or PVR; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD4, IL2RA, or CD69; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD4, IL2RA, or CD69; and CD40, CD80, CD86, CD70, GITRL CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD4, IL2RA, or CD69; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD4, IL2RA, or CD69; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD4, IL2RA, or CD69; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD40, CD80, CD86, CD70, GITRL CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD3D, CD3E, CD2, CD3G,

CD6, TRAT1, CD28, or LCK; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD40, CD80, CD86, CD70, or GITRL; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD40, CD80, CD86, CD70, or GITRL; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD40, CD80, CD86, CD70, or GITRL; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD274, PDL2, IDO1, or PVR; and CD4, IL2RA, CD69 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD274, PDL2, IDO1, or PVR; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD274, PDL2, IDO1, or PVR; and CD40, CD80, CD86, CD70, GITRL CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD274, PDL2, IDO1, or PVR; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD274, PDL2, IDO1, or PVR; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD274, PDL2, IDO1, or PVR; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD4, IL2RA, or CD69; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD4, IL2RA, or CD69; and CD40, CD80, CD86, CD70, GITRL CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD4, IL2RA, or CD69; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD4, IL2RA, or CD69; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD4, IL2RA, or CD69; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD40, CD80, CD86, CD70, GITRL CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD40, CD80, CD86, CD70, or GITRL; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD40, CD80, CD86, CD70, or GITRL; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD40, CD80, CD86, CD70, or GITRL; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14,

TNFSF14, or CD226; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD274, PDL2, IDO1, or PVR; CD4, IL2RA, or CD69; and TAPBP, TAP1, TAP2, PSMB9, PSMB8 CD274, PDL2, IDO1, or PVR; CD4, IL2RA, or CD69; and CD40, CD80, CD86, CD70, GITRL CD274, PDL2, IDO1, or PVR; CD4, IL2RA, or CD69; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD274, PDL2, IDO1, or PVR; CD4, IL2RA, or CD69; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD274, PDL2, IDO1, or PVR; CD4, IL2RA, or CD69; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD274, PDL2, IDO1, or PVR; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD40, CD80, CD86, CD70, GITRL CD274, PDL2, IDO1, or PVR; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD274, PDL2, IDO1, or PVR; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD274, PDL2, IDO1, or PVR; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD274, PDL2, IDO1, or PVR; CD40, CD80, CD86, CD70, or GITRL; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD274, PDL2, IDO1, or PVR; CD40, CD80, CD86, CD70, or GITRL; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD274, PDL2, IDO1, or PVR; CD40, CD80, CD86, CD70, or GITRL; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD274, PDL2, IDO1, or PVR; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD274, PDL2, IDO1, or PVR; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD274, PDL2, IDO1, or PVR; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD4, IL2RA, or CD69; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD40, CD80, CD86, CD70, GITRL CD4, IL2RA, or CD69; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD4, IL2RA, or CD69; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD4, IL2RA, or CD69; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD4, IL2RA, or CD69; CD40, CD80, CD86, CD70, or GITRL; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 CD4, IL2RA, or CD69; CD40, CD80, CD86, CD70, or GITRL; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD4, IL2RA, or CD69; CD40, CD80, CD86, CD70, or GITRL; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD4, IL2RA, or CD69; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD4, IL2RA, or CD69; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD4, IL2RA, or CD69; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 TAPBP, TAP1, TAP2, PSMB9, or PSMB8; CD40, CD80, CD86, CD70, or GITRL; and CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, CD226 TAPBP, TAP1, TAP2, PSMB9, or PSMB8; CD40, CD80, CD86, CD70, or GITRL; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 TAPBP, TAP1, TAP2, PSMB9, or PSMB8; CD40, CD80, CD86, CD70, or GITRL; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 TAPBP, TAP1, TAP2, PSMB9, or PSMB8; CD27, CD28, ICOS, TNFRSF4, TNFRSF14,

TNFRSF18, TNFRSF14, TNFSF14, or CD226; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 TAPBP, TAP1, TAP2, PSMB9, or PSMB8; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 TAPBP, TAP1, TAP2, PSMB9, or PSMB8; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD40, CD80, CD86, CD70, or GITRL; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7 CD40, CD80, CD86, CD70, or GITRL; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD40, CD80, CD86, CD70, or GITRL; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFRSF14, TNFSF14, or CD226; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1

(123) In another embodiment, the expression levels of one or more of the genes in an immune cell gene signature in four particular gene signature sets are determined. For example, combinations of four particular gene signature sets are set forth in Table 4 below.

(124) TABLE-US-00004 TABLE 4 Combinations of four gene signature sets CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; and NCAM1 or NKP46. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; and ITGAM, ITGAX, CD1C, or CLEC4C. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; and ITGAM, ITGAX, CD1C, or CLEC4C. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, CLEC4C, and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, CLEC4C, and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, CLEC4C, and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, CLEC4C, and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; and ITGAM, ITGAX, CD1C, or CLEC4C. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48;

NCAM1 or NKP46; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, CLEC4C, and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, CLEC4C, and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, CLEC4C, and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, CLEC4C, and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, CLEC4C, and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, CLEC4C, and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, CLEC4C, and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, CLEC4C, and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, CLEC4C, IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, CLEC4C, IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, CLEC4C, IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, CLEC4C, CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, CLEC4C, CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, CLEC4C, CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; and ITGAM, ITGAX, CD1C, or CLEC4C.

FOXP3; MS4A1 or CD48; NCAM1 or NKP46; and IL17A or IL17F. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, CLEC4C, and IL17A or IL17F. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, CLEC4C; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; MS4A1 or CD48; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, CLEC4C; and IL17A or IL17F. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, CLEC4C; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; NCAM1 or NKP46; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; NCAM1 or NKP46; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; ITGAM, ITGAX, CD1C, CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; ITGAM, ITGAX, CD1C, CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; ITGAM, ITGAX, CD1C, CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. FOXP3; ITGAM, ITGAX, CD1C, CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; ITGAM, ITGAX, CD1C, CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; ITGAM, ITGAX, CD1C, CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; IL17A or IL17F; ITGAM, ITGAX, CD1C, CLEC4C; and CD276, PDL1, PDL2, or IDO1. FOXP3; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and IL17A or IL17F. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1.

MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and

CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; NCAM1 or NKP46; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; NCAM1 or NKP46; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3,

CCL21, or CCL22. FOXP3; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; NCAM1 or NKP46; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. NCAM1 or NKP46; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3,

HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22.

(125) In some embodiments, a combination of four particular gene signature sets includes, or consists of, a combination including one or more of the following gene signature sets: B cell Signature 2 (CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5); NK cell Signature 2 (KLRC3, KLRK1, KLRC2, KLRD1); Macrophage (CD68, CD163, ITGAM, ITGAX, CD14); M2 Macrophage (LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A); T cell (CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK); IB T cell Signature 2 (CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT); IB APC Signature 2 (CD274, PDL2, IDO1, PVR); Activated CD4 T cell (CD4, IL2RA, CD69); Antigen processing (TAPBP, TAP1, TAP2, PSMB9, PSMB8); Costimulatory ligand (CD40, CD80, CD86, CD70, GITRL); Costimulatory receptor (CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, CD226); Cytolytic (GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7); and/or Active fibroblast (FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1).

(126) In another embodiment, the expression levels of one or more of the genes in an immune cell gene signature in five particular gene signature sets are determined. For example, combinations of five particular gene signature sets are set forth in Table 5 below.

(127) TABLE-US-00005 TABLE 5 Combinations of five gene signature sets CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; and ITGAM, ITGAX, CD1C, or CLEC4C. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and IL17A

or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or

IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and IL17A or IL17F. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or

CLEC4C; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1.

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MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22.

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CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22.

(128) In some embodiments, a combination of five particular gene signature sets includes, or consists of, a combination including one or more of the following gene signature sets: B cell Signature 2 (CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5); NK cell Signature 2 (KLRC3, KLRK1, KLRC2, KLRD1); Macrophage (CD68, CD163, ITGAM, ITGAX, CD14); M2 Macrophage (LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A); T cell (CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK); IB T cell Signature 2 (CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT); IB APC Signature 2 (CD274, PDL2, IDO1, PVR); Activated CD4 T cell (CD4, IL2RA, CD69); Antigen processing (TAPBP, TAP1, TAP2, PSMB9, PSMB8); Costimulatory ligand (CD40, CD80, CD86, CD70, GITRL); Costimulatory receptor (CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, CD226); Cytolytic (GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7); and/or Active fibroblast (FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1).

(129) In another embodiment, the expression levels of one or more of the genes in an immune cell gene signature in six particular gene signature sets are determined. For example, combinations of six particular gene signature sets are set forth in Table 6 below.

(130) TABLE-US-00006 TABLE 6 Combinations of six gene signature sets CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and IL17A or IL17F. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and

CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA,

LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A

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NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3;

ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; L17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. ITGAM, ITGAX, CD1C or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and

CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22.

(131) In some embodiments, a combination of six particular gene signature sets includes, or consists of, a combination including one or more of the following gene signature sets: B cell Signature 2 (CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5); NK cell Signature 2 (KLRC3, KLRK1, KLRC2, KLRD1); Macrophage (CD68, CD163, ITGAM, ITGAX, CD14); M2 Macrophage (LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A); T cell (CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK); IB T cell Signature 2 (CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT); IB APC Signature 2 (CD274, PDL2, IDO1, PVR); Activated CD4 T cell (CD4, IL2RA, CD69); Antigen processing (TAPBP, TAP1, TAP2, PSMB9, PSMB8); Costimulatory ligand (CD40, CD80, CD86, CD70, GITRL); Costimulatory receptor (CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, CD226); Cytolytic (GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7); and/or Active fibroblast (FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1).

(132) In another embodiment, the expression levels of one or more of the genes in an immune cell gene signature in seven particular gene signature sets are determined. For example, combinations of seven particular gene signature sets are set forth in Table 7 below.

(133) TABLE-US-00007 TABLE 7 Combinations of seven gene signature sets CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CCL2, IL1B, IL8, IL6, or PTGS2. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3,

HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F;

and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB,

IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM,

ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C;

CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22.

(134) In some embodiments, a combination of seven particular gene signature sets includes, or consists of, a combination including one or more of the following gene signature sets: B cell Signature 2 (CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5); NK cell Signature 2 (KLRC3, KLRK1, KLRC2, KLRD1); Macrophage (CD68, CD163, ITGAM, ITGAX, CD14);

M2 Macrophage (LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A); T cell (CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK); IB T cell Signature 2 (CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT); IB APC Signature 2 (CD274, PDL2, IDO1, PVR); Activated CD4 T cell (CD4, IL2RA, CD69); Antigen processing (TAPBP, TAP1, TAP2, PSMB9, PSMB8); Costimulatory ligand (CD40, CD80, CD86, CD70, GITRL); Costimulatory receptor (CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, CD226); Cytolytic (GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7); and/or Active fibroblast (FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1).

(135) In another embodiment, the expression levels of one or more of the genes in an immune cell gene signature in eight particular gene signature sets are determined. For example, combinations of eight particular gene signature sets are set forth in Table 8 below.

(136) TABLE-US-00008 TABLE 8 Combinations of eight gene signature sets CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CTLA4, BTLA, LAG3, HAVCR2, or PDCD1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3;

MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB; IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1,

PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22. MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22.

(137) In some embodiments, a combination of eight particular gene signature sets includes, or consists of, a combination including one or more of the following gene signature sets: B cell Signature 2 (CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5); NK cell Signature 2 (KLRC3, KLRK1, KLRC2, KLRD1); Macrophage (CD68, CD163, ITGAM, ITGAX, CD14); M2 Macrophage (LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A); T cell (CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK); IB T cell Signature 2 (CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT); IB APC Signature 2 (CD274, PDL2, IDO1, PVR); Activated CD4 T cell (CD4, IL2RA, CD69); Antigen processing (TAPBP, TAP1, TAP2, PSMB9, PSMB8); Costimulatory ligand (CD40, CD80, CD86, CD70, GITRL); Costimulatory receptor (CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, CD226); Cytolytic (GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7); and/or Active fibroblast (FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2,

COL5A1, COL8A1).

(138) In some embodiment, the expression levels of one or more of the genes in the immune cell gene signature in nine gene signature sets are determined. For example, combinations of nine particular gene signature sets are set forth in Table 9 below.

(139) TABLE-US-00009 TABLE 9 Combinations of nine gene signature sets CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CD276, PDL1, PDL2, or IDO1. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; NCAM1 or NKP46; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22. FOXP3; MS4A1 or CD48; NCAM1 or NKP46; ITGAM, ITGAX, CD1C, or CLEC4C; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CD276, PDL1, PDL2, or IDO1; and CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, CCL22.

(140) In some embodiments, a combination of nine particular gene signature sets includes, or consists of, a combination including one or more of the following gene signature sets: B cell Signature 2 (CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, FCRL5); NK cell Signature 2 (KLRC3, KLRK1, KLRC2, KLRD1); Macrophage (CD68, CD163, ITGAM, ITGAX, CD14); M2 Macrophage (LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, FCGR3A); T cell (CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, LCK); IB T cell Signature 2 (CTLA4, BTLA, LAG3, HAVCR2, PDCD1, TIGIT); IB APC Signature 2 (CD274, PDL2, IDO1, PVR); Activated CD4 T cell (CD4, IL2RA, CD69); Antigen processing (TAPBP, TAP1, TAP2, PSMB9, PSMB8); Costimulatory ligand (CD40, CD80, CD86, CD70, GITRL); Costimulatory receptor (CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, CD226); Cytolytic (GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, NKG7); and/or Active fibroblast (FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1).

(141) In other embodiments, the expression level of one or more of the genes in an immune cell

gene signature in any 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, or 22 particular gene signature sets set forth in Table 1 are determined.

(142) In some embodiments, the expression levels of one or more of the genes in an immune cell gene signature in all 23 gene signature sets are determined. For example: CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1; FOXP3; MS4A1 or CD48; CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, or FCRL5; NCAM1 or NKP46; KLRC3, KLRK1, KLRC2, or KLRD1; ITGAM, ITGAX, CD1C, or CLEC4C; CD68, CD163, ITGAM, ITGAX, or CD14; LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, or FCGR3A; IL17A or IL17F; CCL2, IL1B, IL8, IL6, or PTGS2; CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, or LCK; CTLA4, BTLA, LAG3, HAVCR2, or PDCD1; CTLA4, BTLA, LAG3, HAVCR2, PDCD1, or TIGIT; CD276, PDL1, PDL2, or IDO1; CD274, PDL2, IDO1, or PVR; CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, or CCL22; CD4, IL2RA, or CD69; TAPBP, TAP1, TAP2, PSMB9, or PSMB8; CD40, CD80, CD86, CD70, or GITRL; CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, or CD226; GNLY, KLRK1, KLRB1, GZMH, GZMA, KLRD1, or NKG7; and FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, COL8A1 is determined. In some embodiments, one or more of the genes in Table 14 is further included as an immune cell signature gene in one of the gene sets described herein (e.g., T.sub.eff, B cell, NK cell, T.sub.reg, myeloid, T cell chemotaxis, etc). In other embodiments, one or more of the genes in Table 14 is further included as an immune cell signature gene in a further identified gene set (e.g., Th1, Th2, mast cells, antigen presenting cells (APC), etc).

(143) Optionally, the methods include determining the ratio of expression levels of one or more immune cell gene signatures between gene sets to further identify a cancer patient for treatment with an immunotherapy or who may have the likelihood of benefiting from a particular immunotherapy. For example, the ratio of expression levels of one or more immune cell gene signatures in the T.sub.eff gene set (e.g., one or more of CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1) may be compared to the expression levels of one or more immune cell gene signatures in any of the T.sub.reg gene set (e.g., FOXP3), an IB APC gene signature set (e.g., one or more of CD276, PDL1, PDL2, or IDO1), and/or an IB T cell gene signature set (e.g., one or more of CTLA4, BTLA, LAG3, HAVCR2, or PDCD1) to determine whether the patient should be treated with an immunotherapy or would have a likelihood of benefitting from particular immunotherapy. In other embodiments, the methods include determining the ratio of the presence of the immune cell subtype (e.g., T.sub.eff to T.sub.reg, T.sub.eff to B cells, T.sub.eff to NK cells, T.sub.eff to IB T cell, T.sub.eff to IB APC, T.sub.eff to inflammatory cells) in a sample from a patient with cancer (e.g., bladder cancer, breast cancer, colorectal cancer, gastric cancer, liver cancer, melanoma, lung cancer (e.g., non-small cell lung carcinoma), ovarian cancer, or renal cell carcinoma).

(144) The expression level of an immune cell gene signature may be assessed by any method known in the art suitable for determination of specific protein levels in a patient sample, and is preferably determined by an immunohistochemical ("IHC") method employing antibodies specific for an immune cell gene signature. Such methods are well known and routinely implemented in the art, and corresponding commercial antibodies and/or kits are readily available. Preferably, the expression levels of the marker/indicator proteins of the invention are assessed using the reagents and/or protocol recommendations of the antibody or kit manufacturer. The skilled person will also be aware of further means for determining the expression level of an immune cell gene signature by IHC methods. Therefore, the expression level of one or more of the markers/indicators of the invention can be routinely and reproducibly determined by a person skilled in the art without undue burden. However, to ensure accurate and reproducible results, the invention also encompasses the testing of patient samples in a specialized laboratory that can ensure the validation of testing procedures.

(145) Preferably, the expression level of an immune cell gene signature is assessed in a biological sample that contains or is suspected to contain cancer cells. The sample may be, for example, a

tissue resection, a tissue biopsy, or a metastatic lesion obtained from a patient suffering from, suspected to suffer from, or diagnosed with cancer (e.g., bladder cancer, breast cancer, colorectal cancer, gastric cancer, liver cancer, melanoma, lung cancer (e.g., non-small cell lung carcinoma), ovarian cancer, or renal cell carcinoma). Preferably, the sample is a sample of a tissue, a resection or biopsy of a tumor, a known or suspected metastatic cancer lesion or section, or a blood sample, e.g., a peripheral blood sample, known or suspected to comprise circulating cancer cells. The sample may comprise both cancer cells, i.e., tumor cells, and non-cancerous cells, and, in certain embodiments, comprises both cancerous and non-cancerous cells. In aspects of the invention comprising the determination of gene expression in stroma components, the sample comprises both cancer/tumor cells and non-cancerous cells that are, e.g., associated with the cancer/tumor cells (e.g., tumor associated fibroblasts, endothelial cells, pericytes, the extra-cellular matrix, and/or various classes of leukocytes). In other aspects, the skilled artisan, e.g., a pathologist, can readily discern cancer cells from non-cancerous (e.g., stromal cells, endothelial cells, etc.). Methods of obtaining biological samples including tissue resections, biopsies, and body fluids, e.g., blood samples comprising cancer/tumor cells, are well known in the art. In some embodiments, the sample obtained from the patient is collected prior to beginning any immunotherapy or other treatment regimen or therapy, e.g., chemotherapy or radiation therapy for the treatment of cancer or the management or amelioration of a symptom thereof. Therefore, in some embodiments, the sample is collected before the administration of immunotherapeutic agents or other agents, or the start of immunotherapy or other treatment regimen.

(146) In addition to the methods described above, the invention also encompasses further immunohistochemical methods for assessing the expression level of one or more immune cell gene signatures, such as by Western blotting and ELISA-based detection. As is understood in the art, the expression level of the marker/indicator proteins of the invention may also be assessed at the mRNA level by any suitable method known in the art, such as Northern blotting, real time PCR, and RT PCR. Immunohistochemical- and mRNA-based detection methods and systems are well known in the art and can be deduced from standard textbooks, such as Lottspeich (Bioanalytik, Spektrum Akademisher Verlag, 1998) or Sambrook and Russell (Molecular Cloning: A Laboratory Manual, CSH Press, Cold Spring Harbor, N.Y., U.S.A., 2001). The described methods are of particular use for determining the expression levels of an immune cell gene signature in a patient or group of patients relative to control levels established in a population diagnosed with advanced stages of a cancer (e.g., bladder cancer, breast cancer, colorectal cancer, gastric cancer, liver cancer, melanoma, lung cancer (e.g., non-small cell lung carcinoma), ovarian cancer, or renal cell carcinoma).

(147) For use in the detection methods described herein, the skilled person has the ability to label the polypeptides or oligonucleotides encompassed by the present invention. As routinely practiced in the art, hybridization probes for use in detecting mRNA levels and/or antibodies or antibody fragments for use in IHC methods can be labeled and visualized according to standard methods known in the art. Non-limiting examples of commonly used systems include the use of radiolabels, enzyme labels, fluorescent tags, biotin-avidin complexes, chemiluminescence, and the like.

(148) The expression level of one or more of an immune cell gene signature can also be determined on the protein level by taking advantage of immunoagglutination, immunoprecipitation (e.g., immunodiffusion, immunelectrophoresis, immune fixation), western blotting techniques (e.g., in situ immuno histochemistry, in situ immuno cytochemistry, affinity chromatography, enzyme immunoassays), and the like. Amounts of purified polypeptide may also be determined by physical methods, e.g., photometry. Methods of quantifying a particular polypeptide in a mixture usually rely on specific binding, e.g., of antibodies.

(149) As mentioned above, the expression level of the marker/indicator proteins according to the present invention may also be reflected in increased or decreased expression of the corresponding gene(s) encoding the immune cell gene signature. Therefore, a quantitative assessment of the gene

product prior to translation (e.g. spliced, unspliced or partially spliced mRNA) can be performed in order to evaluate the expression of the corresponding gene(s). The person skilled in the art is aware of standard methods to be used in this context or may deduce these methods from standard textbooks (e.g. Sambrook, 2001). For example, quantitative data on the respective concentration/amounts of mRNA encoding one or more of an immune cell gene signature as described herein can be obtained by Northern Blot, Real Time PCR, and the like.

IV. Methods of Treatment

(150) The invention further provides methods for administering an activating or suppressing immunotherapy to patients with a cancer (e.g., bladder cancer, breast cancer, colorectal cancer, gastric cancer, liver cancer, melanoma, lung cancer (e.g., non-small cell lung carcinoma), ovarian cancer, or renal cell carcinoma that is chemotherapy-resistant, chemotherapy-sensitive, refractory, primary, advanced, or recurrent), if the patient is determined to have a change in the level of expression of one or more immune cell gene signatures in any of the gene sets. In one embodiment, the patient is administered an activating immunotherapy if there is an increase in expression level of one or more immune cell gene signatures in the T.sub.eff gene set (i.e., one or more of CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1) or a decrease in expression level of one or more immune cell gene signatures in the T.sub.reg gene set. In other embodiments, the patient is administered a suppressing immunotherapy if there is an increase in expression level of one or more immune cell gene signatures in the T.sub.reg gene set (i.e., FOXP3) or a decrease in expression level of one or more immune cell gene signatures in the T.sub.eff gene set (i.e., one or more of CD8A, GZMA, GZMB, IFNγ, EOMES, or PRF1). In other embodiments, in addition to determining the expression levels of one or more immune cell gene signatures in the T.sub.eff and/or T.sub.reg gene sets, expression levels of one or more immune cell gene signatures in combinations of any one of the gene sets as set forth in Tables 2-8 can be determined prior to administering a particular immunotherapy regimen to the patient (e.g., an activating immunotherapy regimen or a suppressing immunotherapy regimen).

(151) In some embodiments, the activating immunotherapy includes a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist. In particular embodiments, the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) increases, enhances, or stimulates an immune response or function in a patient having cancer. In some embodiments, the agonist modulates the expression and/or activity of a ligand (e.g., a T cell receptor ligand), and/or increases or stimulates the interaction of the ligand with its immune receptor, and/or increases or stimulates the intracellular signaling mediated by ligand binding to the immune receptor. In other embodiments, the suppressing immunotherapy includes a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist. In particular embodiments, the antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) is an agent that inhibits and/or blocks the interaction of a ligand (e.g., a T cell receptor ligand) with its immune receptor or is an antagonist of ligand and/or receptor expression and/or activity, or is an agent that blocks the intracellular signaling mediated by a ligand (e.g., a T cell receptor ligand) with its immune receptor.

(152) In some embodiments, the methods of the invention may further comprise administering the activating immunotherapy (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or the suppressing immunotherapy (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) with an additional therapy. The additional therapy may be radiation therapy, surgery, chemotherapy, gene therapy, DNA therapy, viral therapy, RNA therapy, bone marrow transplantation, nanotherapy, monoclonal antibody therapy, or a combination of the foregoing. The additional therapy may be in the form of an adjuvant or neoadjuvant therapy. In some embodiments, the additional therapy is the administration of side-effect limiting agents (e.g., agents intended to lessen the occurrence and/or severity of side effects of treatment, such as anti-nausea agents, etc.). In some embodiments, the

additional therapy is radiation therapy. In some embodiments, the additional therapy is surgery. In some embodiments, the additional therapy may be one or more of the chemotherapeutic agents described hereinabove. For example, these methods involve the co-administration of the activating immunotherapy (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or the suppressing immunotherapy (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) with one or more additional chemotherapeutic agents (e.g., carboplatin and/or paclitaxel), as described further below. Immunotherapy optionally in combination with one or more chemotherapeutic agents (e.g., carboplatin and/or paclitaxel) preferably extends and/or improves survival, including progression free survival (PFS) and/or overall survival (OS). In one embodiment, immunotherapy extends survival at least about 20% more than survival achieved by administering an approved anti-tumor agent, or standard of care, for the cancer being treated.

(153) For the prevention or treatment of cancer (e.g., bladder cancer, breast cancer, colorectal cancer, gastric cancer, liver cancer, melanoma, lung cancer (e.g., non-small cell lung carcinoma), ovarian cancer, or renal cell carcinoma), the dose of the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) will depend on the type of cancer to be treated, as defined above, the severity and course of the cancer, whether the antibody is administered for preventive or therapeutic purposes, previous therapy, the patient's clinical history and response to the drug, and the discretion of the attending physician.

(154) In one embodiment, a fixed dose of the agonist or antagonist is administered. The fixed dose may suitably be administered to the patient at one time or over a series of treatments. Where a fixed dose is administered, preferably it is in the range from about 20 mg to about 2000 mg. For example, the fixed dose may be approximately 420 mg, approximately 525 mg, approximately 840 mg, or approximately 1050 mg of the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist). Where a series of doses are administered, these may, for example, be administered approximately every week, approximately every 2 weeks, approximately every 3 weeks, or approximately every 4 weeks, but preferably approximately every 3 weeks. The fixed doses may, for example, continue to be administered until disease progression, adverse event, or other time as determined by the physician. For example, from about two, three, or four, up to about 17 or more fixed doses may be administered.

(155) In one embodiment, one or more loading dose(s) of the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) are administered, followed by one or more maintenance dose(s). In another embodiment, a plurality of the same dose is administered to the patient.

(156) While the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) may be administered as a single anti-tumor agent, the patient is optionally treated with a combination of agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) and one or more (additional) chemotherapeutic agent(s). Exemplary chemotherapeutic agents herein include: gemcitabine, carboplatin, oxaliplatin, irinotecan, fluoropyrimidine (e.g., 5-FU), paclitaxel (e.g., nab-paclitaxel), docetaxel, topotecan, capecitabine, temozolomide, interferon-alpha, and/or liposomal doxorubicin (e.g., pegylated liposomal doxorubicin). The combined administration includes co-administration or concurrent administration, using separate formulations or a single pharmaceutical formulation, and consecutive administration in either order, wherein preferably there is a time period while both (or all) active agents simultaneously exert their biological

activities. Thus, the chemotherapeutic agent may be administered prior to, or following, administration of the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist). In this embodiment, the timing between at least one administration of the chemotherapeutic agent and at least one administration of the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) is preferably approximately 1 month or less (3 weeks, 2, weeks, 1 week, 6 days, 5, days, 4 days, 3 days, 2 days, 1 day). Alternatively, the chemotherapeutic agent and the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) are administered concurrently to the patient, in a single formulation or separate formulations. Treatment with the combination of the chemotherapeutic agent (e.g., carboplatin and/or paclitaxel) and the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) may result in a synergistic, or greater than additive, therapeutic benefit to the patient.

(157) Particularly desired chemotherapeutic agents for combining with the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist), e.g. for therapy of ovarian cancer, include: a chemotherapeutic agent such as a platinum compound (e.g., carboplatin), a taxol such as paclitaxel or docetaxel, topotecan, or liposomal doxorubicin.

(158) Particularly desired chemotherapeutic agents for combining with the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist), e.g., for therapy of breast cancer, include: chemotherapeutic agents such as capecitabine, and a taxol such as paclitaxel (e.g., nab-paclitaxel) or docetaxel.

(159) Particularly desired chemotherapeutic agents for combining with the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist), e.g., for therapy of colorectal cancer, include: chemotherapeutic agents such as a fluoropyrimidine (e.g., 5-FU), paclitaxel, cisplatin, topotecan, irinotecan, fluoropyrimidine-oxaliplatin, fluoropyrimidine-irinotecan, FOLFOX4 (5-FU, lecovorin, oxaliplatin), and IFL (ironotecan, 5-FU, leucovorin).

(160) Particularly desired chemotherapeutic agents for combining with the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist), e.g., for therapy of renal cell carcinoma, include: chemotherapeutic agents such as interferon-alpha2a.

(161) A chemotherapeutic agent, if administered, is usually administered at dosages known therefore, or optionally lowered due to combined action of the drugs or negative side effects attributable to administration of the chemotherapeutic agent. Preparation and dosing schedules for such chemotherapeutic agents may be used according to manufacturers' instructions or as determined empirically by the skilled practitioner. Where the chemotherapeutic agent is paclitaxel, preferably, it is administered at a dose between about 130 mg/m.sup.2 to 200 mg/m.sup.2 (for example approximately 175 mg/m.sup.2), for instance, over 3 hours, once every 3 weeks. Where the chemotherapeutic agent is carboplatin, preferably it is administered by calculating the dose of carboplatin using the Calvert formula which is based on a patient's preexisting renal function or renal function and desired platelet nadir. Renal excretion is the major route of elimination for carboplatin. The use of this dosing formula, as compared to empirical dose calculation based on

body surface area, allows compensation for patient variations in pretreatment renal function that might otherwise result in either underdosing (in patients with above average renal function) or overdosing (in patients with impaired renal function). The target AUC of 4-6 mg/mL/min using single agent carboplatin appears to provide the most appropriate dose range in previously treated patients.

(162) Aside from the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) and chemotherapeutic agent, other therapeutic regimens may be combined therewith. For example, a second (third, fourth, etc.) chemotherapeutic agent(s) may be administered, wherein the second chemotherapeutic agent is an antimetabolite chemotherapeutic agent, or a chemotherapeutic agent that is not an antimetabolite. For example, the second chemotherapeutic agent may be a taxane (such as paclitaxel or docetaxel), capecitabine, or platinum-based chemotherapeutic agent (such as carboplatin, cisplatin, or oxaliplatin), anthracycline (such as doxorubicin, including, liposomal doxorubicin), topotecan, pemetrexed, vinca alkaloid (such as vinorelbine), and TLK 286. "Cocktails" of different chemotherapeutic agents may be administered.

(163) Other therapeutic agents that may be combined with the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist), and/or chemotherapeutic agent include any one or more of: a HER inhibitor, HER dimerization inhibitor (for example, a growth inhibitory HER2 antibody such as trastuzumab, or a HER2 antibody which induces apoptosis of a HER2-overexpressing cell, such as 7C2, 7F3 or humanized variants thereof); an antibody directed against a different tumor associated antigen, such as EGFR, HER3, HE R4; anti-hormonal compound, e.g., an anti-estrogen compound such as tamoxifen, or an aromatase inhibitor; a cardioprotectant (to prevent or reduce any myocardial dysfunction associated with the therapy); a cytokine; an EGFR-targeted drug (such as TARCEVA® IRESSA® or cetuximab); a tyrosine kinase inhibitor; a COX inhibitor (for instance a COX-1 or COX-2 inhibitor); non-steroidal anti-inflammatory drug, celecoxib (CELEBREX®); farnesyl transferase inhibitor (for example, Tipifarnib/ZARNESTRA® R115777 available from Johnson and Johnson or Lonafarnib SCH66336 available from Schering-Plough); antibody that binds oncofetal protein CA 125 such as Oregovomab (MoAb B43.13); HER2 vaccine (such as HER2AutoVac vaccine from Pharmexia, or APC8024 protein vaccine from Dendreon, or HER2 peptide vaccine from GSK/Corixa); another HER targeting therapy (e.g. trastuzumab, cetuximab, ABX-EGF, EMD7200, gefitinib, erlotinib, CP724714, CI1033, GW572016, IMC-11F8, TAK165, etc); Raf and/or ras inhibitor (see, for example, WO 2003/86467); doxorubicin HCl liposome injection (DOXIL®); topoisomerase 1 inhibitor such as topotecan; taxane; HER2 and EGFR dual tyrosine kinase inhibitor such as lapatinib/GW572016; TLK286 (TELCYTA®); EMD-7200; a medicament that treats nausea such as a serotonin antagonist, steroid, or benzodiazepine; a medicament that prevents or treats skin rash or standard acne therapies, including topical or oral antibiotic; a medicament that treats or prevents diarrhea; a body temperature-reducing medicament such as acetaminophen, diphenhydramine, or meperidine; hematopoietic growth factor, etc.

(164) Suitable dosages for any of the above-noted co-administered agents are those presently used and may be lowered due to the combined action (synergy) of the agent and the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist). In addition to the above therapeutic regimes, the patient may be subjected to surgical removal of tumors and/or cancer cells, and/or radiation therapy.

(165) Where the agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) is an antibody, preferably the administered antibody is

a naked antibody. The agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) administered may be conjugated with a cytotoxic agent. Preferably, the conjugate and/or antigen to which it is bound is/are internalized by the cell, resulting in increased therapeutic efficacy of the conjugate in killing the cancer cell to which it binds. In a preferred embodiment, the cytotoxic agent targets or interferes with nucleic acid in the cancer cell. Examples of such cytotoxic agents include maytansinoids, calicheamicins, ribonucleases, and DNA endonucleases.

(166) The agonist (e.g., a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist) or antagonist (e.g., a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist) can be administered by gene therapy. See, for example, WO 96/07321 published Mar. 14, 1996 concerning the use of gene therapy to generate intracellular antibodies. There are two major approaches to getting the nucleic acid (optionally contained in a vector) into the patient's cells; in vivo and ex vivo. For in vivo delivery the nucleic acid is injected directly into the patient, usually at the site where the antibody is required. For ex vivo treatment, the patient's cells are removed, the nucleic acid is introduced into these isolated cells and the modified cells are administered to the patient either directly or, for example, encapsulated within porous membranes which are implanted into the patient (see, e.g. U.S. Pat. Nos. 4,892,538 and 5,283,187). There are a variety of techniques available for introducing nucleic acids into viable cells. The techniques vary depending upon whether the nucleic acid is transferred into cultured cells in vitro or in vivo in the cells of the intended host. Techniques suitable for the transfer of nucleic acid into mammalian cells in vitro include the use of liposomes, electroporation, microinjection, cell fusion, DEAE-dextran, the calcium phosphate precipitation method, etc. A commonly used vector for ex vivo delivery of the gene is a retrovirus. The currently preferred in vivo nucleic acid transfer techniques include transfection with viral vectors (such as adenovirus, Herpes simplex I virus, or adeno-associated virus) and lipid-based systems (useful lipids for lipid-mediated transfer of the gene are DOTMA, DOPE and DC-Chol, for example). In some situations it is desirable to provide the nucleic acid source with an agent that targets the target cells, such as an antibody specific for a cell surface membrane protein or the target cell, a ligand for a receptor on the target cell, etc. Where liposomes are employed, proteins which bind to a cell surface membrane protein associated with endocytosis may be used for targeting and/or to facilitate uptake, e.g. capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, and proteins that target intracellular localization and enhance intracellular half-life. The technique of receptor-mediated endocytosis is described, for example, by Wu et al., *J. Biol. Chem.* 262:44294432 (1987); and Wagner et al., *Proc. Natl. Acad. Sci. USA* 87:3410-3414 (1990). For review of the currently known gene marking and gene therapy protocols see Anderson et al., *Science* 256:808-813 (1992). See also WO 93/25673 and the references cited therein.

EXAMPLES

Materials and Experimental Methods

(167) Statistical Analysis

(168) Statistical analysis was performed using the R statistical software. FLUIDIGM™ and Nanostring data were normalized using the housekeeping gene approach. Specifically, median gene expression of the five housekeeping genes (SP2, GUSB, TMEM55B, VPS33B, and SDHA) was estimated and subtracted from each sample. Gene set expression was represented by the median expression of the member genes. To evaluate between-indication and within-indication variability for each gene signature, linear mixed effects models were used with indications as the random effect. ICC (intraclass correlation), the ratio of the between-indication variance to the total variance, was computed for each gene signature. Differential expression analysis between the clinical response groups was carried out using Wilcoxon rank sum tests. P values were not adjusted

for multiple corrections. Differential expression between primary and metastatic CRC pairs was assessed using Wilcoxon signed rank tests, and the derived p-values were adjusted for multiple testing errors using the Bonferroni method.

Example 1: A High Degree of Correlation was Observed for Immune Cell Signature Genes within a Given Gene Signature Set

(169) To assess the characteristics of the immune landscape in the tumor microenvironment of different tumors, PCR based gene expression signatures were employed to analyze the distribution of immune cell subsets across seven cancer types including urothelial bladder cancer (UBC), breast cancer (BC), non-small cell lung cancer (NSCLC), melanoma, renal cell cancers (RCC), ovarian cancer (OvCa), gastric cancer, liver cancer, and colorectal cancer (CRC). Table 1 depicts the immune gene signatures generated based on exclusive expression of genes in immune cell subsets including effector CD8 T cells (T.sub.eff), regulatory T cells (T.sub.reg), T cells (all), activated CD4 T cells, T cell chemotaxis, myeloid cells, macrophages (all), M2 macrophages, B cells, Th17 cells, NK cells, and innate inflammatory signatures. Expression of immune blockers present in T cells (IB T cells) and antigen presenting cells or tumor cells (IB APC/tumors) were also analyzed (Table 1). Table 1 also depicts the immune gene signature sets of antigen processing, costimulatory ligands, costimulatory receptors, cytolytic, angiogenesis, and active fibroblast signatures. The gene signature sets were analyzed using a 90-gene FLUIDIGM™ panel or an 800-gene custom Nanostring panel, as indicated in Table 1, using RNA extracted from archival FFPE tumor specimens. In general, a high degree of correlation was observed for genes within a given gene set by METHODOLOGY (FIGS. **1-11**): T.sub.eff, 0.72; B cell, 0.8; Myeloid, 0.54; Inflammatory, 0.59; T cell IB, 0.49; IB APC/tumors, 0.5. The only exception was IL17 signatures (R=0.3).

(170) Principal component analysis was applied to decompose the variance for the nine gene signatures. The first two principal components accounted for the majority of the variability (45% and 14% for the first and second components, respectively; FIG. **12**A). Inspection of the factor loading of the first component revealed that the first principal component was related to T.sub.eff, B cell, and IB APC/tumors signatures (FIGS. **12**B and **12**C).

(171) Principal component analysis further suggested that immune landscapes varied between tumor types. To examine whether this between-indication heterogeneity dominates the total variability, linear mixed effects models were used with indications as the random effect to decompose within- and between-indication variability. Intraclass correlation (ICC) was calculated for each gene signature. The ICC is calculated as the ratio of the between-indication variance to the total variance and has a value between 0 and 1. As shown in Table 10, ICCs ranged from 0.11 to 0.29, indicating that there was a substantial amount of within-indication heterogeneity for all gene signatures considered despite clear mean differences between indications.

(172) TABLE-US-00010 TABLE 10 Between-Indication Total Signature Variance Variance ICC Teff 0.65 2.61 0.2 Treg 0.84 2.47 0.25 Bcell 1.02 3.32 0.24 NKcell 1.06 4.18 0.2 Myeloid 0.32 1.57 0.17 IL17 3.23 11.45 0.22 Inflammatory 1.02 2.51 0.29 IB. T 0.58 4.91 0.11 IB. APC 0.53 1.89 0.22

Example 2: T.SUB.eff .Signature Genes Represent CD8 T Cell Infiltration

(173) The expression profile of the signature genes within the T.sub.eff gene set (see, Table 1 above) across cancer types was determined. A survey of the T.sub.eff signature across cancer types showed differences in median expression not just between cancers but also between subtypes within a given indication. While most indications exhibited comparable expression of T.sub.eff genes, NSCLC, melanoma, RCC, and Her2.sup.+ or TN BC had the highest levels of T.sub.eff, while CRC and OvCa had the lowest, followed by hormone receptor positive (HR+) BC (FIG. **13**). Within a cancer type, a wide range of expression patterns was observed suggesting that subpopulations within CRC or OvCa may have T.sub.eff expression levels similar to cancer types like melanoma or RCC.

(174) To determine if the T.sub.eff gene set represented the presence of CD8 T cells, digital

pathology was conducted for CD8 IHC to enumerate the number of CD8 T cells in the tumor center (CN) and the invasive margin (IM) (FIG. **30**).

(175) CD8 IHC were evaluated in three regions, tumor peripheral, invasive margin (IM) and center (Cn). The relationship between IM and Cn CD8 IHC, as well as between CD8 IHC and RNA, was assessed using scattermatrix plot. Raw values of CD8 IHC readings are right skewed; therefore, log 2-transformation was performed to normalize the distribution. CD8 IHC values that were zero were imputed to be half of the minimum non-zero value for log 2 transformation. A high degree of correlation was observed between CD8 IHC and CD8 RNA transcripts across indications (FIG. **29**). A high degree of correlation was observed between IM and CN CD8 IHC readings, with a Spearman correlation coefficient equaling 0.76 for the log 2 transformed values. CD8 RNA was found to be highly correlated with center/IM CD8 IHC positivity, with a Spearman correlation coefficient approximately 0.66 (samples from the same patients were not consolidated for the analyses in this section). When breaking down by indication, high correlation between IM and Cn CD8 IHC positivity persists, with Spearman correlation ranging from 0.69 to 0.82.

(176) In addition, a marked correlation was observed between IM and CN prevalence of CD8 T cells across indications (FIG. **30**). A summary of CD8 positivity by invasive margin (IM) and tumor center (CN) within each indication is presented in Table 11. The empirical cumulative distributions were plotted for both IM and CN in FIG. **31** to detect distributional differences between these two regions and between indications. Among the five indications, melanoma tumors on average had the highest CD8 T cell presence and the largest dynamic range. CRC and bladder tumors, on average, had the lowest CD8 T cell infiltrates and also, the smallest dynamic range. These results were highly correlated with the rank order of the T.sub.eff signatures.

(177) In addition, CD8 T cells were significantly more abundant at invasive margin than at tumor center for melanoma and RCC tumors.

(178) TABLE-US-00011 TABLE 11 IM. IM. Cn. Cn. N Median 25th%-75th% Median 25th%-75th% MELA- 35 3.07 (0.98-5.66) 2.22 (0.57-5.13) NOMA RENAL 56 3.36 (1.11-4.97) 1.835 (0.925-3.503) BLADDER 61 1.47 (1.09-3.19) 1.08 (0.33-1.96) LUNG 68 2.495 (1.245-5.87)   1.66 (0.9275-3.432)   COLO- 22 0.96 (0.785-1.21)   0.34 (0.1275-0.6575) RECTAL

(179) The cancer types that contain a CD8 T cell infiltrate most likely represented tumors that prevent anti-tumor immunity by overexpressing immunosuppressive cells relative to activated T cells. While the general prevalence of T.sub.eff signatures reflected the abundance of tumor infiltrating lymphocytes across indications, the ratio of T.sub.eff signatures to T.sub.reg ranked the cancer types in a manner similar to the ones most likely to respond to immunotherapies. NSCLC, RCC, and melanoma had the highest ratio of T.sub.eff:T.sub.reg reflecting "immunogenic" tumor types. Indications known to have poor responses to immunotherapies like CRC and OvCa were the cancer types with the lowest ratio of T.sub.eff:T.sub.reg (FIG. **15**). While TN and Her2.sup.+ breast cancers exhibited a higher median expression of T.sub.eff signatures, their tumor microenvironment was also shown to be rich in T.sub.reg and this is reflected by the low relative ratio of T.sub.eff to T.sub.reg signatures. Thus, therapies targeting T regulatory cells, such as anti-OX40 (abundantly expressed in T.sub.reg) in combination with checkpoint inhibitors, provide useful therapies for triggering an effective anti-tumor immune response.

Example 3: T.SUB.reg .Signature Genes are Abundant in Breast Cancer

(180) Tumors recruit immunosuppressive cells to inhibit antitumoral T.sub.eff responses. Regulatory T cells (T.sub.reg), characterized by Foxp3 expression, antagonize T.sub.eff action. To test the potential of in-situ immunosuppression, prevalence of Foxp3 was evaluated among tumor indications. Presence of T.sub.reg was highest among BC subtypes (Her2.sup.+ similar to triple negative (TN), both higher than hormone receptor positive (HR.sup.+)) followed by NSCLC, UBC, CRC, OvCa, RCC, and melanoma, with significantly reduced counts (FIG. **14**). Effective T.sub.reg-dependent immunosuppression requires a certain proportion of T.sub.eff:T.sub.reg, thus the proportion of T.sub.eff to T.sub.reg was assessed. T.sub.eff:T.sub.reg ratio was highest in

melanoma, followed by RCC, NSCLC, and UBC (FIG. **15**). Despite differences in independent T.sub.eff and T.sub.reg values, BC (HR.sup.+, Her2.sup.+ and TN), CRC, and ovarian had similarly reduced T.sub.eff:T.sub.reg ratios (FIG. **15**). These results suggest that tumors with low T.sub.eff:T.sub.reg may benefit from therapies targeting T.sub.reg.

Example 4: B Cell, NK Cell, and Myeloid Cell Signature Genes Vary Across Cancer Indications

(181) In preclinical models, B cells were shown to promote intratumoral immunosuppression by recruiting and enabling anti-inflammatory macrophages. On the other hand, NK cells were shown to recognize stress molecules expressed by tumors and direct tumor rejection. The presence of B cells followed a distribution similar to T.sub.eff across indications (FIG. **16**), while NK cells were highest in OvCa, followed by all the other indications (FIG. **17**). Myeloid signature, which encompasses both macrophages and dendritic cells, was similar among indications, except for reduced levels in CRC and OvCa (FIG. **18**), likely representing a low immune infiltrate in these indications. A further distinction was that the median expression of myeloid gene set was higher in non squamous NSCLC compared to squamous NSCLC.

Example 5: Th17 Signature Genes are Distinct in Each Tumor Type

(182) While tumor infiltrating lymphocytes were shown to be associated with better prognosis in several cancer indications, production of IL-17A and IL-17F by Th17 cells was linked to worse prognosis in several tumors, such as CRC, TN BC (Couchad, 20123 Scientific Reports), and ovarian cancer. In some cases, production of IL-17A and IL-17F was associated with better prognosis in indications such as esophageal squamous carcinoma. Analysis of IL-17A and IL-17F across indications showed a complex distribution: tumors expressing IL-17A alone, IL-17F alone, IL-17A.sup.+/IL-17F.sup.+ and IL-17A.sup.−/IL-17F.sup.− (FIG. **20**). The presence of single populations yielded to a gene signature index of 0.3 (FIG. **2**A). Colorectal carcinoma is the indication with the highest levels of IL-17 genes, followed by squamous NSCLC, bladder and non squamous NSCLC (FIG. **19**). Her2.sup.+ BC, HR.sup.+ BC, and OvCa were the indications with the lowest prevalence of IL-17 genes.

(183) When the prevalence of IL-17A and IL-17F was assessed in each indication, heterogeneity in the single and double gene distribution was observed. For instance, IL-17A and IL-17F were mainly co-expressed in CRC, squamous NSCLC, and bladder cancer, while Her2.sup.+ BC exhibited no IL-17A expression (FIG. **20**). These results suggest that IL-17 biology may be distinct in each tumor type and that targeted therapies toward these cytokines may have to consider preponderance of the targeted tissue. For example, IL-17 signature was particularly overrepresented in primary CRC compared to all other tumor types. Th17 cells have been known to be associated with microbial dysbiosis in the colon. To examine if the high expression of Th17 signatures was unique to the primary tumor or if it was translated to distant metastases an analysis of matched primary tumors and metastases expression of IL-17 genes was assessed. Analysis of matched primary tumors and metastases showed that indeed the prevalence of Th17 signatures in CRC may be driven by the colon immunobiology rather than by characteristics of the tumor (FIG. **32**). The liver is abundant in Kuppfer cells, sessile macrophages important in clearing cellular debris and gut derived microbial products. Considering that Arg1 and the myeloid markers are higher in CRC liver metastases, this suggested that resident organ microenvironment is an equally important determinant in contributing to the immunosuppressive microenvironment.

Example 6: Immune Response in the Tumor Microenvironment Changes Between Primary and Metastatic Sites

(184) The immune landscape in the tumor microenvironment may reflect either the endogenous immune responses characteristic of the organ or the specific recruitment by the tumor cells. Thus, it remains to be determined whether the tumor immune microenvironment is maintained when the tumor metastasizes. To test this possibility, the immune gene signatures were compared between 47 pairs of asynchronous matched primary and metastatic CRC tumors. Most of the metastases were located in the liver and lung (36 and 5, respectively) and the rest in other organs.

(185) Differences of gene set expression between primary and metastatic pairs were evaluated using Wilcoxon signed-rank test, and multiplicity of the tests was adjusted using the Bonferroni approach. Table 12 shows log 2 fold change of primary over metastatic samples together with Wilcoxon signed-rank test p values (i.e., Table 12 shows the fold change of the gene signatures using metastases as denominator). A positive fold change indicates higher expression in the CR/PR group compared to the PD group. Boxplot of gene set expression in association with primary metastatic status is shown in FIG. **32**.

(186) TABLE-US-00012 TABLE 12 Bonferroni Signature log2FoldChange raw p corrected p Teff −0.36 0.13 1 Treg 0.74 0.00028 0.00224 Inflammatory 0.67 0.0085 0.068 NKcell 0.5 0.092 0.736 Bcell −0.08 0.55 1 Myeloid −0.49 0.025 0.2 IL17 4 3.8e−07 3.04e−06 Teff/Treg −0.91 5.4e−08 4.32e−07

(187) The IL-17 gene signature, characteristic of primary CRC tumors, was strikingly reduced in CRC metastases, irrespective of location in the liver or lung (−4 fold, p=3.04×10{circumflex over ( )}−6). T.sub.reg were also significantly decreased in metastases (−0.76 fold, p=0.002272). While there were no significant differences in T.sub.eff between primary and metastases, the T.sub.eff:T.sub.reg ratio was significantly increased in the metastases (+0.91 fold, p=4.344×10{circumflex over ( )}−7). Finally, myeloid gene sets tend to be increased in the metastasis while the inflammatory signature is reduced (+0.49 and −67, p=0.1992 and 0.068, respectively).

(188) Differences of immune gene expression between primary and metastatic pairs were evaluated using Wilcoxon signed-rank test for each of the 96 immune genes, and multiplicity of the tests were adjusted using the Bonferroni approach. Genes that were identified as significantly differentially expressed between primary and metastatic samples (Bonferroni corrected p≤0.05) were ARG1, IL17A, VTCN1, IL17F, IL1B, HLA.E, HAVCR2, CD70, FOXP3 and PTGS2.

(189) At the level of individual genes, Arg1, expressed in hepatocytes and anti-inflammatory macrophages, was the single highest upregulated gene between colon primary and liver metastases (FIG. **33**). Taken together, these results suggest that the immune responses in the tumor microenvironment changes between primary and metastatic sites, mirroring the subjacent immune landscape of the organ rather than specific recruitment by tumor cells.

Example 7: Hormone Driven Tumors Display Reduced Inflammation

(190) Tumor-associated inflammation may promote tumor growth, angiogenesis, and recruitment of myeloid suppressor cells, which in turn switch off T cell mediated antitumoral response. Inflammasome products (IL-1β and IL-18), chemokines (CCL2, CCL22) and cytokines (IL-6, IL-8) were described to be part of this process in different indications. By using an inflammatory gene signature, it was observed that the overall inflammation varied across indications (FIG. **21**). The most inflamed tumors were NSCLC, UBC, and RCC, while the least inflamed indications were HR.sup.+ BC, liver, Her2.sup.+ BC, and OvCa. These results suggest that hormone driven tumors display reduced local inflammation.

Example 8: The Presence of T Cell Immune Blockers Trails T.SUB.eff .Distribution Across Cancer Indications

(191) To prevent uncontrolled T.sub.eff activation, inhibitory receptors (IB) are upregulated on immune cells and/or tumor cells upon T cell activation. A mechanism of tumor escape is induction of the ligands for T cell IB, therefore turning off effective anti-tumor responses. To determine the possible impact of these receptor:ligand interactions, prevalence of IB T cell signatures and IB APC/tumor signatures were analyzed. Presence of T cell immune blockers trailed T.sub.eff distribution across indications (FIG. **22**). In all indications, CTLA4 presented the lowest prevalence of IB T cell, while Tim3 (HVACR2) had the highest (FIG. **26**). PD-1 and Lag3 were second in abundance in the IB T cell signature. Expression of BTLA was either reduced in OvCa and CRC or expressed similarly to PD1 and Lag3 in melanoma, RCC, UBC, BC, and NSCLC. These data suggest that, regardless of the tumor type, infiltrating T.sub.eff were similarly equipped with

inhibitory receptors.

(192) Intratumoral antigen presenting cells (APC) and tumors express the inhibitory ligands for IB T cells as well as enzymes that produce catabolites that inhibit T cell activation. To analyze the presence of IB APC/tumor, a gene signature was generated and analyzed across indications. Prevalence of APC-IB signature was similar among indications, except for a marked reduction in HR.sup.+ BC and CRC (FIG. **23**). A granular analysis of genes was conducted to assess the relative expression patterns of individual APC-IB genes across cancer types (FIG. **27**). Expression of CD276 was highest and differentiated from the other genes. PD-L1, PD-L2, and IDO1 were highly correlated (0.7). Of these genes, the highest expressed was IDO1 (FIG. **27**). In addition, the ratio of gene expression of T.sub.eff gene signatures to APC-IB gene signatures was also determined across indications (FIG. **24**). The ratio of gene expression of T.sub.eff gene signatures to each individual gene in the APC-IB gene signature was also determined across indications (FIG. **25**). Of these, OvCa and HR.sup.+ BC had the lowest ratios of Teff/CD276 and Teff/PDL2, while OvCa alone had the lowest T.sub.eff/IDO1 ratio, suggesting that immunotherapy in OvCa may require the blockade of several immune inhibitors to trigger a treatment response.

Example 9: A High Degree of Heterogeneity is Present in the Immune Signature Gene Sets Across Cancer Indications

(193) A hierarchical clustering of the immune gene sets across indications was performed to analyze the immune landscape among tumor type. A high degree of heterogeneity was observed in the immune gene sets across indications, where some tumors showed a remarkable immune presence, while others were "immune deserts" (FIG. **28**).

(194) The unsupervised analysis clustered together the three types of breast cancer and the two types of lung tumors, suggesting that immunological similarities may arise from the tissue where the tumors grow. On the other hand, CRC and OvCa showed an immune desert cluster, devoid of immune gene signatures, except for IL17 and NK, respectively. Overall, the tumors with highest T.sub.eff infiltration were melanoma, RCC, NSCLC(Sq) and Her2+ and TN BC. However, the latter two cancers (i.e., Her2+ and TN BC) also exhibited a high incidence of T.sub.reg, suggesting that the intratumoral immune responses in these tumors may be negated by the effects of T.sub.reg. The most inflamed tumor was NSCLC-non squamous carcinoma, followed by NSCLC-squamous cell carcinoma, and UBC. The tumors with the highest incidence of IB APC/tumors were NSCLC, RCC, UBC, followed by melanoma, and TN BC. On the other hand, CRC, OvCa, HR.sup.+, and Her2.sup.+ BC had no signs of inflammation.

(195) Considering the factors mentioned above, it is predicted that no single factor across indications contributes to responses to checkpoint inhibition but rather the complexity of the tumor immune microenvironment dictates the drivers of resistance or response to immunotherapy. Therefore, analyzing the differences in one or more immune cell gene signatures from multiple gene sets likely provides a more complete prognosis for resistance or response to immunotherapy.

Example 10: Gene Set Expression is not Significantly Associated with Hepatocellular Carcinoma (HCC) Etiology

(196) Differences in gene set expression between the four etiology groups in HCC were evaluated using Kruskal Wallis tests, and multiplicity of the tests was adjusted using the Bonferroni approach. Table 13 shows median expression for each etiology group together with Kruskal-Wallis test p values. No immune subset was found to be significantly associated with HCC etiology although T.sub.eff subset was numerically higher in the virus double positive group (FIGS. **34** and **35**). Differences of immune gene expression were evaluated using Kruskal-Wallis test for each of the 96 immune genes shown in Table 14 and no multiplicity correction was applied. These data suggest that despite disparate tumor etiologies, liver tumors share similar immune microenvironments.

(197) Hierarchical clustering of immune genes having P≤0:1 for etiology differences is shown in FIG. **36**. Genes were median centered across the samples. Euclidean distance and complete linkage were used to generate the dendrogram. Red and green colors indicate higher and lower expression

than median, respectively. Black indicates median expression. The following colors differentiate etiologies: black/History of Alcoholism; red/HBV+; green/HCV+; blue/HBV+HCV+. A high degree of intraclass heterogeneity was present in HCC, with roughly half of tumors with high immune genes, but this difference could not be explained by HCC etiologic subtypes.

(198) TABLE-US-00013 TABLE 13 Alcohol- HBV+ Bonferroni Signature ism HBV+ HCV+ HCV+ raw p corrected p Teff −2.22 −1.8 −2.33 −1.36 0.14 1 Treg −1.36 −1.6 −1.64 −1.68 0.882 1 Inflam- −0.16 −0.04 −1.46 −0.08 0.245 1 matory NKcell −3.18 −2.23 −2.69 −1.7 0.142 1 Bcell −0.67 0.88 −0.22 0.35 0.151 1 Myeloid −2 −1.02 −1.96 −1.53 0.158 1 IL17 −12.4 −14.77 −12.7 −14.61 0.58 1 Teff/Treg −0.56 −0.1 −0.32 0.41 0.201 1

(199) TABLE-US-00014 TABLE 14 ARG1 BTLA CCL2 CCL22 CCL28 CCL5 CCR5 CCR7 CD1C CD244 CD27 CD274 CD274_IvG CD276 CD28 CD3E CD4 CD40 CD40LG CD48 CD69 CD70 CD80 CD8A CD8B CLEC4C CSF2 CTLA4 CX3CL1 CXCL10 CXCL9 CXCR3 EOMES EPCAM FCRL5 FOXP3 GUSB GZMA GZMB HAVCR2 HLA_A HLA_B HLA_C HLA_E ICAM1 ICOS IDO1 IFNγ IL10 IL12A IL13 IL17A IL17F IL1B IL2 IL2RA IL4 IL6 IL7 IL7R IL8 ITGAM ITGAX KLRK1 LAG3 LGALS9 MAP4K1 MICA MICB MS4A1 NCAM1 PDCD1 PDCD1LG2 PRF1 PTGER2 PTGER4 PTGS2 PTPRC PTPRC_2 RORC SDHA SP2 TBX21 TFRC TGFB1 TMEM55B TNF TNFRSF14 TNFRSF4 TNFSF9 VCAM1 VEGFA VPS33B VTCN1 CD86 TNFSF4

Claims

1. A method of treating a human patient having a cancer with an immunotherapy targeting regulatory T (T.sub.reg) cells, the method comprising: (i) determining the expression level of FOXP3 and the expression profile of CD8A, GZMA, GZMB, IFNγ, EOMES, and PRF1 in a biological sample obtained from the patient and determining therefrom that the expression level of FOXP3 is higher than the expression profile of CD8A, GZMA, GZMB, IFNγ, EOMES, and PRF1, thereby identifying the patient for treatment with an immunotherapy targeting T.sub.reg cells; and (ii) administering the immunotherapy targeting T.sub.reg cells to the patient.

2. The method of claim 1, wherein the determining is carried out prior to administering the immunotherapy targeting T.sub.reg cells in order to provide a patient with a pre-administration prognosis for response.

3. The method of claim 1, wherein the cancer is a breast cancer, melanoma, non-small cell lung cancer (NSCLC), bladder cancer, renal cell carcinoma, colorectal cancer, ovarian cancer, gastric cancer, or liver cancer.

4. The method of claim 3, wherein the cancer is primary, advanced, refractory, or recurrent.

5. The method of claim 3, wherein the cancer is a hormone receptor+ (HR+), HER2+, or triple negative (TN) breast cancer.

6. The method of claim 3, wherein the cancer is a non-squamous NSCLC or squamous NSCLC.

7. The method of claim 1, wherein expression of FOXP3, CD8A, GZMA, GZMB, IFNγ, EOMES, and PRF1 in the biological sample obtained from the patient is detected by measuring mRNA or plasma protein levels.

8. The method of claim 1, wherein the immunotherapy targeting T.sub.reg cells enhances tumor immunogenicity.

9. The method of claim 1, wherein the immunotherapy targeting T.sub.reg cells comprises treatment with a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist or treatment with a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist.

10. The method of claim 9, wherein the immunotherapy targeting T.sub.reg cells comprises treatment with a PD-1 axis binding antagonist.

11. The method of claim 10, wherein the PD-1 axis binding antagonist is a PD-L1 binding

antagonist, a PD-1 binding antagonist, or a PD-L2 binding antagonist.

12. The method of claim 1, further comprising determining the expression level of one or more of: (a) MS4A1 and CD48; (b) CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, and FCRL5; (c) NCAM1 and NKP46; (d) KLRC3, KLRK1, KLRC2, and KLRD1; (e) CD68, CD163, ITGAM, ITGAX, and CD14; (f) LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, and FCGR3A; (g) IL17A and IL17F; (h) CCL2, IL1B, IL8, IL6, and PTGS2; (i) CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, and LCK; (j) CTLA4, BTLA, LAG3, HAVCR2, and PDCD1; (k) CTLA4, BTLA, LAG3, HAVCR2, PDCD1, and TIGIT; (l) CD276, PDL1, PDL2, and IDO1; (m) CD274, PDL2, IDO1, and PVR; (n) CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, and CCL22; (o) CD4, IL2RA, and CD69; (p) TAPBP, TAP1, TAP2, PSMB9, and PSMB8; (q) CD40, CD80, CD86, CD70, and GITRL; (r) CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, and CD226; (s) GNLY, KLRK1, KLRB1, GZMH, KLRD1, and NKG7; and (t) FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1, COL4A2, COL5A1, and COL8A1.

13. The method of claim 1, wherein the expression profile is a median expression level.

14. A method of treating a human patient having a cancer, the method comprising administering an immunotherapy targeting T.sub.reg cells to the patient, wherein a biological sample obtained from the patient has been determined to have an expression level of FOXP3 that is higher than the expression profile of CD8A, GZMA, GZMB, IFNγ, EOMES, and PRF1 prior to administering the immunotherapy targeting T.sub.reg cells to the patient.

15. The method of claim 14, wherein the cancer is a breast cancer, melanoma, NSCLC, bladder cancer, renal cell carcinoma, colorectal cancer, ovarian cancer, gastric cancer, or liver cancer.

16. The method of claim 15, wherein the cancer is primary, advanced, refractory, or recurrent.

17. The method of claim 15, wherein the cancer is a HR+, HER2+, or TN breast cancer.

18. The method of claim 15, wherein the cancer is a non-squamous NSCLC or squamous NSCLC.

19. The method of claim 14, wherein expression of FOXP3, CD8A, GZMA, GZMB, IFNγ, EOMES, and PRF1 in the biological sample obtained from the patient was detected by measuring mRNA or plasma protein levels.

20. The method of claim 14, wherein the immunotherapy targeting T.sub.reg cells enhances tumor immunogenicity.

21. The method of claim 14, wherein the immunotherapy targeting T.sub.reg cells comprises treatment with a CD28, OX40, GITR, CD137, CD27, ICOS, HVEM, NKG2D, MICA, or 2B4 agonist or treatment with a CTLA-4, PD-1 axis, TIM-3, BTLA, VISTA, LAG-3, B7H4, CD96, TIGIT, or CD226 antagonist.

22. The method of claim 21, wherein the immunotherapy targeting T.sub.reg cells comprises treatment with a PD-1 axis binding antagonist.

23. The method of claim 22, wherein the PD-1 axis binding antagonist is a PD-L1 binding antagonist, a PD-1 binding antagonist, or a PD-L2 binding antagonist.

24. The method of claim 14, wherein the expression level of one or more of: (a) MS4A1 and CD48; (b) CD79A, MS4A1, CD19, STAP1, KIAA0125, POU2AF1, and FCRL5; (c) NCAM1 and NKP46; (d) KLRC3, KLRK1, KLRC2, and KLRD1; (e) CD68, CD163, ITGAM, ITGAX, and CD14; (f) LAPTM5, LAIR1, CD4, CSF1R, CD163, ADAP2, CD68, MRC1, CD45RO, SLA, MSR1, FPR3, FCGR2A, and FCGR3A; (g) IL17A and IL17F; (h) CCL2, IL1B, IL8, IL6, and PTGS2; (i) CD3D, CD3E, CD2, CD3G, CD6, TRAT1, CD28, and LCK; (j) CTLA4, BTLA, LAG3, HAVCR2, and PDCD1; (k) CTLA4, BTLA, LAG3, HAVCR2, PDCD1, and TIGIT; (l) CD276, PDL1, PDL2, and IDO1; (m) CD274, PDL2, IDO1, and PVR; (n) CX3CL1, CXCL9, CXCL10, CXCR3, CCL21, and CCL22; (o) CD4, IL2RA, and CD69; (p) TAPBP, TAP1, TAP2, PSMB9, and PSMB8; (q) CD40, CD80, CD86, CD70, and GITRL; (r) CD27, CD28, ICOS, TNFRSF4, TNFRSF14, TNFRSF18, TNFSF14, and CD226; (s) GNLY, KLRK1, KLRB1, GZMH, KLRD1, and NKG7; and (t) FAP, FN1, MMP2, BGN, LOXL2, PDPN, PDGFRB, COL4A1,

COL4A2, COL5A1, and COL8A1 has been further determined from the biological sample obtained from the patient prior to administering the immunotherapy targeting T.sub.reg cells to the patient.

25. The method of claim 14, wherein the expression profile is a median expression level.