

CLAIMS

1. A pluripotent human stem cell, wherein the stem cell comprises:
 - (i) a genomic edit that results in loss of function of Cytokine Inducible SH2 Containing Protein (CISH) and
 - (ii) a genomic edit that results in a loss of function of an agonist of the TGF beta signaling pathway, or a genomic edit that results in a loss of function of adenosine A2a receptor (ADORA2A).
2. The pluripotent human stem cell of claim 1, wherein the stem cell comprises a genomic edit that results in a loss of function of an agonist of the TGF beta signaling pathway and a genomic edit that results in a loss of function of ADORA2A.
3. The pluripotent human stem cell of claim 1 or 2, wherein the stem cell comprises a genomic edit that results in a loss of function of a TGF beta receptor or a dominant-negative variant of a TGF beta receptor.
4. The pluripotent human stem cell of claim 3, wherein the TGF beta receptor is a TGF beta receptor II (TGFβRII).
5. The pluripotent human stem cell of any one of the preceding claims, wherein the stem cell expresses one or more pluripotency markers selected from the group consisting of SSEA-3, SSEA-4, TRA-1-60, TRA-1-81, TRA-2-49/6E, ALP, Sox2, E-cadherin, UTF-1, Oct4, Rex1, and Nanog.
6. A differentiated cell, wherein the differentiated cell is a daughter cell of the pluripotent human stem cell of any one of the preceding claims.
7. The differentiated cell of claim 6, wherein the differentiated cell is an immune cell.

8. The differentiated cell of claim 6, wherein the differentiated cell is a lymphocyte.
9. The differentiated daughter cell of claim 6, wherein the differentiated cell is a natural killer cell.
10. The differentiated cell of claim 6, wherein the stem cell is a human induced pluripotent stem cell (iPSC), and wherein the differentiated daughter cell is an iNK cell.
11. The differentiated cell of claim 6, wherein the cell:
- (a) does not express endogenous CD3, CD4, and/or CD8; and
 - (b) expresses at least one endogenous gene encoding:
 - (i) CD56 (NCAM), CD49, CD43, and/or CD45, or any combination thereof;
 - (ii) NK cell receptor immunoglobulin gamma Fc region receptor III (FcγRIII, cluster of differentiation 16 (CD16));
 - (iii) natural killer group-2 member D (NKG2D);
 - (iv) CD69;
 - (v) a natural cytotoxicity receptor;or any combination of two or more thereof.
12. The cell of any of the preceding claims, wherein the cell comprises one or more additional genomic edits.
13. The cell of claim 12, wherein the cell:
- (1) comprises at least one genomic edit characterized by an exogenous nucleic acid expression construct that comprises a nucleic acid sequence encoding:
 - (i) a chimeric antigen receptor (CAR);
 - (ii) a FcγRIII (CD16) or a variant of FcγRIII (CD16);
 - (iii) interleukin 15 (IL-15);
 - (iv) an IL-15 receptor (IL-15R) agonist, or a constitutively active variant of an IL-15 receptor;

(v) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;

(vi) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;

(vii) human leukocyte antigen G (HLA-G);

(viii) human leukocyte antigen E (HLA-E);

(ix) leukocyte surface antigen cluster of differentiation CD47 (CD47);

or any combination of two or more thereof;

and/or

(2) comprises at least one genomic edit that results in a loss of function of at least one of:

(i) ADORA2A;

(ii) T cell immunoreceptor with Ig and ITIM domains (TIGIT);

(iii) β -2 microglobulin (B2M);

(iv) programmed cell death protein 1 (PD-1);

(v) class II, major histocompatibility complex, transactivator (CIITA);

(vi) natural killer cell receptor NKG2A (natural killer group 2A);

(vii) two or more HLA class II histocompatibility antigen alpha chain genes,

and/or two or more HLA class II histocompatibility antigen beta chain genes;

(viii) cluster of differentiation 32B (CD32B, FCGR2B);

(ix) T cell receptor alpha constant (TRAC);

or any combination of two or more thereof.

14. A human induced pluripotent stem cell (iPSC), wherein the iPSC comprises a genomic edit that results in a loss of function of adenosine A2a receptor (ADORA2A).

15. The human iPSC of claim 14, wherein the iPSC comprises a genomic edit that results in a loss of function of an agonist of the TGF beta signaling pathway or a genomic edit that results in loss of function of Cytokine Inducible SH2 Containing Protein (CISH).

16. The human iPSC of claim 15, wherein the iPSC comprises a genomic edit that results in a loss of function of an agonist of the TGF beta signaling pathway and a genomic edit that results in loss of function of CISH.

17. The human iPSC of claim 15 or 16, wherein the iPSC comprises a genomic edit that results in a loss of function of a TGF beta receptor or a dominant-negative variant of a TGF beta receptor.

18. The human iPSC of claim 17, wherein the TGF beta receptor is a TGF beta receptor II (TGFβRII).

19. The human iPSC of any one of claims 14-18, wherein the iPSC expresses one or more pluripotency markers selected from the group consisting of SSEA-3, SSEA-4, TRA-1-60, TRA-1-81, TRA-2-49/6E, ALP, Sox2, E-cadherin, UTF-1, Oct4, Rex1, and Nanog.

20. A differentiated cell, wherein the differentiated cell is a daughter cell of the human iPSC of any one of claims 14-19.

21. The differentiated cell of claim 20, wherein the differentiated cell is an immune cell.

22. The differentiated cell of claim 20, wherein the differentiated cell is a lymphocyte.

23. The differentiated daughter cell of claim 20, wherein the differentiated cell is a natural killer cell.

24. The differentiated cell of claim 20, wherein the differentiated daughter cell is an iNK cell.

25. The differentiated cell of claim 20, wherein the cell:
(a) does not express endogenous CD3, CD4, and/or CD8; and

(b) expresses at least one endogenous gene encoding:

- (i) CD56 (NCAM), CD49, CD43, and/or CD45, or any combination thereof;
 - (ii) NK cell receptor immunoglobulin gamma Fc region receptor III (FcγRIII, cluster of differentiation 16 (CD16));
 - (iii) natural killer group-2 member D (NKG2D);
 - (iv) CD69;
 - (v) a natural cytotoxicity receptor;
- or any combination of two or more thereof.

26. The cell of any of claims 14-25, wherein the cell comprises one or more additional genomic edits.

27. The cell of claim 26, wherein the cell:

(1) comprises at least one genomic edit characterized by an exogenous nucleic acid expression construct that comprises a nucleic acid sequence encoding:

- (i) a chimeric antigen receptor (CAR);
 - (ii) a FcγRIII (CD16) or a variant of FcγRIII (CD16);
 - (iii) interleukin 15 (IL-15);
 - (iv) an IL-15 receptor (IL-15R) agonist, or a constitutively active variant of an IL-15 receptor;
 - (v) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;
 - (vi) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;
 - (vii) human leukocyte antigen G (HLA-G);
 - (viii) human leukocyte antigen E (HLA-E);
 - (ix) leukocyte surface antigen cluster of differentiation CD47 (CD47);
- or any combination of two or more thereof;

and/or

(2) comprises at least one genomic edit that results in a loss of function of at least one of:

- (i) cytokine inducible SH2 containing protein (CISH);

- (ii) T cell immunoreceptor with Ig and ITIM domains (TIGIT);
 - (iii) β -2 microglobulin (B2M);
 - (iv) programmed cell death protein 1 (PD-1);
 - (v) class II, major histocompatibility complex, transactivator (CIITA);
 - (vi) natural killer cell receptor NKG2A (natural killer group 2A);
 - (vii) two or more HLA class II histocompatibility antigen alpha chain genes, and/or two or more HLA class II histocompatibility antigen beta chain genes;
 - (viii) cluster of differentiation 32B (CD32B, FCGR2B);
 - (ix) T cell receptor alpha constant (TRAC);
- or any combination of two or more thereof.

28. The cell of any one of claims 1-27, wherein:

the genomic edit resulting in loss of function of CISH was produced using a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 258-364, 1155, and 1162;

the genomic edit resulting in loss of function of TGF β RII was produced using a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 29-257, 1157, and 1161; and/or

the genomic edit resulting in loss of function of ADORA2A was produced using a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 827-1143, 1159, and 1163.

29. The cell of any one of claims 1-28, wherein:

the genomic edit resulting in loss of function of CISH was produced using a ribonucleoprotein (RNP) complex comprising (i) an RNA-guided nuclease and (ii) a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 258-364, 1155, and 1162;

the genomic edit resulting in loss of function of TGF β RII was produced using a ribonucleoprotein (RNP) complex comprising (i) an RNA-guided nuclease and (ii) a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 29-257, 1157, and 1161; and/or

the genomic edit resulting in loss of function of ADORA2A was produced using a ribonucleoprotein (RNP) complex comprising (i) an RNA-guided nuclease and (ii) a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 827-1143, 1159, and 1163.

30. A method of making the cell of any one of claims 1-29, the method comprising contacting the cell with one or more of:

an RNA-guided nuclease and a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 258-364, 1155, and 1162;

an RNA-guided nuclease and a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 29-257, 1157, and 1161; and/or

an RNA-guided nuclease and a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 827-1143, 1159, and 1163.

31. A method of making the cell of any one of claims 1-30, the method comprising contacting the cell with one or more of:

a ribonucleoprotein (RNP) complex comprising (i) an RNA-guided nuclease and (ii) a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 258-364, 1155, and 1162;

a ribonucleoprotein (RNP) complex comprising (i) an RNA-guided nuclease and (ii) a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 29-257, 1157, and 1161; and/or

a ribonucleoprotein (RNP) complex comprising (i) an RNA-guided nuclease and (ii) a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence according to any one of SEQ ID NO: 827-1143, 1159, and 1163.

32. The method of any one of claims 29-31, wherein the RNA-guided nuclease is a Cas12a variant.

33. The method of claim 32, wherein the Cas12a variant comprises one or more amino acid substitutions selected from M537R, F870L, and H800A.

34. The method of claim 32, wherein the Cas12a variant comprises amino acid substitutions M537R, F870L, and H800A.

35. The method of claim 32, wherein the Cas12a variant comprises the amino acid sequence of SEQ ID NO:1148.

36. The method of any one of claims 30-35, comprising contacting the cell with:

(i) a guide RNA comprising a targeting domain sequence comprising the nucleotide sequence of SEQ ID NO: 1155 or 1162; a guide RNA comprises a targeting domain sequence comprising the nucleotide sequence of SEQ ID NO: 1157 or 1161; and a guide RNA comprises a targeting domain sequence comprising the nucleotide sequence of SEQ ID NO: 1159 or 1163; and

(ii) an RNA-guided nuclease comprising the amino acid sequence of one of SEQ ID NO:1144-1151 (or a portion thereof).

37. A pluripotent human stem cell, wherein the stem cell comprises a disruption in the transforming growth factor beta (TGF beta) signaling pathway.

38. The pluripotent human stem cell of claim 34, wherein the stem cell comprises a genomic edit that results in a loss of function of an agonist of the TGF beta signaling pathway.

39. The pluripotent human stem cell of claim 37 or 38, comprising a loss of function of a TGF beta receptor or a dominant-negative variant of a TGF beta receptor.

40. The pluripotent human stem cell of claim 39, wherein the TGF beta receptor is a TGF beta receptor II (TGFβRII).

41. The pluripotent human stem cell of any one of claims 37-40, further comprising a loss of function of an antagonist of interleukin signaling.

42. The pluripotent human stem cell of any one of claims 37-41, wherein the stem cell further comprises a genomic modification that results in the loss of function of an antagonist of interleukin signaling.

43. The pluripotent human stem cell of claim 41 or 42, wherein the antagonist of interleukin signaling is an antagonist of the IL-15 signaling pathway and/or of the IL-2 signaling pathway.

44. The pluripotent human stem cell of any one of claims 37-43, comprising a loss of function of Cytokine Inducible SH2 Containing Protein (CISH).

45. The pluripotent human stem cell of claim 44, wherein the stem cell comprises a genomic modification that results in the loss of function of CISH.

46. The pluripotent human stem cell of any one of claims 37-45, wherein the stem cell expresses one or more pluripotency markers selected from the group consisting of SSEA-3, SSEA-4, TRA-1-60, TRA-1-81, TRA-2-49/6E, ALP, Sox2, E-cadherin, UTF-1, Oct4, Rex1, and Nanog.

47. A differentiated cell, wherein the differentiated cell is a daughter cell of the pluripotent human stem cell of any one of claims 37-46.

48. The differentiated cell of claim 47, wherein the differentiated cell is an immune cell.

49. The differentiated cell of claim 47, wherein the differentiated cell is a lymphocyte.

50. The differentiated daughter cell of claim 47, wherein the differentiated cell is a natural killer cell.

51. The differentiated cell of claim 47, wherein the stem cell is a human induced pluripotent stem cell (iPSC), and wherein the differentiated daughter cell is an iNK cell.

52. The differentiated cell of claim 47, wherein the cell:

(a) does not express endogenous CD3, CD4, and/or CD8; and

(b) expresses at least one endogenous gene encoding:

(i) CD56 (NCAM), CD49, CD43, and/or CD45, or any combination thereof;

(ii) NK cell receptor immunoglobulin gamma Fc region receptor III (FcγRIII, cluster of differentiation 16 (CD16));

(iii) natural killer group-2 member D (NKG2D);

(iv) CD69;

(v) a natural cytotoxicity receptor;

or any combination of two or more thereof.

53. The cell of any of claims 37-52, wherein the cell comprises one or more additional genomic edits.

54. The cell of claim 53, wherein the cell:

(1) comprises at least one genomic edit characterized by an exogenous nucleic acid expression construct that comprises a nucleic acid sequence encoding:

(i) a chimeric antigen receptor (CAR);

(ii) a FcγRIII (CD16) or a variant of FcγRIII (CD16);

(iii) interleukin 15 (IL-15);

(iv) an IL-15 receptor (IL-15R) agonist, or a constitutively active variant of an IL-15 receptor;

(v) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;

(vi) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;

- (vii) human leukocyte antigen G (HLA-G);
- (viii) human leukocyte antigen E (HLA-E);
- (ix) leukocyte surface antigen cluster of differentiation CD47 (CD47);
- or any combination of two or more thereof;

and/or

(2) comprises at least one genomic edit that results in a loss of function of at least one of:

- (i) cytokine inducible SH2 containing protein (CISH);
 - (ii) adenosine A2a receptor (ADORA2A);
 - (iii) T cell immunoreceptor with Ig and ITIM domains (TIGIT);
 - (iv) β -2 microglobulin (B2M);
 - (v) programmed cell death protein 1 (PD-1);
 - (vi) class II, major histocompatibility complex, transactivator (CIITA);
 - (vii) natural killer cell receptor NKG2A (natural killer group 2A);
 - (viii) two or more HLA class II histocompatibility antigen alpha chain genes,
- and/or two or more HLA class II histocompatibility antigen beta chain genes;
- (ix) cluster of differentiation 32B (CD32B, FCGR2B);
 - (x) T cell receptor alpha constant (TRAC);
 - or any combination of two or more thereof.

55. A method of culturing a pluripotent human stem cell, comprising culturing the stem cell in a medium comprising activin.

56. The method of claim 55, wherein the pluripotent human stem cell is an embryonic stem cell or an induced pluripotent stem cell.

57. The method of claim 55 or 56, wherein the pluripotent human stem cell does not express TGF β RII.

58. The method of any one of claims 55-57, wherein the pluripotent human stem cell is genetically engineered not to express TGF β RII.

59. The method of any one of claims 55-57, wherein the pluripotent human stem cell is genetically engineered to knock out a gene encoding TGF β RII.
60. The method of any one of claims 55-59, wherein the activin is activin A.
61. The method of any one of claims 55-60, wherein the medium does not comprise TGF β .
62. The method of any one of claims 55-61, wherein the culturing is performed for a defined period of time (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 days, or more).
63. The method of any one of claims 55-62, wherein at one or more times during or following the culturing step, the pluripotent human stem cell maintains pluripotency (e.g., exhibits one or more pluripotency markers).
64. The method of claim 63, wherein at one or more times during or following the culturing step, the pluripotent human stem cell expresses a detectable level of one or more of SSEA-3, SSEA-4, TRA-1-60, TRA-1-81, TRA-2-49/6E, ALP, Sox2, E-cadherin, UTF-1, Oct4, Rex1, and Nanog.
65. The method of claim 63, wherein at a time during or following the culturing step, the pluripotent human stem cell is differentiated into cells of endoderm, mesoderm, and/or ectoderm lineage.
66. The method of claim 65, wherein the pluripotent human stem cell, or its progeny, is further differentiated into a natural killer (NK) cell.
67. The method of any one of claims 55-66, wherein the pluripotent human stem cell:
- (1) comprises at least one genomic edit characterized by an exogenous nucleic acid expression construct that comprises a nucleic acid sequence encoding:
- (i) a chimeric antigen receptor (CAR);

- (ii) a FcγRIII (CD16) or a variant of FcγRIII (CD16);
- (iii) interleukin 15 (IL-15);
- (iv) an IL-15 receptor (IL-15R) agonist, or a constitutively active variant of an IL-15 receptor;
- (v) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;
- (vi) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;
- (vii) human leukocyte antigen G (HLA-G);
- (viii) human leukocyte antigen E (HLA-E);
- (ix) leukocyte surface antigen cluster of differentiation CD47 (CD47);
- or any combination of two or more thereof;

and/or

(2) comprises at least one genomic edit that results in a loss of function of at least one of:

- (i) cytokine inducible SH2 containing protein (CISH);
- (ii) adenosine A2a receptor (ADORA2A);
- (iii) T cell immunoreceptor with Ig and ITIM domains (TIGIT);
- (iv) β-2 microglobulin (B2M);
- (v) programmed cell death protein 1 (PD-1);
- (vi) class II, major histocompatibility complex, transactivator (CIITA);
- (vii) natural killer cell receptor NKG2A (natural killer group 2A);
- (viii) two or more HLA class II histocompatibility antigen alpha chain genes, and/or two or more HLA class II histocompatibility antigen beta chain genes;
- (ix) cluster of differentiation 32B (CD32B, FCGR2B);
- (x) T cell receptor alpha constant (TRAC);
- or any combination of two or more thereof.

68. A cell culture comprising (i) a pluripotent human stem cell and (ii) a cell culture medium comprising activin, wherein the pluripotent human stem cell comprises a disruption in the transforming growth factor beta (TGF beta) signaling pathway.

69. The cell culture of claim 68, wherein the stem cell comprises a genomic edit that results in a loss of function of an agonist of the TGF beta signaling pathway.
70. The cell culture of claim 69, wherein the genomic edit is a genomic edit.
71. The cell culture of any one of claims 68-70, wherein the stem cell comprises a loss of function of a TGF beta receptor or a dominant-negative variant of a TGF beta receptor.
72. The cell culture of claim 71, wherein the TGF beta receptor is a TGF beta receptor II (TGFβRII).
73. The cell culture of any one of claims 68-72, wherein the pluripotent human stem cell:
- (1) comprises at least one genomic edit characterized by an exogenous nucleic acid expression construct that comprises a nucleic acid sequence encoding:
 - (i) a chimeric antigen receptor (CAR);
 - (ii) a FcγRIII (CD16) or a variant of FcγRIII (CD16);
 - (iii) interleukin 15 (IL-15);
 - (iv) an IL-15 receptor (IL-15R) agonist, or a constitutively active variant of an IL-15 receptor;
 - (v) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;
 - (vi) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;
 - (vii) human leukocyte antigen G (HLA-G);
 - (viii) human leukocyte antigen E (HLA-E);
 - (ix) leukocyte surface antigen cluster of differentiation CD47 (CD47);
 - or any combination of two or more thereof;
 - and/or
 - (2) comprises at least one genomic edit that results in a loss of function of at least one of:

- (i) cytokine inducible SH2 containing protein (CISH);
 - (ii) adenosine A2a receptor (ADORA2A);
 - (iii) T cell immunoreceptor with Ig and ITIM domains (TIGIT);
 - (iv) β -2 microglobulin (B2M);
 - (v) programmed cell death protein 1 (PD-1);
 - (vi) class II, major histocompatibility complex, transactivator (CIITA);
 - (vii) natural killer cell receptor NKG2A (natural killer group 2A);
 - (viii) two or more HLA class II histocompatibility antigen alpha chain genes, and/or two or more HLA class II histocompatibility antigen beta chain genes;
 - (ix) cluster of differentiation 32B (CD32B, FCGR2B);
 - (x) T cell receptor alpha constant (TRAC);
- or any combination of two or more thereof.

74. A method of increasing a level of iNK cell activity comprising:

- (i) providing a pluripotent human stem cell comprising a disruption in the transforming growth factor beta (TGF beta) signaling pathway; and
- (ii) differentiating the pluripotent human stem cell into an iNK cell,

wherein the iNK cell has a higher level of cell activity as compared to an iNK cell not comprising a disruption of the TGF beta signaling pathway.

75. The method of claim 74, wherein the iNK is differentiated from a pluripotent human stem cell cultured in a medium comprising activin.

76. The method of claim 74 or 75, further comprising culturing the pluripotent human stem cell in a medium comprising activin before and/or during the differentiating step.

77. The method of any one of claims 74-76, further comprising disrupting the transforming growth factor beta (TGF beta) signaling pathway in the pluripotent human stem cell.

78. The method of any one of claims 73-77, wherein the stem cell comprises a genomic edit that results in a loss of function of an agonist of the TGF beta signaling pathway.

79. The method of any one of claims 73-78, wherein the stem cell comprises a loss of function of a TGF beta receptor or a dominant-negative variant of a TGF beta receptor.

80. The method of claim 79, wherein the TGF beta receptor is a TGF beta receptor II (TGFβRII).

81. The method of any one of claims 73-80, wherein the pluripotent human stem cell:

(1) comprises at least one genomic edit characterized by an exogenous nucleic acid expression construct that comprises a nucleic acid sequence encoding:

- (i) a chimeric antigen receptor (CAR);
- (ii) a FcγRIII (CD16) or a variant of FcγRIII (CD16);
- (iii) interleukin 15 (IL-15);
- (iv) an IL-15 receptor (IL-15R) agonist, or a constitutively active variant of an IL-15 receptor;
- (v) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;
- (vi) an IL-12 receptor (IL-12R) agonist, or a constitutively active variant of an IL-12 receptor;
- (vii) human leukocyte antigen G (HLA-G);
- (viii) human leukocyte antigen E (HLA-E);
- (ix) leukocyte surface antigen cluster of differentiation CD47 (CD47);
- or any combination of two or more thereof;

and/or

(2) comprises at least one genomic edit that results in a loss of function of at least one of:

- (i) cytokine inducible SH2 containing protein (CISH);

(ii) adenosine A2a receptor (ADORA2A);
(iii) T cell immunoreceptor with Ig and ITIM domains (TIGIT);
(iv) β -2 microglobulin (B2M);
(v) programmed cell death protein 1 (PD-1);
(vi) class II, major histocompatibility complex, transactivator (CIITA);
(vii) natural killer cell receptor NKG2A (natural killer group 2A);
(viii) two or more HLA class II histocompatibility antigen alpha chain genes,
and/or two or more HLA class II histocompatibility antigen beta chain genes;
(ix) cluster of differentiation 32B (CD32B, FCGR2B);
(x) T cell receptor alpha constant (TRAC);
or any combination of two or more thereof.

82. A method of treating a subject having or at risk of cancer, the method comprising administering to the subject the cell of any one of claims 6-13, 20-29, or 47-54, thereby treating the cancer in the subject.