WHAT IS CLAIMED IS:

1. An isolated hypoimmunogenic ~~induced pluripotent stem (HIP)~~T cell comprising a nucleic acid encoding a chimeric antigen receptor (CAR),

wherein the isolated hypoimmunogenic T cell has reduced expression of ~~endogenous~~ β-2 microglobulin (B2M) ~~gene activity~~ and/or reduced expression of ~~endogenous~~ class II transactivator (CIITA) ~~gene activity have been eliminated and~~compared to a wild-type cell,

wherein the isolated hypoimmunogenic T cell has increased expression of CD47 ~~expression has been increased~~ compared to the wild-type cell, and

wherein the isolated hypoimmunogenic T cell is a naïve T cell, a naïve central memory T cell, an effector memory T cell, or an effector memory RA T cell.

2. The isolated hypoimmunogenic T cell of claim 1, wherein the T cell is a CD3+ T cell, a CD8+ T cell, a CD8+ low T cell, a CD8+ high T cell, a CD4+ T cell, a CD4+/CD8+ high T cell, or a CD4+/CD8+ low T cell.

~~2~~3. The isolated ~~HIP~~ hypoimmunogenic T cell of claim 1 or claim 2, wherein the CAR comprises an extracellular domain, a transmembrane domain, and an intracellular signaling domain.

~~3~~4. The isolated ~~HIP~~ hypoimmunogenic T cell of claim ~~2~~3, wherein the extracellular domain binds to an antigen ~~selected from the group consisting of~~comprising CD19, CD20, CD22, CD38, CD123, CD171, CS1, BCMA, MUC16, ROR1, and/or WT1.

~~4~~5. The isolated ~~HIP~~ hypoimmunogenic T cell of claim ~~2~~ 3 or ~~3~~claim 4, wherein the extracellular domain comprises a single chain variable fragment (scFv).

~~5~~6. The isolated ~~HIP~~ hypoimmunogenic T cell of any one of claims ~~2~~ 3 to ~~4~~5, wherein the transmembrane domain comprises CD3ζ, CD4, CD8α, CD28, 4-1BB, OX40, ICOS, CTLA-4, PD-1, LAG-3, and/or BTLA.

~~6~~7. The isolated ~~HIP~~ hypoimmunogenic T cell of any one of claims ~~2~~ 3 to ~~5~~6, wherein the intracellular signaling domain comprises CD3ζ, CD28, 4-1BB, OX40, ICOS, CTLA-4, PD-1, LAG-3, and/or BTLA.

~~7~~8. The isolated ~~HIP~~ hypoimmunogenic T cell of any one of claims ~~2~~ 1 to ~~6~~7, wherein:

~~the nucleic acid encoding the CAR is introduced into the iPSC after B2M gene activity and CIITA gene have been eliminated and CD4 7 expression has been increased~~the extracellular domain binds to CD19, CD22, or BCMA;

the extracellular domain comprises a single chain variable fragment (scFv);

the transmembrane domain comprises CD8α or CD28; and

the intracellular signaling domain comprises CD3ζ and/or 4-1BB.

~~8~~9. The isolated ~~HIP~~ hypoimmunogenic T cell of any one of claims 1 to ~~7~~8, wherein the ~~HIP~~ isolated hypoimmunogenic T cell is derived from a human induced pluripotent stem cell (iPSC)~~, the B2M gene is human B2M gene, the CIITA gene is human B2M gene, and the increased CD47 expression results from introducing into the iPSC at least one copy of a human CD47 gene under the control of a promoter~~ or a mouse iPSC.

~~9~~10. The isolated ~~HIP~~ hypoimmunogenic T cell of ~~any one of~~ claim~~s 1 to 7~~9, wherein the ~~HIP~~ isolated hypoimmunogenic T cell is ~~a mouse~~ derived from the human iPSC~~induced pluripotent stem cell~~,

wherein the human iPSC has reduced expression of ~~the~~ B2M ~~gene is mouse B2M gene~~, and/or reduced expression of ~~the~~ CIITA ~~gene is mouse B2M gene~~compared to a wild-type cell, and

wherein the human iPSC has increased expression of CD47 ~~expression~~ compared to the wild-type cell, and wherein the increased expression of CD47 results from expression of a ~~results from introducing into the iPSC at least one copy of a mouse~~ CD47 transgene under the control of a constitutive promoter or an inducible promoter.

~~10~~11. The isolated ~~HIP~~ hypoimmunogenic T cell of claim ~~8 or 9~~10, wherein the ~~human~~ CD47 transgene comprises a human CD47 gene, and wherein the CD47 transgene is under the control of ~~promoter is~~ a constitutive promoter.

~~11. The isolated HIP cell of any one of claim 1 to 10, wherein the elimination of B2M gene activity results from a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/Cas9 reaction that disrupts both alleles of the B2M gene.~~

~~12. The isolated HIP cell of any one of claims 1 to 11, wherein the elimination of CIITA gene activity results from a CRISPR/Cas9 reaction that disrupts both alleles of the CIITA gene.~~

12. The isolated hypoimmunogenic T cell of any one of claims 1 to 11, further comprising a safety switch.

13. The isolated ~~HIP~~ hypoimmunogenic T cell of ~~any one of~~ claim~~s 1 to~~ 12, ~~further comprising~~wherein the safety switch is a suicide gene and the suicide gene ~~that~~ is activated by a trigger agent ~~that induces the hypoimmunogenic pluripotent cell to die~~.

14. The isolated ~~HIP~~ hypoimmunogenic T cell of claim 13, wherein the suicide gene is a herpes simplex virus thymidine kinase (HSV-tk) gene and the trigger agent is ganciclovir.

~~15. The isolated HIP cell of claim 14, wherein the HSV-tk gene encodes a protein comprising at least 90% sequence identity to SEQ ID NO:4.~~

~~16. The isolated HIP cell of claim 14, wherein the HSV-tk gene encodes a protein comprising the amino acid sequence of SEQ ID NO:4.~~

~~17~~15. The isolated ~~HIP~~ hypoimmunogenic T cell of claim 13, wherein the suicide gene is an *Escherichia coli* cytosine deaminase (CD) gene and the trigger agent is 5-fluorocytosine (5-FC).

~~18. The isolated HIP cell of claim 1 7, wherein the CD gene encodes a protein comprising at least 90% sequence identity to SEQ ID NO:5.~~

~~19. The isolated HIP cell of claim 17, wherein the CD gene encodes a protein comprising the amino acid sequence of SEQ ID NO:5.~~

~~20~~16. The isolated ~~HIP~~ hypoimmunogenic T cell of claim 13, wherein the suicide gene encodes an inducible caspase 9 protein and the trigger agent is a chemical inducer of dimerization (CID).

~~21. The isolated HIP cell of claim 20, wherein the inducible caspase 9 protein comprises at least 90% sequence identity to SEQ ID NO:6.~~

~~22. The isolated HIP cell of claim 20, wherein the inducible caspase 9 protein comprises the amino acid sequence of SEQ ID NO:6.~~

~~23~~17. The isolated ~~HIP~~ hypoimmunogenic T cell of ~~any one of~~ claim~~s 20 to 22~~ 16, wherein the CID is compound AP 1903.

~~24. An isolated hypoimmune CAR-T cell produced by in vitro differentiation of the HIP cell of any one of claims 1 to 23.~~

2518. The isolated hypoimmune CAR-Thypoimmunogenic T cell of any one of claims 241 to 17, wherein the isolated hypoimmunogenic T cellCAR-T cell is a hypoimmune hypoimmunogenic cytotoxic CAR-T cell.

26. The isolated hypoimmune CAR-T cell of claim 24 or 25, wherein the in vitro differentiation comprises culturing the HIP cell in a culture media comprising one or more growth factors or cytokines selected from the group consisting of bFGF, EPO, Flt3L, IGF, IL-2, IL-3, IL-6, IL-7, IL-15, GM-CSF, SCF, and VEGF.

27. The isolated hypoimmune CAR-T cell of any one of claims 24 to 26, wherein the culture media further comprises one or more selected from the group consisting of a BMP activator, a GSK3 inhibitor, a ROCK inhibitor, a TGFβ receptor/ALK inhibitor, and a NOTCH activator.

28. The isolated hypoimmune CAR-T cell of any one of claims 24 to 27, wherein the *in vitro* differentiation comprises culturing the HIP cell on feeder cells.

29. The isolated hypoimmune CAR-T cell of any one of claims 24 to 28, wherein the in vitro differentiation comprises culturing in simulated microgravity.

30. The isolated hypoimmune CAR-T cell of claim 29, wherein the culturing in simulated microgravity is for at least 72 hours.

3119. The isolated hypoimmune CAR-Thypoimmunogenic T cell of any one of claims 24 1 to 30 18 for use as in a treatment of a cancer.

20. The isolated hypoimmunogenic T cell of claim 19, wherein the cancer is a blood cancer, a solid tumor cancer, or a liquid tumor cancer.

~~32. A method of treating a patient with cancer by administering a composition comprising a therapeutically effective amount of the isolated hypoimmune CAR-T cells of any one of claims 24 to 27.~~

~~33. The method of claim 32, wherein the composition further comprises a therapeutically effective carrier.~~

~~34. The method of claim 32 or 33, wherein the administration comprises intravenous administration, subcutaneous administration, intranodal administration, intratumoral administration, intrathecal administration, intrapleural administration, and intraperitoneal administration.~~

~~35. The method of any one of claims 32 to 34, wherein the administration further comprises a bolus or by continuous perfusion.~~

~~36~~21. The ~~method of any one~~isolated hypoimmunogenic T cell of claim~~s~~ ~~32 to 35~~19, wherein the cancer is ~~a blood cancer selected from the group consisting of~~ leukemia, lymphoma~~, and~~ myeloma, glioblastoma, melanoma, neuroblastoma, adenocarcinoma, glioma, soft tissue sarcoma, astrocytoma, fibrosarcoma, myxosarcoma, liposarcoma, oligodendroglioma, ependymoma, medulloblastoma, primitive neural ectodermal tumor (PNET), chondrosarcoma, osteogenic sarcoma, pancreatic ductal adenocarcinoma, small cell lung adenocarcinoma, large cell lung adenocarcinoma, chordoma, angiosarcoma, endotheliosarcoma, squamous cell carcinoma, bronchoalveolarcarcinoma, epithelial adenocarcinoma, epithelial adenocarcinoma, lymphangiosarcoma, lymphangioendotheliosarcoma, hepatoma, cholangiocarcinoma, synovioma, mesothelioma, Ewing's tumor, rhabdomyosarcoma, colon carcinoma, basal cell carcinoma, sweat gland carcinoma, papillary carcinoma, sebaceous gland carcinoma, papillary adenocarcinoma, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, testicular tumor, medulloblastoma, craniopharyngioma, ependymoma, pinealoma,

hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, neuroblastoma, retinoblastoma, Waldenstrom's macroglobulinemia, heavy chain disease, breast tumor, ductal adenocarcinoma, lobular adenocarcinoma, squamous and adenocarcinoma of the uterine cervix, uterine and ovarian epithelial carcinoma, prostatic adenocarcinoma, transitional squamous cell carcinoma of the bladder, B and T cell lymphoma, plasmacytoma, malignant melanoma, soft tissue sarcoma or leiomyosarcoma.

22. A method for producing an isolated hypoimmunogenic T cell comprising a nucleic acid encoding a chimeric antigen receptor (CAR), comprising:

reducing or eliminating endogenous β-2 microglobulin (B2M) gene expression and/or endogenous class II transactivator (CIITA) gene expression in a parent cell using CRISPR/Cas, TALEN, or Zinc Finger technology;

introducing a CD47 transgene in the parent cell; and

introducing the nucleic acid encoding the CAR in the parent cell;

wherein the isolated hypoimmunogenic T cell comprises a naïve T cell, a naïve central memory T cell, an effector memory T cell, or an effector memory RA T cell.

23. The method of claim 22, wherein the method further comprises introducing a safety switch in the parent cell, wherein the safety switch is a suicide gene and the suicide gene is activated by a trigger agent.

24. The method of claim 22 or claim 23, wherein the parent cell is a human induced pluripotent stem cell (iPSC).

25. The method of any one of claims 22-24, wherein the method further comprises subjecting the iPSC to *in vitro* differentiation into the isolated hypoimmunogenic T cell.

~~37. The method of any one of claims 32 to 35, wherein the cancer is a solid tumor cancer or a liquid tumor cancer.~~

~~38. A pure population of hypoimmune CAR-T cells derived from a population of isolated HIP cells by a method comprising in vitro differentiation,~~

~~wherein the isolated HIP cells comprise a nucleic acid encoding a chimeric antigen receptor (CAR) and a suicide gene that is activated by a trigger agent that can induce the HIP cells to die, and~~

~~wherein endogenous β-2 microglobulin (B2M) gene activity and endogenous class II transactivator (CIITA) gene activity have been eliminated and CD47 expression has been increased in the HIP cells.~~

~~39. The pure population of isolated hypoimmune CAR-T cells of claim 38, wherein the suicide gene is a herpes simplex virus thymidine kinase (HSV-tk) gene and the trigger agent is ganciclovir, the suicide gene is an *Escherichia coli* cytosine deaminase (CD) gene and the trigger agent is 5-fluorocytosine (5-FC), or the suicide gene is an inducible caspase 9 protein and the trigger agent is a chemical inducer of dimerization (CID).~~

~~40. The pure population of isolated hypoimmune CAR-T cells of claim 38 or 39, wherein the CAR-T cells are hypoimmune cytotoxic CAR-T cells.~~

~~41. The pure population of isolated hypoimmune CAR-T cells of any one of claims 38 to 40, wherein the in vitro differentiation comprises culturing the HIP cells in a culture media comprising one or more growth factors or cytokines selected from the group consisting of bFGF, EPO, Flt3L, IGF, IL-2, IL-3, IL-6, IL-7, IL-15, GM-CSF, SCF, and VEGF.~~

~~42. The pure population of isolated hypoimmune CAR-T cells of any one of claims 38 to 41, wherein the culture media further comprises one or more selected from the group consisting of a BMP activator, a GSK3 inhibitor, a ROCK inhibitor, a TGFβ receptor/ALK inhibitor, and a NOTCH activator.~~

~~43. The pure population of isolated hypoimmune CAR-T cells of any one of claims 38 to 42, wherein the in vitro differentiation comprises culturing the HIP cells on feeder cells.~~

~~44. The pure population of isolated hypoimmune CAR-T cells of any one of claims 38 to 43, wherein the in vitro differentiation comprises culturing in simulated microgravity.~~

~~45. The pure population of isolated hypoimmune CAR-T cells of claim 44, wherein the culturing in simulated microgravity is for at least 72 hours.~~

~~46. The pure population of isolated hypoimmune CAR-T cells of any one of claims 38 to 42, wherein the method further comprises culturing the hypoimmune CAR-T cells in a negative selection media comprising the trigger agent to induce the HIP cells to die, thereby producing a population of isolated hypoimmune CAR-T cells that is substantially free or free of the hypoimmunogenic iPSCs.~~

~~47. A method of treating a patient with cancer by administering a composition comprising a therapeutically effective amount of the pure population of isolated hypoimmune CAR-T cells of any one of claims 38 to 46.~~

~~48. The method of claim 47, wherein the composition further comprises a therapeutically effective carrier.~~

~~49. The method of claim 47 or 48, wherein the administration comprises intravenous administration, subcutaneous administration, intranodal administration, intratumoral administration, intrathecal administration, intrapleural administration, and intraperitoneal administration.~~

~~50. The method of any one of claims 47 to 49, wherein the administration further comprise a bolus or by continuous perfusion.~~

~~51. The method of any one of claims 47 to 50, wherein the cancer is a blood cancer selected from the group consisting of leukemia, lymphoma, and myeloma.~~

~~52. The method of any one of claims 47 to 50, wherein the cancer is a solid tumor cancer or a liquid tumor cancer.~~

~~53~~26. ~~A~~ The method of ~~making the isolated hypoimmune CAR-T cells of any one of claims 24 to 27 comprising in vitro differentiating of any one of the HIP cells of any one of~~ claim~~s 1 to 23~~25, wherein *in vitro* ~~differentiating~~ differentiation comprises culturing the iPSC in culture medium comprising ~~one or more growth factors or cytokines selected from the group consisting of~~ bFGF, EPO, Flt3L, IGF, IL-2, IL-3, IL-6, IL-7, IL-15, GM-CSF, SCF, ~~and~~ VEGF, or a combination thereof.

~~54~~27. The method of claim ~~53~~26, wherein the culture ~~media~~ medium further comprises ~~one or more selected from the group consisting of~~ a BMP activator, a GSK3 inhibitor, a ROCK inhibitor, a TGFβ receptor/ALK inhibitor, ~~and~~ a NOTCH activator, or a combination thereof.

~~55~~28. The method of any one of claim~~s 53 or 54~~25 to 27, wherein the *in vitro* ~~differentiating~~ differentiation comprises culturing the ~~HIP cells~~ iPSC on feeder cells.

~~56. The method of any one of claims 53 to 55, wherein the in vitro differentiating comprises culturing the HIP cells on feeder cells.~~

~~57~~29. The method of any one of claims ~~53~~ 25 to ~~56~~28, wherein the *in vitro* ~~differentiating~~ differentiation comprises culturing the iPSC in simulated microgravity.

~~58. The method of claim 57, wherein the culturing in simulated microgravity is for at least 72 hours.~~

30. A composition comprising a therapeutically effective amount of one or more isolated hypoimmunogenic T cells of any one of claims 1-21, for use in ~~treating a patient with~~the treatment of ~~a~~ cancer.

31. The composition for use of claim 30, wherein the one or more isolated hypoimmunogenic T cells comprise:

one or more naïve T cells,
one or more naïve central memory T cells,
one or more effector memory T cells,
one or more effector memory RA T cells, or
a combination thereof.

32. The composition for use of claim 30 or 31, wherein the one or more isolated hypoimmunogenic T cells comprise:

one or more CD3+ T cells,
one or more CD8+ T cells,
one or more CD8+ low T cells,
one or more CD8+ high T cells,
one or more CD4+ T cells,
one or more CD4+/CD8+ high T cells,
one or more CD4+/CD8+ low T cells, or
a combination thereof.

33. The composition for use of any one of claims 30-32, wherein the composition

further comprises a therapeutically effective carrier for intravenous administration, subcutaneous administration, intranodal administration, intratumoral administration, intrathecal administration, intrapleural administration, intraperitoneal administration, a bolus or continuous perfusion.

34. The composition for use of any one of claims 30-33, wherein the cancer is a blood cancer, a solid tumor cancer, or a liquid tumor cancer.

35. The composition for use of any one of claims 30-34, wherein the cancer is leukemia, lymphoma, myeloma, glioblastoma, melanoma, neuroblastoma, adenocarcinoma, glioma, soft tissue sarcoma, astrocytoma, fibrosarcoma, myxosarcoma, liposarcoma, oligodendroglioma, ependymoma, medulloblastoma, primitive neural ectodermal tumor (PNET), chondrosarcoma, osteogenic sarcoma, pancreatic ductal adenocarcinoma, small cell lung adenocarcinoma, large cell lung adenocarcinoma, chordoma, angiosarcoma, endotheliosarcoma, squamous cell carcinoma, bronchoalveolarcarcinoma, epithelial adenocarcinoma, epithelial adenocarcinoma, lymphangiosarcoma, lymphangioendotheliosarcoma, hepatoma, cholangiocarcinoma, synovioma, mesothelioma, Ewing's tumor, rhabdomyosarcoma, colon carcinoma, basal cell carcinoma, sweat gland carcinoma, papillary carcinoma, sebaceous gland carcinoma, papillary adenocarcinoma, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, testicular tumor, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, neuroblastoma, retinoblastoma, Waldenstrom's macroglobulinemia, heavy chain disease, breast tumor, ductal adenocarcinoma, lobular adenocarcinoma, squamous and adenocarcinoma of the uterine cervix, uterine and ovarian epithelial carcinoma, prostatic adenocarcinoma, transitional squamous cell carcinoma of the bladder, B and T cell lymphoma, plasmacytoma, malignant melanoma, soft tissue sarcoma or leiomyosarcoma.

36. The composition for use of any one of claims 30-35, wherein the one or more isolated hypoimmunogenic T cells comprise a safety switch and wherein the safety switch is activated by a trigger agent.