WHAT IS CLAIMED IS:

1. A method of manufacturing a genetically engineered lymphocyte comprising:

contacting in vitro one or more lymphocytes from a subject with an anti-CD81 antibody, an exogenous Interleukin-7 (IL-7) and an exogenous Interleukin-21 (IL-21);

transforming the contacted lymphocyte with a vector containing a gene of interest; and harvesting the lymphocyte.

2. The method of claim 1, wherein the lymphocyte is selected from the group consisting of natural killer cells (NK cells), B cells, T cells, NK-T cells, and tumor infiltrating lymphocytes (TILs).

3. The method of claim 2, wherein the lymphocyte is a T cell.

4. The method of any one of claims 1 to 3, wherein the lymphocyte is contacted with an anti-CD3 antibody and an anti-CD28 antibody.

5. The method of any one of claims 1 to 4, wherein the T cells comprise CD8+ T cells and CD4+ T cells.

6. The method of claim 5, wherein:
the CD8+ T cells express CCR7+ CD45RA+; and/or
the CD4+ T cells express CCR7+ CD45RA+; and/or
the CD8+ T cells express CD27+ CD28+; and/or
the CD4+ T cells express CD27+ CD28+.

7. The method of claim 6, wherein the CD8+ T cells and/or the CD4+ T cells express CD27+ CD28+ CCR7+ CD45RA+.

8. The method of any one of claims 1 to 7, wherein the T cells express a chimeric antigen receptor (CAR) wherein the T cells are transformed with a vector containing the chimeric antigen receptor (CAR).

9. The method of claim 8, wherein the chimeric antigen receptor (CAR):
is bicistronic or bispecific; and/or
comprises CD19; and/or

comprises a single chain variable fragment (scFv) targeting an identified tumor antigen comprising CD20, BCMA, CLL-1, CTLA4, CD30, CD40, NKp44, NKp30, GPC-3, CD79a, CD79b, BAFF-R, CS-1, PSMA, NKG2D, CLL-1, CD33, CD22 or NKp46.

10. The method of any one of claims 1 to 9, wherein the vector is a retroviral vector, a DNA vector, a plasmid, an RNA vector, an adenoviral vector, an adenovirus associated vector, a lentiviral vector, or any combination thereof.

11. The method of claim 10 wherein the DNA vector is a transposon.

12. The method of any one of claims 1 to 11, wherein the lymphocytes have not been contacted with an exogenous Interleukin-2 (IL-2).

13. The method of any one of claims 1 to 12, wherein the subject is a subject in need of a T cell therapy.

14. The method of claim 10, wherein the lymphocytes are transduced with a vector containing a gene of interest.

15. The method of claim 14, wherein the vector is a lentiviral vector or the vector is a retroviral vector.

16. The method of any one of claims 1 to 15, wherein the lymphocytes are harvested no more than 24 hours after transformation.

17. The method of any one of claims 1 to 16, wherein the lymphocytes are harvested no more than 2 days, 3 days, 5 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days after transformation.

18. A genetically engineered lymphocyte produced by a method comprising:

contacting in vitro one or more lymphocytes from a subject with an anti-CD81 antibody, an exogenous Interleukin-7 (IL-7) and an exogenous Interleukin-21 (IL-21);

transforming the contacted lymphocyte with a vector containing a gene of interest; and harvesting the lymphocyte.

19. The lymphocyte of claim 18, wherein the lymphocyte is selected from the group consisting of natural killer cells (NK cells), B cells, T cells, NK-T cells, and tumor infiltrating lymphocytes (TILs).

20. A genetically engineered lymphocyte produced by a method comprising:

contacting in vitro one or more lymphocytes from a subject with an anti-CD81 antibody, an exogenous Interleukin-7 (IL-7) and an exogenous Interleukin-21 (IL-21);

transforming the contacted lymphocyte with a vector containing a gene of interest; and harvesting the lymphocyte, wherein the genetically engineered lymphocyte has a higher juvenile and a less differentiated CAR-T phenotype compared to the genetically engineered lymphocyte produced by contacting in vitro one or more lymphocytes from a subject with an exogenous Interleukin-2 (IL-2).

21. The genetically engineered lymphocyte of claim 20, wherein the lymphocyte is contacted with an anti-CD3 antibody and an anti-CD28 antibody.

22. The genetically engineered lymphocyte of claim 20 or 21, wherein the lymphocyte is T cell.

23. The genetically engineered lymphocyte of any one of claims 20 to 22, wherein the higher juvenile and less differentiated CAR-T phenotype comprises CCR7+ CD45RA+ CD4+ T cells and/or CCR7+ CD45RA+ CD8+ T cells.

24. The genetically engineered lymphocyte of any one of claims 20 to 23, wherein the higher juvenile and less differentiated CAR-T phenotype is produced when the lymphocytes are harvested no more than 6 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days after the transformation.

25. The genetically engineered lymphocyte of any one of claims 20 to 24, wherein the higher juvenile and less differentiated CAR-T phenotype is produced when the lymphocytes are harvested no more than 14 days after the transformation.

26. A genetically engineered lymphocyte produced by a method comprising: contacting in vitro one or more lymphocytes from a subject with an anti-CD81 antibody, an exogenous Interleukin-7 (IL-7) and an exogenous Interleukin-21 (IL-21); transforming the contacted

lymphocyte with a vector containing a gene of interest; and harvesting the lymphocyte, wherein the genetically engineered lymphocyte secretes a lower effector cytokine compared to the genetically engineered lymphocyte produced by contacting in vitro one or more lymphocytes from a subject with an exogenous Interleukin-2 (IL-2).

27. The genetically engineered lymphocyte of claim 26, wherein the lower effector cytokine is Granzyme A or wherein the lower effector cytokine is IFN-γ.

28. The isolated genetically engineered lymphocyte of claim 26 or 27, wherein the lymphocytes further secrete higher IL2.

29. A genetically engineered lymphocyte produced by a method comprising:

contacting in vitro one or more lymphocytes from a subject with an anti-CD81 antibody, an exogenous Interleukin-7 (IL-7) and an exogenous Interleukin-21 (IL-21); transforming the contacted lymphocyte with a vector containing a gene of interest; and harvesting the lymphocyte, wherein the genetically engineered lymphocytes exhibit a more juvenile phenotype compared to the genetically engineered lymphocyte produced by contacting in vitro one or more lymphocytes from a subject with an exogenous Interleukin-2 (IL-2).

30. A composition comprising the genetically engineered lymphocytes of any one of claims 18 to 29.

31. Use of a genetically engineered lymphocyte of any one of claims 18 to 29 for the manufacture of a composition for the treatment of a cancer, wherein the genetically engineered lymphocyte is a T cell.

32. The use of claim 31, wherein the cancer is selected from the group consisting of acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), adenoid cystic carcinoma, adrenocortical, carcinoma, AIDS-related cancers, anal cancer, appendix cancer, astrocytomas, atypical teratoid/rhabdoid tumor, central nervous system, B-cell leukemia, lymphoma, refractory B-cell malignancy or other B cell malignancies, basal cell carcinoma, bile duct cancer, bladder cancer, bone cancer, osteosarcoma and malignant fibrous histiocytoma, brain stem glioma, brain tumors, breast cancer, bronchial tumors, burkitt lymphoma, carcinoid tumors, central nervous system cancers, cervical cancer, chordoma, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), chronic myeloproliferative disorders, colon cancer, colorectal

cancer, craniopharyngioma, cutaneous t-cell lymphoma, embryonal tumors, central nervous system, endometrial cancer, ependymoblastoma, ependymoma, esophageal cancer, esthesioneuroblastoma, ewing sarcoma family of tumors extracranial germ cell tumor, extragonadal germ cell tumor extrahepatic bile duct cancer, eye cancer fibrous histiocytoma of bone, malignant, and osteosarcoma, gallbladder cancer, gastric (stomach) cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumors (GIST), soft tissue sarcoma, germ cell tumor, gestational trophoblastic tumor, glioma, hairy cell leukemia, head and neck cancer, heart cancer, hepatocellular (liver) cancer, histiocytosis, Hodgkin lymphoma, hypopharyngeal cancer, intraocular melanoma, islet cell tumors (endocrine pancreas), kaposi sarcoma, kidney cancer, langerhans cell histiocytosis, laryngeal cancer, leukemia, lip and oral cavity cancer, liver cancer (primary), lobular carcinoma in situ (LCIS), lung cancer, lymphoma, macroglobulinemia, male breast cancer, malignant fibrous histiocytoma of bone and osteosarcoma, medulloblastoma, medulloepithelioma, melanoma, merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer with occult primary midline tract carcinoma involving NUT gene, mouth cancer, multiple endocrine neoplasia syndromes, multiple myeloma/plasma cell neoplasm, mycosis fungoides, myelodysplastic syndromes, myelodysplastic/myeloproliferative neoplasms, myelogenous leukemia, chronic (CML), Myeloid leukemia, acute (AML), myeloma, multiple, myeloproliferative disorders, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-Hodgkin lymphoma, non-small cell lung cancer, oral cancer, oral cavity cancer, oropharyngeal cancer, osteosarcoma and malignant fibrous histiocytoma of bone, ovarian cancer, pancreatic cancer, papillomatosis, paraganglioma, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytoma, pineal parenchymal tumors of intermediate differentiation, pineoblastoma and supratentorial primitive neuroectodermal tumors, pituitary tumor, plasma cell neoplasm/multiple myeloma, pleuropulmonary blastoma, pregnancy and breast cancer, primary central nervous system (CNS) lymphoma, prostate cancer, rectal cancer, renal cell (kidney) cancer, renal pelvis and ureter, transitional cell cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, sarcoma, sézary syndrome, small cell lung cancer, small intestine cancer, soft tissue sarcoma, squamous cell carcinoma, squamous neck cancer, stomach (gastric) cancer, supratentorial primitive neuroectodermal tumors, t-cell lymphoma, cutaneous, testicular cancer, throat cancer, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal pelvis and ureter, trophoblastic tumor, ureter and renal pelvis cancer, urethral cancer, uterine cancer, uterine sarcoma, vaginal cancer, vulvar cancer, Waldenström macroglobulinemia and Wilms Tumor.

33. Use of one or more lymphocytes that have been contacted with an anti-CD81 antibody, an exogenous Interleukin-7 (IL-7) and an exogenous Interleukin-21 (IL-21), in the manufacture of a medicament for treating a tumor in a subject in need of a T cell therapy.

34. Use of one or more lymphocytes that have been contacted with an anti-CD81 antibody, an exogenous Interleukin-7 (IL-7) and an exogenous Interleukin-21 (IL-21), in the manufacture of a medicament for reducing or decreasing the size of a tumor or inhibiting growth of a tumor in a subject in need of a T cell therapy.

35. The method of any one of claims 1 to 17, or the isolated genetically engineered lymphocytes of any one of claims 18 to 29, wherein the lymphocytes can be used in autologous cell therapy or allogeneic cell therapy.

36. The method of any one of claims 1 to 17 or 35, or the genetically engineered lymphocytes of any one of claims 18 to 29 or 35, wherein the lymphocytes produce more cytokines compared to lymphocytes produced by a process of making genetically engineered lymphocytes in the presence of IL-2.

37. The method of any one of claims 1 to 17 or 35 to 36, or the genetically engineered lymphocytes of any one of claims 18 to 29 or 35 to 36, wherein the lymphocytes:
produce more IL-2;and/or
are more juvenile; and/or
are more proliferative or robust;
compared to lymphocytes produced by a process of making genetically engineered lymphocytes in the presence of IL-2.