CLAIMS

What Is Claimed Is:

1. A composition comprising isolated T cells modified to overexpress and/or contain elevated levels of one or more AP-1 transcription factors.

2. The composition of claim 1, wherein the isolated T cells are further modified to express a recombinant receptor.

3, The composition of claim 2, wherein the recombinant receptor is a T cell receptor (TCR).

4. The composition of claim 2, wherein the recombinant receptor is a chimeric antigen receptor (CAR).

5. The composition of claim 2, wherein the recombinant receptor is specific for a tumor antigen.

6. The composition of claim 5, wherein the tumor antigen is selected from the group consisting of CD19, CD20, CD22, ROR1, GD2, EBV protein or antigen, folate receptor, Mesothelin, human carcinoembryonic antigen, CD33/IL3Ra, c-Met, PSMA, Glycolipid F77, EGFRvIII, NY-ESO-1, MAGE-A3, MART-1, GP1000 and p53.

7. The composition of claim 1, wherein the isolated T cells are native, naturally occurring T cells.

8. The composition of claim 7, wherein the native, naturally occurring T cells are obtained from resected tumors.

9. The composition of claim 7, wherein the native, naturally occurring T cells are obtained by leukapheresis of a blood sample.

10. The composition of claim 9, wherein the T cells are expanded ex vivo.

11. The composition of claim 1, wherein the T cells are selected from the group consisting of CD3+ T cells, CD8+ T cells, CD4+ T cells, natural killer (NK) T cells, gamma delta T cells, a combination of CD4+ and CD8 T+ cells, memory T cells, cytokine-induced killer cells, and combinations thereof.

12. The composition of claim 1, wherein the one or more AP-1 transcription factors are selected from the group consisting of c-Fos, c-Jun, Activating transcription factor (ATF) and Jun dimerization protein (JDP).

13. The composition of claim 1, wherein the AP-1 transcription factor is c-Jun.

14. The composition of claim 1, wherein the AP-1 transcription factor is a mutated/truncated AP-1 transcription factor.

15. The composition of claim 1, wherein the mutated/truncated AP-1 transcription factor comprises an N-terminal deletion.

16. The composition of claim 1, wherein the mutated/truncated AP-1 transcription factor (i) lacks a transactivation domain or (ii) comprises an inactive transactication domain.

17. The composition of claim 1, wherein the isolated T cells co-express c-Jun and an engineered receptor.

18. The composition of claim 17, wherein c-Jun and the engineered receptor are expressed from separate expression vector constructs.

19. The composition of claim 17, wherein c-Jun and the engineered receptor are co-expressed from a single expression vector construct.

20. The composition of claim 1, wherein the isolated T cells are T cells with specificity for and activity against a tumor.

21. The composition of claim 20, wherein the T cells are peripheral blood derived T cells genetically modified to express a receptor that recognizes and responds to tumor.

22. The composition of claim 1, wherein the T cells are further modified to reduce and/or eliminate expression and/or activity of one or more AP-1 inhibitory complex members.

23. The composition of claim 22, wherein the AP-1 inhibitory complex member is selected from the group consisting of JunB, a BATF family member, IRF4, an ATF family member, or a combination thereof.

24. The composition of claim 22, wherein the AP-1 inhibitory complex member is JunB and/or BATF3.

25. A method of treating a disease or pathologic condition in a subject comprising administering to the subject having the disease or pathologic condition an effective amount of a composition comprising T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors.

26. The method of claim 25, wherein the AP-1 transcription factor is c-Jun.

27. The method of claim 26, wherein the AP-1 transcription factor is a mutated/truncated transcription factor.

28. The method of claim 26, wherein the T cells are further modified to express a recombinant receptor.

29. The method of claim 28,

wherein c-Jun and the recombinant receptor are expressed from separate expression vector constructs, or

wherein c-Jun and the recombinant receptor are co-expressed from a single expression vector construct.

30. The method of claim 25, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors are less susceptible to experiencing T cell exhaustion.

31. The method of claim 25, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors have increased reactivity against low antigen density on target cells of the T cells.

32. The method of claim 25, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors are less susceptible to experiencing diminished memory formation.

33. The method of claim 25, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors are less susceptible to experiencing diminished proliferative capacity.

34. The method of claim 25, wherein the disease or condition is a tumor or cancer.

35. The method of claim 34, wherein the T cells are modified to express a recombinant receptor specific for the tumor or cancer.

36. The method of claim 35, wherein the recombinant receptor is a chimeric antigen receptor (CAR).

37. The method of claim 36, wherein the CAR is specific for a tumor antigen selected from the group consisting of CD19, CD20, CD22, ROR1, GD2, EBV protein or antigen, folate receptor, Mesothelin, human carcinoembryonic antigen, CD33/IL3Ra, c-Met, PSMA, Glycolipid F77, EGFRvIII, NY-ESO-1, MAGE-A3, MART-1, GP1000 and p53.

38. The method of claim 25, wherein the disease or condition is a viral, bacterial and/or parasitic infection.

39. The method of claim 25, wherein the T cells are further modified to reduce and/or eliminate expression and/or activity of one or more AP-1 inhibitory complex members.

40. The method of claim 39, wherein the AP-1 inhibitory complex member is selected from the group consisting of JunB, a BATF family member, IRF4, an ATF family member, or a combination thereof.

41. The method of claim 40, wherein the AP-1 inhibitory complex member is JunB and/or BATF3.

42. A method of treating or delaying the progression of cancer in a patient comprising administering to the patient a therapeutically effective amount of a composition comprising T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors and to express a chimeric antigen receptor (CAR) specific for a tumor antigen.

43. The method of claim 42, wherein the administering reduces the number of cancerous cells in the patient.

44. The method of claim 42, wherein the administering reduces and/or clears tumor burden in the patient.

45 The method of claim 42, further comprising administering to the patient one or more anticancer agents and/or one or more chemotherapeutic agents.

46. The method of claim 42, wherein the administering occurs before, at the same time, and/or after the patient receives radiation therapy.

47. The method of claim 42, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors and to express a chimeric antigen receptor (CAR) specific for a tumor antigen are less susceptible to experiencing T cell exhaustion .

48. The method of claim 42, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors and to express a chimeric antigen receptor (CAR) specific for a tumor antigen have increased reactivity against low antigen density on target cells of the T cells.

49. The method of claim 42, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors and to express a chimeric antigen receptor (CAR) specific for a tumor antigen are less susceptible to experiencing diminished memory formation.

50. The method of claim 42, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors and to express a chimeric antigen receptor (CAR) specific for a tumor antigen are less susceptible to experiencing diminished proliferative capacity.

51. A therapeutically effective amount of a composition comprising T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors and to express a chimeric antigen receptor (CAR) specific for a tumor antigen for use in treating or delaying the progression of cancer in a subject.

52. The composition for use of claim 51, further comprising one or more anticancer agents and/or one or more chemotherapeutic agents.

53. The composition for use of claim 51, wherein the composition reduces the number of cancerous cells in the patient, and reduces or eliminates the tumor burden in the patient.

54. The method of claim 51, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors and to express a chimeric antigen receptor (CAR) specific for a tumor antigen are less susceptible to experiencing T cell exhaustion .

55. The method of claim 51, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors and to express a chimeric antigen

receptor (CAR) specific for a tumor antigen have increased reactivity against low antigen density on target cells of the T cells.

56. The method of claim 51, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors and to express a chimeric antigen receptor (CAR) specific for a tumor antigen are less susceptible to experiencing diminished memory formation.

57. The method of claim 51, wherein the T cells modified to express and/or contain elevated levels of one or more AP-1 transcription factors and to express a chimeric antigen receptor (CAR) specific for a tumor antigen are less susceptible to experiencing diminished proliferative capacity.

58. A method of treating a disease or condition in a patient comprising administering to the patient having the disease or condition an effective amount of a composition comprising T cells modified to reduce and/or eliminate expression and/or activity of one or more AP-1 inhibitory complex members.

59. The method of claim 58, wherein the disease or condition is cancer.

60. The method of claim 59, wherein the AP-1 inhibitory complex member is selected from the group consisting of JunB, BATF3, a BATF family member, IRF4, an IRF family member, an ATF family member, or a combination thereof.

61. The method of claim 58, wherein the AP-1 inhibitory complex member is JunB, BATF3, and/or IRF4.

62. The method of claim 58, wherein the T cells are modified by CRISPR-Cas9, shRNA, siRNA, RNAi, micro-RNA, degron, regulatable promoter, or pharmacological inhibition.

63. A composition comprising isolated T cells modified to reduce and/or eliminate expression and/or activity of one or more AP-1 inhibitory complex members.

64. The composition of claim 63, wherein the AP-1 inhibitory complex member is selected from the group consisting of JunB, BATF3, a BATF family member, IRF4, an IRF family member, an ATF family member, or a combination thereof.

65. The composition of claim 63, wherein the AP-1 inhibitory complex member is JunB, BATF3, and/or IRF4.

66. The composition of claim 1, wherein the isolated T cells modified to overexpress and/or contain elevated levels of one or more AP-1 transcription factors are less susceptible to experiencing T cell exhaustion .

67. The composition of claim 1, wherein the isolated T cells modified to overexpress and/or contain elevated levels of one or more AP-1 transcription factors have increased reactivity against low antigen density on target cells of the T cells.

68. The composition of claim 1, wherein the isolated T cells modified to overexpress and/or contain elevated levels of one or more AP-1 transcription factors are less susceptible to experiencing diminished memory formation.

69. The composition of claim 1, wherein the isolated T cells modified to overexpress and/or contain elevated levels of one or more AP-1 transcription factors are less susceptible to experiencing diminished proliferative capacity.