CLAIMS

WHAT IS CLAIMED IS:

1. A composition comprising:

(a) a tissue-specific antigen peptide comprising an epitope sequence of a protein encoded by a gene selected from the group consisting of *ANKRD30A*, *COL10A1*, *CTCFL*, *PPIAL4G*, *POTEE*, *DLL3*, *MMP13*, *SSX1*, *DCAF4L2*, *MAGEA4*, *MAGEA11*, *MAGEC2*, *MAGEA12*, *PRAME*, *CLDN6*, *EPYC*, *KLK3*, *KLK2*, *KLK4*, *TGM4*, *POTEG*, *RLN1*, *POTEH*, *SLC45A2*, *TSPAN10*, *PAGE5*, *CSAG1*, *PRDM7*, *TG*, *TSHR*, *RSPH6A*, *SCXB*, *HIST1H4K*, *ALPPL2*, *PRM2*, *PRM1*, *TNP1*, *LELP1*, *HMGB4*, *AKAP4*, *CETN1*, *UBQLN3*, *ACTL7A*, *ACTL9*, *ACTRT2*, *PGK2*, *C2orf53*, *KIF2B*, *ADAD1*, *SPATA8*, *CCDC70*, *TPD52L3*, *ACTL7B*, *DMRTB1*, *SYCN*, *CELA2A*, *CELA2B*, *PNLIPRP1*, *CTRC*, *AMY2A*, *SERPINI2*, *RBPJL*, *AQP12A*, *IAPP*, *KIRREL2*, *G6PC2*, *AQP12B*, *CYP11B1*, *CYP11B2*, *STAR*, *CYP11A1*, and *MC2R*, wherein the protein is expressed by a cancer;

(b) a polynucleotide encoding the tissue-specific antigen peptide;

(c) one or more antigen presenting cells (APCs) presenting the tissue-specific antigen peptide;

(d) a T cell receptor (TCR) or an antibody, or a functional part thereof that is specific to a complex of (i) the epitope sequence and (ii) a protein encoded by an HLA allele; or

(e) a population of immune cells from a biological sample comprising at least one antigen specific T cell comprising the TCR.

2. A composition comprising

(a) a tissue-specific antigen peptide comprising an epitope sequence of a protein, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs 1-8962, wherein the protein is expressed by a cancer;

(b) a polynucleotide encoding the tissue-specific antigen peptide;

(c) one or more antigen presenting cells (APCs) presenting the tissue-specific antigen peptide;

(d) a T cell receptor (TCR) or an antibody, or a functional part thereof that is specific to a complex of (i) the epitope sequence and (ii) a protein encoded by an HLA allele; or

(e) a population of immune cells from a biological sample comprising at least one antigen specific T cell comprising the TCR.

3. A composition comprising:

(a) a tissue specific antigen peptide comprising an epitope sequence of a protein, wherein the protein is expressed by a tumor of a target tissue;

(b) a polynucleotide encoding the tissue-specific antigen peptide;

(c) one or more antigen presenting cells (APCs) presenting the tissue-specific antigen peptide;

(d) a T cell receptor (TCR) or an antibody, or a functional part thereof that is specific to a complex of (i) the epitope sequence and (ii) a protein encoded by an HLA allele; or

(e) a population of immune cells from a biological sample comprising at least one antigen specific T cell comprising the TCR;

wherein the epitope sequence binds to or is predicted to bind to a protein encoded by a protein encoded by an HLA allele expressed by a human subject, and wherein the protein is encoded by a tissue-specific antigen epitope gene that has an expression level in the target tissue that is at least 2 fold more than an expression level of the tissue-specific antigen gene in each tissue of a plurality of non-target tissues that are different than the target tissue.

4. The composition of any one of claims 1-3, wherein the protein comprises TSHR, TG, RSPH6A, SCXB, SSX1, or any combination thereof, and wherein the cancer comprises thyroid cancer.

5. The composition of any one of claims 1-4, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs 6846-7061, 7359-7448, 7629-8099, and 8619-8744, and wherein the cancer comprises thyroid cancer.

6. The composition of any one of claims 1-3, wherein the protein comprises RBPJL, AQP12A, AQP12B, IAPP, CELA2A, CELA2B, AMY2A, CTRC, G6PC2, KIRREL2, PNLIPRP1, SERPINI2, SYNC, or any combination thereof, and wherein the cancer comprises pancreatic cancer.

7. The composition of any one of claims 1-3 and 6, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs 720-814, 989-1182, 1373-1565, 2120-2211, 2920-3009, 3101-3196, 3320-3440, 5193-5284, 6487-6579, 7062-7150, and 7539-7628, and wherein the cancer comprises pancreatic cancer.

8. The composition of any one of claims 1-3, wherein the protein comprises CYP11A1, CYP11B1, CYP11B2, MC2R, STAR, or any combination thereof, and wherein the cancer comprises adrenal cancer.

9. The composition of any one of claims 1-3 and 8, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs 22122523, 4817-4915, and 7449-7538, and wherein the cancer comprises adrenal cancer.

10. The composition of any one of claims 1-3, wherein the protein comprises ALPPL2, POTEE, PRAME, or any combination thereof, and wherein the cancer comprises uterine cancer.

11. The composition of any one of claims 1-3 and 10, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs 627-719, 5285-5431, and 6085-6183, and wherein the cancer comprises uterine cancer.

12. The composition of any one of claims 1-3, wherein the protein comprises KLK2, KLK3, KLK4, POTEH, POTEG, TGM4, RLN1, POTEE, PPIAL4G or any combination thereof, and wherein the cancer comprises prostate cancer.
13. The composition of any one of claims 13 and 12, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs 3441-4274, 5285-6084, 6580-6845, and 8100-8434, and wherein the cancer comprises prostate cancer.
14. The composition of any one of claims 1-3, wherein the protein comprises ANKRD30A, COL10A1, or a combination thereof and wherein the cancer comprises breast cancer.
15. The composition of any one of claims 1-3 and 14, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs 815-988, and 1749-1867, and wherein the cancer comprises breast cancer.
16. The composition of any one of claims 1-3, wherein the protein comprises CTCFL, PRAME, CLDN6, EPYC, or any combination thereof, and wherein the cancer comprises ovarian cancer.
17. The composition of any one of claims 1-3 and 16, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs 1659-1748, 1964-2119, 2827-2919, and 6085-6183, and wherein the cancer comprises ovarian cancer.
18. The composition of any one of claims 1-3, wherein the protein comprises CTCFL, and wherein the cancer comprises cervical cancer.
19. The composition of any one of claims 1-3 and 18, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs 1964-2119, and wherein the cancer comprises cervical cancer.
20. The composition of any one of claims 1-3, wherein the protein comprises POTEE, PPIAL4G, or a combination thereof, and wherein the cancer comprises colorectal cancer.
21. The composition of any one of claims 1-3 and 20, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID Nos 5285-5431, and 5996-6084, and wherein the cancer comprises colorectal cancer.
22. The composition of any one of claims 1-3, wherein the protein comprises DLL3, and wherein the cancer comprises glioma.
23. The composition of any one of claims 1-3 and 22, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID Nos 2619-2736, and wherein the cancer comprises glioma.
24. The composition of any one of claims 1-3, wherein the protein comprises MMP13, and wherein the cancer comprises head and neck cancer.

25. The composition of any one of claims 1-3 and 24, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID Nos 4916-5010, and wherein the cancer comprises head and neck cancer.

26. The composition of any one of claims 1-3, wherein the protein comprises DCAF4L2, SSX1, or a combination thereof, and wherein the cancer comprises liver cancer.

27. The composition of any one of claims 1-3 and 26, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID Nos 2524-2618, and 7359-7448, and wherein the cancer comprises liver cancer.

28. The composition of any one of claims 1-3, wherein the protein comprises SSX1, MAGEA4, PRAME, CSAG1, MAGEA12, MAGEA2, MAGEC2, PAGE5, PRDM7, SLC45A2, TSPAN10, or any combination thereof, and wherein the cancer comprises melanoma.

29. The composition of any one of claims 1-3 and 28, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID Nos 1868-1963, 4458-4550, 4551-4637, 4638-4728, 4729-4816, 5011-5100, 6085-6183, 6184-6307, 7151-7264, 7359-7448, and 8745-8835, and wherein the cancer comprises melanoma.

30. The composition of any one of claims 1-3, wherein the protein comprises MAGEA11, MAGEA4, PRAME, or any combination thereof, and wherein the cancer comprises lung squamous cell carcinoma.

31. The composition of any one of claims 1-3 and 30, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID Nos 4368-4457, 4638-4728, and 6085-6183, and wherein the cancer comprises lung squamous cell carcinoma.

32. The composition of any one of claims 1-3, wherein the protein comprises ACTL7A, ACTL7B, ACTL9, ACTRT2, ADAD1, AKAP4, C2orf53, CCDC70, CETN1, DMRTB1, HMGB4, KIF2B, LELP1, PGK2, PRM1, PRM2, SPATA8, TNP1, TPD52L3, UBQLN3, or any combination thereof, and wherein the cancer comprises testis cancer.

33. The composition of any one of claims 1-3 and 32, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID Nos 1-626, 1183-1372, 1566-1658, 2737-2826, 3010-3100, 3197-3319, 4275-4367, 5101-5192, 6308-6486, 7265-7358, 8435-8618, and 8836-8962, and wherein the cancer comprises testis cancer.

34. The composition of any one of claims 1-3, wherein the tissue specific antigen peptide comprises an epitope sequence of a protein encoded by a gene selected from the group consisting of: ANKRD30A, DLL3, PRAME, CLDN6, EPYC, SLC45A2, TSPAN10, TSHR, LELP1, AQP12A, KIRREL2, G6PC2, AQP12B, and MC2R.

35. The composition of any one of claims 1-3, wherein the protein comprises KLK2, KLK3, KLK4, ANKRD30A, PRAME, MAGE4, or a combination thereof.

36. The composition of claim 35, wherein the protein comprises KLK2, KLK3 or KLK4; and wherein the cancer comprises prostate cancer.

37. The composition of any one of claims 1-3 and 36, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of AYSEKVTEF (SEQ ID NO: 3534), GLWTGGKDTCGV (SEQ ID NO: 3468), HPEDTGQVF (SEQ ID NO: 3988), HPEYNRPLL (SEQ ID NO: 4143), QRVPVSHSF (SEQ ID NO: 3544), SESDTIRSI (SEQ ID NO: 4176), SLFHPEDTGQV (SEQ ID NO: 3775), SLQCVSLHL (SEQ ID NO: 3456), VILLGRHSL (SEQ ID NO: 3891), VLVHPQWVL (SEQ ID NO: 3757), LFHPEDTGQVF (SEQ ID NO: 3827), RPRSLQCVSL (SEQ ID NO: 3578), GYLQGLVSF (SEQ ID NO: 4094), IRNKSVILL (SEQ ID NO: 3974), KLQCVDLHV (SEQ ID NO: 3740), LLANGRMPTV (SEQ ID NO: 4029), LRPGDDSTL (SEQ ID NO: 3767), MPALPMVL (SEQ ID NO: 3874), NRPLLANDL (SEQ ID NO: 4216), SLQCVSLHL (SEQ ID NO: 3456), TWIAPPLQV (SEQ ID NO: 3784), VFQVSHSF (SEQ ID NO: 3828) and YSEKVTEFML (SEQ ID NO: 3454).

38. The composition of any one of claims 1-3 and 36, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of AYSEKVTEF (SEQ ID NO: 3534), HPEDTGQVF (SEQ ID NO: 3988), HPEYNRPLL (SEQ ID NO: 4143), QRVPVSHSF (SEQ ID NO: 3544), LFHPEDTGQVF (SEQ ID NO: 3827), GYLQGLVSF (SEQ ID NO: 4094), IRNKSVILL (SEQ ID NO: 3974), KLQCVDLHV (SEQ ID NO: 3740), LLANGRMPTV (SEQ ID NO: 4029), LRPGDDSTL (SEQ ID NO: 3767), MPALPMVL (SEQ ID NO: 3874), NRPLLANDL (SEQ ID NO: 4216), SLQCVSLHL (SEQ ID NO: 3456), TWIAPPLQV (SEQ ID NO: 3784), VFQVSHSF (SEQ ID NO: 3828) and YSEKVTEFML (SEQ ID NO: 3454).

39. The composition of claim 35, wherein the protein comprises ANKRD30A; and wherein the cancer comprises breast cancer.

40. The composition of any one of claims 1-3 and 38, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of LLSHGAVIEV (SEQ ID NO: 831), SIPTKALEL (SEQ ID NO: 942), SQYSGQLKV (SEQ ID NO: 927), SVPNKALEL (SEQ ID NO: 941), SLSKILDTV (SEQ ID NO: 826) and SLDQKLFQL (SEQ ID NO: 827).

41. The composition of any one of claims 1-3 and 38, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of LLSHGAVIEV (SEQ ID NO: 831), SIPTKALEL (SEQ ID NO: 942), SVPNKALEL (SEQ ID NO: 941), SLSKILDTV (SEQ ID NO: 826) and SLDQKLFQL (SEQ ID NO: 827).

42. The composition of claim 35, wherein the protein comprises PRAME; and wherein the cancer comprises squamous cell lung cancer; melanoma; ovarian cancer, uterine cancer, or any combination thereof.

43. The composition of any one of claims 1-3 and 42, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of DSLFFLRGR (SEQ ID NO: 6132), ELFSYLIEK (SEQ ID NO: 6108), FYDPEPILC (SEQ ID NO: 6166), ISISALQSL (SEQ ID NO: 6161), ITDDQLLAL (SEQ ID NO: 6158), KRKKNVLRL (SEQ ID NO: 6173), LQSLLQHLI (SEQ ID NO: 6146), LSHIHASSY (SEQ ID NO: 6152), PYLGQMINL (SEQ ID NO: 6120), QLLALLPSL (SEQ ID NO: 6093), SFYGNSISI (SEQ ID NO: 6174), SLLQHLIGL (SEQ ID NO: 6095), SPSVSQLSVL (SEQ ID NO: 6139), SPYLGQMINL (SEQ ID NO: 6138), TSPRRLVEL (SEQ ID NO: 6159), VLYPVPLESY (SEQ ID NO: 6154), VSPEPLQAL (SEQ ID NO: 6156), YLHARLREL (SEQ ID NO:6157) and RLDQLLRHV (SEQ ID NO:6104).

44. The composition of any one of claims 1-3 and 42, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence of SLLQHLIGL (SEQ ID NO: 6095).

45. The composition of claim 35, wherein the protein comprises MAGE4; and wherein the cancer comprises squamous cell lung cancer.

46. The composition of any one of claims 1-3 and 45, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of EVDPASNTY (SEQ ID NO: 4638), GVYDGREHTV (SEQ ID NO: 4653), KEVDPASNTY (SEQ ID NO: 4640), KVDELAHFL (SEQ ID NO: 4648), QIFPKTGL (SEQ ID NO: 4692), QSPQGASAL (SEQ ID NO: 4707), SALPTTISF (SEQ ID NO: 4699),, TVYGEPRKL (SEQ ID NO: 4722), VYGEPRKL (SEQ ID NO: 4727), YPSLREAAL (SEQ ID NO: 4689), ALLEEEEGV (SEQ ID NO: 4698) and KVLEHVVRV (SEQ ID NO: 4697).

47. The composition of any one of claims 1-3 and 45, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of EVDPASNTY (SEQ ID NO: 4638), GVYDGREHTV (SEQ ID NO: 4653), KVDELAHFL (SEQ ID NO: 4648) and KVLEHVVRV (SEQ ID NO: 4697).

48. The composition of any one of claims 3-47, wherein the target tissue is a non-essential tissue.

49. The composition of any one of claims 3-48, wherein each non-target tissue is an essential tissue.

50. The composition of any one of claims 1-49, wherein the tissue-specific antigen peptide is an isolated, purified, and/or synthetic peptide.

51. The composition of any one of claims 1-49, wherein the tissue-specific antigen peptide further comprises an accessory sequence flanking the epitope sequence.

52. The composition of any one of claims 1-51, wherein the polynucleotide comprises deoxyribonucleic acid (DNA).

53. The composition of any one of claims 1-52, wherein the polynucleotide comprises ribonucleic acid (RNA).

54. The composition of any one of claims 1-53, comprising a viral vector containing the polynucleotide.

55. The composition of claim 54, wherein the viral vector is an adenovirus viral vector, an adeno-associated virus (AAV) viral vector, a Herpes Simplex virus (HSV) viral vector, a Semliki Forest Virus (SFV) viral vector, a lentivirus viral vector, a retrovirus viral vector, a poxvirus viral vector, an alpha virus viral vector, a vaccinia virus viral vector, a hepatitis B virus (HBV) viral vector, a human papillomavirus viral vector, or a pseudotype thereof, or any combination thereof.

56. The composition of any one of claims 1-55, wherein the tissue-specific antigen peptide activates $CD8^+$ T cells, $CD4^+$ T cells, or both.

57. The composition of any one of claims 1-56, wherein the TCR is specific to the tissue-specific antigen peptide in a complex with a class I MHC protein or a class II MHC protein.

58. The composition of any one of claims 1-57, wherein the at least one antigen specific T cell expresses CD8 or CD4.

59. The composition of any one of claims 1-58, wherein the at least one antigen specific T cell comprise an exogenous polynucleotide encoding the TCR.

60. The composition of any one of claims 1-59, wherein the biological sample is from a subject with the cancer or a donor other than a subject with the cancer.

61. The composition of claim 60, wherein the donor has a natural immune response to the tissue-specific antigen peptide.

62. The composition of claim 60, wherein the cancer comprises prostate cancer, and wherein the donor is female.

63. The composition of any one of claims 1-62, wherein the protein is encoded by a tissue specific antigen epitope gene that has an mRNA expression level in each non-target tissue of a plurality of non-target tissues that are different than a target tissue of the tumor that is at most about 5 mRNA transcripts per one million total mRNA transcripts in each respective non-target tissue.

64. The composition of any one of claims 1-63, wherein the protein is encoded by a tissue specific antigen epitope gene that has an mRNA expression level in a target tissue that is at least about 100 mRNA transcripts per one million total mRNA transcripts in the target tissue.

65. A pharmaceutical composition comprising

(a) the composition of any one of claims 1-64, and

(b) a pharmaceutically acceptable carrier.

66. A method comprising identifying an epitope sequence, wherein the epitope sequence

(a) binds to or is predicted to bind to a protein encoded by a MHC allele expressed by a human subject, and

(b) is encoded by a tissue-specific antigen epitope gene that has an expression level in a tumor from a target tissue that is at least 2 fold greater than an expression level of the tissue-specific antigen epitope gene in each tissue of a plurality of non-target tissues that are different than the target tissue

67. A method of preparing T cells comprising a T cell receptor (TCR) specific to a complex of (i) a epitope sequence of a tissue specific antigen peptide of a protein and (ii) a protein encoded by an HLA allele of a human subject, the method comprising: incubating T cells in the presence of antigen presenting cells (APCs) comprising the epitope sequence, wherein the APCs express the protein encoded by an HLA allele of a human subject.

68. The method of claim 67, wherein the APCs comprise a polypeptide comprising the epitope sequence or a polynucleotide encoding a polypeptide comprising the epitope sequence.

69. The method of claim 67 or 68, wherein the APCs are APCs from a human subject.

70. The method of any one of claims 67-69, wherein the T cells are T cells from a human subject.

71. The method of any one of claims 67-70, wherein the method further comprises administering the T cells to a human subject in need thereof.

1~~72~~. Use of a composition in the manufacture of a medicament for treating a disease or a condition in ~~A method of treatment, comprising:~~

~~administering a composition to~~ a human subject in need thereof, wherein the composition comprises:

(a) a tissue-specific antigen peptide comprising an epitope sequence of a protein, wherein the epitope sequence is expressed by a diseased cell of a target tissue of the human subject~~the tumor~~;

(b) a polynucleotide encoding the tissue-specific antigen peptide;

(c) one or more antigen presenting cells (APCs) presenting the ~~tissue-specific antigen~~ epitope sequence;

(d) a T cell receptor (TCR) specific to a complex of (i) the epitope sequence and (ii) a protein encoded by an HLA allele of ~~a~~the human subject; or

(e) a population of immune cells from a biological sample comprising at least one antigen specific T cell comprising the TCR;

wherein the epitope sequence binds to or is predicted to bind to a protein encoded by an HLA allele expressed by the human subject, and wherein the ~~protein is encoded by a~~ tissue-specific antigen epitope gene ~~that~~ has an expression level in the diseased cell of a target tissue of the human subject ~~tumor~~ that is at least 2 fold more than an expression level of the tissue-specific antigen epitope gene in cells of each non-target tissue of the subject, wherein the tissue-specific antigen is specific to a non-essential tissue, and wherein the non-essential tissue is a tissue not required for survival of a human~~each tissue of a plurality of non-target tissues that are different than the target tissue~~.

2. The use of claim 1, wherein the human subject does not have the non-essential tissue or the function of the non-essential tissue is substituted.

3. The use of claim 1 or 2, wherein the human subject has the non-essential tissue.

4. The use of any one of claims 1-3, wherein the diseased cell is a tumor cell of the target tissue.

5. The use of any one of claims 1-4, wherein an mRNA expression level of a gene encoding the tissue-specific antigen peptide is at the most about 5 mRNA transcripts in a non-target essential tissue per one million total mRNA transcripts in each respective non-target tissue of the subject; and wherein an mRNA expression level of the gene encoding the tissue-specific antigen peptide is at least about 100 mRNA transcripts per one million total mRNA transcripts in the target tissue.

~~73. The method of claim 66, 67 or 72, wherein each tissue of the plurality of tissues is an essential tissue.~~

~~74. The method of any one of claims 66, 67, 72 and 73, wherein the plurality of tissues comprise skeletal muscle, coronary artery, heart, adipose, uterus, vagina, skin, salivary gland, brain, lung, esophagus, stomach, colon, small intestine, nerve, or any combination thereof.~~

~~75. The method of any one of claims 66, 67 and 72-74, wherein each non-target tissue of the plurality of non-target tissues is a non-essential tissue.~~

~~76. The method of any one of claims 66, 67 and 72-75, wherein the MHC allele is a class I MHC allele or a class II MHC allele.~~

~~77. A method of treating a cancer, comprising: administering the composition of any one of claims 1-64 to a subject in need thereof.~~

~~78. The method of any one of claims 66-77, wherein the cancer comprises adrenal gland cancer, breast cancer, cervical cancer, colorectal cancer, fallopian tube cancer, glioma, head and neck cancer, liver cancer, squamous cell lung cancer, melanoma, ovarian cancer, pancreatic cancer, prostate cancer, testicular cancer, thyroid cancer, uterine cancer, or any combination thereof.~~

~~79. The method of claim 67, 72 or 77, wherein the protein comprises KLK2, KLK3, KLK4, ANKRD30A, PRAME, MAGE4, or a combination thereof.~~

~~80. The method of claim 79, wherein the protein comprises KLK2, KLK3 or KLK4; and wherein the cancer comprises prostate cancer.~~

~~81. The method of any one of claims 67, 72, 77 and 80, wherein~~

~~(a) the epitope sequence is AYSEKVTEF (SEQ ID NO: 3534) and the human subject expresses a protein encoded by an HLA-C06:02 or HLA-A24:02 allele,~~

~~(b) the epitope sequence is GLWTGGKDTCGV (SEQ ID NO: 3468) and the human subject expresses a protein encoded by an HLA-A02:01 allele,~~

~~(c) the epitope sequence is HPEDTGQVF (SEQ ID NO: 3988) and the human subject expresses a protein encoded by an HLA-C*04:01 or HLA-C07:01 allele,~~

(d) the epitope sequence is HPEYNRPLL (SEQ ID NO: 4143) and the human subject expresses a protein encoded by an HLA-C*07:01 or HLA-B07:02 allele,

(e) the epitope sequence is QRVPVSHSF (SEQ ID NO: 3544) and the human subject expresses a protein encoded by an HLA-C*07:01, HLA-C*07:02 or HLA-A24:02 allele,

(f) the epitope sequence is SESDTIRSI (SEQ ID NO: 4176) and the human subject expresses a protein encoded by an HLA-B13:02 allele,

(g) the epitope sequence is SLFHPEDTGQV (SEQ ID NO: 3775) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(h) the epitope sequence is SLQCVSLHL (SEQ ID NO: 3456) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(i) the epitope sequence is VILLGRHSL (SEQ ID NO: 3891) and the human subject expresses a protein encoded by an HLA-B08:01 allele,

(j) the epitope sequence is VLVHPQWVL (SEQ ID NO: 3757) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(k) the epitope sequence is LFHPEDTGQVF (SEQ ID NO: 3827) and the human subject expresses a protein encoded by an HLA-A24:02 allele,

(l) the epitope sequence is RPRSLQCVSL (SEQ ID NO: 3578) and the human subject expresses a protein encoded by an HLA-B07:02 allele,

(m) the epitope sequence is GYLQGLVSF (SEQ ID NO: 4094) and the human subject expresses a protein encoded by an HLA-A24:02 allele,

(n) the epitope sequence is IRNKSVILL (SEQ ID NO: 3974) and the human subject expresses a protein encoded by an HLA-C*06:02, HLA-C*07:02 or HLA-C07:01 allele,

(o) the epitope sequence is KLQCVDLHV (SEQ ID NO: 3740) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(p) the epitope sequence is LLANGRMPTV (SEQ ID NO: 4029) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(q) the epitope sequence is LRPGDDSTL (SEQ ID NO: 3767) and the human subject expresses a protein encoded by an HLA-C07:02 allele,

(r) the epitope sequence is MPALPMVL (SEQ ID NO: 3874) and the human subject expresses a protein encoded by an HLA-B07:02 allele,

(s) the epitope sequence is NRPLLANDL (SEQ ID NO: 4216) and the human subject expresses a protein encoded by an HLA-C*06:02, HLA-C*07:02 or HLA-C01:02 allele,

(t) the epitope sequence is SLQCVSLHL (SEQ ID NO: 3456) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(u) the epitope sequence is TWIAPPLQV (SEQ ID NO: 3784) and the human subject expresses a protein encoded by an HLA-C*04:01 or HLA-A02:01 allele,

(v) the epitope sequence is VFQVSHSF (SEQ ID NO: 3828) and the human subject expresses a protein encoded by an HLA-C*07:02 or HLA-A24:02 allele, or

(w) the epitope sequence is YSEKVTEFML (SEQ ID NO: 3454) and the human subject expresses a protein encoded by an HLA-A01:01 allele.

82. The method of claim 79, wherein the protein comprises ANKRD30A; and wherein the cancer comprises breast cancer.

83. The method of any one of claims 72, 77 and 82, wherein

(a) the epitope sequence is LLSHGAVIEV (SEQ ID NO: 831) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(b) the epitope sequence is SQYSGQLKV (SEQ ID NO: 927) and the human subject expresses a protein encoded by an HLA-B13:02 allele,

(c) the epitope sequence is SVPNKALEL (SEQ ID NO: 941) and the human subject expresses a protein encoded by an HLA-C*04:01 or HLA-C01:02 allele,

(d) the epitope sequence is SLSKILDTV (SEQ ID NO: 826) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(e) the epitope sequence is SIPTKALEL (SEQ ID NO: 942) and the human subject expresses a protein encoded by an HLA-C*04:01 or HLA-C01:02 allele, or

(f) the epitope sequence is SLDQKLFQL (SEQ ID NO: 827) and the human subject expresses a protein encoded by an HLA-A02:01 allele.

84. The method of claim 79, wherein the protein comprises PRAME; and wherein the cancer comprises squamous cell lung cancer; melanoma; ovarian cancer, uterine cancer, or any combination thereof.

85. The method of any one of claims 72, 77 and 84, wherein

(a) the epitope sequence is DSLFFLRGR (SEQ ID NO: 6132) and the human subject expresses a protein encoded by an HLA-A33:03 allele,

(b) the epitope sequence is ELFSYLIEK (SEQ ID NO: 6108) and the human subject expresses a protein encoded by an HLA-A03:01 allele,

(c) the epitope sequence is FYDPEPILC (SEQ ID NO: 6166) and the human subject expresses a protein encoded by an HLA-C04:01 allele,

(d) the epitope sequence is ISISALQSL (SEQ ID NO: 6161) and the human subject expresses a protein encoded by an HLA-C03:04 allele,

(e) the epitope sequence is ITDDQLLAL (SEQ ID NO: 6158) and the human subject expresses a protein encoded by an HLA-A01:01 allele,

(f) the epitope sequence is KRKKNVLRL (SEQ ID NO: 6173) and the human subject expresses a protein encoded by an HLA-C07:01 allele,

(g) the epitope sequence is LQSLLQHLI (SEQ ID NO: 6146) and the human subject expresses a protein encoded by an HLA-B13:02 allele,

(h) the epitope sequence is LSHIHASSY (SEQ ID NO: 6152) and the human subject expresses a protein encoded by an HLA-B46:01 allele,

(i) the epitope sequence is PYLGQMINL (SEQ ID NO: 6120) and the human subject expresses a protein encoded by an HLA-A24:02 allele,

(j) the epitope sequence is QLLALLPSL (SEQ ID NO: 6093) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(k) the epitope sequence is SFYGNSISI (SEQ ID NO: 6174) and the human subject expresses a protein encoded by an HLA-C07:01 allele,

(l) the epitope sequence is SLLQHLIGL (SEQ ID NO: 6095) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(m) the epitope sequence is SPSVSQLSVL (SEQ ID NO: 6139) and the human subject expresses a protein encoded by an HLA-B07:02 allele,

(n) the epitope sequence is SPYLGQMINL (SEQ ID NO: 6138) and the human subject expresses a protein encoded by an HLA-B07:02 allele,

(o) the epitope sequence is TSPRRLVEL (SEQ ID NO: 6159) and the human subject expresses a protein encoded by an HLA-C01:02 allele,

(p) the epitope sequence is VLYPVPLESY (SEQ ID NO: 6154) and the human subject expresses a protein encoded by an HLA-A03:01 allele,

(q) the epitope sequence is VSPEPLQAL (SEQ ID NO: 6156) and the human subject expresses a protein encoded by an HLA-C01:02 allele,

(r) the epitope sequence is YLHARLREL (SEQ ID NO:6157) and the human subject expresses a protein encoded by an HLA-B08:01 allele, or

(s) the epitope sequence is RLDQLLRHV (SEQ ID NO:6104) and the human subject expresses a protein encoded by an HLA-A02:01 allele.

86. The method of claim 79, wherein the protein comprises MAGE4; and wherein the cancer comprises squamous cell lung cancer.

87. The method of any one of claims 72, 77 and 86, wherein

(a) the epitope sequence is EVDPASNTY (SEQ ID NO: 4638) and the human subject expresses a protein encoded by an HLA-A01:01 allele,

(b) the epitope sequence is GVYDGREHTV (SEQ ID NO: 4653) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(c) the epitope sequence is KEVDPASNTY (SEQ ID NO: 4640) and the human subject expresses a protein encoded by an HLA-A01:01 allele,

(d) the epitope sequence is KVDELAHFL (SEQ ID NO: 4648) and the human subject expresses a protein encoded by an HLA-A02:01 allele,

(e) the epitope sequence is QIFPKTGL (SEQ ID NO: 4692) and the human subject expresses a protein encoded by an HLA-B08:01 allele,

(f) the epitope sequence is QSPQGASAL (SEQ ID NO: 4707) and the human subject expresses a protein encoded by an HLA-C01:02 allele,

(g) the epitope sequence is SALPTTISF (SEQ ID NO: 4699) and the human subject expresses a protein encoded by an HLA-B46:01 allele,

(h) the epitope sequence is TVYGEPRKL (SEQ ID NO: 4722) and the human subject expresses a protein encoded by an HLA-C07:01 allele,

(i) the epitope sequence is VYGEPRKL (SEQ ID NO: 4727) and the human subject expresses a protein encoded by an HLA-C07:02 allele,

(j) the epitope sequence is YPSLREAAL (SEQ ID NO: 4689) and the human subject expresses a protein encoded by an HLA-B07:02 allele,

(k) the epitope sequence is ALLEEEEGV (SEQ ID NO: 4698) and the human subject expresses a protein encoded by an HLA-A02:01 allele, or

(l) the epitope sequence is KVLEHVVRV (SEQ ID NO: 4697) and the human subject expresses a protein encoded by an HLA-A02:01 allele.

88. A method comprising (a) contacting a T cell with an antigen peptide in complex with an HLA of an APC; and (b) determining a sequence of a TCR of the T cell that recognizes the antigen peptide in complex with the HLA, wherein the T cell is suspected to have zero or reduced immune tolerance to a tissue of origin of the antigen peptide.

689. The method use of any one of claims 1-5 88, wherein

(i) the human subject the T cell is from a female subject, and the tissue-specific antigen peptide is specific to a non-essential tissue selected from the group consisting of: Bulbourethral gland, epididymis, penis, prostate, scrotum, seminal vesicle, testicle, and any combination thereof;

(ii) the human subject is a male subject, and the tissue-specific antigen is specific to a non-essential tissue selected from the group consisting of: Bartholin's gland, fallopian tube, ovary, Skene's gland, uterus, cervix, vagina, and any combination thereof;

(iii) the human subject is a Type I diabetes patient, and the tissue-specific antigen is specific to pancreas; or

(iv) the human subject has auto-immune thyroid condition, and the tissue-specific antigen is specific to thyroid.

790. The usemethod of any one of claims 1-6 88, wherein the human subject T cell is from a female subject, and the tissue-specific antigen peptide is specific to prostate.

8. The use of any one of claims 1-7, wherein the tissue-specific antigen peptide of (a) is an isolated, purified, and/or synthetic peptide; and wherein the tissue-specific antigen peptide further comprises an accessory sequence flanking the epitope sequence.

9. The use of any one of claims 1-8, wherein the polynucleotide encoding the tissue-specific antigen peptide of (b) is an mRNA.

10. The use of any one of claims 1-9, wherein the at least one antigen specific T cell comprises an exogenous sequence encoding the TCR.

11. The use of any one of claims 1-10, wherein the tissue-specific antigen peptide comprising the epitope sequence of the polypeptide is encoded by the gene selected from the group consisting of *ANKRD30A*, *COL10A1*, *CTCFL*, *PPIAL4G*, *POTEE*, *DLL3*, *MMP13*, *SSX1*, *DCAF4L2*, *MAGEA4*, *MAGEA11*, *MAGEC2*, *MAGEA12*, *PRAME*, *CLDN6*, *EPYC*, *KLK3*, *KLK2*, *KLK4*, *TGM4*, *POTEG*, *RLN1*, *POTEH*, *SLC45A2*, *TSPAN10*, *PAGE5*, *CSAG1*, *PRDM7*, *TG*, *TSHR*, *RSPH6A*, *SCXB*, *HIST1H4K*, *ALPPL2*, *PRM2*, *PRM1*, *TNP1*, *LELP1*, *HMGB4*, *AKAP4*, *CETN1*, *UBQLN3*, *ACTL7A*, *ACTL9*, *ACTRT2*, *PGK2*, *C2orf53*, *KIF2B*, *ADAD1*, *SPATA8*, *CCDC70*, *TPD52L3*, *ACTL7B*, *DMRTB1*, *SYCN*, *CELA2A*, *CELA2B*, *PNLIPRP1*, *CTRC*, *AMY2A*, *SERPINI2*, *RBPJL*, *AQP12A*, *IAPP*, *KIRREL2*, *G6PC2*, *AQP12B*, *CYP11B1*, *CYP11B2*, *STAR*, *CYP11A1*, and *MC2R*; or

wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs 1-8962.

12. The use of any one of claims 1-11, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs: 3441-4274, 5285-6084, 6580-6845, and 8100-8434.

13. The use of any one of claims 1-12, wherein the protein comprising the tissue-specific antigen peptide comprising the epitope sequence is KLK2, KLK3 or KLK4, and wherein the non-essential tissue is prostate.

14. The use of any one of claims 1-13, wherein the protein comprising the tissue-specific antigen peptide comprising the epitope sequence is KLK2, and wherein the non-essential tissue is prostate.

15. The use of any one of claims 1-14, wherein the epitope sequence has from 70% to 100% sequence identity to a peptide sequence selected from the group consisting of SEQ ID NOs: 3441-3721, 3723, 3729, 3736, 3744, 3752, 3757, 3778, 3794, 3804, 3811, 3813, 3816, 3822, 3824, 3829, 3831, 3833, 3835, 3844, 3850, 3854, 3854, 3869, 3879, 3905, 3916, 3923, 3928, 3944, 3959, 3961, 3972, 3975, 3993, 3998, 3999, and 4001.

16. The use of any one of claims 1-15, wherein the epitope sequence is selected from the group consisting of AYSEKVTEF (SEQ ID NO: 3534), GLWTGGKDTCGV (SEQ ID NO: 3468), QRVPVSHSF (SEQ ID NO: 3544), SLQCVSLHL (SEQ ID NO: 3456), VILLGRHSL (SEQ ID NO: 3891), RPRSLQCVSL (SEQ ID NO: 3578), SLQCVSLHL (SEQ ID NO: 3456), and YSEKVTEFML (SEQ ID NO: 3454).

17. The use of any one of claims 1-16, wherein the TCR is specific to a complex of:

1) the epitope sequence is AYSEKVTEF (SEQ ID NO: 3534) and the human subject expresses a protein encoded by an HLA-C06:02 or HLA-A24:02 allele,
2) the epitope sequence is GLWTGGKDTCGV (SEQ ID NO: 3468) and the human subject expresses a protein encoded by an HLA-A02:01 allele,
3) the epitope sequence is QRVPVSHSF (SEQ ID NO: 3544) and the human subject expresses a protein encoded by an HLA-C*07:01, HLA-C*07:02 or HLA-A24:02 allele,
4) the epitope sequence is SLQCVSLHL (SEQ ID NO: 3456) and the human subject expresses a protein encoded by an HLA-A02:01 allele,
5) the epitope sequence is RPRSLQCVSL (SEQ ID NO: 3578) and the human subject expresses a protein encoded by an HLA-B07:02 allele,
6) the epitope sequence is SLQCVSLHL (SEQ ID NO: 3456) and the human subject expresses a protein encoded by an HLA-A02:01 allele, or
7) the epitope sequence is YSEKVTEFML (SEQ ID NO: 3454) and the human subject expresses a protein encoded by an HLA-A01:01 allele.

18. The use of claim 17, wherein the antigen specific T cell comprises the TCR of any one of 1) – 7).

19. A method of preparing T cells comprising a T cell receptor (TCR) specific to a complex of (i) an epitope sequence of a tissue specific antigen peptide and (ii) a protein encoded by an HLA allele of a human subject, the method comprising:

(a) contacting a T cell *ex vivo* with an antigen peptide in complex with an HLA of an APC, wherein the T cell has reduced on no tolerance for the antigenic peptide,

(b) determining a sequence of a TCR of the T cell that recognizes the antigen peptide in complex with the HLA, wherein the T cell has reduced or no immune tolerance to a tissue of origin of the antigen peptide;

(c) (i) expanding the T cell in presence of the antigen peptide in complex with the HLA, or (ii) expressing a recombinant polynucleic acid encoding the sequence of the TCR in isolated T cells;

thereby preparing the T cells comprising the TCR; and

wherein the T cell is from a subject, wherein the tissue-specific antigen is specific to a non-essential tissue, and wherein the non-essential tissue is a tissue not required for survival of a human.

20. A composition comprising:

(a) a tissue-specific antigen peptide comprising an epitope sequence of a polypeptide encoded by a gene selected from the group consisting of KLK2, KLK3 and KLK4;

(b) a polynucleotide encoding the tissue-specific antigen peptide;

(c) one or more antigen presenting cells (APCs) presenting the epitope sequence;

(d) a T cell receptor (TCR) or an antibody, or a functional part thereof that is specific to a complex of (i) the epitope sequence and (ii) a protein encoded by an HLA allele; or

(e) a population of immune cells from a biological sample comprising at least one antigen specific T cell comprising the TCR.

~~91. The method of claim 88, wherein the T cell is from a male subject, and the antigen peptide is specific to a tissue selected from the group consisting of: Bartholin's gland, fallopian tube, ovary, Skene's gland, uterus, cervix, vagina, and any combination thereof.~~

~~92. The method of claim 88, wherein the T cell is from a male subject, and the antigen peptide is specific to ovary.~~

~~93. The method of claim 88, wherein the T cell is from a Type I diabetes patient, and the antigen peptide is specific to pancreas.~~

~~94. The method of claim 88, wherein the T cell is from a subject that has auto-immune thyroid condition, and the antigen peptide is specific to thyroid.~~