CLAIMS

WHAT IS CLAIMED IS:

1. Use of a composition in the manufacture of a medicament for treating a disease or a condition in 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;

   (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) specific to a complex of (i) the epitope sequence and (ii) a protein encoded by an HLA allele of 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 tissue-specific antigen epitope gene has an expression level in the diseased cell of a target tissue of the human subject 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.

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.

6. The use of any one of claims 1-5, wherein

   (i) the human subject is a female subject, and the tissue-specific antigen 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.

7. The use of any one of claims 1-6, wherein the human subject is a female subject, and the tissue-specific antigen 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.