CLAIMS

1. A T cell receptor (TCR) capable of binding to a PRAME peptide having the amino acid sequence SLLQHLIGL (SEQ ID NO: 1) or a portion thereof, or its HLA-A2 bound form, wherein the TCR comprises:
   a) a CDR3 of the TCR alpha chain variable region comprising or consisting of the amino acid sequence of (SEQ ID NO: 6), or an amino acid sequence having at least 95 % identity to SEQ ID NO: 6, a CDR1 of the TCR alpha chain variable region comprising or consisting of the amino acid sequence of SEQ ID NO: 2, and a CDR2 of the TCR alpha chain variable region comprising or consisting of the amino acid sequence of SEQ ID NO: 4, and
   b) a CDR3 of the TCR beta chain variable region comprising or consisting of the amino acid sequence of (SEQ ID NO: 7), or an amino acid sequence having at least 95 % identity to SEQ ID NO: 7, a CDR1 of the TCR beta chain variable region comprising or consisting of the amino acid sequence of SEQ ID NO: 3, and a CDR2 of the TCR beta chain variable region comprising or consisting of the amino acid sequence of SEQ ID NO: 5.

2. The TCR according to claim 1, wherein the HLA-A2 is a HLA-A*02:01, HLA-A*02:02 or HLA-A*02:04 encoded molecule.

3. The TCR according to claim 1 or 2, wherein binding to sequence SLLQHLIGL (SEQ ID NO: 1) or a portion thereof, or its HLA-A2 bound form induces IFN-gamma secretion by cells transduced or transfected with the TCR.

4. The TCR according to any one of claims 1 to 3, wherein the half-maximal IFN-gamma secretion is less than 1 M, as measured by an IFN-gamma immunoassay.

5. The TCR according to any of the preceding claims, wherein the TCR comprises:
   a) a TCR alpha chain comprising a CDR1 having the amino acid sequence of SEQ ID NO: 2, a CDR2 having the amino acid sequence of SEQ ID NO: 4 and a CDR3 having the amino acid sequence of SEQ ID NO: 6, and
   b) a TCR beta chain comprising a CDR1 having the amino acid sequence of SEQ ID NO: 3, a CDR2 having the amino acid sequence of SEQ ID NO: 5 and a CDR3 having the amino acid sequence of SEQ ID NO: 7.

6. The TCR according to any of the preceding claims, comprising

a) a TCR alpha chain variable region comprising or consisting of the amino acid sequence of SEQ ID NO: 8, and
b) a TCR beta chain variable region comprising or consisting of the amino acid sequence of SEQ ID NO: 9.

7. The TCR according to any of the preceding claims, comprising
a) a TCR alpha chain comprising or consisting of an amino acid sequence selected from SEQ ID NO: 10; or an amino acid sequence having at least 80 % identity, preferably at least 85 % identity, more preferably 90 % or 95 % to SEQ ID NO: 10; and
b) a TCR beta chain comprising or consisting of an amino acid sequence selected from of SEQ ID NO: 11, or an amino acid sequence having at least 80 % identity, preferably at least 85 % identity, more preferably 90 % or 95 % to SEQ ID NO: 11.

8. The TCR according to any of the preceding claims, comprising at least one TCR alpha chain(s) and at least one TCR beta chain(s) covalently linked to each other to form TCR heterodimers or multimers.

9. The TCR according to any one of the preceding claims, said TCR being selected from a native TCR, a TCR variant, a TCR fragment, or a TCR construct.

10. The TCR according to any of the preceding claims, further comprising one or more fusion component(s) optionally selected from Fe receptors; Fe domains, including lgA, lgD, lgG, lgE, and lgM; cytokines, including IL-2 or IL-15; toxins; antibodies or antigen-binding fragments thereof, including anti-CD3, anti-CD28, anti-CDS, anti-CD16 or anti-CD56 antibodies or antigen-binding fragments thereof; CD247 (CD3-zeta), CD28, CD137, CD134 domain, or combinations thereof, optionally further comprising at least one linker.

11. The TCR according to any one of the preceding claims, comprising
a) at least one TCR alpha chain as defined in any one of claims 1 to 10; and/or
b) at least one TCR beta chain as defined in any one of claims 1 to 10; and/or
c) an antibody or a single chain antibody fragment (scFv) which is directed against an antigen or epitope on the surface of lymphocytes,

wherein the TCR alpha chain(s) and TCR beta chain(s) are linked to each other and fused, optionally via a linker, to said antibody or scFv.

12. The TCR according to claim 11, wherein said antigen is selected from CD3, CD28, CD5, CD16 or CD56.

13. The TCR according to any one of the preceding claims, further comprising at least one molecular marker.

14. The TCR according to any one of the preceding claims which is soluble.

15. A nucleic acid encoding the TCR according to any one of the preceding claims.

16. The nucleic acid according to claim 15, comprising the nucleic acid sequence of SEQ ID NO: 13, 14, 15, 16, 17, 18, 19, 20, 21, or 22.

17. A vector comprising the nucleic acid according to claim 15 or 16.

18. A host cell comprising the TCR according to any one of claims 1 to 14, the nucleic acid sequence according to claim 15 or 16 or the vector according to claim 17.

19. The host cell according to claim 18, which is selected from lymphocytes including but not limited to cytotoxic T lymphocytes (CTLs), CD8+ T cells, CD4+ T cells, natural killer (NK) cells, natural killer T (NKT) cells, gamma/ delta-T cells.

20. A method for obtaining a TCR according to any of the preceding claims, comprising
    a) incubating a host cell according to claim 18 or 19 under conditions causing expression of said TCR,
    b) purifying said TCR.

21. A pharmaceutical or diagnostic composition comprising one or more of:
    a) the TCR according to any one of claims 1 to 14;
    b) the nucleic acid according to claim 15 or 16;
    c) the vector according to claim 17; and/or
    d) the host cell according to claim 18 or 19,

    and, optionally, pharmaceutically excipient(s); wherein the host cell is a cytotoxic T lymphocyte (CTL), CD8+ T cell, CD4+ T cell, natural killer (NK) cell, natural killer T (NKT) cell, or gamma/delta-T cell.

22. The pharmaceutical composition according to claim 21, further comprising a checkpoint inhibitor.

23. The pharmaceutical composition according to claim 22, wherein said checkpoint inhibitor is selected from the group consisting of a CTLA-4 inhibitor, a PD-1 inhibitor and a PD-L1 inhibitor.

24. The TCR according to any one of claims 1 to 14, the nucleic acid according to claim 15 or 16, the vector according to claim 17 and/or the host cell according to claim 18 or 19 for use as a medicament; wherein the host cell is a cytotoxic T lymphocyte (CTL), CD8+ T cell, CD4+ T cell, natural killer (NK) cell, natural killer T (NKT) cell, or gamma/delta-T cell.

25. Use of the TCR according to any one of claims 1 to 14, the nucleic acid according to claim 15 or 16, the vector according to claim 17 and/or the host cell according to claim 18 or 19 in the manufacture of a medicament for the detection, diagnosis, prognosis, and/or treatment of cancer; wherein the host cell is a cytotoxic T lymphocyte (CTL), CD8+ T cell, CD4+ T cell, natural killer (NK) cell, natural killer T (NKT) cell, or gamma/delta-T cell.

26. The use of claim 25, wherein the cancer is preferably selected from the group consisting of melanoma, bladder carcinoma, colon carcinoma, and breast adenocarcinoma, sarcoma, prostate cancer, uterine cancer, uveal cancer, uveal melanoma, squamous head and neck cancer, synovial carcinoma, Ewing's sarcoma, triple negative breast cancer, thyroid cancer, testicular cancer, renal cancer, pancreatic cancer, ovarian cancer, esophageal cancer, non-small-cell lung cancer, non-Hodgkin's lymphoma, multiple myeloma, melanoma, hepatocellular carcinoma, head and neck cancer, gastric cancer, endometrial cancer, colorectal cancer, cholangiocarcinoma, breast cancer, bladder cancer, myeloid leukemia and acute lymphoblastic leukemia, preferably wherein the cancer is selected from the group consisting of NSCLC, SCLC, breast, ovarian or colorectal cancer, sarcoma or osteosarcoma.

27. The use of claim 25, wherein treatment of cancer comprises:
    a) providing one or more of
        (i) the TCR according to any one of claims 1 to 14;
        (ii) the nucleic acid according to claim 15 or 16;
        (iii) the vector according to claim 17;

(iv) the host cell according to claim 18 or 19; and

(v) the pharmaceutical composition according to any one of claims 21 to 23; and

b) wherein at least one of (i) to (v) is to be administered to a subject in need thereof.

28. The use of any one of claims 25 to 27, wherein treatment of cancer comprises:

a) providing a sample of a subject, said sample comprising lymphocytes;

b) providing one or more of

(i) the TCR according to any one of claims 1 to 14;

(ii) the nucleic acid according to claim 15 or 16;

(iii) the vector according to claim 17;

(iv) the host cell according to claim 18 or 19; and

(v) the pharmaceutical composition according to any one of claims 21 to 23;

c) introducing one or more of (i) to (v) of step (b) into the lymphocytes of step (a) and, thereby, obtaining modified lymphocytes,

d) wherein the modified lymphocytes of step (c) are to be administered to a subject or patient in need thereof.

29. A method of detecting the presence of a cancer in a subject in vitro, comprising:

a) providing a sample of a subject, said sample comprising one or more cells;

b) contacting said sample with

(i) the TCR according to any one of claims 1 to 14;

(ii) the host cell according to claim 18 or 19; and/or

(iii) the pharmaceutical composition according to claim 21;

thereby forming a complex, and

c) detecting the complex,

wherein detection of the complex is indicative of the presence of the cancer in the subject; wherein the host cell is a cytotoxic T lymphocyte (CTL), CD8+ T cell, CD4+ T cell, natural killer (NK) cell, natural killer T (NKT) cell, or gamma/delta-T cell.

30. Use of a TCR according to any one of claims 1 to 14, a nucleic acid according to claim 15 or 16 and/or a vector according to claim 17 for generating modified lymphocytes, wherein the use is in vitro or ex vivo.

31. The TCR according to claim 1, wherein the CDR3 of the TCR alpha chain variable region comprises or consists of the amino acid sequence of (SEQ ID NO: 6), and wherein the CDR3 of the TCR beta chain variable region comprises or consists of the

amino acid sequence of (SEQ ID NO: 7).

32. The TCR according to claim 31, comprising

a) a TCR alpha chain comprising or consisting of an amino acid sequence selected from SEQ ID NO: 10; or an amino acid sequence having at least 80 % identity, preferably at least 85 % identity, more preferably 90 % or 95 % to SEQ ID NO: 10; and

b) a TCR beta chain comprising or consisting of an amino acid sequence selected from of SEQ ID NO: 11, or an amino acid sequence having at least 80 % identity, preferably at least 85 % identity, more preferably 90 % or 95 % to SEQ ID NO: 11.

33. The TCR according to claim 1, comprising:

a) a TCR alpha chain comprising or consisting of the amino acid sequence of SEQ ID NO: 10; and

b) a TCR beta chain comprising or consisting of the amino acid sequence of SEQ ID NO: 11.