(iv) an amino acid sequence comprising Homeobox B13 (HOXB13), an immunogenic variant thereof, or an immunogenic fragment of the HOXB13 or the immunogenic variant thereof; and

(v) an amino acid sequence comprising NK3 Homeobox 1 (NKX3-1), an immunogenic variant thereof, or an immunogenic fragment of the NKX3-1 or the immunogenic variant thereof, wherein the immunogenic fragment or the immunogenic variant is immunologically equivalent to KLK2, PSA, PAP, HOXB13 or NKX3-1, respectively.

In another aspect, the present disclosure provides the composition or medical preparation as described herein for use as a pharmaceutical. In yet another aspect, the present disclosure provides a use of the composition or medical preparation as described herein in the manufacture of a medicament for treating or preventing prostate cancer.

In a further aspect, the present disclosure provides a use of at least one RNA in the manufacture of a medicament for treating prostate cancer in a subject, wherein the at least one RNA encodes the following amino acid sequences:

(i) an amino acid sequence comprising Kallikrein-2 (KLK2), an immunogenic variant thereof, or an immunogenic fragment of the KLK2 or the immunogenic variant thereof;

(ii) an amino acid sequence comprising Prostate Specific Antigen (PSA), an immunogenic variant thereof, or an immunogenic fragment of the PSA or the immunogenic variant thereof;

(iii) an amino acid sequence comprising Prostatic Acid Phosphatase (PAP), an immunogenic variant thereof, or an immunogenic fragment of the PAP or the immunogenic variant thereof;

(iv) an amino acid sequence comprising Homeobox B13 (HOXB13), an immunogenic variant thereof, or an immunogenic fragment of the HOXB13 or the immunogenic variant thereof; and

(v) an amino acid sequence comprising NK3 Homeobox 1 (NKX3-1), an immunogenic variant thereof, or an immunogenic fragment of the NKX3-1 or the immunogenic variant thereof,

wherein the immunogenic fragment or the immunogenic variant is immunologically equivalent to KLK2, PSA, PAP, HOXB13 or NKX3-1, respectively.

Claims

1. A composition or medical preparation comprising at least one RNA, wherein the at least one RNA encodes the following amino acid sequences:
(i) an amino acid sequence comprising Kallikrein-2 (KLK2), an immunogenic variant thereof, or an immunogenic fragment of the KLK2 or the immunogenic variant thereof;
(ii) an amino acid sequence comprising Prostate Specific Antigen (PSA), an immunogenic variant thereof, or an immunogenic fragment of the PSA or the immunogenic variant thereof;
(iii) an amino acid sequence comprising Prostatic Acid Phosphatase (PAP), an immunogenic variant thereof, or an immunogenic fragment of the PAP or the immunogenic variant thereof;
(iv) an amino acid sequence comprising Homeobox B13 (HOXB13), an immunogenic variant thereof, or an immunogenic fragment of the HOXB13 or the immunogenic variant thereof; and
(v) an amino acid sequence comprising NK3 Homeobox 1 (NKX3-1), an immunogenic variant thereof, or an immunogenic fragment of the NKX3-1 or the immunogenic variant thereof, wherein the immunogenic fragment or the immunogenic variant is immunologically equivalent to KLK2, PSA, PAP, HOXB13 or NKX3-1, respectively.

2. The composition or medical preparation of claim 1, wherein each of the amino acid sequences under (i), (ii), (iii), (iv), or (v) is encoded by a separate RNA.

3. The composition or medical preparation of claim 1 or 2, wherein

the RNA encoding the amino acid sequence under (i) comprises the nucleotide sequence of SEQ ID NO: 3 or 4, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 3 or 4; and/or

the amino acid sequence under (i) comprises the amino acid sequence of SEQ ID NO: 1 or 2, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 1 or 2; and/or

the RNA encoding the amino acid sequence under (ii) comprises the nucleotide sequence of SEQ ID NO: 7 or 8, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 7 or 8; and/or

the amino acid sequence under (ii) comprises the amino acid sequence of SEQ ID NO: 5 or 6, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 5 or 6; and/or

the RNA encoding the amino acid sequence under (iii) comprises the nucleotide sequence of SEQ ID NO: 11 or 12, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 11 or 12; and/or

the amino acid sequence under (iii) comprises the amino acid sequence of SEQ ID NO: 9 or 10, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 9 or 10; and/or

the RNA encoding the amino acid sequence under (iv) comprises the nucleotide sequence of SEQ ID NO: 15 or 16, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 15 or 16; and/or

the amino acid sequence under (iv) comprises the amino acid sequence of SEQ ID NO: 13 or 14, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 13 or 14; and/or

the RNA encoding the amino acid sequence under (v) comprises the nucleotide sequence of SEQ ID NO: 19 or 20, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 19 or 20; and/or

the amino acid sequence under (v) comprises the amino acid sequence of SEQ ID NO: 17 or 18, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 17 or 18.

4. The composition or medical preparation of any one of claims 1 to 3, wherein at least one or each of the amino acid sequences under (i), (ii), (iii), (iv), or (v) is encoded by a coding sequence which is codon-optimized and/or the G/C content of which is increased compared to wild type coding sequence, wherein the codon-optimization and/or the increase in the G/C content preferably does not change the sequence of the encoded amino acid sequence.

5. The composition or medical preparation of any one of claims 1 to 4, wherein at least one or each RNA comprises the 5' cap $m_2^{7,2'\text{-}O}Gpp_sp(5')G$.

6. The composition or medical preparation of any one of claims 1 to 5, wherein at least one or each RNA comprises a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 21, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 21.

7. The composition or medical preparation of any one of claims 1 to 6, wherein at least one or each amino acid sequence under (i), (ii), (iii), (iv), or (v) comprises an amino acid sequence enhancing antigen processing and/or presentation,

wherein, preferably the amino acid sequence enhancing antigen processing and/or presentation comprises an amino acid sequence corresponding to the transmembrane and cytoplasmic domain of a MHC molecule, preferably a MHC class I molecule,

wherein, more preferably, the RNA encoding the amino acid sequence enhancing antigen processing and/or presentation comprises the nucleotide sequence of SEQ ID NO: 25, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 25; and/or

wherein, more preferably, the amino acid sequence enhancing antigen processing and/or presentation comprises the amino acid sequence of SEQ ID NO: 24, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 24.

8. The composition or medical preparation of any one of claims 1 to 7, wherein at least one or each amino acid sequence under (i), (ii), (iii), (iv), or (v) comprises an amino acid sequence which breaks immunological tolerance,

wherein, preferably, the amino acid sequence which breaks immunological tolerance comprises helper epitopes, preferably tetanus toxoid-derived helper epitopes; and/or.

wherein the RNA encoding the amino acid sequence which breaks immunological tolerance, preferably, comprises the nucleotide sequence of SEQ ID NO: 27, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 27; and/or

wherein the amino acid sequence which breaks immunological tolerance, preferably, comprises the amino acid sequence of SEQ ID NO: 26, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 26.

9. The composition or medical preparation of any one of claims 1 to 8, wherein at least one or each RNA comprises a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 28, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 28.

10. The composition or medical preparation of any one of claims 1 to 9, wherein at least one or each RNA comprises a poly-A sequence,

wherein the poly-A sequence, preferably, comprises at least 100 nucleotides; and/or

wherein the poly-A sequence comprises or consists of the nucleotide sequence of SEQ ID NO: 29.

11. The composition or medical preparation of any one of claims 1 to 10, wherein the RNA is formulated as a liquid, formulated as a solid, or a combination thereof; or

wherein the RNA is formulated for injection; or

wherein the RNA is formulated for intravenous administration; or

wherein the RNA is formulated or is to be formulated as lipoplex particles; or

wherein the RNA is formulated or is to be formulated as lipoplex particles which are obtainable by mixing the RNA with liposomes.

12. The composition or medical preparation of any one of claims 1 to 11, wherein the composition or medical preparation is

(i) a pharmaceutical composition; or

(ii) a kit.

13. The composition or medical preparation of claim 12, wherein the kit comprises the RNAs in separate vials or wherein the kit comprises the RNAs and liposomes in separate vials; and/or

wherein the kit further comprises instructions for use of the RNAs and optionally the liposomes for treating or preventing prostate cancer.

14. The composition or medical preparation of any one of claims 1 to 13 for use as a pharmaceutical.

15. Use of the composition or medical preparation of any one of claims 1 to 13 in the manufacture of a medicament for treating or preventing prostate cancer.

16. The composition or medical preparation of any one of claims 1 to 13, which is for administration to a human.

17. The use according to claim 15, wherein a further therapy is to be administered,

wherein, preferably, the further therapy comprises one or more selected from the group consisting of: (i) surgery to excise, resect, or debulk a tumor, (ii) radiotherapy, and (iii) chemotherapy; and/or

wherein, preferably, the further therapy comprises that a further therapeutic agent is to be administered,

wherein, more preferably, the further therapeutic agent comprises an anti-cancer therapeutic agent and/or a checkpoint modulator.

18. The use of claim 17 wherein the checkpoint modulator is an anti-PD1 antibody, an anti-CTLA-4 antibody, or a combination of an anti-PD1 antibody and an anti-CTLA-4 antibody.

19. Use of at least one RNA in the manufacture of a medicament for treating prostate cancer in a subject, wherein the at least one RNA encodes the following amino acid sequences:
(i) an amino acid sequence comprising Kallikrein-2 (KLK2), an immunogenic variant thereof, or an immunogenic fragment of the KLK2 or the immunogenic variant thereof;
(ii) an amino acid sequence comprising Prostate Specific Antigen (PSA), an immunogenic variant thereof, or an immunogenic fragment of the PSA or the immunogenic variant thereof;
(iii) an amino acid sequence comprising Prostatic Acid Phosphatase (PAP), an immunogenic variant thereof, or an immunogenic fragment of the PAP or the immunogenic variant thereof;

(iv) an amino acid sequence comprising Homeobox B13 (HOXB13), an immunogenic variant thereof, or an immunogenic fragment of the HOXB13 or the immunogenic variant thereof; and

(v) an amino acid sequence comprising NK3 Homeobox 1 (NKX3-1), an immunogenic variant thereof, or an immunogenic fragment of the NKX3-1 or the immunogenic variant thereof, wherein the immunogenic fragment or the immunogenic variant is immunologically equivalent to KLK2, PSA, PAP, HOXB13 or NKX3-1, respectively.

20. The use of claim 19, wherein each of the amino acid sequences under (i), (ii), (iii), (iv), or (v) is encoded by a separate RNA.

21. The use of claim 19 or 20, wherein

the RNA encoding the amino acid sequence under (i) comprises the nucleotide sequence of SEQ ID NO: 3 or 4, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 3 or 4; and/or

the amino acid sequence under (i) comprises the amino acid sequence of SEQ ID NO: 1 or 2, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 1 or 2; and/or

the RNA encoding the amino acid sequence under (ii) comprises the nucleotide sequence of SEQ ID NO: 7 or 8, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 7 or 8; and/or

the amino acid sequence under (ii) comprises the amino acid sequence of SEQ ID NO: 5 or 6, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 5 or 6; and/or

the RNA encoding the amino acid sequence under (iii) comprises the nucleotide sequence of SEQ ID NO: 11 or 12, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 11 or 12; and/or

the amino acid sequence under (iii) comprises the amino acid sequence of SEQ ID NO: 9 or 10, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 9 or 10; and/or

the RNA encoding the amino acid sequence under (iv) comprises the nucleotide sequence of SEQ ID NO: 15 or 16, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 15 or 16; and/or

the amino acid sequence under (iv) comprises the amino acid sequence of SEQ ID NO: 13 or 14, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 13 or 14; and/or

the RNA encoding the amino acid sequence under (v) comprises the nucleotide sequence of SEQ ID NO: 19 or 20, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 19 or 20; and/or

the amino acid sequence under (v) comprises the amino acid sequence of SEQ ID NO: 17 or 18, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 17 or 18.

22. The use of any one of claims 19 to 21, wherein at least one or each of the amino acid sequences under (i), (ii), (iii), (iv), or (v) is encoded by a coding sequence which is codon-optimized and/or the G/C content of which is increased compared to wild type coding sequence, wherein the codon-optimization and/or the increase in the G/C content preferably does not change the sequence of the encoded amino acid sequence.

23. The use of any one of claims 19 to 22, wherein at least one or each RNA comprises the 5' cap $m_2^{7,2'\text{-}O}Gpp_sp(5')G$.

24. The use of any one of claims 19 to 23, wherein at least one or each RNA comprises a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 21, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 21.

25. The use of any one of claims 19 to 24, wherein at least or each one amino acid sequence under (i), (ii), (iii), (iv), or (v) comprises an amino acid sequence enhancing antigen processing and/or presentation,

wherein, preferably, the amino acid sequence enhancing antigen processing and/or presentation comprises an amino acid sequence corresponding to the transmembrane and cytoplasmic domain of a MHC molecule, preferably a MHC class I molecule,

wherein, more preferably, the RNA encoding the amino acid sequence enhancing antigen processing and/or presentation comprises the nucleotide sequence of SEQ ID NO: 25, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 25; and/or

wherein, more preferably, the amino acid sequence enhancing antigen processing and/or presentation comprises the amino acid sequence of SEQ ID NO: 24, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 24.

26. The use of any one of claims 19 to 25, wherein at least one or each amino acid sequence under (i), (ii), (iii), (iv), or (v) comprises an amino acid sequence which breaks immunological tolerance,

wherein, preferably, the amino acid sequence which breaks immunological tolerance comprises helper epitopes, preferably tetanus toxoid-derived helper epitopes; and/or

wherein the RNA encoding the amino acid sequence which breaks immunological tolerance, preferably, comprises the nucleotide sequence of SEQ ID NO: 27, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 27; and/or

the amino acid sequence which breaks immunological tolerance, preferably, comprises the amino acid sequence of SEQ ID NO: 26, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 26.

27. The use of any one of claims 19 to 26, wherein at least one or each RNA comprises a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 28, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 28.

28. The use of any one of claims 19 to 27, wherein at least one or each RNA comprises a poly-A sequence,

wherein, preferably, the poly-A sequence comprises at least 100 nucleotides; and/or

wherein, preferably, the poly-A sequence comprises or consists of the nucleotide sequence of SEQ ID NO: 29.

29. The use of any one of claims 19 to 28,

wherein the RNA is to be administered by injection; or

wherein the RNA is to be administered by intravenous administration; or

wherein the RNA is formulated as lipoplex particles; or

wherein the RNA lipoplex particles are obtainable by mixing the RNA with liposomes.

30. The use of any one of claims 19 to 29, wherein the subject is a human.

31. The use of any one of claims 19 to 30, which further comprises that a further therapy is to be administered,

wherein, preferably, the further therapy comprises one or more selected from the group consisting of: (i) surgery to excise, resect, or debulk a tumor, (ii) radiotherapy, and (iii) chemotherapy; and/or

wherein, preferably, the further therapy comprises that a further therapeutic agent is to be administered,

wherein, more preferably, the further therapeutic agent comprises an anti-cancer therapeutic agent, and/or a checkpoint modulator.

32. The use of claim 31, wherein the checkpoint modulator is an anti-PD1 antibody, an anti-CTLA-4 antibody, or a combination of an anti-PD1 antibody and an anti-CTLA-4 antibody.