CLAIMS

1. A C68 vector comprising:

(a) a C68 nucleotide sequence; and

(b) a multi-antigen construct that comprises at least one nucleotide sequence encoding an immunogenic PSA polypeptide, at least one nucleotide sequence encoding an immunogenic PSCA polypeptide, and at least one nucleotide sequence encoding an immunogenic PSMA polypeptide.

2. The C68 vector according to claim 1, wherein the C68 nucleotide sequence is the sequence of SEQ ID NO: 57 lacking at least one gene selected from the group consisting of E1A, E1B, E2A, E2B, E3, E4, L1, L2, L3, L4 and L5 genes, wherein the immunogenic PSA polypeptide comprises amino acids 27-263 of SEQ ID NO:15 or amino acids 4 - 240 of SEQ ID NO:17, wherein the immunogenic PSCA polypeptide comprises the amino acid sequence of SEQ ID NO:21 or amino acids 4-125 0f SEQ ID NO:21, and wherein the immunogenic PSMA polypeptide is selected from the group consisting of:

1) a polypeptide comprising amino acids 15-750 of SEQ ID NO: 1;

2) a polypeptide comprising the amino acid sequence of SEQ ID NO:3;

3) a polypeptide comprising the amino acid sequence of SEQ ID NO:5;

4) a polypeptide comprising the amino acid sequence of SEQ ID NO:7;

5) a polypeptide comprising the amino acids 4 – 739 of SEQ ID NO:9;

6) a polypeptide comprising the amino acids 4 – 739 of SEQ ID NO:3;

7) a polypeptide comprising the amino acids 4 - 739 of SEQ ID NO:5;

8) a polypeptide comprising the amino acids 4 - 739 of SEQ ID NO:7; and

9) a polypeptide comprising the amino acid sequence of SEQ ID NO: 9.

3. The C68 vector according to claim 2, wherein the C68 nucleotide sequence is the sequence of SEQ ID NO: 57 lacking the genes of E1A, E1B, and E3, and wherein the multi-antigen construct further comprises a separator sequence between two nucleotide sequences encoding two different immunogenic polyppetides and has the structure of formula (I):

1. PAA1-SS1-PAA2-SS2-PAA3 (I)
2. wherein in formula (I):

(i) PAA1, PAA2, and PAA3 each is a nucleotide sequence encoding an immunogenic PSA polypeptide, a nucleotide sequence encoding immunogenic PSCA

polypeptide, or a nucleotide sequence encoding immunogenic PSMA polypeptide, provided the PAA1, PAA2, and PAA3 encode different PAA polypeptides, and

(ii) SS1 and SS2 are separator sequences and can be the same or different.

4. The C68 vector according to claim 3, wherein the separator sequences are selected from 2A peptide sequences and IRESs.

5. The C68 vector according to claim 4, wherein the 2A peptide sequence is selected from the group consisting of the 2A-peptide sequence of FMDV, ERAV, PTV1, EMC-B, EMCV, TME-GD7, ERBV, TaV, DrosC, CrPV, ABPV, IFV, Porcine rotavirus, human rotavirus, T brucei TSR1, and T cruzi AP endonuclease; and wherein the IRES is a EMCV IRES.

. 6. The vector according to claim 5, wherein PAA1 in formula (I) is a nucleotide sequence encoding the immunogenic PSA polypeptide or a nucleotide sequence encoding the immunogenic PSCA polypeptide.

7. The vector according to claim 6, wherein:

(i) PAA1 is a nucleotide sequence encoding the immunogenic PSA polypeptide;

(ii) PAA2 is a nucleotide sequence encoding an immunogenic PSCA or PSMA polypeptide;

(iii) SS1 is a 2A-peptide sequence; and

(iv) SS2 is a 2A-peptide sequence or an EMCV IRES.

8. The C68 vector according to claim 7, wherein the 2A-peptide sequence is the FMDV 2A-peptide sequence or the TAV 2A-peptide sequence.

9. The C68 vector according to claim 8, wherein:

(1) the nucleotide sequence encoding the immunogenic PSA polypeptide is selected from the group consisting of: (i) the nucleotide sequence of SEQ ID NO: 18; (ii) the nucleotide sequence of SEQ ID NO: 20; (iii) the nucleotide sequence comprising nucleotides 10-720 of SEQ ID NO:18; (iv) the nucleotide sequence comprising nucleotides 1115-1825 of SEQ ID NO:58; and (v) the nucleotide sequence comprising nucleotides 1106-1825 of SEQ ID NO:58;

(2) the nucleotide sequence encoding the immunogenic PSCA polypeptide is selected from the group consisting of: (i) the nucleotide sequence of SEQ ID NO:22; (ii) a nucleotide sequence comprising nucleotides 10- 372 of SEQ ID NO:22; (iii) a nucleotide sequence comprising nucleotides 1892-2257 of SEQ ID NO:58; and (iv) a nucleotide sequence comprising nucleotides 1886-2257 of SEQ ID NO:58; and

(3) the nucleotide sequence encoding the immunogenic PSMA polypeptide is selected from the group consisting of: (i) the nucleotide sequence comprising nucleotides 43-2250 of SEQ ID NO:2; (ii) the nucleotide sequence of SEQ ID NO:4; (iii) the nucleotide sequence of SEQ ID NO:6; (iv) the nucleotide sequence of SEQ ID NO:8; (v) the nucleotide sequence of SEQ ID NO:10; (vi) a nucleotide sequence comprising nucleotides 10 – 2217 of SEQ ID NO:4; (vii) a nucleotide sequence comprising nucleotides 10 – 2217 of SEQ ID NO:6; (viii) a nucleotide sequence comprising nucleotides 10 – 2217 of SEQ ID NO:8; (ix) a nucleotide sequence comprising nucleotides 10 – 2217 of SEQ ID NO:10; (x) a nucleotide sequence comprising nucleotides 2333-4543 of SEQ ID NO:58; and (xi) a nucleotide sequence comprising nucleotides 2324-4543 of SEQ ID NO:58.

10. The C68 vector according to claim 3, wherein in formula (I):

(1) PAA1 is a nucleotide sequence encoding an immunogenic PSA polypeptide and comprises nucleotides 1115-1825 of SEQ ID NO: 58 or comprises 1106-1114 of SEQ ID NO: 58;

(2) PAA2 is a nucleotide sequence encoding an immunogenic PSCA polypeptide and comprises nucleotides 1892-2257 of SEQ ID NO: 58 or comprises 1886-2257 of SEQ ID NO: 58;

(3) PAA3 is a nucleotide sequence encoding an immunogenic PSMA polypeptide and comprises nucleotides 2333-4543 of SEQ ID NO: 58 or comprises 2324-4543 of SEQ ID NO: 58;

(4) SS1 is a nucleotide sequence encoding T2A; and

(5) SS2 is a nucleotide sequence encoding F2A.

11. The C68 vector according to claim 1, wherein the multi-antigen construct comprises a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:60 or SEQ ID NO:64.

12. The C68 vector according to claim 1, wherein the multi-antigen construct comprises a nucleotide sequence of SEQ ID NO:61, SEQ ID NO:65, SEQ ID NO:66, or a degenerate variant of the nucleotide sequence of SEQ ID NO:61, SEQ ID NO:65, SEQ ID NO:66.

13. The C68 vector according to claim 11 or claim 12, further comprising a CMV promoter.

14. The C68 vector according to claim 1, which comprises the nucleotide sequence of SEQ ID NO:58, nucleotides 9-34811 of SEQ ID NO:58, or the nucleotide sequence of SEQ ID NO:63.

15. A composition comprising a C68 vector according to any one of claims 1-14.

16. A cell comprising a C68 vector according to any one of claims 1-14.

17. A pharmaceutical composition comprising a vector according to any one of claims 1-14 and a pharmaceutically acceptable excipient.

18. A method of treating prostate cancer in a human, comprising administering to the human an effective amount of the pharmaceutical composition according to claim 17.

19. The method according to claim 18, further comprising administering to the human an effective amount of an immune modulator.

20. The method according to claim 18, further comprising administering to the human (a) an effective amount of at least one immune- suppressive-cell inhibitor and (b) an effective amount of at least one immune-effector-cell enhancer.

21. The method according to claim 20, wherein the immune-suppressive-cell inhibitor is selected from the group consisting of a protein kinase inhibitor, a COX-2 inhibitor, and a PDE5 inhibitor, and wherein the immune-effector-cell enhancer is selected from the group consisting of a CTLA-4 inhibitor, a CD40 agonist, a TLR agonist, a 4-1BB agonist, a OX40 agonist, a GITR agonist, a PD-1 antagonist, and a PD-L1 antagonist.

22. The method according to claim 21, wherein:

(1) the protein kinase inhibitor is selected from the group consisting of imatinib, sorafenib, lapatinib, zactima MP-412, dasatinib, lestaurtinib, sunitinib malate, axitinib, erlotinib, gefitinib, bosutinib, temsirolismus, and nilotinib;

(2) the CTLA-4 inhibitor is selected from the group consisting of ipilimumab and tremelimumab;

(3) the CD40 agonist is an anti-CD40 antibody selected from the group consisting of G28-5, mAb89, EA-5 , S2C6, CP870893, and dacetuzumab; and

(4) the TLR agonist is a CpG oligonucleotide selected from the group consisting of CpG 24555, CpG 10103, CpG7909, and CpG1018.

23. The method according to claim 22, wherein the immune-suppressive-cell inhibitor is a protein kinase inhibitor selected from the group consisting of sorafenib, dasatinib, imatinib, axitinib, and sunitinib malate, and wherein the immune-effector-cell enhancer is tremelimumab.

24. The method according to claim 22, wherein the immune-suppressive-cell inhibitor is a protein kinase inhibitor selected from the group consisting of sorafenib, dasatinib, imatinib, axitinib, and sunitinib malate, and wherein the immune-effector-cell enhancer is a CpG oligonucleotide selected from the group consisting of CpG24555, CpG10103, CpG7909, and CpG1018.

CLAIMS

1. A C68 vector comprising:

(a) a C68 nucleotide sequence; and

(b) a multi-antigen construct that comprises at least one nucleotide sequence encoding an immunogenic PSA polypeptide, at least one nucleotide sequence encoding an immunogenic PSCA polypeptide, and at least one nucleotide sequence encoding an immunogenic PSMA polypeptide.

2. The C68 vector according to claim 1, wherein the C68 nucleotide sequence is the sequence of SEQ ID NO: 57 lacking at least one gene selected from the group consisting of E1A, E1B, E2A, E2B, E3, E4, L1, L2, L3, L4 and L5 genes, wherein the immunogenic PSA polypeptide comprises amino acids 27-263 of SEQ ID NO:15 or amino acids 4 - 240 of SEQ ID NO:17, wherein the immunogenic PSCA polypeptide comprises the amino acid sequence of SEQ ID NO:21 or amino acids 4-125 0f SEQ ID NO:21, and wherein the immunogenic PSMA polypeptide is selected from the group consisting of:

1) a polypeptide comprising amino acids 15-750 of SEQ ID NO: 1;

2) a polypeptide comprising the amino acid sequence of SEQ ID NO:3;

3) a polypeptide comprising the amino acid sequence of SEQ ID NO:5;

4) a polypeptide comprising the amino acid sequence of SEQ ID NO:7;

5) a polypeptide comprising the amino acids 4 – 739 of SEQ ID NO:9;

6) a polypeptide comprising the amino acids 4 – 739 of SEQ ID NO:3;

7) a polypeptide comprising the amino acids 4 - 739 of SEQ ID NO:5;

8) a polypeptide comprising the amino acids 4 - 739 of SEQ ID NO:7; and

9) a polypeptide comprising the amino acid sequence of SEQ ID NO: 9.

3. The C68 vector according to claim 2, wherein the C68 nucleotide sequence is the sequence of SEQ ID NO: 57 lacking the genes of E1A, E1B, and E3, and wherein the multi-antigen construct further comprises a separator sequence between two nucleotide sequences encoding two different immunogenic polyppetides and has the structure of formula (I):

1. PAA1-SS1-PAA2-SS2-PAA3 (I)

2. wherein in formula (I):

(i) PAA1, PAA2, and PAA3 each is a nucleotide sequence encoding an immunogenic PSA polypeptide, a nucleotide sequence encoding immunogenic PSCA polypeptide, or a nucleotide sequence encoding immunogenic PSMA polypeptide, provided the PAA1, PAA2, and PAA3 encode different PAA polypeptides, and

(ii) SS1 and SS2 are separator sequences and can be the same or different.

4. The C68 vector according to claim 3, wherein the separator sequences are selected from 2A peptide sequences and IRESs.

5. The C68 vector according to claim 4, wherein the 2A peptide sequence is selected from the group consisting of the 2A-peptide sequence of FMDV, ERAV, PTV1, EMC-B, EMCV, TME-GD7, ERBV, TaV, DrosC, CrPV, ABPV, IFV, Porcine rotavirus, human rotavirus, T brucei TSR1, and T cruzi AP endonuclease; and wherein the IRES is a EMCV IRES.

6. The vector according to claim 5, wherein PAA1 in formula (I) is a nucleotide sequence encoding the immunogenic PSA polypeptide or a nucleotide sequence encoding the immunogenic PSCA polypeptide.

7. The vector according to claim 6, wherein:

(i) PAA1 is a nucleotide sequence encoding the immunogenic PSA polypeptide;

(ii) PAA2 is a nucleotide sequence encoding an immunogenic PSCA or PSMA polypeptide;

(iii) SS1 is a 2A-peptide sequence; and

(iv) SS2 is a 2A-peptide sequence or an EMCV IRES.

8. The C68 vector according to claim 7, wherein the 2A-peptide sequence is the FMDV 2A-peptide sequence or the TAV 2A-peptide sequence.

9. The C68 vector according to claim 8, wherein:

(1) the nucleotide sequence encoding the immunogenic PSA polypeptide is selected from the group consisting of: (i) the nucleotide sequence of SEQ ID NO: 18; (ii)

the nucleotide sequence of SEQ ID NO: 20; (iii) the nucleotide sequence comprising nucleotides 10-720 of SEQ ID NO:18; (iv) the nucleotide sequence comprising nucleotides 1115-1825 of SEQ ID NO:58; and (v) the nucleotide sequence comprising nucleotides 1106-1825 of SEQ ID NO:58;

(2) the nucleotide sequence encoding the immunogenic PSCA polypeptide is selected from the group consisting of: (i) the nucleotide sequence of SEQ ID NO:22; (ii) a nucleotide sequence comprising nucleotides 10- 372 of SEQ ID NO:22; (iii) a nucleotide sequence comprising nucleotides 1892-2257 of SEQ ID NO:58; and (iv) a nucleotide sequence comprising nucleotides 1886-2257 of SEQ ID NO:58; and

(3) the nucleotide sequence encoding the immunogenic PSMA polypeptide is selected from the group consisting of: (i) the nucleotide sequence comprising nucleotides 43-2250 of SEQ ID NO:2; (ii) the nucleotide sequence of SEQ ID NO:4; (iii) the nucleotide sequence of SEQ ID NO:6; (iv) the nucleotide sequence of SEQ ID NO:8; (v) the nucleotide sequence of SEQ ID NO:10; (vi) a nucleotide sequence comprising nucleotides 10 – 2217 of SEQ ID NO:4; (vii) a nucleotide sequence comprising nucleotides 10 – 2217 of SEQ ID NO:6; (viii) a nucleotide sequence comprising nucleotides 10 – 2217 of SEQ ID NO:8; (ix) a nucleotide sequence comprising nucleotides 10 – 2217 of SEQ ID NO:10; (x) a nucleotide sequence comprising nucleotides 2333-4543 of SEQ ID NO:58; and (xi) a nucleotide sequence comprising nucleotides 2324-4543 of SEQ ID NO:58.

10. The C68 vector according to claim 3, wherein in formula (I):

(1) PAA1 is a nucleotide sequence encoding an immunogenic PSA polypeptide and comprises nucleotides 1115-1825 of SEQ ID NO: 58 or comprises 1106-1114 of SEQ ID NO: 58;

(2) PAA2 is a nucleotide sequence encoding an immunogenic PSCA polypeptide and comprises nucleotides 1892-2257 of SEQ ID NO: 58 or comprises 1886-2257 of SEQ ID NO: 58;

(3) PAA3 is a nucleotide sequence encoding an immunogenic PSMA polypeptide and comprises nucleotides 2333-4543 of SEQ ID NO: 58 or comprises 2324-4543 of SEQ ID NO: 58;

(4) SS1 is a nucleotide sequence encoding T2A; and

(5) SS2 is a nucleotide sequence encoding F2A.

11. The C68 vector according to claim 1, wherein the multi-antigen construct comprises a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:60 or SEQ ID NO:64.

12. The C68 vector according to claim 1, wherein the multi-antigen construct comprises a nucleotide sequence of SEQ ID NO:61, SEQ ID NO:65, SEQ ID NO:66, or a degenerate variant of the nucleotide sequence of SEQ ID NO:61, SEQ ID NO:65, SEQ ID NO:66.

13. The C68 vector according to claim 11 or claim 12, further comprising a CMV promoter.

14. The C68 vector according to claim 1, which comprises the nucleotide sequence of SEQ ID NO:58, nucleotides 9-34811 of SEQ ID NO:58, or the nucleotide sequence of SEQ ID NO:63.

15. A composition comprising a C68 vector according to any one of claims 1-14.

16. A cell comprising a C68 vector according to any one of claims 1-14.

17. A pharmaceutical composition comprising a vector according to any one of claims 1-14 and a pharmaceutically acceptable excipient.

18. A pharmaceutical composition according to claim 17 for use in the treatment of prostate cancer.

19. The composition according to claim 18, wherein an effective amount of an immune modulator is also to be administered during the treatment.

20. The composition according to claim 18, wherein (a) an effective amount of at least one immune- suppressive-cell inhibitor and (b) an effective amount of at least one immune-effector-cell enhancer is also to be administered during the treatment.

21. The composition according to claim 20, wherein the immune-suppressive-cell inhibitor is selected from the group consisting of a protein kinase inhibitor, a COX-2 inhibitor, and a PDE5 inhibitor, and wherein the immune-effector-cell enhancer is selected from the group consisting of a CTLA-4 inhibitor, a CD40 agonist, a TLR agonist, a 4-1BB agonist, a OX40 agonist, a GITR agonist, a PD-1 antagonist, and a PD-L1 antagonist.

22. The composition according to claim 21, wherein:

(1) the protein kinase inhibitor is selected from the group consisting of imatinib, sorafenib, lapatinib, zactima MP-412, dasatinib, lestaurtinib, sunitinib malate, axitinib, erlotinib, gefitinib, bosutinib, temsirolismus, and nilotinib;

(2) the CTLA-4 inhibitor is selected from the group consisting of ipilimumab and tremelimumab;

(3) the CD40 agonist is an anti-CD40 antibody selected from the group consisting of G28-5, mAb89, EA-5 , S2C6, CP870893, and dacetuzumab; and

(4) the TLR agonist is a CpG oligonucleotide selected from the group consisting of CpG 24555, CpG 10103, CpG7909, and CpG1018.

23. The composition according to claim 22, wherein the immune-suppressive-cell inhibitor is a protein kinase inhibitor selected from the group consisting of sorafenib, dasatinib, imatinib, axitinib, and sunitinib malate, and wherein the immune-effector-cell enhancer is tremelimumab.

24. The composition according to claim 22, wherein the immune-suppressive-cell inhibitor is a protein kinase inhibitor selected from the group consisting of sorafenib, dasatinib, imatinib, axitinib, and sunitinib malate, and wherein the immune-effector-cell enhancer is a CpG oligonucleotide selected from the group consisting of CpG24555, CpG10103, CpG7909, and CpG1018.

25. The use of a pharmaceutical composition according to claim 17, in the manufacture of a medicament for the treatment of prostate cancer.

26. The ~~use~~ according to claim 25, wherein an effective amount of an immune

modulator is to be administered as well as the medicament.

27. The use according to claim 25, wherein (a) an effective amount of at least one immune-suppressive-cell inhibitor and (b) an effective amount of at least one immune-effector-cell enhancer is to be administered as well as the medicament.

28. The use according to claim 27, wherein the immune-suppressive-cell inhibitor is selected from the group consisting of a protein kinase inhibitor, a COX-2 inhibitor, and a PDE5 inhibitor, and wherein the immune-effector-cell enhancer is selected from the group consisting of a CTLA-4 inhibitor, a CD40 agonist, a TLR agonist, a 4-1BB agonist, a OX40 agonist, a GITR agonist, a PD-1 antagonist, and a PD-L1 antagonist.

29. The use according to claim 28, wherein:

(1) the protein kinase inhibitor is selected from the group consisting of imatinib, sorafenib, lapatinib, zactima MP-412, dasatinib, lestaurtinib, sunitinib malate, axitinib, erlotinib, gefitinib, bosutinib, temsirolismus, and nilotinib;

(2) the CTLA-4 inhibitor is selected from the group consisting of ipilimumab and tremelimumab;

(3) the CD40 agonist is an anti-CD40 antibody selected from the group consisting of G28-5, mAb89, EA-5 , S2C6, CP870893, and dacetuzumab; and

(4) the TLR agonist is a CpG oligonucleotide selected from the group consisting of CpG 24555, CpG 10103, CpG7909, and CpG1018.

30. The use according to claim 29, wherein the immune-suppressive-cell inhibitor is a protein kinase inhibitor selected from the group consisting of sorafenib, dasatinib, imatinib, axitinib, and sunitinib malate, and wherein the immune-effector-cell enhancer is tremelimumab.

31. The use according to claim 29, wherein the immune-suppressive-cell inhibitor is a protein kinase inhibitor selected from the group consisting of sorafenib, dasatinib, imatinib, axitinib, and sunitinib malate, and wherein the immune-effector-cell enhancer is a CpG oligonucleotide selected from the group consisting of CpG24555, CpG10103, CpG7909, and CpG1018.