

VECTOR FOR CANCER TREATMENT

Field of Invention

The present invention relates to vectors which are capable of eliciting an inflating memory CD8+ T cell response. These vectors which elicit an inflating memory CD8+ T cell response are suitable for use in the treatment of cancer. The present invention also relates to methods for making the vectors and methods for inducing an inflating memory CD8+ T cell response.

Introduction

Anti-cancer strategies aiming to activate the CD8 T cell arm of immunity have shown remarkable efficacy. There is considerable overlap between the requirements for a good CD8 T cell response against a chronic infection with that against cancer – they have to be durable, functional, sustained and able to home to the correct site and resist exhaustion owing to prolonged TCR stimulation.

Epitope based cancer vaccines are one strategy that has been used to activate a T cell response to specific tumour associated antigens. Initially, peptide-based single epitope vaccines were used, however these provided poor clinical responses as they did not adequately active the innate immune system. To enhance the immune activation multi-peptide vaccines were developed, wherein multiple epitopes were administered together.

This approach of administering multiple epitopes has also been performed using adenoviral vectors. By using an adenoviral vector, which has the capacity to encode large transgenes, multiple epitopes can be encoded and delivered as a concatemer (Bei and Scardino., J Biomed Biotechnol 2010;2010:102758). Alternatively, full length antigens can be encoded and delivered. However, there is still a need to improve immune activation against cancer cells.

Summary of the Invention

In one aspect, the present disclosure relates to a viral vector comprising a nucleotide sequence encoding a single cancer specific CD8+ T cell epitope, wherein the vector is an adenoviral vector or adeno-associated viral vector, wherein the vector does not comprise a nucleic acid encoding any other cancer specific T cell epitopes other than the single cancer specific CD8+ T cell epitope, and wherein the viral vector induces an inflating memory CD8+ T cell response when administered to a subject.

In another aspect, disclosed herein is a composition, comprising at least two viral vectors wherein each of the at least two viral vectors is a viral vector disclosed herein and wherein each of the at least two viral vectors encodes a different single cancer specific CD8+ T cell epitope

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In another aspect, disclosed herein is a pharmaceutical composition comprising the viral vector disclosed herein and a pharmaceutically acceptable carrier, diluent, excipient or adjuvant.

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In yet another aspect, disclosed herein is a host cell, comprising the viral vector disclosed herein, the composition disclosed herein, or the pharmaceutical composition disclosed herein.

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In yet another aspect, disclosed herein is the use of a viral vector disclosed herein, the composition disclosed herein, the pharmaceutical composition disclosed herein, or the host cell disclosed herein, in the manufacture of a medicament for the treatment of a cancer, in a subject in need thereof.

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In yet another aspect, disclosed herein is the use of a viral vector disclosed herein, the composition disclosed herein, the pharmaceutical composition disclosed herein, or the host cell disclosed herein, in the manufacture of a medicament for inducing an inflating memory CD8+ T cell response in a subject in need thereof.

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In yet another aspect, disclosed herein is the use of a viral vector disclosed herein, the composition disclosed herein, the pharmaceutical composition disclosed herein, or the host cell disclosed herein in the manufacture of a medicament for inducing an inflating memory CD8+ T cell response in a subject in need thereof wherein the inflating memory CD8+ T cell response comprises production of CD8+/CX3CR1+/KLRG-1+ T cells.

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In yet another aspect, disclosed herein is a viral vector disclosed herein, the composition of claim disclosed herein, the pharmaceutical composition disclosed herein, or the host cell disclosed herein for use in therapy.

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In yet another aspect, disclosed herein is the use of a composition disclosed herein in the manufacture of a medicament for the treatment of a cancer, in a subject in need thereof wherein each of the at least two viral vectors are present in the medicament at an amount that is not therapeutically effective individually, thereby treating the cancer in the subject, optionally wherein the cancer is selected from colorectal cancer, prostate cancer, oesophageal cancer, liver cancer, renal cancer, lung cancer, breast cancer, pancreatic cancer, brain cancer, hepatocellular cancer, lymphoma, leukaemia, gastric cancer, cervical cancer, ovarian cancer, thyroid cancer, melanoma, carcinoma, head and neck cancer, skin cancer, nasopharyngeal cancer, Epstein Barr driven cancers, Human Papilloma virus driven cancers, or soft tissue sarcoma.

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The present ~~invention~~disclosure arises from the surprising finding that a vector encoding a single cancer specific CD8+ and/or CD4+ T cell epitope, referred to herein as a minigene vector, can

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induce an inflating memory CD8+ T cell response. Memory inflation describes the longitudinal development of stable, expanded CD8+ T cell memory pools, wherein the cells have distinct phenotype and function. This inflating memory response results in a long-lived pool of epitope specific T cells which remain abundant and functional even beyond the acute phase of infection
5 (Klerner et al., Immunol Rev 2018 283(1):99-111). It is believed that the features of inflating memory cells, may result in an enhanced anti-tumour response.

The present inventors have developed a vaccine platform based on the replication-deficient AdHu5 adenoviral vector backbone in which only the CD8+ T cell epitope of interest is inserted.

cells are generated from a single injection of the minigene. These long-lived tumour specific CD8+ T cell responses are found in the blood and so are present systemically. Therefore, they may play an important role in suppressing micrometastasis after primary tumour control. Finally, the adenoviral vector minigenes also have the advantage of being easy to design and produce, due to the simplicity of the vector and encoded sequence.

As such, the [inventiondisclosure](#) relates to an adenoviral vector comprising a nucleotide sequence encoding a single cancer specific CD8+ and/or CD4+ T cell epitope, wherein the vector is capable of inducing an inflating memory CD8+ T cell response.

In an [embodimentexample](#) the [inventiondisclosure](#) relates to an adenoviral vector or an adeno-associated virus (AAV) vector comprising a nucleotide sequence encoding a single cancer specific CD8+ T cell epitope, wherein the vector is capable of inducing an inflating memory CD8+ T cell response. In an [embodimentexample](#) the vector is capable of inducing production of CD8+ T cells characterised by markers selected from the group comprising CX3CR1+, KLRG-1+, CD44+, CD62L-. In an [embodimentexample](#) the vector is capable of inducing production of CD8+ T cells characterised by markers selected from the group comprising CX3CR1+, KLRG-1+, CD44+, CD62L-, CD27(low), CD127(low). In an [embodimentexample](#) the nucleotide sequence encoding the cancer specific CD8+ or CD4+ T cell epitope comprises from 12 to 45 nucleotide base pairs. In an [embodimentexample](#) the nucleotide sequence encoding the cancer specific CD8+ and/or CD4+ T cell epitope comprises from 24 to 45 nucleotide base pairs. In an [embodimentexample](#) the cancer specific CD8+ and/or CD4+ T cell epitope is derived from a tumour associated antigen. In an [embodimentexample](#) the cancer specific CD8+ and/ or CD4+ T cell epitope is mutated in a cancer cell. In an [embodimentexample](#) the cancer specific CD8+ and/or CD4+ T cell epitope is overexpressed in a cancer cell. In an [embodimentexample](#) the cancer specific CD8+ and/or CD4+ T cell epitope is derived from a tumour associated antigen selected from the group consisting of TRP-1, CEA, TAG-72, 9D7, Ep-CAM, EphA3, telomerase, mesothelin, SAP-1 Melan-A/MART-1, tyrosinase, CLPP, cyclin-A1, cyclin-B1 MAGE-A1, MAGE-C1, MAGE-C2, SSX2, XAGE1b/GAGED2a, CD45, glypican-3, IGF2B3, kallikrein-4, KIF20A, lengsin, meloe, MUC5AC, survivin, PRAME, SSX-2, NY-ESO-1/LAGE1, gp70, MC1R, TRP-1/-2, β -catenin, BRCA1/2, CDK4, foetal protein SIM1. In an [embodimentexample](#) the cancer specific CD8+ or CD4+ T cell epitope comprises SEQ ID NO:1 (SPSYVYHQF) or SEQ ID NO:2 (SLLMWITQC). In an [embodimentexample](#) the cancer specific CD8+ and/or CD4+ T cell epitope is specific for colorectal cancer, prostate cancer, oesophageal cancer, liver cancer, renal cancer, lung cancer, breast cancer, breast cancer, pancreatic cancer, brain cancer, hepatocellular cancer, lymphoma, leukaemia, gastric cancer, cervical cancer, ovarian cancer, thyroid cancer, melanoma, carcinoma, head and neck cancer, skin cancer, nasopharyngeal cancer, Epstein Barr driven cancers, Human Papilloma virus driven cancers and soft tissue sarcoma. In an [embodimentexample](#) the vector is human serotype 5 (AdHu5). In an [embodimentexample](#) the vector comprises a CMV promoter. In an [embodimentexample](#) the vector comprises a TATA box. In an [embodimentexample](#) the

vector lacks the E1 and E3 proteins. In an [embodimentexample](#) the vector does not comprise any additional nucleotide sequence encoding a cancer specific CD8+ and/or CD4+ T cell epitope. Thus, the vector has a nucleotide sequence encoding a single cancer specific CD8+ T cell epitope and may comprise other vector elements necessary for the transcription of the nucleic acid, but it does not include a nucleic acid sequence that encodes a cancer specific epitope that is not a CD8+ T cell epitope, e.g. a CD4+ T cell epitope. Moreover, it does not include more than one cancer specific CD8+ or CD4+ T cell epitope. Thus, the presence of multiple anti-cancer T cell epitopes in the vector is excluded. This excludes multiple copies of the same anti-cancer T cell epitope or copies of different anti-cancer T cell epitopes. The vector does not have a concatemer, that is a long continuous DNA molecule that contains multiple copies of the same cancer specific T cell epitope linked in series.

In an [aspectexample](#) the [inventiondisclosure](#) relates to an immunogenic composition, comprising the vector according to the [inventiondisclosure](#).

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In an [aspectexample](#) the [inventiondisclosure](#) relates to an immunogenic composition or vaccine composition comprising at least 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10, up to 20, 30, 40 or 50 vectors according to the [inventiondisclosure](#).

In an [aspectexample](#) the [inventiondisclosure](#) relates to a host cell, comprising the vector according to the [inventiondisclosure](#), or the immunogenic composition according to the [inventiondisclosure](#).

In an [aspectexample](#) the [inventiondisclosure](#) related to the vector or composition according to the [inventiondisclosure](#), for use in therapy.

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In an [aspectexample](#) the [inventiondisclosure](#) relates to a method of treating or preventing a cancer, comprising administering a therapeutically effective amount of the vector or composition according to the [inventiondisclosure](#).

In an [aspectexample](#) the [inventiondisclosure](#) relates to a method of inducing an inflating memory CD8+ T cell response, comprising the step of; administering a therapeutically effective amount of the vector or composition according to the [inventiondisclosure](#), to a subject in need thereof, wherein the CD8+ T cells are characterised by markers selected from the group comprising CX3CR1+, KLRG-1+, CD44+ and CD62L-.

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In an [aspectexample](#) the [inventiondisclosure](#) relates to a method of producing the vector are described above, comprising the steps of;

- i) synthesising the nucleic acid sequence encoding the epitope, as a sense and antisense primer,

- ii) cloning the nucleic acid sequence encoding epitope sequence into a first plasmid,
- iii) cloning the sequence comprising the nucleic acid sequence encoding epitope into a second plasmid comprising the adenoviral DNA

5 In an [aspectexample](#) the [inventiondisclosure](#) relates to a kit comprising the vector according to the [inventiondisclosure](#), one or more additional active ingredients, pharmaceutically acceptable carrier, diluent, excipient or adjuvant, and optionally instructions for use.

10 In an [aspectexample](#) the [inventiondisclosure](#) relates to a method for inducing a T cell immune response in an animal against a cancer specific CD8+ and/or CD4+ T cell epitope, comprising contacting a cell with the vector or composition according to the [inventiondisclosure](#).

Figures

15 **Figure 1.** Immunization of Balb/c mice with an AdHu5 replication-deficient vector encoding an AH1 CD8+ T cell tumour epitope stimulates a durable CD8+ T response in the periphery. (A) Schematic representation of the constructs used for the production of AdHu5 vector expressing a MHC-1 binding CT26-specific cancer epitope. (B) FACs plots showing %CD8+ AH1 tetramer + (tet+) cells in the blood from AH1 (left) and Ad-I8V (right) vaccinated mice. (C) AH1-tetramer-specific CD8 + T cell responses in the blood at day 7 (left) and day 50 (right) from two independent experiments. (D) FACS plots showing the presence of indicated markers on CD8+ AH1-tet+ (left) and AH1-tet-(right) populations in the blood from the same sample. (E) Phenotype of AH1-tet+ CD8+ T cells compared to AH1-tet-CD8+ T cells from the same groups at day 7 (left) and day 50 (right) from two independent experiments. Geo M FI = geometric mean fluorescence intensity.

25 **Figure 2.** Memory inflationary AH1-specific T cells demonstrate inhibition of CT26 tumour growth in Balb/c mice after both prophylactic and therapeutic vaccination with Ad-AH1. (A) Experimental setup for prophylactic vaccination (independently performed twice, P1 and P2) and therapeutic vaccination (T1). A star indicates presence of palpable tumours. (B-D) Tumour growth curves for the different groups (N =5 per group) in a prophylactic (P1 and P2)(B and C) and therapeutic vaccination setting (T1) (D). In T1, the arrow indicates the time-point of vaccination. Mice vaccinated with Ad-AH1 (1×10^8 IU) are shown in green, Ad-A H 1 Low (1×10^7 IU) in orange, Ad-AH1 (1×10^8 IU) + Ad-GSW11 (1×10^8 IU) in red , Ad-GSW11 (1×10^8 IU) in lilac, Ad-I8V (1×10^8 IU) in grey, and naïve mice in black. TF = tumour free. (E, G, L) Statistically significant differences in tumour sizes between groups at day 18 post-challenge. Dots indicate individual mice. (F,H,J) Graphs show the slope of the tumour growth curves determined by linear regression from the day tumours show clear tumour growth (day 7 post-challenge for controls and day 18 post-challenge for Ad-AH1 vaccinated mice). (K) The tumour growth rate was recalculated to determine the specific growth rate. The tumor growth rate between implantation and humane endpoint was quantified using the parameter of specific

CLAIMS

1. ~~An adenoviral vector or adeno-associated virus~~ A viral vector comprising a nucleotide sequence encoding a single cancer specific CD8+ T cell epitope, wherein the vector is ~~capable of inducing an inflating memory CD8+ T cell response~~ an adenoviral vector or adeno-associated viral vector, wherein ~~said~~the vector does not comprise a nucleic acid encoding ~~further any other~~ cancer specific T cell epitopes other than the single cancer specific CD8+ T cell epitope, and wherein the viral vector induces an inflating memory CD8+ T cell response when administered to a subject.
2. The viral vector according to claim 1, wherein the ~~vector is capable of inducing~~ inflating memory CD8+ T cell response comprises production of CD8+ T cells ~~characterised by markers selected from the group comprising +/CX3CR1+, +/KLRG-1+, +/CD44+, +/CD62L-~~ T cells -.
3. The viral vector according to claim 1, ~~wherein the vector is capable of inducing production of CD8+ T cells characterised by markers selected from the group comprising CX3CR1+, KLRG-1+, CD44+, CD62L-, CD27 (low), CD127 (low).~~
4. ~~The vector according to any of claims 1 to 3 or 2,~~ wherein the nucleotide sequence encoding the cancer specific CD8+ T cell epitope comprises from 12 to 45 nucleotide base pairs in length optionally wherein the nucleotide sequence encoding the cancer specific CD8+ T cell epitope comprises from 24 to 45 nucleotide base pairs in length.
4. The viral vector according to any of claims 1 to 3, wherein the cancer specific CD8+ T cell epitope is a viral antigen, a tumour associated antigen that is overexpressed in a cancer cell, or an antigen that is mutated in a cancer cell.
5. The viral vector according to any of claims 1 to 4, wherein the nucleotide sequence encoding the cancer specific CD8+ T cell epitope ~~comprises from 24 to 45 nucleotide base pairs, encodes a polypeptide comprising the cancer specific CD8+ T cell epitope, and wherein the polypeptide comprising the cancer specific CD8+ T cell epitope is not processed by antigen presenting cells.~~
6. The viral vector according to any of claims 1 to 5, wherein the ~~cancer specific~~ inflating memory CD8+ T cell ~~epitope is derived from response comprises~~ a tumour associated antigen,) production of CD8+/CX3CR1+/KLRG-1+ T cells that have sustained expression of Tbx21 and/or E2f2;

b) production of CD8+/CX3CR1+/KLRG-1+ T cells that have low expression of Eomes; and/or
c) production of: CD8+/CX3CR1+/KLRG-1+ T cells that have low expression of PD-1, Tim-3, and/or
Lag-3.

7. The viral vector according to any of claims 1 to 6, wherein the inflating memory CD8+ T cell epitope is
mutated response is capable of controlling tumour growth in a cancer cell the subject greater than 50 days after
the pharmaceutical composition is administered.

8. The viral vector according to any of claims 12 to 7, wherein the T cell epitope is overexpressed
a) the CD8+/CX3CR1+/KLRG-1+ T cells form 2 percent to 20 percent of total circulating CD8+ T cells
in the subject; and/or
b) the CD8+/CX3CR1+/KLRG-1+ T cells maintain a cancer cell memory effector phenotype for at least
30 days

9. The viral vector according to any of claims 1 to 8, wherein the T cell epitope is derived from a tumour
 associated antigen selected from the group consisting of TRP-1, CEA, TAG-72, 9D7, Ep-CAM, EphA3,
 telomerase, mesothelin, SAP-1 Melan-A/MART-1, tyrosinase, CLPP, cyclin-A1, cyclin-B1 MAGE-A1, MAGE-
 C1, MAGE-C2, SSX2, XAGE1b/GAGED2a, CD45, glypican-3, IGF2B3, kallikrein-4, KIF20A, lengsin, meloe,
 MUC5AC, survivin, PRAME, SSX-2, NY-ESO-1/LAGE1, gp70, MC1R, TRP-1/-2, β -catenin, BRCA1/2, CDK4,
and foetal protein SIM1.

10. The viral vector according to claim any of claims 1 to 9, wherein the T cell epitope viral vector comprises
a sequence with at least 90% sequence identity to SEQ ID NO: 2 (SLLMWITQC), 13 and a sequence with at
least 90% sequence identity to SEQ ID NO: 14.

11. The viral vector according to any of claims 1 to 610, wherein the viral vector further comprises a
sequence with at least 90% sequence identity to SEQ ID NO: 15 and a sequence with at least 90% sequence
identity to SEQ ID NO: 33.

12. The viral vector according to any of claims 1 to 11, wherein the cancer specific CD8+ T cell epitope is
 specific for colorectal cancer, prostate cancer, oesophageal cancer, liver cancer, renal cancer, lung cancer,
 breast cancer, pancreatic cancer, brain cancer, hepatocellular cancer, lymphoma, leukaemia, gastric cancer,
cervical cancer, ovarian cancer, thyroid cancer, melanoma, carcinoma, head and neck cancer, skin cancer,

nasopharyngeal cancer, Epstein Barr driven cancers, Human Papilloma virus driven cancers or soft tissue sarcoma.

13. The viral vector according to any of claims 1 to 12, wherein the viral vector

- a) is human serotype 5 (AdHu5);
- b) is human serotype 2;
- c) comprises a CMV promoter;
- d) comprises a TATA box; and/or
- e) lacks a sequence encoding the E1 and E3 proteins.

14. The viral vector according to any of claims 1 to 13, wherein the vector is a replication-deficient AdHu5 adenoviral vector.

15. A composition, comprising at least two viral vectors wherein each of the at least two viral vectors is a viral vector according to any of claims 1 to 14 and wherein each of the at least two viral vectors encodes a different single cancer specific CD8+ T cell epitope.

16. A pharmaceutical composition comprising the viral vector according to any of claims 1-14 and a pharmaceutically acceptable carrier, diluent, excipient or adjuvant.

17. A host cell, comprising the viral vector according to any of claims 1 to 14, the composition of claim 15, or the pharmaceutical composition according to claim 16.

18. Use of a viral vector according to any of claims 1 to 14, the composition of claim 15, the pharmaceutical composition of claim 16, or the host cell of claim 17, in the manufacture of a medicament for the treatment of a cancer, in a subject in need thereof.

19. Use of a viral vector according to any of claims 1 to 14, the composition of claim 15, the pharmaceutical composition of claim 16, or the host cell of claim 17, in the manufacture of a medicament for inducing an inflating memory CD8+ T cell response in a subject in need thereof.

20. Use of a viral vector according to any of claims 1 to 14, the composition of claim 15, the pharmaceutical composition of claim 16, or the host cell of claim 17 in the manufacture of a medicament for inducing an inflating

memory CD8+ T cell response in a subject in need thereof wherein the inflating memory CD8+ T cell response comprises production of CD8+/CX3CR1+/KLRG-1+ T cells.

21. Use of any one of claims 18 to 20, wherein,

a) the vector, the composition, the pharmaceutical composition or the host cell is to be administered intravenously or intramuscularly;

b) the vector, the composition, the pharmaceutical composition or the host cell is to be administered as a single dose;

c) the vector, the composition, the pharmaceutical composition or the host cell is to be administered as multiple doses;

d) the vector, the composition, the pharmaceutical composition or the host cell is to be administered prophylactically;

e) the vector, the composition, the pharmaceutical composition or the host cell is to be administered therapeutically

f) the vector, the composition, the pharmaceutical composition or the host cell is to be administered in combination with a therapy or therapeutic agent; and/or.

g) the vector, the composition, the pharmaceutical composition or the host cell is to be administered in combination with an immunomodulatory molecule either separately, sequentially or simultaneously.

22. Use of any one claims 18 to 20, wherein the immunomodulatory molecule is an immune checkpoint inhibitor selected from the group consisting of CTLA-4, PD-1, PD-L1, PD-L2, TIM3, LAG -3, B7-H3, B7-H4, B7-H6, A2aR, BTLA, GAL9 and IDO.

23. Use of claim 19 or 20, wherein the inflating memory CD8+ T cell response comprises production of

a) CD8+/CX3CR1+/KLRG-1+/CD44+ T cells;

b) CD8+/CX3CR1+/KLRG-1+/CD62L- T cells; or

c) CD8+/CX3CR1+/KLRG-1+/CD44+/CD62L- T cells.

24. Use of claim 19 or 20, wherein the inflating memory CD8+ T cell response

a) is capable of controlling tumour growth in the subject greater than 50 days after the pharmaceutical composition is administered; and/or

b) comprises production of CD8+/CX3CR1+/KLRG-1+ T cells that

i) have sustained expression of Tbx21 and/or E2f2;

ii) have low expression of Eomes;

iii) have low expression of PD-1, Tim-3, and/or Lag-3;

iv) form 2 percent to 20 percent of total circulating CD8+ T cells in the subject; and/or

v) maintain a memory effector phenotype for at least 30 days.

25. Use of claim 18, wherein the cancer is colorectal cancer, prostate cancer, oesophageal cancer, liver cancer, renal cancer, lung cancer, breast cancer, pancreatic cancer, brain cancer, hepatocellular cancer, lymphoma, leukaemia, gastric cancer, cervical cancer, ovarian cancer, thyroid cancer, melanoma, carcinoma, head and neck cancer, skin cancer, nasopharyngeal cancer, Epstein Barr driven cancers, Human Papilloma virus driven cancers ~~and, or~~ soft tissue sarcoma.

~~12. The~~26. A viral vector according to any of claims 1 to ~~11, wherein~~14, the composition of claim 15, the pharmaceutical composition of claim 16, or the host cell of claim 17 for use in therapy. vector is human serotype 5 (AdHu5).

~~13. The vector according to any of claims 1 to 12, wherein the vector comprises a CMV promoter.~~

~~14. The vector according to any of claims 1 to 13, wherein the vector comprises a TATA box.~~

~~15. The vector according to any of claims 1 to 14, wherein the vector lacks the E1 and E3 proteins.~~

~~16. An immunogenic composition, comprising the vector according to any of claims 1 to 15.~~

~~17. An immunogenic composition, comprising at least two vectors according to any of claims 1 to 15.~~

~~18. The composition according to claim 17, wherein each vector encodes a different cancer specific CD8+ T-cell epitope.~~

~~19. The composition of any of claims 16 to 18, comprising one or more additional active ingredients, pharmaceutically acceptable carrier, diluent, excipient or adjuvant.~~

~~20. A host cell, comprising the vector according to any of claims 1 to 15, or the immunogenic composition according to any of claims 16 to 19.~~

~~21. The vector or composition according to any of claims 1 to 19, for use in therapy.~~

~~22. — The vector or composition according to any of claims 1 to 19, for use in the treatment or prevention of cancer.~~

~~23. — A method of treating or preventing a cancer, comprising administering a therapeutically effective amount of the vector according to claims 1 to 15 or a composition according to claims 16 to 19.~~

~~27. — Use of a composition of claim 15 in the manufacture of a medicament for the treatment of a cancer, in a subject in need thereof wherein each of the at least two viral vectors are present in the medicament at an amount that is not therapeutically effective individually, thereby treating the cancer in the subject, optionally wherein the cancer is selected from colorectal cancer, prostate cancer, oesophageal cancer, liver cancer, renal cancer, lung cancer, breast cancer, pancreatic cancer, brain cancer, hepatocellular cancer, lymphoma, leukaemia, gastric cancer, cervical cancer, ovarian cancer, thyroid cancer, melanoma, carcinoma, head and neck cancer, skin cancer, nasopharyngeal cancer, Epstein Barr driven cancers, Human Papilloma virus driven cancers, or soft tissue sarcoma.~~

~~24. — A method of inducing an inflating memory CD8⁺ T cell response, comprising the step of; administering a therapeutically effective amount of the vector according to any of claims 1 to 15, or composition according to any of claims 16 to 19, to a subject in need thereof, wherein the CD8⁺ T cells are characterised by markers selected from the group comprising CX3CR1⁺, KLRG-1⁺, CD44⁺ and CD62L⁻.~~

~~25. — The vector or composition according to claim 21 or 22, the method according to claim 23 or 24, wherein the vector or composition is administered intravenously or intramuscularly.~~

~~26. — The vector or composition according to claim 21 or 22, the method according to claim 23 or 24, wherein the vector or composition is administered as a single dose.~~

~~27. — The vector or composition according to claim 21 or 22, the method according to claim 23 or 24, wherein the vector or composition is administered as multiple doses.~~

~~28. — The vector or composition according to claim 21 or 22, the method according to claim 23 or 24, wherein the vector or immunogenic composition is administered prophylactically to the subject.~~

~~29. — The vector or composition according to claim 21 or 22, the method according to claim 23 or 24, wherein the vector or immunogenic composition is administered therapeutically to the subject.~~

~~30. — The vector or composition according to claim 21 or 22, the method according to claim 23 or 24, wherein the vector or composition is administered in combination with an immunomodulatory molecule either separately, sequentially or simultaneously.~~

~~31. — The method, vector or composition according to claim 30, wherein the immunomodulatory molecule is an immune checkpoint inhibitor.~~

~~32. — The method, vector or composition according to claim 31, wherein the immune check point inhibitor is an inhibitor of an immune checkpoint protein selected from the group consisting of CTLA-4, PD-1, PD-L1, PD-L2, TIM3, LAG-3, B7-H3, B7-H4, B7-H6, A2aR, BTLA, GAL9 and IDO.~~

~~33. — A method of producing the vector according to any of claim 1 to 15, comprising the steps of;~~
~~i) synthesising the nucleic acid sequence encoding the epitope, as a sense and antisense primer,~~
~~ii) cloning the nucleic acid sequence encoding epitope sequence into a first plasmid,~~
~~iii) cloning the sequence comprising the nucleic acid sequence encoding epitope into a second vector comprising the adenoviral DNA.~~

~~34. — A kit comprising the vector according to any of claims 1 to 15 or a composition according to claims 16 to 19, one or more additional active ingredients, pharmaceutically acceptable carrier, diluent, excipient or adjuvant, and optionally instructions for use.~~

~~35. — A method for inducing a T cell immune response in an animal against a cancer specific CD8+ T cell epitope, comprising contacting a cell with the vector to claims 1 to 15 or a composition according to claims 16 to 19.~~