The vaccine of the present invention has therefore been demonstrated to have the capacity to alter the microenvironment surrounding a tumour, making it "visible" to the immune system, permitting T cell infiltration, not only to provoke an immune response to the tumour itself, but further to cancer associated fibroblasts which entirely unexpectedly have been shown to express the MAGED4B protein too. Thus, a vaccine according to the present invention has the capacity to alter cells surrounding the tumour that act to protect such cancer cells from the immune system and anti-cancer agents. Thus, the vaccine of the invention has far-reaching implications for the modulation of the cancer microenvironment, exposing the tumour to the immune system, enhancing the immune response against the tumour and thus greatly assisting tumour cell death.

Notably, the present inventors have found that the vaccine of the invention is very unlikely to cause harm to the normal tissues in the body, since patterns of expression in other tissues is minimal. Thus, this makes the vaccine clinically relevant.

Thus, the present invention provides vaccines that treat and provide protection against tumour growth.

An aim of the present invention is to provide a cancer vaccine that can provide an appropriate immune response against cancer cells, particularly oral and oropharyngeal cancer cells.

Summary

The present disclosure relates to the provision of a nucleic acid vaccine. The vaccine according to any part hereof may be formulated as a vaccine composition. The nucleic acid vaccine is a cancer vaccine, for use in treating cancer. Various alternative vaccines are described. As used herein, either protein may be described as a cancer antigen.

In one aspect, the present disclosure refers to an anti-cancer agent comprising a DNA encoding an immunologically active truncated version of MAGED4B protein, wherein said immunologically active truncated version of MAGED4B protein comprises between 400 and 700 amino acids of a sequence which has at least 85% sequence identity to the MAGED4B sequence as set forth in in any one of sequence SEQ ID No. 3, 31, 41, 42 or 43, wherein said truncated version comprises the removal of all or part of a MAGE homology domain corresponding to residues 412-682 of SEQ ID No. 3.

In another aspect, the present disclosure refers to the anti-cancer agent as disclosed herein for use in therapy.

In another aspect, the present disclosure refers to the use of the anti-cancer agent as disclosed herein in the manufacture of a medicament for treating cancer in a human or animal subject, wherein the cancer overexpresses MAGED4B.

In another aspect, the present disclosure refers to the use of the anti-cancer agent as disclosed herein in the manufacture of a medicament for revealing a tumour to the immune system, wherein the cancer overexpresses MAGED4B.

In another aspect, the present disclosure refers to the use of the anti-cancer agent as disclosed herein in the manufacture of a medicament for sensitising a tumour to a second anticancer agent, wherein the cancer overexpresses MAGED4B.

In another aspect, the present disclosure refers to the use of an anti-cancer agent as disclosed herein in the manufacture of a medicament for sensitising a tumour to infiltration by CD8+ T cells in a human or animal subject.

In another aspect, the present disclosure refers to a method of selecting a cancer for treatment with the anti-cancer agent as disclosed herein, said method comprising determining whether a cancer is associated with the expression of MAGED4B alone, or in combination with FJX1.

In yet another aspect, the present disclosure refers to the use of an anti-cancer agent as disclosed herein in the manufacture of a medicament for treating cancer by increasing the efficacy of immune checkpoint blockade in a patient in need thereof.

The cancer vaccine may comprise a nucleic acid which encodes a MAGED4B protein or a variant thereof. This may be the full length protein as described in SEQ ID No. 3 or SEQ ID No. 31, but this can be truncated or modified, such that a sufficient amount of the protein is provided by the nucleic acid, to enable the protein to be processed within the cell and presented to the immune system. Suitable truncations are described in SEQ ID No. 35 to SEQ ID No. 37. Thus, the MAGED4B protein may be an immunogenic fragment of the full length protein as described herein. The sequence MADGED4B protein may further be modified, such that amino acid substitutions are made. Such variants, modifications and truncations are discussed further herein.

Known isoforms (variants) of MAGED4B are described in No. 41-43.

Alternatively defined, the cancer vaccine may include a nucleic acid encoding a MAGED4B protein, said nucleic acid sequence as described in SEQ ID No. 7, SEQ ID No. 16, SEQ ID No. 17, SEQ ID No. 24, SEQ ID No. 25 or SEQ ID No. 26, or variants and truncated versions thereof. Variants and truncations are as defined herein.

Optionally, the composition may also include a nucleic acid which encodes a FJX1 protein or a variant thereof. The protein may be a full length protein as described in SEQ ID No. 4 or SEQ ID No. 33 or may be truncated or modified. Such variants, modifications and truncations are discussed further herein.

CLAIMS

1. An anti-cancer agent comprising a DNA encoding an immunologically active truncated version of MAGED4B protein, wherein said immunologically active truncated version of MAGED4B protein comprises between 400 and 700 amino acids of a sequence which has at least 85% sequence identity to the MAGED4B sequence as set forth in in any one of sequence SEQ ID No. 3, 31, 41, 42 or 43, wherein said truncated version comprises the removal of all or part of a MAGE homology domain corresponding to residues 412-682 of SEQ ID No. 3.

2. The anti-cancer agent according to claim 1 wherein said DNA encodes a MAGED4B protein as set forth in any one of SEQ ID No. 35 to SEQ ID No. 37.

3. The anti-cancer agent according to any preceding claim wherein the nucleic acid sequence has at least 85% sequence identity to the sequence set forth in any one of SEQ ID No. 7, SEQ ID No. 16, SEQ ID No. 17, SEQ ID No. 24, SEQ ID No. 25 or SEQ ID No. 26.

4. The anti-cancer agent according to any preceding claim further comprising a helper motif.

5. The anti-cancer agent according to claim 4 wherein said helper motif encodes a protein which stimulates an immunological response.

6. The anti-cancer agent as described in claim 4 or claim 5 wherein said helper motif encodes an immunological fragment of a protein.

7. The anti-cancer agent as described in claim 6 wherein said helper motif encodes a helper epitope.

8. The anti-cancer agent of any one of claims 4 to 7 wherein the helper motif is an immunogenic fragment of tetanus toxin.

9. The anti-cancer agent of claim 8 wherein the helper motif is the p30 MHCII epitope of tetanus toxin.

10. The anti-cancer agent of claim 8 or claim 9 wherein the helper motif is DOM.

11. The anti-cancer agent according to any preceding claim wherein said anti-cancer agent further comprises a nucleic acid encoding a FJX1 protein, wherein said FJX1 protein has at least 85% identity to a sequence as set forth in SEQ ID No. 4 or SEQ ID No. 33.

12. The anti-cancer agent of claim 11, wherein said FJX1 protein is optionally encoded by a nucleic acid that has at least 85% identity to a nucleic acid sequence as described in SEQ ID No. 8, SEQ ID No. 20 or SEQ ID No. 21.

13. The anti-cancer agent of claim 11 or claim 12 wherein said MAGED4B and FJX1 are encoded by the same DNA as a fusion protein.

14. The anti-cancer agent of claim 13 wherein the fusion protein further comprises an immunological fragment of a protein.

15. The anti-cancer agent of claim 13 or claim 14 wherein the fusion protein includes one or more linker proteins between MAGED4B and/or FJX1 and/or the immunological fragment of a protein.

16. The anti-cancer agent of any preceding claim wherein at least one nucleic acid encodes a signal peptide.

17. The anti-cancer agent of any preceding claim wherein said DNA is a plasmid, a closed linear DNA, a minicircle DNA or a single stranded circular DNA.

18. The anti-cancer agent of any preceding claim in which the DNA further comprises a promoter operably linked to the coding sequences.

19. The anti-cancer agent of claim 18 wherein the promoter further comprises a polyadenylation signal downstream of the encoding sequences.

20. An anti-cancer agent as claimed in any one of claims 1 to 19 for use in therapy.

21. Use of the anti-cancer agent as claimed in any one of claims 1 to 19 in the manufacture of a medicament for treating cancer in a human or animal subject, wherein the cancer overexpresses MAGED4B.

22. Use of the anti-cancer agent as claimed in any one of claims 1 to 19 in the manufacture of a medicament for revealing a tumour to the immune system, wherein the tumour overexpresses MAGED4B.

23. Use of the anti-cancer agent as claimed in any one of claims 1 to 19 in the manufacture of a medicament for sensitising a tumour to a second anticancer agent, wherein the tumour overexpresses MAGED4B.

24. The use of claim 23 wherein the second anticancer agent is an immune checkpoint inhibitor.

25. The anti-cancer agent for use as claimed in claim 20, or the use of claims 21-24, wherein said anti-cancer agent is to be used in combination with a second anti-cancer agent.

26. The anti-cancer agent for use as claimed in claim 25, or the use of claim 25, wherein the second anti-cancer agent is an immune checkpoint inhibitor.

27. Use of an anti-cancer agent of any one of claims 1 to 19 in the manufacture of a medicament for sensitising a tumour to infiltration by $CD8^+$ T cells in a human or animal subject.

28. The use of claim 21 or 27, wherein said use further comprises the use of a second anti-cancer agent.

29. The use of claim 28, wherein the second anti-cancer agent is an immune checkpoint inhibitor.

30. The use of any one of claim 22 to 29 or the anti-cancer agent for use of claim 25, wherein said checkpoint inhibitor is an agent capable of blocking the action of PD-1, PD-L1, PD-L2 or CTLA-4.

31. The use of claim 30 or the anti-cancer agent for use of claim 30, wherein the agent is an antibody or aptamer.

32. The anti-cancer agent for use of claim 20, 25 or 26, or the use according to any one of claims 21-31, wherein said cancer or tumour is any one or more of head and neck cancer, oral cancer, oropharyngeal cancer, nasopharyngeal cancer, lung cancer, breast cancer, oesophageal cancer, stomach cancer, liver cancer, colon cancer, kidney cancer, cholangiocarcinoma, cutaneous melanoma, rectal cancer, thyroid cancer, bladder urothelial carcinoma, renal cancer and stomach adenocarcinoma.

33. A method of selecting a cancer for treatment with the anti-cancer agent of any one of claims 1-19, said method comprising determining whether a cancer is associated with the expression of MAGED4B alone, or in combination with FJX1.

34. Use of an anti-cancer agent of any one of claims 1 to 19 in the manufacture of a medicament for treating cancer by increasing the efficacy of immune checkpoint blockade in a patient in need thereof.

35. The anti-cancer agent of any one of claims 1 to 19 wherein said truncated version comprises the removal of the MAGED4B common homology domain (residues 412 to 682 of SEQ ID No. 3).