

In a first aspect, the present disclosure provides a polypeptide comprising a fragment of an invariant chain (INV) of a *Teleostei*, which has T cell response enhancer activity, comprising or consisting of between 16 to 27 amino acids of the membrane proximal domain (MPD) of an INV of the *Teleostei*, wherein the MPD is characterized by the following amino acid sequence (SEQ ID NO: 31):

5 X<sub>1</sub> QKX<sub>2</sub> QIHTLQKX<sub>3</sub> SX<sub>4</sub> RX<sub>5</sub> X<sub>6</sub> X<sub>7</sub> QX<sub>8</sub> TRX<sub>9</sub> SX<sub>10</sub> AV

wherein

X<sub>1</sub> is G, D, S or N;

X<sub>2</sub> is E or Q;

X<sub>3</sub> is N or S;

10 X<sub>4</sub> is D or E;

X<sub>5</sub> is M or L;

X<sub>6</sub> is G, N, S or T;

X<sub>7</sub> is K or R;

X<sub>8</sub> is L or M;

15 X<sub>9</sub> is S, T or A; and

X<sub>10</sub> is Q or H;

and wherein the 16 to 27 amino acids of the MPD are preferably at least 70% identical to SEQ ID NO: 7;

and optionally one or more antigens and/or one or more antigenic fragments thereof.

20 In one example, the present disclosure provides a polypeptide comprising:

- (a) a fragment of an invariant chain (INV) of a *Teleostei*, which has T cell response enhancer activity, comprising or consisting of between 16 to 27 amino acids of the membrane proximal domain (MPD) of an INV of the *Teleostei*, wherein the MPD is preferably characterized by the following amino acid sequence:

25 X<sub>1</sub> QKX<sub>2</sub> QIHTLQKX<sub>3</sub> SX<sub>4</sub> RX<sub>5</sub> X<sub>6</sub> X<sub>7</sub> QX<sub>8</sub> TRX<sub>9</sub> SX<sub>10</sub> AV

wherein

X<sub>1</sub> is G, D, S or N;

X<sub>2</sub> is E or Q;

X<sub>3</sub> is N or S;

30 X<sub>4</sub> is D or E;

X<sub>5</sub> is M or L;

X<sub>6</sub> is G, N, S or T;

X<sub>7</sub> is K or R;

X<sub>8</sub> is L or M;

35 X<sub>9</sub> is S, T or A; and

X<sub>10</sub> is Q or H;

and wherein the 16 to 27 amino acids of the MPD are preferably at least 70% identical to SEQ ID NO: 7;

and optionally one or more antigens or antigenic fragments thereof;

5 or

- (b) a full length *Teleostei* INV of SEQ ID NO: 1 or a variant thereof, which has T cell response enhancer activity, wherein the amino acid sequence of the MPD of the variant is at least 80% identical to SEQ ID NO: 7 and one or more antigens or antigenic fragments thereof.

10 In a second aspect the present disclosure relates to a polynucleotide encoding the polypeptide according to the first aspect of the present disclosure, wherein the polynucleotide is preferably DNA or RNA, more preferably a DNA.

In a third aspect the present disclosure relates to a vector comprising the polynucleotide according to the second aspect of the disclosure.

15 In a fourth aspect the present disclosure relates to a collection of two or more different vectors, wherein the different vectors each comprise a polynucleotide according to the second aspect of the present disclosure encoding a different polypeptide according to the first aspect of the present disclosure.

20 In a fifth aspect the present disclosure relates to a pharmaceutical composition comprising the polypeptide of the first aspect of the present disclosure, a polynucleotide of the second aspect of the present disclosure or a vector of the third aspect of the present disclosure or collection of vectors of the fourth aspect of the disclosure and a pharmaceutically acceptable excipient and optionally one or more adjuvants.

25 In another aspect, the present disclosure refers to a kit of parts comprising the pharmaceutical composition as described herein and separately packaged at least one immunomodulator, or at least one polynucleotide encoding the immunomodulator, or a vector comprising the polynucleotide encoding the immunomodulator.

30 In an example the present disclosure relates to a kit of parts comprising the pharmaceutical composition of the fifth aspect of the present disclosure and separately packaged at least one immunomodulator, for example a modulator of a checkpoint molecule (MCM), or at least one polynucleotide encoding the immunomodulator, for example a MCM, or a vector comprising the polynucleotide encoding the immunomodulator, for example a MCM.

35 In yet another aspect, the present disclosure refers to the use of a polypeptide as described herein, the polynucleotide as described herein, a vector or a collection of vectors as described herein, or a pharmaceutical composition or kits comprising such pharmaceutical compositions as described herein in the manufacture of a medicament for preventing or treating a proliferative disease, preferably cancer,

viral disease, fungal disease or bacterial disease. In a further aspect, the present disclosure refers to the use of the pharmaceutical composition as described herein, or the kit of parts as described herein, in the manufacture of a medicament for preventing or treating a proliferative disease, preferably cancer, viral disease, fungal disease or bacterial disease, wherein the at least one immunomodulator, or the at least one polynucleotide encoding the immunomodulator, or the vector or liposomal particle comprising the polynucleotide encoding the immunomodulator, is to be administered prior to, concomitantly with or subsequently to the administration of said medicament.

In an example the present disclosure relates to a polypeptide according to the first aspect of the disclosure, a polynucleotide according to the second aspect of the disclosure, or a vector or a collection of vectors according to third or fourth aspect of the disclosure for use as a medicament.

In another example the present disclosure relates to polypeptide according to the first aspect of the disclosure, a polynucleotide according to the second aspect of the disclosure, or a vector or a collection of vectors according to third or fourth aspect of the disclosure, or a pharmaceutical composition according to the fifth aspect of the disclosure or kits comprising such pharmaceutical compositions according to the sixth aspect of the disclosure for use in preventing or treating a proliferative disease, preferably cancer, viral disease or bacterial disease.

#### FIGURE LEGENDS

**Fig. 1:** Immunogenicity of GAd vectors at doses of  $5 \times 10^7$  vp or  $5 \times 10^8$  vp. Vectors encode for Mandarin Fish INV full length (MF\_INV\_FL), Mandarin Fish INV short version (residue 1 to 81, MF\_INV\_SH), Mandarin Fish INV variants A (residue 62 to 88, MF\_INV\_A) and B (residue 66 to 81, MF\_INV\_B) linked to the CT26 pentatope antigen. Penta represents the CT26 pentatope antigen without the Mandarin Fish INV sequence or a fragment thereof and with only an initial methionine. Values reported were obtained by an ELISpot assay on spleen cells of immunized animals. Splenocytes were stimulated ex vivo two weeks post vaccination with a pool of five synthetic peptides corresponding to the sequences of the five cancer specific neoantigens containing the mutation. Responses are expressed as number of T cells producing  $\text{IFN}\gamma$  per millions of splenocytes. Shown at the bottom is the number of mice showing a positive response out of a total number of 6 immunized mice for each tested vector construct. The dashed line represents the threshold for a positive response.

**Fig. 2:** Alignment of invariant chains of various *Teleostei* species. The first box characterizes the 26 amino acid long transmembrane domain (TMD). The membrane proximal domain (MPD) is immediately C-terminally of the TMD and highlighted with a second box. The location and extend of the short 16 amino acid long invariant chain fragment MF\_INV\_B comprised in the MPD is highlighted by a series of asterisk (\*) below the second box. The INV sequences are from top to

## CLAIMS

1. A polypeptide comprising a fragment of an invariant chain (INV) of a *Teleostei*, which has T cell response enhancer activity, comprising or consisting of between 16 to 27 amino acids of the membrane proximal domain (MPD) of an INV of the *Teleostei*, wherein the MPD is characterized by the following amino acid sequence (SEQ ID NO: 31):

X<sub>1</sub> QKX<sub>2</sub> QIHTLQKX<sub>3</sub> SX<sub>4</sub> RX<sub>5</sub> X<sub>6</sub> X<sub>7</sub> QX<sub>8</sub> TRX<sub>9</sub> SX<sub>10</sub> AV

wherein

X<sub>1</sub> is G, D, S or N;

X<sub>2</sub> is E or Q;

X<sub>3</sub> is N or S;

X<sub>4</sub> is D or E;

X<sub>5</sub> is M or L;

X<sub>6</sub> is G, N, S or T;

X<sub>7</sub> is K or R;

X<sub>8</sub> is L or M;

X<sub>9</sub> is S, T or A; and

X<sub>10</sub> is Q or H;

and wherein the 16 to 27 amino acids of the MPD are preferably at least 70% identical to SEQ ID NO: 7;

and optionally one or more antigens and/or one or more antigenic fragments thereof.

2. The polypeptide of claim 1, wherein the amino acid sequence of:

(a) the MPD according to claim 1 is any of SEQ ID NOs: 7 to 12; or

(b) the fragment according to claim 1 comprises or consists of any of SEQ ID NOs: 7 to 18.

3. The polypeptide of claim 1 (a) or claim 2 alternative (a) or (b), wherein the fragment consists of at least 16 to 27 N-terminal amino acids of the MPD and:

- (i) 1 to 26 consecutive amino acids of the transmembrane domain (TMD) of an INV of a *Teleostei* immediately N-terminal of the MPD, wherein the TMD of the INV of the *Teleostei* is preferably characterized by the following amino acid sequence (SEQ ID NO: 32):

AY<sub>1</sub>KY<sub>2</sub>AY<sub>3</sub>LTTLY<sub>4</sub>CLLY<sub>5</sub>Y<sub>6</sub>SQVFTAYY<sub>7</sub>VF

wherein

Y<sub>1</sub> is L or F;

Y<sub>2</sub> is I or V;

Y<sub>3</sub> is G or A;

Y<sub>4</sub> is T or A;

Y<sub>5</sub> is L or V;

5 Y<sub>6</sub> is A or S; and

Y<sub>7</sub> is M or T;

and/or

(ii) 1 to 19 consecutive amino acids of the INV of a *Teleostei* immediately C-terminal of the MPD preferably characterized by the following amino acid sequence (SEQ ID NO: 33):

10 APZ<sub>1</sub>Z<sub>2</sub>MZ<sub>3</sub>Z<sub>4</sub>PMZ<sub>5</sub>SLPZ<sub>6</sub>Z<sub>7</sub>Z<sub>8</sub>DZ<sub>9</sub>Z<sub>10</sub>

wherein

Z<sub>1</sub> is M, V or A;

Z<sub>2</sub> is R or K;

Z<sub>3</sub> is H, A or Q;

15 Z<sub>4</sub> is M or L;

Z<sub>5</sub> is N or S;

Z<sub>6</sub> is M or L;

Z<sub>7</sub> is M, L or V;

Z<sub>8</sub> is M or S;

20 Z<sub>9</sub> is F or Y; and

Z<sub>10</sub> is T or S.

4. The polypeptide according to any of claims 1 to 3, wherein the antigen in each case is independently selected from the group consisting of a cancer-specific antigen, a cancer specific neoantigen or, a viral protein, a bacterial protein, wherein preferably:

25 (i) the polypeptide comprises at least five different antigens and/or antigenic fragments thereof;

and/or

(ii) the one or more antigens and/or one or more antigenic fragments thereof are C-terminally of the fragment of the INV according to alternative (a) of claim 1 or the full length INV according to alternative (b) of claim 1.

30 5. A polynucleotide encoding the polypeptide according to any one of claims 1 to 4, wherein the polynucleotide is preferably DNA or RNA, more preferably a DNA.

6. A vector comprising the polynucleotide according to claim 5.
7. A collection of two or more different vectors, wherein the different vectors each comprise a polynucleotide according to claim 5 encoding a different polypeptide according to claims 1 to 4.
8. The vector of claim 6 or the collection of vectors of claim 7, wherein the vector in each case is independently selected from the group consisting of a plasmid; a cosmid; a liposomal particle, a viral vector or a virus like particle; preferably an alphavirus vector, a venezuelan equine encephalitis (VEE) virus vector, a sindbis (SIN) virus vector, a semliki forest virus (SFV) virus vector, a simian or human cytomegalovirus (CMV) vector, a Lymphocyte choriomeningitis virus (LCMV) vector, a retroviral vector, a lentiviral vector, an adenoviral vector, an adeno-associated virus vector a poxvirus vector, a vaccinia virus vector or a modified vaccinia ankara (MVA) vector, wherein the adenoviral vector is preferably a Great Apes adenoviral vector, more preferably a chimpanzee or bonobo or gorilla adenoviral vector.
9. A pharmaceutical composition comprising the polypeptide of any of claims 1 to 4, polynucleotide of claim 5, or a vector(s) of claim 6 to 8, a pharmaceutically acceptable excipient and optionally one or more adjuvants.
10. The pharmaceutical composition of claim 9, further comprising at least one immunomodulator, or at least one polynucleotide encoding the immunomodulator, or a vector or liposomal particle comprising the polynucleotide encoding the immunomodulator.
11. A kit of parts comprising the pharmaceutical composition of claim 9 and separately packaged at least one immunomodulator, or at least one polynucleotide encoding the immunomodulator, or a vector comprising the polynucleotide encoding the immunomodulator.
12. The pharmaceutical composition of claim 10 or the kit of parts of claim 11, wherein:
  - (i) the immunomodulator is a MCM and is selected from the group consisting of:
    - (a) an agonist of a tumor necrosis factor (TNF) receptor superfamily member, preferably of CD27, CD40 (e.g. CP-870,893), OX40, GITR or CD137; and/or
    - (b) an antagonist of PD-1, CD274, A2AR, B7-H3 (e.g. MGA271), B7-H4, BTLA, CTLA-4, IDO, KIR, LAG3, TIM-3, or VISTA or an antagonist of a B7-CD28 superfamily member, preferably of CD28 or ICOS or an antagonist of a ligand thereof;

and/or

(ii) the immunomodulator is a T cell growth factor, preferably IL-2, IL-12, or IL-15.

- 5 13. Use of a polypeptide according to claims 1 to 4, the polynucleotide according to claim 5, a vector or a collection of vectors according to claim 6 to 8, or a pharmaceutical composition or kits comprising such pharmaceutical compositions according to claims 9 to 12 in the manufacture of a medicament for preventing or treating a proliferative disease, preferably cancer, viral disease, fungal disease or bacterial disease.
- 10 14. The use according to claim 13, wherein the cancer is selected from the group consisting of malignant neoplasms of lip, oral cavity, pharynx, a digestive organ, respiratory organ, intrathoracic organ, bone, articular cartilage, skin, mesothelial tissue, soft tissue, breast, female genital organs, male genital organs, urinary tract, brain and other parts of central nervous system, thyroid gland, endocrine glands, lymphoid tissue, and haematopoietic tissue.
- 15 15. Use of the pharmaceutical composition according to claim 10 or 12, or the kit of parts according to claim 11 or 12, in the manufacture of a medicament for preventing or treating a proliferative disease, preferably cancer, viral disease, fungal disease or bacterial disease, wherein the at least one immunomodulator, or the at least one polynucleotide encoding the immunomodulator, or
   
20 the vector or liposomal particle comprising the polynucleotide encoding the immunomodulator, is to be administered prior to, concomitantly with or subsequently to the administration of said medicament.