

CLAIMS:

1. A peptide mixture comprising a first and a second peptide, each independently selected from:

5 a peptide capable of inducing an immune response against a TGF β R2 -1a frameshift mutant protein, wherein the peptide comprises i) an immunogenic fragment of SEQ ID NO: 3, wherein the fragment comprises at least 8 consecutive amino acids of SEQ ID NO: 3 including at least one of positions 121 and 135 of SEQ ID NO: 3, or ii) an immunogenic fragment of SEQ ID NO: 2, wherein the fragment comprises at least
10 10 consecutive amino acids of SEQ ID NO: 19;

a peptide capable of inducing an immune response against a ASTE1 -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of SEQ ID NO: 5, wherein the fragment comprises at least 10 consecutive amino acids of SEQ ID NO: 26 ;

15 a peptide capable of inducing an immune response against a TAF1 β -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of SEQ ID NO: 7, wherein the fragment comprises at least 8 consecutive amino acids of SEQ ID NO: 27;

a peptide capable of inducing an immune response against a KIAA2018 -1a frameshift mutant protein, wherein the peptide comprises a immunogenic fragment of one of SEQ ID NOs: 9-12, wherein the fragment comprises at least 8 consecutive amino acids of one of one of SEQ ID NOs: 9-12, respectively, including at least one amino acid from positions 13 to 37 of SEQ ID NO: 9, positions 91 to 109 of SEQ ID NO: 10, positions 147 to 167 of SEQ ID NO: 11 and positions 1016 to 1037 of SEQ ID
20 NO: 12, respectively; and
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a peptide capable of inducing an immune response against a SLC22A9 -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of one of SEQ ID NO: 14-18, wherein the fragment comprises at least 8 consecutive amino acids of one of SEQ ID NOs: 14-18, respectively, including at least one amino
30 acid from positions 327 to 400 of SEQ ID NO: 14, positions 335 to 400 of SEQ ID NO: 15, positions 533 to 549 of SEQ ID NO: 16, positions 327 to 400 of SEQ ID NO: 17 and positions 335 to 400 of SEQ ID NO: 18, respectively;

wherein the first peptide is capable of inducing an immune response against a different frameshift mutant protein from the second peptide.

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2. A peptide mixture according to claim 1, wherein the peptide comprising an immunogenic fragment of SEQ ID NO: 3 comprises at least 9, preferably at least 10, consecutive amino acids of SEQ ID NO: 3, or the peptide comprising an immunogenic fragment of SEQ ID NO: 2 comprises at least 9, preferably at least 10, consecutive amino acids of SEQ ID NO: 19.

3. A peptide mixture according to claim 1 or 2, wherein the peptide capable of inducing an immune response against a TGF β R2 -1a frameshift mutant protein comprises position 121 to 132 of SEQ ID NO: 3, positions 129 to 137 of SEQ ID NO: 3, positions 135 to 146 of SEQ ID NO: 3 or positions 2 to 17 of SEQ ID NO: 19, positions 10 to 18 of SEQ ID NO: 19 or positions 16 to 33 of SEQ ID NO: 19, preferably wherein the amino acid corresponding to position 121 or 135 of SEQ ID NO: 3 is glycine.

4. A peptide mixture according to any one of the preceding claims, wherein the peptide capable of inducing an immune response against a TGF β R2 -1a frameshift mutant protein comprises the amino acid sequence of one of SEQ ID NOs: 19 to 25, 124 and 125, preferably wherein the peptide consists of one of SEQ ID NOs: 19 to 25, 124 and 125.

5. A peptide mixture according to any one of the preceding claims, wherein the immunogenic fragment of SEQ ID NO: 5 comprises at least 10 consecutive amino acids, preferably at least 15 consecutive amino acids, of SEQ ID NO: 26, preferably wherein the peptide capable of inducing an immune response against a ASTE1 -1a frameshift mutant protein comprises the sequence of SEQ ID NO: 26, preferably wherein the peptide capable of inducing an immune response against a ASTE1 -1a frameshift mutant protein consists of SEQ ID NO: 26.

6. A peptide mixture according to any one of the preceding claims, wherein the immunogenic fragment of SEQ ID NO: 7 comprises at least 10 consecutive amino acids, preferably at least 13 consecutive amino acids, of SEQ ID NO: 27, preferably wherein the peptide capable of inducing an immune response against a TAF1 β -1a frameshift mutant protein comprises the sequence of SEQ ID NO: 27, preferably wherein the peptide capable of inducing an immune response against a TAF1 β -1a frameshift mutant protein consists of SEQ ID NO: 27.

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7. A peptide mixture according to any one of the preceding claims, wherein the immunogenic fragment of one of SEQ ID NOs: 9-12 comprises at least 10 consecutive amino acids, preferably at least 15 consecutive amino acids, of one of SEQ ID NOs: 9-12, preferably wherein the peptide comprises the sequence of SEQ ID NO: 28,
5 preferably wherein the peptide consists of SEQ ID NO: 28.

8. A peptide mixture according to any one of the preceding claims, wherein the immunogenic fragment of one of SEQ ID NOs: 14-18 comprises at least 10 consecutive amino acids, preferably at least 15 consecutive amino acids, of one of
10 SEQ ID NOs: 14-18, respectively, including at least one amino acid from positions 327 to 400 of SEQ ID NO: 14, positions 335 to 400 of SEQ ID NO: 15, positions 533 to 549 of SEQ ID NO: 16, positions 327 to 400 of SEQ ID NO: 17 and positions 335 to 400 of SEQ ID NO: 18, respectively, preferably, wherein the peptide capable of inducing an immune response against a SLC22A9 -1a frameshift mutant protein comprises the
15 sequence of one of SEQ ID NOs: 29-32, preferably wherein the peptide consists of one of SEQ ID NOs: 29-32.

9. A peptide mixture according to any one of the preceding claims wherein the first peptide is a peptide capable of inducing an immune response to against a TGF β R2 -1a frameshift mutant protein, and the second peptide is a peptide capable of inducing an
20 immune response against a ASTE1 -1a frameshift mutant protein or a TAF1 β -1a frameshift mutant protein.

10. A peptide mixture according to any one of the preceding claims, wherein the peptide mixture comprises at least one further peptide selected from the peptides defined in claim 1, wherein the at least one further peptide is capable of inducing an immune response against a different frameshift mutant protein from each of the first and second peptides, preferably wherein the first peptide is a peptide capable of inducing an immune response against a TGF β R2 -1a frameshift mutant protein, the
25 second peptide is a peptide capable of inducing an immune response against a ASTE1 -1a frameshift mutant protein, and the at least one further peptide is a peptide capable of inducing an immune response against a TAF1 β -1a frameshift mutant protein, and preferably wherein the peptide mixture further comprises a peptide capable of inducing an immune response against a KIAA2018 -1a frameshift mutant protein and/or a
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peptide capable of inducing an immune response against a SLC22A9 -1a frameshift mutant protein.

11. A peptide mixture according to any one of the preceding claims, wherein at least one of the peptides in the peptide mixture comprises a glycine residue at its C-terminus.

12. A peptide capable of inducing an immune response against:
a ASTE1 -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of SEQ ID NO: 5, wherein the fragment comprises at least 10 consecutive amino acids of SEQ ID NO: 26;

a TAF1 β -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of SEQ ID NO: 7, wherein the fragment comprises at least 12 consecutive amino acids of SEQ ID NO: 27, and wherein the peptide comprises no more than 27 amino acids;

a KIAA2018 -1a frameshift mutant protein, wherein the peptide comprises a immunogenic fragment of one of SEQ ID NOs: 9-12, wherein the fragment comprises at least 8 consecutive amino acids of one of one of SEQ ID NOs: 9-12, including at least one amino acid from positions 13 to 37 of SEQ ID NO: 9, positions 91 to 109 of SEQ ID NO: 10, positions 147 to 167 of SEQ ID NO: 11 and positions 1016 to 1037 of SEQ ID NO: 12; or

a SLC22A9 -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of one of SEQ ID NO: 14-18, wherein the fragment comprises at least 8 consecutive amino acids of one of SEQ ID NOs: 14-18, including at least one amino acid from positions 327 to 400 of SEQ ID NO: 14, positions 335 to 400 of SEQ ID NO: 15, positions 533 to 549 of SEQ ID NO: 16, positions 327 to 400 of SEQ ID NO: 17 and positions 335 to 400 of SEQ ID NO: 18.

13. A peptide according to claim 12, wherein the peptide comprises a glycine residue at its C-terminus.

14. A T-cell mixture comprising a first and a second T-cell each independently selected from:

a T-cell specific for a peptide capable of inducing an immune response against TGF β R2 -1a frameshift mutant protein as defined in claim 1, wherein the T-cell is a non-transfected T-cell;

5 a T-cell specific for a peptide capable of inducing an immune response against a -1a ASTE1 frameshift mutant protein as defined in claim 1;

a T-cell specific for a peptide capable of inducing an immune response against a TAF1 β -1a frameshift mutant protein as defined in claim 1;

a T-cell specific for a peptide capable of inducing an immune response against a KIAA2018 -1a frameshift mutant protein as defined in claim 1; and

10 a T-cell specific for a peptide capable of inducing an immune response against a SLC22A9 -1a frameshift mutant protein as defined in claim 1,
wherein the first T-cell is specific for a peptide which is capable of inducing an immune response against a different frameshift mutant protein from the peptide for which the second T-cell is specific.

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15. A T-cell specific for a peptide capable of inducing an immune response against:

20 a ASTE1 -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of SEQ ID NO: 5, wherein the fragment comprises at least 10 consecutive amino acids of SEQ ID NO: 26;

a TAF1 β -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of SEQ ID NO: 7, wherein the fragment comprises at least 10 consecutive amino acids of SEQ ID NO: 27, and wherein the peptide comprises no more than 35 amino acids;

25 a KIAA2018 -1a frameshift mutant protein, wherein the peptide comprises a immunogenic fragment of one of SEQ ID NOs: 9-12, wherein the fragment comprises at least 8 consecutive amino acids of one of one of SEQ ID NOs: 9-12, including at least one amino acid from positions 13 to 37 of SEQ ID NO: 9, positions 91 to 109 of SEQ ID NO: 10, positions 147 to 167 of SEQ ID NO: 11 and positions 1016 to 1037 of
30 SEQ ID NO: 12; or

a SLC22A9 -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of one of SEQ ID NO: 14-18, wherein the fragment comprises at least 8 consecutive amino acids of one of SEQ ID NOs: 14-18, including at least one amino acid from positions 327 to 400 of SEQ ID NO: 14, positions 335 to 400 of SEQ

ID NO: 15, positions 533 to 549 of SEQ ID NO: 16, positions 327 to 400 of SEQ ID NO: 17 and positions 335 to 400 of SEQ ID NO: 18,
for use in the treatment and/or prophylaxis of cancer, preferably wherein the cancer is colorectal cancer.

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16. A T-cell receptor, or an antigen-binding fragment thereof, specific for a peptide capable of inducing an immune response against:

a ASTE1 -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of SEQ ID NO: 5, wherein the fragment comprises at least 10 consecutive amino acids of SEQ ID NO: 26;

a TAF1 β -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of SEQ ID NO: 7, wherein the fragment comprises at least 10 consecutive amino acids of SEQ ID NO: 27, and wherein the peptide comprises no more than 35 amino acids;

a KIAA2018 -1a frameshift mutant protein, wherein the peptide comprises a immunogenic fragment of one of SEQ ID NOs: 9-12, wherein the fragment comprises at least 8 consecutive amino acids of one of one of SEQ ID NOs: 9-12, including at least one amino acid from positions 13 to 37 of SEQ ID NO: 9, positions 91 to 109 of SEQ ID NO: 10, positions 147 to 167 of SEQ ID NO: 11 and positions 1016 to 1037 of SEQ ID NO: 12; or

a SLC22A9 -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of one of SEQ ID NO: 14-18, wherein the fragment comprises at least 8 consecutive amino acids of one of SEQ ID NOs: 14-18, including at least one amino acid from positions 327 to 400 of SEQ ID NO: 14, positions 335 to 400 of SEQ ID NO: 15, positions 533 to 549 of SEQ ID NO: 16, positions 327 to 400 of SEQ ID NO: 17 and positions 335 to 400 of SEQ ID NO: 18,
for use in the treatment and/or prophylaxis of cancer, preferably wherein the cancer is colorectal cancer.

17. At least one nucleic acid molecule, wherein the nucleic acid molecule or molecules individually or collectively comprise nucleotide sequences encoding at least two of the peptides defined in claims 1 to 11 or the or each nucleic acid molecule comprises a nucleotide sequence encoding at least one of the peptides defined in claim 12 or 13.

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18. A vector comprising the nucleic acid molecule as defined in claim 17.
19. A host cell comprising the vector as defined in claim 18.
- 5 20. A pharmaceutical composition comprising a peptide mixture as defined in any one of claims 1-11, a peptide as defined in claim 12 or 13, a T-cell mixture as defined in claim 14, a T-cell as defined in claim 15, a nucleic acid molecule as defined in claim 17, a vector as defined in claim 18 or a host cell as defined in claim 19, and a pharmaceutically-acceptable carrier, diluent or excipient.
- 10 21. A peptide mixture as defined in any one of claims 1 to 11, , a T-cell mixture as defined in claim 14, a T-cell as defined in claim 15, a T-cell receptor, or an antigen-binding fragment thereof, as defined in claim 16, a nucleic acid molecule as defined in claim 17, a vector as defined in claim 18, a host cell as defined in claim 19, or a
- 15 pharmaceutical composition as defined in claim 20, for use in the treatment and/or prophylaxis of cancer, preferably wherein the cancer is colorectal cancer.
22. A peptide capable of inducing an immune response against:
- 20 a ASTE1 -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of SEQ ID NO: 5, wherein the fragment comprises at least 10 consecutive amino acids of SEQ ID NO: 26;
- a TAF1 β -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of SEQ ID NO: 7, wherein the fragment comprises at least 10 consecutive amino acids of SEQ ID NO: 27, and wherein the peptide comprises no
- 25 more than 35 amino acids;
- a KIAA2018 -1a frameshift mutant protein, wherein the peptide comprises a immunogenic fragment of one of SEQ ID NOs: 9-12, wherein the fragment comprises at least 8 consecutive amino acids of one of one of SEQ ID NOs: 9-12, including at least one amino acid from positions 13 to 37 of SEQ ID NO: 9, positions 91 to 109 of
- 30 SEQ ID NO: 10, positions 147 to 167 of SEQ ID NO: 11 and positions 1016 to 1037 of SEQ ID NO: 12; or
- a SLC22A9 -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of one of SEQ ID NO: 14-18, wherein the fragment comprises at least 8 consecutive amino acids of one of SEQ ID NOs: 14-18, including at least one
- 35 amino acid from positions 327 to 400 of SEQ ID NO: 14, positions 335 to 400 of SEQ

ID NO: 15, positions 533 to 549 of SEQ ID NO: 16, positions 327 to 400 of SEQ ID NO: 17 and positions 335 to 400 of SEQ ID NO: 18,
for use in the treatment and/or prophylaxis of cancer, preferably wherein the cancer is colorectal cancer.

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23. A method of selecting a peptide mixture, peptide, nucleic acid molecule, vector, host cell, T-cell mixture, T-cell, T-cell receptor or a pharmaceutical composition for administration to a patient, comprising:

10 i) identifying whether a cancer patient has a frameshift mutation in one or more of the TGF β R2 protein, ASTE1 protein, TAF1 β protein, KIAA2018 protein and SLC22A9 protein and, if so,

15 ii) selecting a peptide mixture as defined in any one of claims 1 to 11, a peptide as defined in claim 12 or 13, a T-cell mixture as defined in claim 14, a T-cell as defined in claim 15, a T-cell receptor, or an antigen-binding fragment thereof, as defined in claim 16, a nucleic acid molecule as defined in claim 17, a vector as defined in claim 18, a host cell as defined in claim 19, a pharmaceutical composition as defined in claim 20, or a peptide for use as defined in claim 21.