

CLAIMS:

1. 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, and wherein the peptide comprises at least 22 amino acids and no more than 31 amino acids;

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, and wherein the peptide has only 2 or 3 amino acids from the wild-type amino acid sequence of KIAA 2018 (SEQ ID NO: 8); 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, and wherein the peptide comprises at least 18 amino acids and no more than 28 amino acids.

2. A peptide according to claim 1, wherein the peptide comprises a glycine residue at its C-terminus.

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

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 consecutive amino acids of SEQ ID NO: 19;

5 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-;

10 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;

15 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 NO: 12, respectively; and

20 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 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;

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

30 42. A peptide mixture according to claim 31, 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.

35 53. A peptide mixture according to claim 4 or 23 or 4, 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.

5 64. A peptide mixture according to any one of ~~the preceding claims 3 to 5~~, 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.

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75. A peptide mixture according to any one of ~~the preceding claims 3 to 6~~, 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.

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86. A peptide mixture according to any one of ~~the preceding claims 3 to 7~~, 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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97. A peptide mixture according to any one of ~~the preceding claims 3 to 8~~, 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, preferably wherein the peptide consists of SEQ ID NO: 28.

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108. A peptide mixture according to any one of ~~the preceding claims 3 to 9~~, 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 SEQ ID NOs: 14-18, respectively, including at least one amino acid from positions 327 to 400

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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 sequence of one of SEQ ID NOs: 29-32, preferably wherein the peptide consists of one of SEQ ID NOs: 29-32.

~~119.~~ A peptide mixture according to any one of ~~the preceding claims 3 to 10,~~ 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 immune response against a ASTE1 -1a frameshift mutant protein or a TAF1 β -1a frameshift mutant protein.

~~1012.~~ A peptide mixture according to any one of ~~the preceding claims 3 to 11,~~ wherein the peptide mixture comprises at least one further peptide selected from the peptides defined in claim ~~34,~~ 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 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 peptide capable of inducing an immune response against a SLC22A9 -1a frameshift mutant protein.

~~1113.~~ A peptide mixture according to any one of ~~the preceding claims 3 to 12,~~ wherein at least one of the peptides in the peptide mixture comprises a glycine residue at its C-terminus.

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~~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;~~

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~~—— 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 an 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 34, wherein the T-cell is a non-transfected T-cell;

a T-cell specific for a peptide capable of inducing an immune response against a -1a ASTE1 frameshift mutant protein as defined in claim 34;

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 34;

a T-cell specific for a peptide capable of inducing an immune response against a KIAA2018 -1a frameshift mutant protein as defined in claim 34; and

a T-cell specific for a peptide capable of inducing an immune response against a SLC22A9 -1a frameshift mutant protein as defined in claim 34,

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.

15. A T-cell 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, and wherein the peptide comprises at least 22 amino acids and no more than 31 amino acids;

5 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;

10 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, and wherein the peptide has only 2 or 3 amino acids from the wild-type amino acid sequence of KIAA 2018 (SEQ ID NO: 8); or

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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, and wherein the peptide comprises at least 18 amino acids and no more than 28 amino acids;

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~~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:

30 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, and wherein the peptide comprises at least 22 amino acids and no more than 31 amino acids;

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;

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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, and wherein the peptide has only 2 or 3 amino acids from the wild-type amino acid sequence of KIAA 2018 (SEQ ID NO: 8); or

a SLC22A9 -1a frameshift mutant protein, wherein the peptide comprises an immunogenic fragment of one of SEQ ID NOs: 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, and wherein the peptide comprises at least 18 amino acids and no more than 28 amino acids,
~~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 or the or each nucleic acid molecule comprises a nucleotide sequence encoding at least one of the peptides defined in claim 1 or 2 or 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~~ 3 to 13 ~~or the or each nucleic acid molecule comprises a nucleotide sequence encoding at least one of the peptides defined in claim 12 or 13.~~

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.

20. A pharmaceutical composition comprising a peptide as defined in claim 1 or 2, a peptide mixture as defined in any one of claims 3 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 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.

21. A peptide as defined in claim 1 or 2, a peptide mixture as defined in any one of claims 3 to 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, or a 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. Use of a peptide as defined in claim 1 or 2, a peptide mixture as defined in any one of claims 3 to 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, or a pharmaceutical composition as defined in claim 20, in the preparation of a medicament for the treatment and/or prophylaxis of cancer.

2223. 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.

24. Use of a peptide in the preparation of a medicament for the treatment and/or prophylaxis of cancer, wherein the peptide is 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.

25. The use according to claim 22 or claim 24, wherein the cancer is colorectal cancer.

2326. 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:

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,

ii) selecting a peptide as defined in claim 1 or 2, a peptide mixture as defined in any one of claims 4 to 113 to 13, 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 ~~23~~²⁴.