

Claims

1. A vaccine comprising an immunologically effective amount of:

(i) a polynucleotide comprising a nucleotide sequence encoding a targeting unit, a dimerization unit and an antigenic unit, wherein the antigenic unit comprises at least one betacoronavirus epitope; or

(ii) a polypeptide encoded by the polynucleotide as defined in (i), or

(iii) a dimeric protein consisting of two polypeptides encoded by the polynucleotide as defined in (i); and

a pharmaceutically acceptable carrier.

2. The vaccine according to claim 1, wherein the at least one betacoronavirus epitope is a full-length viral surface protein of a betacoronavirus or a part thereof, preferably

~~3. The vaccine according to claim 2, wherein the viral surface protein is selected from the group consisting of envelope protein, spike protein, membrane protein and hemagglutinin esterase, preferably~~

~~4. The vaccine according to any of claims 2 to 3 wherein the at least one betacoronavirus epitope comprises or is the spike protein.~~

~~5. The vaccine according to any of claims 2 to 4, wherein the at least one betacoronavirus epitope comprises or is the full-length spike protein.~~

~~6. The vaccine according to claim 5, wherein the at least one betacoronavirus epitope comprises or consists of an amino acid sequence having at least 70% sequence identity to the amino acid sequence 243 to 1437 of SEQ ID NO: 275, such as at least 75%, such as at least 77%, such as at least 80%, such as at least 85%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98% or such as at least 99% sequence identity or such as 100% sequence identity.~~

~~7. The vaccine according to any of claims 2 to 4, wherein the at least one betacoronavirus epitope comprises or is a part of the spike protein, preferably~~

8. The vaccine according to claim 7, wherein the part of the spike protein is one selected from the group consisting of receptor binding domain (RBD), heptad repeat 1 (HR1) domain and heptad repeat 2 (HR2) domain.

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94. The vaccine according to claim 83, wherein the at least one betacoronavirus epitope comprises or is the RBD or a part of the RBD, preferably

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10. The vaccine according to claim 9, wherein the at least one betacoronavirus epitope comprises or consists of an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO: 231 or SEQ ID NO: 802, or SEQ ID NO: 803, preferably SEQ ID NO: 803 or SEQ ID NO: 804 or SEQ ID NO: 805, such as at least 75%, such as at least 77%, such as at least 80%, such as at least 85%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98% or such as at least 99% sequence identity or such as 100% sequence identity, and/or

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11. The vaccine according to claim 9, wherein the at least one betacoronavirus epitope comprises or consists of an amino acid sequence having at least 70% sequence identity to the amino acid sequence 243 to 465 of SEQ ID NO: 255, such as at least 75%, such as at least 77%, such as at least 80%, such as at least 85%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98% or such as at least 99% sequence identity or such as 100% sequence identity.

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12. The vaccine according to claim 9, wherein the at least one betacoronavirus epitope comprises or consists of an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO: 246, such as at least 75%, such as at least 77%, such as at least 80%, such as at least 85%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98% or such as at least 99% sequence identity or such as 100% sequence identity.

~~13. The vaccine according to any of claims 9 to 12, wherein the antigenic unit comprises multiple copies of the RBD or parts thereof which copies are identical or differ in their amino acid sequences.~~

5 ~~14~~5. The vaccine according to any of claims 2 to ~~13~~4, wherein the at least one betacoronavirus epitope is a B cell epitope comprised in the viral surface protein or a part thereof, and/or

10 ~~15. The vaccine according to any of claims 2 to 14, wherein the antigenic unit comprises multiple B cell epitopes comprised in the viral surface protein or a part thereof.~~

~~16~~6. The vaccine according to claim 1, wherein the at least one betacoronavirus epitope is a T cell epitope, preferably

15 ~~17. The vaccine to claim 16, wherein the antigenic unit comprises multiple T cell epitopes, and/or~~

20 ~~18. The vaccine according to any of claims 16 to 17, wherein the T cell epitope is conserved between different genus and/or species and/or strains of betacoronaviruses, preferably between SARS-Cov2 and SARS-CoV, and/or~~

25 ~~19. The vaccine according to any of claims 16 to 18, wherein the T cell epitope has a length of from 7 to about 200 amino acids, preferably of from 7 to 100 amino acids or the T cell epitope has a length suitable for presentation by HLA class I/II alleles, preferably a length of from 7 to 30 amino acids, more preferably a length of from 8 to 15 amino acids, and/or~~

30 ~~20. The vaccine according to any of claims 16 to 19, wherein the T cell epitope is known to be immunogenic or is selected based on the predicted ability to bind to HLA class I/II alleles, and/or~~

~~21. The vaccine according to any of claims 16 to 20, wherein the T cell epitope is selected from epitopes having an amino acid sequence of any of SEQ ID NO: 1 to SEQ ID NO: 444.~~

22. The vaccine according to any of claims 16 to 20, wherein the T cell epitope is selected from the list consisting of RSFIEDLLFNKVTLA, MTYRRLISMMGFKMNYQVNGYPNMF, LMIERFVSLAIDAYP, RAMPNMLRIMASLVL, MVYMPASWVMRIMTW, FLNRFTTTTLNDFNLVAM, SSVELKHFFFAQDGNAAL, HFAIGLALYYPSARIVYTACSHAAV, YFIKGLNNLNRMVL, YLNTLT LAVPYNMRV, AQFAPSASAFFGMSRI, EIVDTV SALVYDNKL, SSGDATTAYANSVFNICQAVTANVNALL, HVISTSHKLVLVSNPYV, MLSDTLKNLSDRVVFVLWAHGFEL, TANPKTPKYKFVRIQPGQTF, ASIKNFKSVLYYQNNVFM, FVNEFYAYLRKHFSMM, RVWTL MNVLT LVYKV, FAYANRNRF LYI IKL and LVKPSFYVYSRVKNL.

23. The vaccine according to any of claims 16 to 20, wherein the T cell epitope is selected from the list consisting of RAMPNMLRIMASLVL, HVISTSHKLVLVSNPYV and LVKPSFYVYSRVKNL.

24. The vaccine according to any of claim 16 to 23, wherein the antigenic unit further comprises at least one betacoronavirus epitope which is a full-length viral surface protein of a betacoronavirus or a part thereof, such as

25. The vaccine according to claim 24, wherein the viral surface protein is selected from the group consisting of envelope protein, spike protein, membrane protein and hemagglutinin esterase.

26. The vaccine according to any of claims 24 to 25, wherein the at least one betacoronavirus epitope comprises or is the spike protein, and/or

27. The vaccine according to any of claims 24 to 26, wherein the at least one betacoronavirus epitope comprises or is the full-length spike protein, and/or

28. The vaccine according to claim 27, wherein the at least one betacoronavirus epitope comprises or consists of an amino acid sequence having at least 70% sequence identity to the amino acid sequence 243 to 1437 of SEQ ID NO: 275, such as at least 75%, such as at least 77%, such as at least 80%, such as at least 85%, such as at least 90%, such

~~as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98% or such as at least 99% sequence identity or such as 100% sequence identity.~~

5 ~~29. The vaccine according to any of claims 24 to 26, wherein the at least one betacoronavirus epitope comprises or is a part of the spike protein-, preferably~~

~~30 The vaccine according to claim 29, wherein the at least one betacoronavirus epitope comprises or is the RBD or a part thereof.~~

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~~31. The vaccine according to claim 30, wherein the at least one betacoronavirus epitope comprises or consists of an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO: 231 or SEQ ID NO: 802, or SEQ ID NO: 803 or SEQ ID NO: 804 or SEQ ID NO: 805, such as at least 75%, such as at least 77%,
15 such as at least 80%, such as at least 85%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98% or such as at least 99% sequence identity or such as 100% sequence identity.~~

20 ~~32 The vaccine according to claim 30, wherein the at least one betacoronavirus epitope comprises or consists of an amino acid sequence having at least 70% sequence identity to the amino acid sequence 243 to 465 of SEQ ID NO: 255, such as at least 75%, such as at least 77%, such as at least 80%, such as at least 85%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such
25 as at least 95%, such as at least 96%, such as at least 97%, such as at least 98% or such as at least 99% sequence identity or such as 100% sequence identity.~~

~~33 The vaccine according to claim 30, wherein the at least one betacoronavirus epitope comprises or consists of an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO: 246, such as at least 75%, such as at least 77%, such as at least 80%, such as at least 85%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98% or such as at
30 least 99% sequence identity or such as 100% sequence identity.~~

34. The vaccine according to any of claims 30 to 33, wherein the antigenic unit comprises multiple copies of the RBD or parts thereof which copies are identical or differ in their amino acid sequences.

35. The vaccine according to any of claims 24 to 34, wherein the at least one betacoronavirus epitope is a B cell epitope comprised in the viral surface protein or a part thereof.

36. The vaccine according to any of claims 24 to 35, wherein the antigenic unit comprises multiple B cell epitopes comprised in the viral surface protein or a part thereof.

37. The vaccine according to claim 24, wherein the antigenic unit comprises a T cell epitope selected from the list consisting of RSFIEDLLFNKVTLA, MTYRRLISMMGFKMNYQVNGYPNMF, LMIERFVSLAIDAYP, RAMPNMLRIMASLVL, MVYMPASWVMRIMTW, FLNRFTTTLNDFNLVAM, SSVELKHFFFAQDGNAAI, HFAIGLALYYPSARIVYTACSHAAV, YFIKGLNNLNRMVL, YLNTLTLAVPYNMRV, AQFAPSASAFFGMSRI, EIVDTVSALVYDNKL, SSGDATTAYANSVFNICQAVTANVNALL, HVISTSHKLVLVSNPYV, MLSDTLKNLSDRVVEVLWAHGFEL, TANPKTPKYKEVRIQPGQTF, ASIKNFKSVLYYQNNVFM, FVNEFYAYLRKHFSMM, RVWTLNMNVLTLYYKV, FAYANRNRFLYIIKL and LVKPSFYVYSRVKN and wherein the antigenic unit further comprises an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO: 231 or SEQ ID NO: 802, or SEQ ID NO: 803 or SEQ ID NO: 804 or SEQ ID NO: 805, such as at least 75%, such as at least 77%, such as at least 80%, such as at least 85%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98% or such as at least 99% sequence identity or such as 100% sequence identity.

38. The vaccine according to claim 24, wherein the antigenic unit comprises one or more T cell epitopes selected from the list consisting of RAMPNMLRIMASLVL, HVISTSHKLVLVSNPYV and LVKPSFYVYSRVKNL and wherein the antigenic unit

5 ~~further comprises an amino acid sequence having at least 70% sequence identity to the amino acid sequence 243 to 465 of SEQ ID NO: 255, such as at least 75%, such as at least 77%, such as at least 80%, such as at least 85%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98% or such as at least 99% sequence identity or such as 100% sequence identity.~~

10 ~~398. The vaccine according to any of the preceding claims, wherein the antigenic unit comprises up to 3500 amino acids, such as from 21 to 3500 amino acids, preferably from about 30 amino acids to about 2000 amino acids such as from about 50 to about 1500 amino acids, more preferably from about 100 to about 1500 amino acids, such as from about 100 to about 1000 amino acids or from about 100 to about 500 amino acids or from about 100 to about 300 amino acids-, and/or~~

15 ~~40. The vaccine according to any of the preceding claims, wherein the antigenic unit comprises one or more linkers, preferably one or more non-immunogenic and/or flexible linkers-, and/or~~

20 ~~41. The vaccine according to any of the preceding claims, wherein the antigenic unit comprises 10, 20, 30, 40 or 50 epitopes, preferably T cell epitopes.~~

25 ~~429. The vaccine according to any of the preceding claims, wherein said targeting unit comprises antibody binding regions with specificity for surface molecules or receptors on antigen presenting cells (APCs), preferably specificity for CD14, CD40, Toll- like receptor, CCR1, CCR3, CCR5, MHC class I proteins or MHC class II proteins-, and/or~~

~~43. The vaccine according to any of the preceding claims, wherein the targeting unit has affinity for a chemokine receptor selected from CCR1, CCR3 and CCR5-, or~~

30 ~~44. The vaccine according to any of claims 42 to 43, wherein said targeting unit has affinity for MHC class II proteins, preferably MHC class II proteins selected from the group consisting of anti-HLA-DP, anti-HLA-DR and anti-pan HLA class II-, preferably~~

~~45. The vaccine according to any of the preceding claims, wherein the targeting unit is selected from anti-pan HLA class II and MIP-1 α and preferably selected from anti-pan HLA class II and human MIP-1 α .~~

5 ~~46~~10. The vaccine according to claim ~~9~~45, wherein the targeting unit is ~~MIP-1 α~~ , preferably human MIP-1 α .

10 11. The vaccine according to any of the preceding claims, wherein the targeting unit comprises or consists of an amino acid sequence having at least 80% sequence identity to the amino acid sequence 24-93 of SEQ ID NO: 234.

~~47. The vaccine according to claim 45, wherein the targeting unit is anti-pan HLA class II.~~

15 ~~48~~12. The vaccine according to any of the preceding claims, wherein the dimerization unit comprises a hinge region-, preferably

~~49. The vaccine according to any of claims 48, wherein the dimerization unit further comprises another domain that facilitates dimerization-, preferably~~

20 ~~50. The vaccine according to claim 49, wherein the other domain is an immunoglobulin domain, preferably an immunoglobulin constant domain-, preferably~~

25 ~~51. The vaccine according to any of claims 48 to 49, wherein the dimerization unit further comprises a dimerization unit linker, which connects the hinge region and the other domain that facilitates dimerization.~~

30 13. The vaccine according to any of the preceding claims, wherein the dimerization unit comprises or consists of an amino acid sequence having at least 80% sequence identity to the amino acid sequence 94-237 of SEQ ID NO: 233.

~~52~~14. The vaccine according to any of the preceding claims, wherein the vaccine comprises the polynucleotide-, preferably

53. ~~The vaccine according to claim 52, wherein the polynucleotide further comprises a nucleotide sequence encoding a signal peptide, preferably wherein the signal peptide comprises or consists of an amino acid sequence having at least 80% sequence identity to the amino acid sequence 1-23 of SEQ ID NO: 234 and preferably~~

54. ~~The vaccine according to any of the preceding claims, wherein the vaccine comprises the polypeptide encoded by said polynucleotide or the dimeric protein and comprises said targeting unit, dimerization unit and antigenic unit in said peptide or dimeric protein are in the N-terminal to C-terminal order of targeting unit, dimerization unit and antigenic unit.~~

55. ~~15. The vaccine according to any of the preceding claims, wherein said betacoronavirus is one selected from the group consisting of SARS-CoV, MERS-CoV, SARS-CoV-2, HCoV-OC43 and HCoV-HKU1, preferably selected from the group consisting of SARS-CoV and SARS-CoV2, most preferably wherein said betacoronavirus is SARS-CoV2.~~

56. ~~16. A polynucleotide as defined in any of the claims 1 to 15~~53.

57. ~~17. A vector comprising the polynucleotide according to claim 16~~56.

58. ~~A host cell comprising the polynucleotide as defined in any of the claims 1 to 53 or comprising the vector according to claim 57.~~

59. ~~18. A polypeptide encoded by the polynucleotide as defined in any of claims 1 to 15~~53 or-

60. ~~A dimeric protein consisting of two of said polypeptides as defined in claim 59.~~

61. ~~The dimeric protein according to claim 60, wherein the dimeric protein is a homodimeric protein.~~

62. ~~19. The polynucleotide according to claim 56-16 or the polypeptide according to claim 59 or the dimeric protein according to any of claims 60 or 61~~18 for use as a medicament.

6320. A method of preparing the vaccine according to any one of the preceding claims 1 to ~~1551~~ and ~~54 to 55~~, wherein the vaccine comprises the polypeptide or the dimeric protein and wherein said method comprises:

- a) transfecting cells with the polynucleotide as defined in any of the claims 1 to ~~53~~15;
- b) culturing the cells;
- c) collecting and purifying the dimeric protein or the polypeptide expressed from the cells; and
- d) mixing the dimeric protein or polypeptide obtained from step c) with the pharmaceutically acceptable carrier.

6421. A method for preparing the vaccine according to any one of the preceding claims 1 to ~~53~~ and ~~55~~15, wherein the vaccine comprises the polynucleotide and wherein the method comprises:

- a) preparing the polynucleotide;
- b) optionally cloning the polynucleotide into an expression vector; and
- c) mixing the polynucleotide obtained from step a) or the vector obtained from step b) with the pharmaceutically acceptable carrier.

6522. Use of the polynucleotide according to claim 16 or the polypeptide or the dimeric protein according to claim 18 in the manufacture of a vaccine A method for treating a subject ~~having~~suffering from a betacoronavirus infection or being in need of prevention thereof, ~~the method comprising administering to the subject the vaccine as defined in any of claims 1 to 55.~~

66. ~~A vaccine as defined in any of claims 1 to 55 for use in the treatment of an infection with a betacoronavirus or for use in the prevention of a betacoronavirus infection.~~