Claims

1. A mutant of a wild-type RSV F protein, which mutant comprises a F1 polypeptide and a F2 polypeptide, wherein the mutant comprises at least one introduced amino acid mutation relative to the amino acid sequence of the wild-type RSV F protein, wherein the introduced amino acid mutation is a pair of cysteine mutations selected from the group consisting of: (1) 55C and 188C; (2) 103C and 148C; and (3) 142C and 371C, and wherein amino acid positions are numbered according to SEQ ID NO:1.

2. The mutant according to claim 1, wherein the mutant further comprises at least one cavity filling mutation, and at least one electrostatic mutation, wherein the cavity filling mutation is selected from the group consisting of:

(1) substitution of the amino acid at position 62, 155, 190, or 290 with I, Y, L, H, or M;

(2) substitution of the amino acid at position 54, 58, 189, 219, or 397 with I, Y, L, H, or M;

(3) substitution of the amino acid at position 151 with A or H;

(4) substitution of the amino acid at position 147 or 298 with I, L, H, or M; and

(5) substitution of the amino acid at position 164, 187, 192, 207, 220, 296, 300, or 495 with I, Y, or H,

and wherein the electrostatic mutation is selected from the group consisting of:

(1) substitution of the amino acid at position 82, 92, or 487 by D, F, Q, T, S, L, or H;

(2) substitution of the amino acid at position 315, 394, or 399 by F, M, R, S, L, I, Q, or T;

(3) substitution of the amino acid at position 392, 486, or 489 by H, S, N, T, or P; and

(4) substitution of the amino acid at position 106 or 339 by F, Q, N, or W.

3. The mutant according to claim 1, wherein the C-terminus of the F1 polypeptide is linked to a trimerization domain.

4. The mutant according to claim 1, wherein the F2 polypeptide comprises RSV F amino acid positions 26-109 and F1 polypeptide comprises RSV F amino acid positions 137-513.

5. The mutant according to claim 1, wherein the wild-type RSV is subtype A, subtype B, strain A2, strain Ontario, or strain Buenos Aires.

6. The mutant according to claim 2, wherein the pair of cysteine mutations is selected from the group consisting of: (1) 55C and 188C; and (2) 103C and 148C.

7. The mutant according to claim 2, wherein the cavity filling mutation is selected from the group consisting of:

(1) substitution of the amino acid at position 190 with I, Y, or M;

(2) substitution of the amino acid at position 54 with I or H; and

(3) substitution of the amino acid at position 296 with I.

8. The mutant according to claim 2, wherein the electrostatic mutation is selected from the group consisting of:

(1) substitution of the amino acid at position 487 with D, Q, or H;

(2) substitution of the amino acid at position 489 with H, S, or N; and

(3) substitution of the amino acid at position 486 with H, S, or T.

9. The mutant according to claim 2, wherein:

(i) the pair of cysteine mutations is selected from the group consisting of: (1) 55C and 188C; and (2) 103C and 148C;

(ii) the cavity filling mutation is selected from the group consisting of:

(1) substitution of the amino acid at positions 190 with I, Y, or M;

(2) substitution of the amino acid at position 54 with I or H; and

(3) substitution of the amino acid at position 296 with I; and

(iii) the electrostatic mutation is selected from the group consisting of:

(1) substitution of the amino acid at position 487 with D, Q, or H;

(2) substitution of the amino acid at position 486 with H, S, or T; and

(3) substitution of the amino acid at position 489 with H, S, or N.

10. The mutant according to claim 9, wherein the mutant comprises a combination of introduced amino acid mutations selected from the group consisting of:

(1) combination of 103C, 148C, 190I, and 486S;

(2) combination of 54H, 55C, 188C, and 486S;

(3) combination of 54H, 103C, 148C, 190I, 296I, and 486S;

(4) combination of 54H, 55C, 142C, 188C, 296I, and 371C;

(5) combination of 55C, 188C, and 486S;

(6) combination of 54H, 55C, 188C, and 190I;

(7) combination of 55C, 188C, 190I, and 486S; and

(8) combination of 54H, 55C, 188C, 190I, and 486S.

11. The mutant according to claim 4, wherein the mutant comprises a cysteine (C) at position 103 (103C) and at position 148 (148C), an isoleucine (I) at position 190 (190I), and a serine (S) at position 486 (486S), and wherein the mutant comprises a F1 polypeptide and a F2 polypeptide selected from the group consisting of:

(1) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:41 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:42;

(2) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:41 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:42;

(3) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO: 43 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:44;

(4) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:43 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:44;

(5) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO: 45 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:46;

(6) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:45 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:46;

(7) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO: 47 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:48;

(8) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:47 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:48;

(9) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO: 49 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:50;

(10) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:49 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:50.

(11) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:279 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:280;

(12) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:279 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:280;

(13) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:281 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:282;

(14) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:281 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:282;

(15) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:283 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:284;

(16) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:283 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:284;

(17) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:285 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:286;

(18) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:285 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:286;

(19) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:287 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:288;

(20) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:287 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:288;

(21) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:289 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:290; and

(22) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:289 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:290.

12. The mutant according to claim 4, wherein the mutant comprises a histidine (H) at position 54, a cysteine (C) at positions 103 and 148, a isoleucine (I) at positions 190, and 296, and a serine (S) at position 486, and wherein the mutant comprises a F1 polypeptide and a F2 polypeptide selected from the group consisting of:

(1) F2 polypeptide comprising the amino acid sequence of SEQ ID NO: 51 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:52;

(2) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:51 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:52;

(3) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:53 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:54;

(4) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:53 and a F1 polypeptide comprising

an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:54;

(5) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:55 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:56;

(6) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:55 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:56;

(7) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:57 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:58;

(8) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:57 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:58;

(9) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:59 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:60;

(10) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:59 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:60;

(11) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:291 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:292;

(12) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:291 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:292;

(13) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:293 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:294;

(14) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:293 and a F1 polypeptide

comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:294;

(15) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:295 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:296;

(16) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:295 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:296;

(17) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:297 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:298;

(18) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:297 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:298;

(19) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:299 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:300;

(20) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:299 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:300;

(21) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:301 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:302; and

(22) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:301 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:302.

13. The mutant according to claim 4, wherein the mutant comprises a histidine (H) at position 54, a cysteine (C) at positions 55 and 188, and a serine (S) at position 486, and wherein the mutant comprises a F1 polypeptide and a F2 polypeptide selected from the group consisting of:

(1) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:61 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:62;

(2) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:61 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:62;

(3) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:63 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:64;

(4) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:63 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:64;

(5) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:65 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:66;

(6) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:65 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:66;

(7) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:67 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:68;

(8) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:67 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:68;

(9) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:69 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:70;

(10) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:69 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:70;

(11) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:303 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:304;

(12) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:303 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:304;

(13) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:305 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:306;

(14) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:305 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:306;

(15) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:307 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:308;

(16) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:307 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:308;

(17) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:309 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:310;

(18) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:309 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:310;

(19) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:311 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:312;

(20) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:311 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:312.

(21) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:313 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:314; and

(22) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:313 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:314.

14. The mutant according to claim 4, wherein the mutant comprises a histidine (H) at position 54, a cysteine (C) at positions 55 and 188, an isoleucine (I) at position 190 (190I), and a serine (S) at position 486, and wherein the mutant comprises a F1 polypeptide and a F2 polypeptide selected from the group consisting of:

(1) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:71 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:72;

(2) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:71 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:72;

(3) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:73 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:74;

(4) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:73 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:74;

(5) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:75 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:76;

(6) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:75 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:76;

(7) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:77 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:78;

(8) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:77 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:78;

(9) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:79 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:80;

(10) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:79 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:80;

(11) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:315 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:316;

(12) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:315 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:316;

(13) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:317 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:318;

(14) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:317 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:318;

(15) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:319 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:320;

(16) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:319 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:320;

(17) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:321 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:322;

(18) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:321 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:322;

(19) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:323 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:324;

(20) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:323 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:324.

(21) a F2 polypeptide comprising the amino acid sequence of SEQ ID NO:325 and a F1 polypeptide comprising the amino acid sequence of SEQ ID NO:326; and

(22) a F2 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:325 and a F1 polypeptide comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO:326.

15. The mutant according to claim 1, which comprises amino acids 26-109 and 137-513 of any one of the amino acid sequences of SEQ ID NOs:19-21 and 32-39.

16. The mutant according to claim 1, further comprising at least one pair of introduced cysteine mutations in the HRB region.

17. The mutant according to claim 16, wherein the at least one pair of cysteine mutations in the HRB region is selected from the group consisting of:

(1) 508C and 509C;

(2) 515C and 516C; and

(3) 522C and 523C.

18. A pharmaceutical composition comprising (i) a RSV F protein mutant according to claim 2 and (ii) a pharmaceutically acceptable carrier.

19. The pharmaceutical composition according to claim 18, wherein the F1 polypeptide and F2 polypeptide are from the F protein of RSV subtype B.

20. The pharmaceutical composition according to claim 18, wherein the F1 polypeptide and F2 polypeptide are from the F protein of RSV subtype A.

21. The pharmaceutical composition according to claim 20, further comprising a second mutant according to claim 2, wherein the F1 polypeptide and F2 polypeptide of the second mutant are from the F protein of RSV subtype B.

22. The pharmaceutical composition according to claim 18, which is a vaccine.

23. A nucleic acid molecule comprising a nucleotide sequence that encodes an amino acid sequence of a RSV F protein mutant according to claim [[9]] 1.

24. The nucleic acid molecule according to claim 23, wherein the mutant comprises amino acids 26-513 of any of the amino acid sequences of SEQ ID NOs:19-21 and 32-39.

25. The nucleic acid molecule according to claim 23, which comprises a nucleotide sequence, or a degenerate variant thereof, selected from the group consisting of:

(1) a nucleotide sequence comprising nucleotides 76-1539 of SEQ ID NO:8;

(2) a nucleotide sequence comprising nucleotides 76-1539 of SEQ ID NO:9 ;

(3) a nucleotide sequence comprising nucleotides 76-1539 of SEQ ID NO:10;

(4) a nucleotide sequence comprising nucleotides 76-1539 of SEQ ID NO:11;

(5) a nucleotide sequence comprising nucleotides 76-1539 of SEQ ID NO:12;

(6) a nucleotide sequence comprising nucleotides 76-1539 of SEQ ID NO:13;

(7) a nucleotide sequence comprising nucleotides 76-1539 of SEQ ID NO:14;

(8) a nucleotide sequence comprising nucleotides 76-1539 of SEQ ID NO:15;

(9) a nucleotide sequence comprising nucleotides 76-1539 of SEQ ID NO:16;

(10) a nucleotide sequence comprising nucleotides 76-1539 of SEQ ID NO:17; and

(11) a nucleotide sequence comprising nucleotides 76-1539 of SEQ ID NO:18.

26. The pharmaceutical composition according to claim 18, further comprising an adjuvant.

27. The pharmaceutical composition according to claim 26, wherein the adjuvant is an aluminum salt.

28. The pharmaceutical composition according to claim 18, wherein the C-terminus of the F1 polypeptide of the mutant is linked to a trimerization domain.

29. The pharmaceutical composition according to claim 28, wherein the trimerization domain is a phage T4 foldon domain.

30. The pharmaceutical composition according to claim 21, wherein the F2 polypeptide and F1 polypeptide of the mutant from the F protein of RSV subtype A comprise the amino acid sequence of SEQ ID NO:45 and the amino acid sequence of SEQ ID NO:46, respectively, and wherein the F2 polypeptide and F1 polypeptide of the second mutant from the F protein of RSV subtype B comprise the amino acid sequence of SEQ ID NO:49 and the amino acid sequence of SEQ ID NO:50, respectively.

31. The pharmaceutical composition according to claim 30, further comprising an adjuvant.

32. The pharmaceutical composition according to claim 31, wherein the adjuvant is an aluminum salt.

33. The pharmaceutical composition according to claim 30, wherein the C-terminus of the F1 polypeptide of the mutant from the F protein of RSV subtype A and the C-terminus of the F1 polypeptide of the second mutant from the F protein of RSV subtype B is each linked to a trimerization domain.

34. The pharmaceutical composition according to claim 33, wherein the trimerization domain is a phage T4 fibritin foldon domain.

35. The pharmaceutical composition according to claim 34, further comprising an adjuvant.

36. The pharmaceutical composition according to claim 35, wherein the adjuvant is an aluminum salt.

37. The mutant according to claim 1, further comprising a cavity filling mutation, or an electrostatic mutation, wherein cavity filling mutation is selected from the group consisting of:

(1) substitution of the amino acid at position 62, 155, 190, or 290 with I, Y, L, H, or M;

(2) substitution of the amino acid at position 54, 58, 189, 219, or 397 with I, Y, L, H, or M;

(3) substitution of the amino acid at position 151 with A or H;

(4) substitution of the amino acid at position 147 or 298 with I, L, H, or M; and

(5) substitution of the amino acid at position 164, 187, 192, 207, 220, 296, 300, or 495 with I, Y, H;

and wherein the introduced electrostatic mutation is selected from the group consisting of:

(1) substitution of the amino acid at position 82, 92, or 487 by D, F, Q, T, S, L, or H;

(2) substitution of the amino acid at position 315, 394, or 399 by F, M, R, S, L, I, Q, or T;

(3) substitution of the amino acid at position 392, 486, or 489 by H, S, N, T, or P; and

(4) substitution of the amino acid at position 106 or 339 by F, Q, N, or W.

38. The mutant according to claim 37, wherein the cavity filling mutation is selected from the group consisting of:

(1) substitution of the amino acid at position 190 with I, Y, or M;

(2) substitution of the amino acid at position 54 with I or H; and

(3) substitution of the amino acid at position 296 with I.

39. The mutant according to claim 37, wherein the electrostatic mutation is selected from the group consisting of:

(1) substitution of the amino acid at position 487 with D, Q, or H;

(2) substitution of the amino acid at position 489 with H, S, or N; and

(3) substitution of the amino acid at position 486 with H, S, or T.

40. The mutant according to claim 38, wherein the electrostatic mutation is selected from the group consisting of:

(1) substitution of the amino acid at position 487 with D, Q, or H;

(2) substitution of the amino acid at position 489 with H, S, or N; and

(3) substitution of the amino acid at position 486 with H, S, or T.

41. The mutant according to claim 40, wherein the pair of cysteine mutations is selected from the group consisting of: (1) 55C and 188C; and (2) 103C and 148C.

42. A pharmaceutical composition, comprising a mutant according to claim 1 and a pharmaceutically acceptable carrier.

43. The pharmaceutical composition according to claim 42, further comprising an adjuvant.

44. The pharmaceutical composition according to claim 42, wherein the C-terminus of the F1 polypeptide of the mutant is linked to a trimerization domain.