claims

1. mRNA sequence comprising a coding region encoding a mutant of fusion protein F of Respiratory syncytial virus (RSV), wherein the amino acid residues 554-574 of the amino acid sequence of the fusion protein F are deleted in the mutant of fusion protein F;
   wherein the G/C content of the coding region is increased by substituting at least 70% of the substitutable codons in the coding region compared with the G/C content of the coding region of the wild type mRNA, and wherein the coded amino acid sequence of said GC-enriched mRNA is not being modified compared with the coded amino acid sequence of the wild type mRNA.

2. The mRNA sequence according to claim 1, wherein the mutant of fusion protein F is derived from the RSV strain ATCC VR-26 long.

3. The mRNA sequence according to claim 1 or 2 comprising additionally
   a) a 5'-CAP structure,
   b) a poly(A) sequence,
   c) and optionally a poly (C) sequence.

4. The mRNA sequence according to claim 3, wherein the poly(A) sequence comprises a sequence of 25 to 400 adenosine nucleotides.

5. The mRNA sequence according to any one of claims 1 to 4 comprising additionally at least one histone stem-loop.

6. The mRNA sequence according to claim 5, wherein the at least one histone stem-loop is selected from following formulae (I) or (II):

   formula (I) (stem-loop sequence without stem bordering elements):

$$\underbrace{[N_{0-2}GN_{3-5}]}_{\text{stem1}}\ \underbrace{[N_{0-4}(U/T)N_{0-4}]}_{\text{loop}}\ \underbrace{[N_{3-5}CN_{0-2}]}_{\text{stem2}}$$

formula (II) (stem-loop sequence with stem bordering elements):

$$\underbrace{N_{1\text{-}6}}_{\text{stem1 bordering element}}\ \underbrace{[N_{0\text{-}2}GN_{3\text{-}5}]}_{\text{stem1}}\ \underbrace{[N_{0\text{-}4}(U/T)N_{0\text{-}4}]}_{\text{loop}}\ \underbrace{[N_{3\text{-}5}CN_{0\text{-}2}]}_{\text{stem2}}\ \underbrace{N_{1\text{-}6}}_{\text{stem2 bordering element}}$$

wherein:

stem1 or stem2 bordering elements $N_{1\text{-}6}$ is a consecutive sequence of 1 to 6 N, wherein each N is independently from another selected from a nucleotide selected from A, U, T, G and C, or a nucleotide analogue thereof;

stem1 $[N_{0\text{-}2}GN_{3\text{-}5}]$ is reverse complementary or partially reverse complementary with element stem2, and is a consecutive sequence between of 5 to 7 nucleotides;

wherein $N_{0\text{-}2}$ is a consecutive sequence of 0 to 2 N, wherein each N is independently from another selected from a nucleotide selected from A, U, T, G and C or a nucleotide analogue thereof;

wherein $N_{3\text{-}5}$ is a consecutive sequence of 3 to 5 N, wherein each N is independently from another selected from a nucleotide selected from A, U, T, G and C or a nucleotide analogue thereof, and

wherein G is guanosine or an analogue thereof, and may be optionally replaced by a cytidine or an analogue thereof, provided that its complementary nucleotide cytidine in stem2 is replaced by guanosine;

loop sequence $[N_{0-4}(U/T)N_{0-4}]$ is located between elements stem1 and stem2, and is a consecutive sequence of 3 to 5 nucleotides;

wherein each N_{0-4} is independent from another a consecutive sequence of 0 to 4 N, wherein each N is independently from another selected from a nucleotide selected from A, U, T, G and C or a nucleotide analogue thereof; and

wherein U/T represents uridine, or optionally thymidine;

stem2 $[N_{3-5}CN_{0-2}]$ is reverse complementary or partially reverse complementary with element stem1, and is a consecutive sequence between of 5 to 7 nucleotides;

wherein N_{3-5} is a consecutive sequence of 3 to 5 N, wherein each N is independently from another selected from a nucleotide selected from A, U, T, G and C or a nucleotide analogue thereof;

wherein N_{0-2} is a consecutive sequence of 0 to 2 N, wherein each N is independently from another selected from a nucleotide selected from A, U, T, G and C or a nucleotide analogue thereof; and

wherein C is cytidine or an analogue thereof, and may be optionally replaced by a guanosine or an analogue thereof provided that its complementary nucleotide guanosine in stem1 is replaced by cytidine;

wherein

stem1 and stem2 are capable of base pairing with each other

forming a reverse complementary sequence, wherein base pairing may occur between stem1 and stem2, or

forming a partially reverse complementary sequence, wherein an incomplete base pairing may occur between stem1 and stem2.

7. The mRNA sequence according to claim 6, wherein the at least one histone stem-loop is selected from at least one of following formulae (Ia) or (IIa):

$$\underbrace{[N_{0-1}GN_{3-5}]}_{\text{stem1}}\ \underbrace{[N_{1-3}(U/T)N_{0-2}]}_{\text{loop}}\ \underbrace{[N_{3-5}CN_{0-1}]}_{\text{stem2}}$$

formula (Ia) (stem-loop sequence without stem bordering elements)

$$\underbrace{N_{2-5}}_{\text{stem1 bordering element}}\ \underbrace{[N_{0-1}GN_{3-5}]}_{\text{stem1}}\ \underbrace{[N_{1-3}(U/T)N_{0-2}]}_{\text{loop}}\ \underbrace{[N_{3-5}CN_{0-1}]}_{\text{stem2}}\ \underbrace{N_{2-5}}_{\text{stem2 bordering element}}$$

formula (IIa) (stem-loop sequence with stem bordering elements)

8. The mRNA sequence according to any of claims 1 to 7 comprising additionally a 3'-UTR element.

9. The mRNA sequence according to claim 8, wherein the at least one 3'UTR element comprises or consists of a nucleic acid sequence, which is derived from a 3'UTR of a gene providing a stable mRNA, wherein the 3'UTR element preferably comprises or consists of a nucleic acid sequence derived from a 3'UTR of a gene selected from the group consisting of an albumin gene, an α-globin gene, a β-globin gene, a tyrosine hydroxylase gene, a lipoxygenase gene, and a collagen alpha gene, wherein the 3'-UTR element more preferably comprises or consists of a nucleic acid sequence derived from a 3'UTR of α-globin gene, most preferably comprising the corresponding RNA sequence of the nucleic acid sequence according to SEQ ID NO. 29.

10. The mRNA sequence according to any of claims 8 or 9, wherein the mRNA sequence comprises, preferably in 5'- to 3'-direction:

a.) a 5'-CAP structure, preferably m7GpppN;

b.) a coding region encoding the mutant of fusion protein F of Respiratory syncytial virus (RSV);

c.) a 3'-UTR element comprising or consisting of a nucleic acid sequence, which is derived from a alpha globin gene, preferably comprising the corresponding RNA sequence of the nucleic acid sequence according to SEQ ID NO. 29;

d.) a poly(A) sequence, preferably comprising 64 adenosines;

e.) a poly(C) sequence, preferably comprising 30 cytosines; and

f.) a histone-stem-loop, preferably comprising the corresponding RNA sequence to the nucleic acid sequence according to SEQ ID No 30.

11. The mRNA sequence according to claim 8, wherein the at least one 3'UTR element comprises or consist of a nucleic acid sequence, which is derived from the 3'UTR of a human albumin gene.

12. The mRNA sequence according to claim 11, wherein the 3'UTR element is derived from a nucleic acid sequence according to SEQ ID NO. 25, preferably from a corresponding RNA sequence.

13. The mRNA sequence according to any of claims 1 to 12 comprising additionally a 5'-UTR element, which comprises or consists of a nucleic acid sequence, which is derived from the 5'UTR of a TOP gene, preferably from a corresponding RNA sequence, preferably lacking the 5'TOP motif.

14. The mRNA sequence according to claim 13, wherein the 5'UTR element comprises or consists of a nucleic acid sequence, which is derived from a 5'UTR of a TOP gene encoding a ribosomal protein, preferably from a corresponding RNA sequence, preferably lacking the 5'TOP motif.

15. The mRNA sequence according to claim 14, wherein the 5'UTR element comprises or consists of a nucleic acid sequence, which is derived from a 5'UTR of a TOP gene encoding a ribosomal Large protein (RPL), preferably lacking the 5'TOP motif and

more preferably comprising or consisting of a corresponding RNA sequence of the nucleic acid sequence according to SEQ ID NO. 23.

16. The mRNA sequence according to claim 15, wherein the mRNA sequence comprises, preferably in 5'- to 3'-direction:

a.) a 5'-CAP structure;

b.) a 5'-UTR element which comprises or consists of a nucleic acid sequence, which is derived from the 5'-UTR of a TOP gene, preferably comprising or consisting of the corresponding RNA sequence of the nucleic acid sequence according to SEQ ID NO. 23;

c.) a coding region encoding the mutant of fusion protein F of Respiratory syncytial virus (RSV);

d.) a 3'UTR element comprising or consisting of a nucleic acid sequence, which is derived from a gene providing a stable mRNA, preferably comprising or consisting of the corresponding RNA sequence of a nucleic acid sequence according to SEQ ID NO. 18;

e.) a poly(A) sequence preferably comprising 64 adenosines;

f.) a poly(C) sequence, preferably comprising 30 cytosines; and

g.) a histone-stem-loop, preferably comprising the corresponding RNA sequence of the nucleic acid sequence according to SEQ ID No 30.

17. The mRNA sequence according to claim 16, wherein the mRNA sequence comprises the RNA sequence according to SEQ ID No. 33.

18. The mRNA sequence according to claims 1 to 17, wherein the mRNA sequence is associated with or complexed with a cationic or polycationic compound or a polymeric carrier, optionally in a weight ratio selected from a range of 6:1 (w/w) to 0.25:1 (w/w) of mRNA to cationic or polycationic compound and/or with a polymeric carrier; or optionally in a nitrogen/phosphate ratio of mRNA to cationic or polycationic compound and/or polymeric carrier in the range of 0.1-10.

19. The mRNA sequence according to claim 18, wherein the mRNA sequence is associated or complexed with a cationic protein or peptide, preferably protamine, or with a cationic lipid.

20. A composition comprising a plurality or more than one of mRNA sequences each according to any of claims 1 to 19.

21. Pharmaceutical composition comprising an mRNA sequence as defined according to any of claims 1 to 19 or a composition as defined according to claim 20 and optionally a pharmaceutically acceptable carrier.

22. Pharmaceutical composition according to claim 21, wherein the mRNA sequence is complexed at least partially with a cationic or polycationic compound and/or a polymeric carrier, preferably cationic proteins or peptides, most preferably protamine, or cationic lipids.

23. Pharmaceutical composition according to claim 22, wherein the ratio of complexed mRNA to free mRNA is selected from a range of 5:1 (w/w) to 1:10 (w/w).

24. Pharmaceutical composition according to any one of claims 21 to 23, for use as a vaccine.

25. Kit or kit of parts comprising the mRNA sequence as defined according to any of claims 1 to 19, the composition as defined according to claim 20, the pharmaceutical composition as defined according to any of claims 21 to 24 and optionally technical instructions with information on the administration and dosage of the components.

26. mRNA sequence as defined according to any of claims 1 to 19, composition as defined according to claim 20, pharmaceutical composition as defined according to any of claims 21 to 24, and kit or kit of parts as defined according to claim 25 for use as a medicament.

27. mRNA sequence as defined according to any of claims 1 to 19, composition as defined according to claim 20, pharmaceutical composition as defined according to

any of claims 21 to 24, and kit or kit of parts as defined according to claim 25 for use in the treatment or prophylaxis of RSV infections.

28. mRNA sequence, composition, pharmaceutical composition and kit or kit of parts for use according to claim 27, wherein the treatment is combined with administration of RSV immue globuline, particularly Palivizumab.