Claims

1. An artificial nucleic acid molecule comprising:

a. at least one 5'-untranslated region element (5'UTR element) which comprises or consists of

a nucleic acid sequence, which consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in the full-length 5'UTR of a TOP gene, which represents at least 80% of the full-length 5'UTR of a TOP gene,

or

a nucleic acid sequence, which consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in a variant of the 5'UTR of a TOP gene, which represents at least 80% of the variant of the 5'UTR of a TOP gene, wherein the variant of the 5'UTR of a TOP gene is at least 80% identical to the naturally occuring 5'UTR, from which the variant is derived,

wherein the at least one 5'UTR element does not comprise a functional 5'TOP motif;

b. at least one open reading frame (ORF); and

c. at least one 3'UTR element, which comprises or consists of

a nucleic acid sequence which consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in the full-length 3'UTR of an albumin gene, which represents at least 80% of the full-length 3'UTR of an albumin gene,

or

a nucleic acid sequence which consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in a variant of a 3'UTR of an albumin gene, which represents at least 80% of the variant of the 3'UTR of an albumin gene, wherein the variant of the 3'UTR of an albumin gene is at least 80% identical to the naturally occuring 3'UTR the variant is derived from.

2. The artificial nucleic acid molecule according to claim 1, 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 vertebrate albumin gene or from a variant thereof, preferably from the 3'UTR of a mammalian albumin gene or from a variant thereof, more preferably from the 3'UTR of a human albumin gene or from a variant thereof, even more preferably from the 3'UTR of the human albumin gene according to GenBank Accession number NM_000477.5 or from a variant thereof.

3. The artificial nucleic acid molecule according to claims 1 or 2, wherein the at least one 3'UTR element exhibits a length of at least about 50 nucleotides, preferably of at least about 75 nucleotides, more preferably of at least about 100 nucleotides, even more preferably of at least about 125 nucleotides, most preferably of at least about 150 nucleotides.

4. The artificial nucleic acid molecule according to claims 1-3, wherein the 5'UTR element and the open reading frame are heterologous.

5. The artificial nucleic acid molecule according to claim 1 to 4, wherein the 5'UTR element is suitable for increasing protein production from the artificial nucleic acid molecule.

6. The artificial nucleic acid molecule according to any one of claims 1-5, wherein the nucleic acid sequence which is derived from a 5'UTR of a TOP gene, preferably the 5'UTR element, starts at its 5'-end with a nucleotide located at position 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 downstream of the TOP-motif of the 5'UTR of the TOP gene.

7. The artificial nucleic acid molecule according to any one of claims 1-6, wherein the nucleic acid sequence which is derived from a 5'UTR of a TOP gene, preferably the 5'UTR element terminates at its 3'-end with a nucleotide located at position 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 upstream of the start codon of the open reading frame of the gene or mRNA it is derived from.

8. The artificial nucleic acid molecule according to any one of claims 1-7, wherein the nucleic acid sequence which is derived from the 5'UTR of a TOP gene is derived from the 5'UTR of a eukaryotic TOP gene or from a variant thereof, preferably from the 5'UTR of a plant or animal TOP gene or from a variant thereof, more preferably from the 5'UTR of a chordate TOP gene or from a variant thereof, even more preferably from the 5'UTR of a vertebrate TOP gene or from a variant thereof, most

preferably from the 5'UTR of a mammalian TOP gene, such as a human TOP gene, or from a variant thereof.

9. The artificial nucleic acid molecule according to any of claims 1 to 8, wherein the at least one 3'UTR element and the at least one 5'UTR element act at least additively, preferably synergistically to increase protein production from said artificial nucleic acid molecule.

10. The artificial nucleic acid molecule according to any one of claims 1-9, further comprising

d. a poly(A) sequence and/or a polyadenylation signal.

11. The artificial nucleic acid molecule according to claim 10, wherein the polyadenylation signal is located within the 3'UTR element.

12. The artificial nucleic acid molecule according to claim 10 or 11, wherein the polyadenylation signal comprises the consensus sequence NN(U/T)ANA, with N = A or U, preferably AA(U/T)AAA or A(U/T)(U/T)AAA.

13. The artificial nucleic acid molecule according to any one of claims 10-12, wherein the polyadenylation signal, preferably the consensus sequence NNUANA, is located less than about 50 nucleotides upstream of the 3'-end of the 3'UTR.

14. The artificial nucleic acid molecule according to any one of claims 10-13, wherein the poly(A) sequence has a length of about 20 to about 300 adenine nucleotides, preferably of about 40 to about 200 adenine nucleotides, more preferably of about 50 to about 100 adenine nucleotides.

15. The artificial nucleic acid molecule according to any one of claims 1 to 14, which further comprises a histone stem-loop sequence.

16. The artificial nucleic acid molecule according to any one of claims 1-15, wherein the 5'UTR element is derived from a 5'UTR of a TOP gene encoding a ribosomal Large protein (RPL) or from a variant of a 5'UTR of a TOP gene encoding a ribosomal Large protein (RPL).

17. The artificial nucleic acid molecule according to any one of claims 1-16, wherein the 5'UTR element comprises or consists of a nucleic acid sequence having an identity of

at least about 80%, more preferably of at least about 90%, even more preferably of at least about 95%, even more preferably of at least about 99% to a nucleic acid sequence extending from nucleotide position 5 to the nucleotide position immediately 5' to the start codon of a nucleic acid sequence according to any of SEQ ID NOs. 1-1363, 1395, 1421 or 1422 or to a corresponding RNA sequence, or wherein the at least one 5'UTR element comprises or consists of a fragment of a nucleic acid sequence which has an identity of at least about 80%, more preferably of at least about 90%, even more preferably of at least about 95%, even more preferably of at least about 99% to a nucleic acid sequence extending from nucleotide position 5 to the nucleotide position immediately 5' to the start codon of a nucleic acid sequence according to SEQ ID NOs. 1-1363, 1395, 1421 or 1422 or to a corresponding RNA sequence.

18. The artificial nucleic acid molecule according to any one of claims 1-17, wherein the 5'UTR element comprises or consists of a nucleic acid sequence having an identity of at least about 80%, more preferably of at least about 90%, even more preferably of at least about 95%, even more preferably of at least about 99% to the 5'UTR of a nucleic acid sequence according to any of SEQ ID NOs. 67, 259, 1284-1318, 1344, 1346, 1348-1354, 1357, 1358, 1421 or 1422 or to a corresponding RNA sequence, or wherein the at least one 5'UTR element comprises or consists of a fragment of a nucleic acid sequence which has an identity of at least about 80%, more preferably of at least about 90%, even more preferably of at least about 95%, even more preferably of at least about 99% to the 5'UTR of a nucleic acid sequence according to SEQ ID No. SEQ ID NOs: 67, 259, 1284-1318, 1344, 1346, 1348-1354, 1357, and 1358, 1421 or 1422 or to a corresponding RNA sequence.

19. The artificial nucleic acid molecule according to any one of claims 1-18, wherein the 5'UTR element comprises or consists of a nucleic acid sequence which is derived from the 5'UTR a ribosomal protein Large 32 gene (RPL32), a ribosomal protein Large 35 gene (RPL35), a ribosomal protein Large 21 gene (RPL21), an ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle (ATP5A1) gene, an hydroxysteroid (17-beta) dehydrogenase 4 gene (HSD17B4), an androgen-induced 1 gene (AIG1), cytochrome c oxidase subunit VIc gene (COX6C), or a N-acylsphingosine amidohydrolase (acid ceramidase) 1 gene (ASAH1) or from a variant thereof, preferably from a vertebrate ribosomal protein Large 32 gene (RPL32), a vertebrate ribosomal protein Large 35 gene (RPL35), a

vertebrate ribosomal protein Large 21 gene (RPL21), a vertebrate ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle (ATP5A1) gene, a vertebrate hydroxysteroid (17-beta) dehydrogenase 4 gene (HSD17B4), a vertebrate androgen-induced 1 gene (AIG1), a vertebrate cytochrome c oxidase subunit VIc gene (COX6C), or a vertebrate N-acylsphingosine amidohydrolase (acid ceramidase) 1 gene (ASAH1) or from a variant thereof, more preferably from a mammalian ribosomal protein Large 32 gene (RPL32), a ribosomal protein Large 35 gene (RPL35), a ribosomal protein Large 21 gene (RPL21), a mammalian ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle (ATP5A1) gene, a mammalian hydroxysteroid (17-beta) dehydrogenase 4 gene (HSD17B4), a mammalian androgen-induced 1 gene (AIG1), a mammalian cytochrome c oxidase subunit VIc gene (COX6C), or a mammalian N-acylsphingosine amidohydrolase (acid ceramidase) 1 gene (ASAH1) or from a variant thereof, most preferably from a human ribosomal protein Large 32 gene (RPL32), a human ribosomal protein Large 35 gene (RPL35), a human ribosomal protein Large 21 gene (RPL21), a human ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle (ATP5A1) gene, a human hydroxysteroid (17-beta) dehydrogenase 4 gene (HSD17B4), a human androgen-induced 1 gene (AIG1), a human cytochrome c oxidase subunit VIc gene (COX6C), or a human N-acylsphingosine amidohydrolase (acid ceramidase) 1 gene (ASAH1) or from a variant thereof.

20. The artificial nucleic acid molecule according to any one of claims 1-19, wherein the 5'UTR element comprises or consists of a nucleic acid sequence which has an identity of at least about 80%, more preferably of at least about 90%, even more preferably of at least about 95%, even more preferably of at least about 99% to the nucleic acid sequence according to SEQ ID NO. 1368 or SEQ ID NOs 1412-1420, or to a corresponding RNA sequence, or wherein the at least one 5'UTR element comprises or consists of a fragment of a nucleic acid sequence which has an identity of at least about 80%, more preferably of at least about 90%, even more preferably of at least about 95%, even more preferably of at least about 99% to the nucleic acid sequence according to SEQ ID No. 1368 or SEQ ID NOs 1412-1420, or to a corresponding RNA sequence.

21. The artificial nucleic acid molecule according to any one of claims 18 or 20, wherein the fragment consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in the full-length sequence, which represents at

least 80%, preferably at least 90%, of the full-length sequence the fragment is derived from.

22. The artificial nucleic acid molecule according to any one of claims 1-21, wherein the at least one 5'UTR element exhibits a length of at least about 20 nucleotides, preferably of at least about 30 nucleotides, more preferably of at least about 40 nucleotides.

23. The artificial nucleic acid molecule according to any one of claims 1-22, wherein the at least one 3'UTR element comprises or consists of a nucleic acid sequence which has an identity of at least about 80%, more preferably of at least about 90%, even more preferably of at least about 95%, even more preferably of at least about 99% to a nucleic acid sequence selected from SEQ ID NOs. 1369-1393 or to a corresponding RNA sequence, or wherein the at least one 3'UTR element comprises or consists of a fragment of a nucleic acid sequence which has an identity of at least about 80%, more preferably of at least about 90%, even more preferably of at least about 95%, even more preferably of at least about 99% to a nucleic acid sequence selected from SEQ ID NOs. 1369-1393 or to a corresponding RNA sequence.

24. The artificial nucleic acid molecule according to claim 23, wherein the fragment consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in the full-length sequence, which represents at least 80%, preferably at least 90%, of the full-length sequence the fragment is derived from.

25. The artificial nucleic acid molecule according to claim 23 or 24, wherein the fragment exhibits a length of at least about 50 nucleotides, preferably of at least about 75 nucleotides, more preferably of at least about 100 nucleotides, even more preferably of at least about 125 nucleotides, most preferably of at least about 150 nucleotides.

26. The artificial nucleic acid molecule according to any one of claims 1-25, wherein the at least one 3'UTR element exhibits a length of at least about 50 nucleotides, preferably of at least about 75 nucleotides, more preferably of at least about 100 nucleotides, even more preferably of at least about 125 nucleotides, most preferably of at least about 150 nucleotides.

27. The artificial nucleic acid molecule according to any one of claims 1-26, wherein the open reading frame does not code for a reporter protein, such as a GFP protein, a

luciferase protein, a globin protein, human growth hormon, or human albumin, preferably not for albumin.

28. The artificial nucleic acid molecule according to any one of claims 1-27, further comprising a 5'-cap structure, a poly(C) sequence and/or an IRES-motif.

29. The artificial nucleic acid molecule according to any one of claims 1-28, further comprising a promoter containing-sequence.

30. The artificial nucleic acid molecule according to any one of claims 1-29, wherein the artificial nucleic acid molecule, preferably the open reading frame, is at least partially G/C modified, preferably wherein the G/C content of the open reading frame is increased compared to the wild type open reading frame.

31. The artificial nucleic acid molecule according to any one of claims 1-30, wherein the open reading frame comprises a codon-optimized region, preferably, wherein the open reading frame is codon-optimized.

32. The artificial nucleic acid molecule according to any one of claims 1-31, which is an RNA, preferably an mRNA molecule.

33. A vector comprising:

a. at least one 5'-untranslated region element (5'UTR element) which comprises or consists of
a nucleic acid sequence which consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in the full-length 5'UTR of a TOP gene, which represents at least 80% of the full-length 5'UTR of a TOP gene, or
a nucleic acid sequence which consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in a variant of the 5'UTR of a TOP gene, which represents at least 80% of the variant of the 5'UTR of a TOP gene, wherein the variant of the 5'UTR of a TOP gene is at least 80% identical to the naturally occuring 5'UTR the variant is derived from,
wherein the at least one 5'UTR element does not comprise a functional 5'TOP motif;

b. at least one open reading frame (ORF) and/or at least one cloning site; and

c. at least one 3'UTR element, which comprises or consists of
a nucleic acid sequence which consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in the full-length 3'UTR of an albumin gene, which represents at least 80% of the full-length 3'UTR of an albumin gene, or
a nucleic acid sequence which consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in a variant of a 3'UTR of an albumin gene, which represents at least 80% of the variant of the 3'UTR of an albumin gene, wherein the variant of the 3'UTR of an albumin gene is at least 80% identical to the naturally occuring 3'UTR the variant is derived from.

34. The vector according to claim 33, wherein the 5'UTR element and the open reading frame are heterologous.

35. The vector according to claim 33 or 34, which is an RNA or DNA vector.

36. The vector according to any one of claims 33-35, which is a plasmid vector or a viral vector, preferably a plasmid vector.

37. The vector according to any one of claims 33-36, which comprises or codes for an artificial nucleic acid molecule according to any one of claims 1-32.

38. The vector according to any one of claims 33-37, which is a circular molecule.

39. The vector according to claim 38, wherein the ORF, the poly(A) sequence or the 3'UTR element of the coding strand is followed in 5'→3' direction by a restriction site for linearization of the circular vector molecule.

40. A cell comprising the artificial nucleic acid molecule according to any one of claims 1-32 or the vector according to any one of claims 33-39, preferably a mammalian cell, more preferably an isolated cell of a mammalian subject, preferably of a human subject.

41. A pharmaceutical composition comprising the artificial nucleic acid molecule according to any one of claims 1-32, the vector according to any one of claims 33-39, or the cell according to claim 40, preferably further comprising one or more pharmaceutically acceptable diluents and/or excipients and/or one or more adjuvants.

42. The artificial nucleic acid molecule according to any one of claims 1-32, the vector according to any one of claims 33-39, the cell according to claim 40, or the pharmaceutical composition according to claim 41 for use as a medicament.

43. The artificial nucleic acid molecule according to any one of claims 1-32, the vector according to any one of claims 33-39, the cell according to claim 40, or the pharmaceutical composition according to claim 41 for use as a vaccine or for use in gene therapy.