Claims

1. Nucleic acid sequence comprising or coding for
   a) a coding region, encoding at least one peptide or protein;
   b) at least one histone stem-loop, and
   c) a poly(A) sequence or a polyadenylation signal;
   wherein said peptide or protein comprises a tumour antigen a fragment, variant or derivative of said tumour antigen.

2. The nucleic acid sequence according to claim 1, wherein the tumour antigen is a melanocyte-specific antigen, a cancer-testis antigen or a tumour-specific antigen, preferably a CT-X antigen, a non-X CT-antigen, a binding partner for a CT-X antigen or a binding partner for a non-X CT-antigen or a tumour-specific antigen, more preferably a CT-X antigen, a binding partner for a non-X CT-antigen or a tumour-specific antigen or a fragment, variant or derivative of said tumour antigen.

3. The nucleic acid sequence according to claim 1 or claim 2, wherein the tumour antigen is selected from the list of:
   5T4, 707-AP, 9D7, AFP, AlbZIP HPG1, alpha-5-beta-1-integrin, alpha-5-beta-6-integrin, alpha-actinin-4/m, alpha-methylacyl-coenzyme A racemase, ART-4, ARTC1/m, B7H4, BAGE-1, BCL-2, bcr/abl, beta-catenin/m, BING-4, BRCA1/m, BRCA2/m, CA 15-3/CA 27-29, CA 19-9, CA72-4, CA125, calreticulin, CAMEL, CASP-8/m, cathepsin B, cathepsin L, CD19, CD20, CD22, CD25, CDE30, CD33, CD4, CD52, CD55, CD56, CD80, CDC27/m, CDK4/m, CDKN2A/m, CEA, CLCA2, CML28, CML66, COA-1/m, coactosin-like protein, collage XXIII, COX-2, CT-9/BRD6, Cten, cyclin B1, cyclin D1, cyp-B, CYPB1, DAM-10, DAM-6, DEK-CAN, EFTUD2/m, EGFR, ELF2/m, EMMPRIN, EpCam, EphA2, EphA3, ErbB3, ETV6-AML1, EZH2, FGF-5, FN, Frau-1, G250, GAGE-1, GAGE-2, GAGE-3, GAGE-4, GAGE-5, GAGE-6, GAGE7b, GAGE-8, GDEP, GnT-V, gp100, GPC3, GPNMB/m, HAGE, HAST-2, hepsin, Her2/neu, HERV-K-MEL, HLA-A*0201-R17I, HLA-A11/m, HLA-A2/m, HNE, homeobox NKX3.1, HOM-TES-14/SCP-1, HOM-TES-85, HPV-E6, HPV-E7, HSP70-2M, HST-2, hTERT, iCE, IGF-1R, IL-13Ra2, IL-2R, IL-5, immature laminin receptor, kallikrein-2, kallikrein-4, Ki67, KIAA0205, KIAA0205/m, KK-LC-1, K-

Ras/m, LAGE-A1, LDLR-FUT, MAGE-A1, MAGE-A2, MAGE-A3, MAGE-A4, MAGE-A6, MAGE-A9, MAGE-A10, MAGE-A12, MAGE-B1, MAGE-B2, MAGE-B3, MAGE-B4, MAGE-B5, MAGE-B6, MAGE-B10, MAGE-B16, MAGE-B17, MAGE-C1, MAGE-C2, MAGE-C3, MAGE-D1, MAGE-D2, MAGE-D4, MAGE-E1, MAGE-E2, MAGE-F1, MAGE-H1, MAGEL2, mammaglobin A, MART-1/melan-A, MART-2, MART-2/m, matrix protein 22, MC1R, M-CSF, ME1/m, mesothelin, MG50/PXDN, MMP11, MN/CA IX-antigen, MRP-3, MUC-1, MUC-2, MUM-1/m, MUM-2/m, MUM-3/m, myosin class I/m, NA88-A, N-acetylglucosaminyltransferase-V, Neo-PAP, Neo-PAP/m, NFYC/m, NGEP, NMP22, NPM/ALK, N-Ras/m, NSE, NY-ESO-B, OA1, OFA-iLRP, OGT, OGT/m, OS-9, OS-9/m, osteocalcin, osteopontin, p15, p190 minor bcr-abl, p53, p53/m, PAGE-4, PAI-1, PAI-2, PAP, PART-1, PATE, PDEF, Pim-1-Kinase, Pin-1, Pml/PARalpha, POTE, PRAME, PRDX5/m, prostein, proteinase-3, PSA, PSCA, PSGR, PSM, PSMA, PTPRK/m, RAGE-1, RBAF600/m, RHAMM/CD168, RU1, RU2, S-100, SAGE, SART-1, SART-2, SART-3, SCC, SIRT2/m, Sp17, SSX-1, SSX-2/HOM-MEL-40, SSX-4, STAMP-1, STEAP-1, survivin, survivin-2B, SYT-SSX-1, SYT-SSX-2, TA-90, TAG-72, TARP, TEL-AML1, TGFbeta, TGFbetaRII, TGM-4, TPI/m, TRAG-3, TRG, TRP-1, TRP-2/6b, TRP/INT2, TRP-p8, tyrosinase, UPA, VEGFR1, VEGFR-2/FLK-1, WT1 and a immunoglobulin idiotype of a lymphoid blood cell or a T cell receptor idiotype of a lymphoid blood cell, or a fragment, variant or derivative of said tumour antigen; preferably survivin or a homologue thereof, an antigen from the MAGE-family or a binding partner thereof or a fragment, variant or derivative of said tumour antigen.

4. The nucleic acid according to claims 1 to 3, wherein the at least one histone stem loop is heterologous to the coding region encoding the at least one peptide or protein, preferably, wherein the coding region does not encode a histone protein or fragment, derivate of variant thereof having histone or histone-like function.

5. The nucleic acid according to claims 1 or 4, wherein the peptide or protein encoded by the coding region comprises a tumour antigenic protein or a fragment, variant or derivative thereof, the fragment, variant or derivative of the tumour antigenic protein retaining at least 50% of the biological activity of the tumour antigenic protein.

6. The nucleic acid of any of claims 1 to 5, wherein its coding region does not encode a reporter protein or a marker or selection protein.

7. Nucleic acid sequence according to any of claims 1 to 6, wherein the nucleic acid is an RNA, preferably an mRNA.

8. Nucleic acid sequence according to any of claims 1 to 7, 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):

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

wherein:

stem1 or stem2 bordering elements N_{1-6} is a consecutive sequence of 1 to 6, preferably of 2 to 6, more preferably of 2 to 5, even more preferably of 3 to 5, most preferably of 4 to 5 or 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;

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

wherein N_{0-2} is a consecutive sequence of 0 to 2, preferably of 0 to 1, more preferably of 1 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_{3-5} is a consecutive sequence of 3 to 5, preferably of 4 to 5, more preferably of 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 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, more preferably of 4 nucleotides;

wherein each N_{0-4} is independent from another a consecutive sequence of 0 to 4, preferably of 1 to 3, more preferably of 1 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 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, preferably of 4 to 5, more preferably of 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;

wherein N_{0-2} is a consecutive sequence of 0 to 2, preferably of 0 to 1, more preferably of 1 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.

9. The nucleic acid according to claim 8 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)

10. The nucleic acid sequence according to any of claims 1 to 9, wherein the poly(A) sequence comprises a sequence of about 25 to about 400 adenosine nucleotides, preferably a sequence of about 50 to about 400 adenosine nucleotides, more preferably a sequence of about 50 to about 300 adenosine nucleotides, even more preferably a sequence of about 50 to about 250 adenosine nucleotides, most preferably a sequence of about 60 to about 250 adenosine nucleotides.

11. Nucleic acid sequence according to any of claims 1 to 10, wherein the polyadenylation signal comprises the consensus sequence NN(U/T)ANA, preferably AA(U/T)AAA or A(U/T)(U/T)AAA.

12. Nucleic acid sequence according to any of claims 1 to 11, wherein the nucleic acid sequence is a modified nucleic acid, in particular a stabilized nucleic acid.

13. Nucleic acid sequence according to claim 12, wherein the G/C content of the coding region encoding at least one peptide or protein of said modified nucleic acid is increased compared with the G/C content of the coding region of the wild-type nucleic acid, the coded amino acid sequence of said modified nucleic acid

preferably not being modified compared with the coded amino acid sequence of the wild-type nucleic acid.

14. A composition comprising at least one type of nucleic acid sequences according to any of claims 1 to 13.

15. The composition according to claim 14, wherein the composition comprises at least two types of nucleic acid sequences wherein each type of nucleic acid sequence encodes for a different peptide or protein, preferably for a different tumour antigen.

16. The composition according to claim 14 or claim 15, wherein one type of the contained nucleic acid sequences encodes for PSA, PSMA, PSCA, STEAP-1, NY-ESO-1, 5T4, Survivin, MAGE-C1, or MAGE-C2.

17. The composition according to any of claims 14 to 16, wherein the nucleic acid sequence does not encode for NY-ESO1, provided that the composition contains only one type of nucleic acid sequence.

18. A kit or kit of parts comprising at least one, preferably a plurality or more than one of nucleic acid sequences each according to any of claims 1 to 13.

19. The composition or kit or kit of parts according to any of claims 14 to 18, comprising at least:

a) a nucleic acid sequence of any of claims 1 to 13 wherein said encoded peptide or protein comprises the tumour antigen PSA, or a fragment, variant or derivative thereof; and

b) a nucleic acid sequence of any of claims 1 to 13 wherein said encoded peptide or protein comprises the tumour antigen PSMA, or a fragment, variant or derivative thereof; and

c) a nucleic acid sequence of any of claims 1 to 13 wherein said encoded peptide or protein comprises the tumour antigen PSCA, or a fragment, variant or derivative thereof; and

d) a nucleic acid sequence of any of claims 1 to 13 wherein said encoded peptide or protein comprises the tumour antigen STEAP-1, or a fragment, variant or derivative thereof.

20. A composition or kit or kit of parts according to any of claims 14 to 18, comprising at least:

a) a nucleic acid sequence comprising or coding for

i. a coding region, encoding at least one peptide or protein which comprises the tumour antigen NY-ESO-1, or a fragment, variant or derivative thereof,

ii. at least one histone stem-loop, and

iii. a poly(A) sequence or a polyadenylation signal;

b) a nucleic acid sequence of any of claims 1 to 13 wherein said encoded peptide or protein comprises the tumour antigen 5T4, or a fragment, variant or derivative thereof; and

c) a nucleic acid sequence of any of claims 1 to 13 wherein said encoded peptide or protein comprises the tumour antigen Survivin, or a fragment, variant or derivative thereof.

21. The composition or kit or kit of parts according to any of claims 11 to 17, further comprising at least:

a) a nucleic acid sequence of any of claims 1 to 13 wherein said encoded peptide or protein comprises the tumour antigen MAGE-C1, or a fragment, variant or derivative thereof; and

b) a nucleic acid sequence of any of claims 1 to 13 wherein said encoded peptide or protein comprises the tumour antigen MAGE-C2, or a fragment, variant or derivative thereof.

22. Nucleic acid sequence as defined according to any of claims 1 to 13 or composition or kit or kit of parts as defined according to any of claims 14 to 21 for use as a medicament.

23. Nucleic acid sequence as defined according to any of claims 1 to 13 or composition or kit or kit of parts as defined according to any of claims 14 to 21 for use in the treatment of cancer or tumour diseases.

24. Pharmaceutical composition comprising a nucleic acid sequence as defined according to any of claims 1 to 13 or a composition as defined according to any of claims 14 to 21 and optionally a pharmaceutically acceptable carrier.

25. Use of a nucleic acid sequence as defined according to any of claims 1 to 13 or a composition or kit or kit of parts as defined according to any of claims 14 to 21 for increasing the expression of said encoded peptide or protein.

26. Use of a nucleic acid sequence as defined according to any of claims 1 to 13 or composition or kit or kit of parts as defined according to any of claims 14 to 21 for increasing the expression of said encoded peptide or protein in the treatment of cancer or tumour diseases.

27. A method for increasing the expression of an encoded peptide or protein comprising the steps:

a) providing the nucleic acid sequence as defined according to any of claims 1 to 13 or the composition as defined according to any of claims 14 to 21,

b) applying or administering the nucleic acid sequence or the composition to a cell-free expression system, a cell, a tissue or an organism.

What is claimed is:

1. An invention not claimed in any divisional application.