Applicant:
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ARTIFICIAL NUCLEIC ACID MOLECULES

The present invention was made with support from the Government under Agreement No. HR0011-11-3-0001 awarded by DARPA. The Government has certain rights in the invention.This application claims the priority of international patent application PCT/EP2014/003479 filed on December 30, 2014, which is incorporated herein by reference.

The invention relates to artificial nucleic acid molecules comprising an open reading frame, a 3'-untranslated region element (3'-UTR element) and/or a 5'-untranslated region element (5'-UTR element) and optionally a poly(A) sequence and/or a polyadenylation-signal. The invention relates further to a vector comprising a 3'-UTR element and/or a 5'-UTR element, to a cell comprising the artificial nucleic acid molecule or the vector, to a pharmaceutical composition comprising the artificial nucleic acid molecule or the vector and to a kit comprising the artificial nucleic acid molecule, the vector and/or the pharmaceutical composition, preferably for use in the field of gene therapy and/or genetic vaccination.
Gene therapy and genetic vaccination belong to the most promising and quickly developing methods of modern medicine. They may provide highly specific and individual options for therapy of a large variety of diseases. Particularly, inherited genetic diseases but also autoimmune diseases, cancerous or tumour-related diseases as well as inflammatory diseases may be the subject of such treatment approaches. Also, it is envisaged to prevent early onset of such diseases by these approaches.

The main conceptual rational behind gene therapy is appropriate modulation of impaired gene expression associated with pathological conditions of specific diseases. Pathologically altered gene expression may result in lack or overproduction of essential gene products, for example, signalling factors such as hormones, housekeeping factors, metabolic enzymes, structural proteins or the like. Altered gene expression may not only be due to mis-regulation of transcription and/or translation, but also due to mutations within the ORF coding for a particular protein. Pathological mutations may be caused by e.g. chromosomal aberration, or by more specific mutations, such as point or frame-shift-mutations, all of them resulting in

limited functionality and, potentially, total loss of function of the gene product. However, misregulation of transcription or translation may also occur, if mutations affect genes encoding proteins which are involved in the transcriptional or translational machinery of the cell. Such mutations may lead to pathological up- or down-regulation of genes which are – as such – functional. Genes encoding gene products which exert such regulating functions, may be, e.g., transcription factors, signal receptors, messenger proteins or the like. However, loss of function of such genes encoding regulatory proteins may, under certain circumstances, be reversed by artificial introduction of other factors acting further downstream of the impaired gene product. Such gene defects may also be compensated by gene therapy via substitution of the affected gene itself.

Genetic vaccination allows evoking a desired immune response to selected antigens, such as characteristic components of bacterial surfaces, viral particles, tumour antigens or the like. Generally, vaccination is one of the pivotal achievements of modern medicine. However, effective vaccines are currently available only for a limited number of diseases. Accordingly, infections that are not preventable by vaccination still affect millions of people every year.

Commonly, vaccines may be subdivided into "first", "second" and "third" generation vaccines. "First generation" vaccines are, typically, whole-organism vaccines. They are based on either live and attenuated or killed pathogens, e.g. viruses, bacteria or the like. The major drawback of live and attenuated vaccines is the risk for a reversion to life-threatening variants. Thus, although attenuated, such pathogens may still intrinsically bear unpredictable risks. Killed pathogens may not be as effective as desired for generating a specific immune response. In order to minimize these risks, "second generation" vaccines were developed. These are, typically, subunit vaccines, consisting of defined antigens or recombinant protein components which are derived from pathogens.

Genetic vaccines, i.e. vaccines for genetic vaccination, are usually understood as "third generation" vaccines. They are typically composed of genetically engineered nucleic acid molecules which allow expression of peptide or protein (antigen) fragments characteristic for a pathogen or a tumor antigen *in vivo*. Genetic vaccines are expressed upon administration to a patient after uptake by target cells. Expression of the administered nucleic acids results in production of the encoded proteins. In the event these proteins are recognized as foreign by the patient's immune system, an immune response is triggered.

As can be seen from the above, both methods, gene therapy and genetic vaccination, are essentially based on the administration of nucleic acid molecules to a patient and subsequent transcription and/or translation of the encoded genetic information. Alternatively, genetic vaccination or gene therapy may also comprise methods which include isolation of specific body cells from a patient to be treated, subsequent *in ex vivo* transfection of such cells, and re-administration of the treated cells to the patient.

DNA as well as RNA may be used as nucleic acid molecules for administration in the context of gene therapy or genetic vaccination. DNA is known to be relatively stable and easy to handle. However, the use of DNA bears the risk of undesired insertion of the administered DNA-fragments into the patient's genome potentially resulting mutagenic events such as in loss of function of the impaired genes. As a further risk, the undesired generation of anti-DNA antibodies has emerged. Another drawback is the limited expression level of the encoded peptide or protein that is achievable upon DNA administration because the DNA must enter the nucleus in order to be transcribed before the resulting mRNA can be translated. Among other reasons, the expression level of the administered DNA will be dependent on the presence of specific transcription factors which regulate DNA transcription. In the absence of such factors, DNA transcription will not yield satisfying amounts of RNA. As a result, the level of translated peptide or protein obtained is limited.

By using RNA instead of DNA for gene therapy or genetic vaccination, the risk of undesired genomic integration and generation of anti-DNA antibodies is minimized or avoided. However, RNA is considered to be a rather unstable molecular species which may readily be degraded by ubiquitous RNAses.

Typically, RNA degradation contributes to the regulation of the RNA half-life time. That effect was considered and proven to fine tune the regulation of eukaryotic gene expression (Friedel *et al.*, 2009. Conserved principles of mammalian transcriptional regulation revealed by RNA half-life, Nucleic Acid Research 37(17): 1-12). Accordingly, each naturally occurring mRNA has its individual half-life depending on the gene from which the mRNA is derived and in which cell type it is expressed. It contributes to the regulation of the expression level of this gene. Unstable RNAs are important to realize transient gene expression at distinct points in time. However, long-lived RNAs may be associated with accumulation of distinct proteins or continuous expression of genes. *In vivo*, the half-life of mRNAs may also be dependent on

environmental factors, such as hormonal treatment, as has been shown, e.g., for insulin-like growth factor I, actin, and albumin mRNA (Johnson *et al.*, Newly synthesized RNA: Simultaneous measurement in intact cells of transcription rates and RNA stability of insulin-like growth factor I, actin, and albumin in growth hormone-stimulated hepatocytes, Proc. Natl. Acad. Sci., Vol. 88, pp. 5287-5291, 1991).

For gene therapy and genetic vaccination, usually stable RNA is desired. This is, on the one hand, due to the fact that it is usually desired that the product encoded by the RNA sequence accumulates *in vivo*. On the other hand, the RNA has to maintain its structural and functional integrity when prepared for a suitable dosage form, in the course of its storage, and when administered. Thus, efforts were made to provide stable RNA molecules for gene therapy or genetic vaccination in order to prevent them from being subject to early degradation or decay.

It has been reported that the G/C-content of nucleic acid molecules may influence their stability. Thus, nucleic acids comprising an increased amount of guanine (G) and/or cytosine (C) residues may be functionally more stable than nucleic acids containing a large amount of adenine (A) and thymine (T) or uracil (U) nucleotides. In this context, WO02/098443 provides a pharmaceutical composition containing an mRNA that is stabilised by sequence modifications in the coding region. Such a sequence modification takes advantage of the degeneracy of the genetic code. Accordingly, codons which contain a less favourable combination of nucleotides (less favourable in terms of RNA stability) may be substituted by alternative codons without altering the encoded amino acid sequence. This method of RNA stabilization is limited by the provisions of the specific nucleotide sequence of each single RNA molecule which is not allowed to leave the space of the desired amino acid sequence. Also, that approach is restricted to coding regions of the RNA.

As an alternative option for mRNA stabilisation, it has been found that naturally occurring eukaryotic mRNA molecules contain characteristic stabilising elements. For example, they may comprise so-called untranslated regions (UTR) at their 5'-end (5'-UTR) and/or at their 3'-end (3'-UTR) as well as other structural features, such as a 5'-cap structure or a 3'-poly(A) tail. Both, 5'-UTR and 3'-UTR are typically transcribed from the genomic DNA and are, thus, an element of the premature mRNA. Characteristic structural features of mature mRNA, such as the 5'-cap and the 3'-poly(A) tail (also called poly(A) tail or poly(A) sequence) are usually added to the transcribed (premature) mRNA during mRNA processing.

A 3'-poly(A) tail is typically a monotonous sequence stretch of adenosine nucleotides added to the 3'-end of the transcribed mRNA. It may comprise up to about 400 adenosine nucleotides. It was found that the length of such a 3'-poly(A) tail is a potentially critical element for the stability of the individual mRNA.

Also, it was shown that the 3'-UTR of α-globin mRNA may be an important factor for the well-known stability of α-globin mRNA (Rodgers *et al.*, Regulated α-globin mRNA decay is a cytoplasmic event proceeding through 3'-to-5' exosome-dependent decapping, RNA, 8, pp. 1526-1537, 2002). The 3'-UTR of α–globin mRNA is apparently involved in the formation of a specific ribonucleoprotein-complex, the α-complex, whose presence correlates with mRNA stability *in vitro* (Wang *et al.*, An mRNA stability complex functions with poly(A)-binding protein to stabilize mRNA *in vitro,* Molecular and Cellular biology, Vol 19, No. 7, July 1999, p. 4552-4560).

An interesting regulatory function has further been demonstrated for the UTRs in ribosomal protein mRNAs: while the 5'-UTR of ribosomal protein mRNAs controls the growth-associated translation of the mRNA, the stringency of that regulation is conferred by the respective 3'-UTR in ribosomal protein mRNAs (Ledda et al., Effect of the 3'-UTR length on the translational regulation of 5'-terminal oligopyrimidine mRNAs, Gene, Vol. 344, 2005, p. 213-220). This mechanism contributes to the specific expression pattern of ribosomal proteins, which are typically transcribed in a constant manner so that some ribosomal protein mRNAs such as ribosomal protein S9 or ribosomal protein L32 are referred to as housekeeping genes (Janovick-Guretzky et al., Housekeeping Gene Expression in Bovine Liver is Affected by Physiological State, Feed Intake, and Dietary Treatment, J. Dairy Sci., Vol. 90, 2007, p. 2246-2252). The growth-associated expression pattern of ribosomal proteins is thus mainly due to regulation on the level of translation.

Irrespective of factors influencing mRNA stability, effective translation of the administered nucleic acid molecules by the target cells or tissue is crucial for any approach using nucleic acid molecules for gene therapy or genetic vaccination. As can be seen from the examples cited above, along with the regulation of stability, also translation of the majority of mRNAs is regulated by structural features like UTRs, 5'-cap and 3'-poly(A) tail. In this context, it has been reported that the length of the poly(A) tail may play an important role for translational

efficiency as well. Stabilizing 3'-elements, however, may also have an attenuating effect on translation.

It is the object of the invention to provide nucleic acid molecules which may be suitable for application in gene therapy and/or genetic vaccination. Particularly, it is the object of the invention to provide an mRNA species which is stabilized against preterm degradation or decay without exhibiting significant functional loss in translational efficiency. It is also an object of the invention to provide an artificial nucleic acid molecule, preferably an mRNA, which is characterized by enhanced expression of the respective protein encoded by said nucleic acid molecule. One particular object of the invention is the provision of an mRNA, wherein the efficiency of translation of the respective encoded protein is enhanced. Another object of the present invention is to provide nucleic acid molecules coding for such a superior mRNA species which may be amenable for use in gene therapy and/or genetic vaccination. It is a further object of the present invention to provide a pharmaceutical composition for use in gene therapy and/or genetic vaccination. In summary, it is the object of the present invention to provide improved nucleic acid species which overcome the above discussed disadvantages of the prior art by a cost-effective and straight-forward approach.

The object underlying the present invention is solved by the claimed subject matter.

For the sake of clarity and readability the following definitions are provided. Any technical feature mentioned for these definitions may be read on each and every embodiment of the invention. Additional definitions and explanations may be specifically provided in the context of these embodiments.

Adaptive immune response: The adaptive immune response is typically understood to be an antigen-specific response of the immune system. Antigen specificity allows for the generation of responses that are tailored to specific pathogens or pathogen-infected cells. The ability to mount these tailored responses is usually maintained in the body by "memory cells". Should a pathogen infect the body more than once, these specific memory cells are used to quickly eliminate it. In this context, the first step of an adaptive immune response is the activation of naïve antigen-specific T cells or different immune cells able to induce an antigen-specific immune response by antigen-presenting cells. This occurs in the lymphoid tissues and organs through which naïve T cells are constantly passing. The three cell types that may serve as antigen-presenting cells are dendritic cells, macrophages, and B cells. Each of these cells has

a distinct function in eliciting immune responses. Dendritic cells may take up antigens by phagocytosis and macropinocytosis and may become stimulated by contact with e.g. a foreign antigen to migrate to the local lymphoid tissue, where they differentiate into mature dendritic cells. Macrophages ingest particulate antigens such as bacteria and are induced by infectious agents or other appropriate stimuli to express MHC molecules. The unique ability of B cells to bind and internalize soluble protein antigens via their receptors may also be important to induce T cells. MHC-molecules are, typically, responsible for presentation of an antigen to T-cells. Therein, presenting the antigen on MHC molecules leads to activation of T cells which induces their proliferation and differentiation into armed effector T cells. The most important function of effector T cells is the killing of infected cells by CD8+ cytotoxic T cells and the activation of macrophages by Th1 cells which together make up cell-mediated immunity, and the activation of B cells by both Th2 and Th1 cells to produce different classes of antibody, thus driving the humoral immune response. T cells recognize an antigen by their T cell receptors which do not recognize and bind the antigen directly, but instead recognize short peptide fragments e.g. of pathogen-derived protein antigens, e.g. so-called epitopes, which are bound to MHC molecules on the surfaces of other cells.

Adaptive immune system: The adaptive immune system is essentially dedicated to eliminate or prevent pathogenic growth. It typically regulates the adaptive immune response by providing the vertebrate immune system with the ability to recognize and remember specific pathogens (to generate immunity), and to mount stronger attacks each time the pathogen is encountered. The system is highly adaptable because of somatic hypermutation (a process of accelerated somatic mutations), and V(D)J recombination (an irreversible genetic recombination of antigen receptor gene segments). This mechanism allows a small number of genes to generate a vast number of different antigen receptors, which are then uniquely expressed on each individual lymphocyte. Because the gene rearrangement leads to an irreversible change in the DNA of each cell, all of the progeny (offspring) of such a cell will then inherit genes encoding the same receptor specificity, including the Memory B cells and Memory T cells that are the keys to long-lived specific immunity.

Adjuvant/adjuvant component: An adjuvant or an adjuvant component in the broadest sense is typically a pharmacological and/or immunological agent that may modify, e.g. enhance, the effect of other agents, such as a drug or vaccine. It is to be interpreted in a broad sense and refers to a broad spectrum of substances. Typically, these substances are able to increase

the immunogenicity of antigens. For example, adjuvants may be recognized by the innate immune systems and, e.g., may elicit an innate immune response. "Adjuvants" typically do not elicit an adaptive immune response. Insofar, "adjuvants" do not qualify as antigens. Their mode of action is distinct from the effects triggered by antigens resulting in an adaptive immune response.

Antigen: In the context of the present invention "antigen" refers typically to a substance which may be recognized by the immune system, preferably by the adaptive immune system, and is capable of triggering an antigen-specific immune response, e.g. by formation of antibodies and/or antigen-specific T cells as part of an adaptive immune response. Typically, an antigen may be or may comprise a peptide or protein which may be presented by the MHC to T-cells. In the sense of the present invention an antigen may be the product of translation of a provided nucleic acid molecule, preferably an mRNA as defined herein. In this context, also fragments, variants and derivatives of peptides and proteins comprising at least one epitope are understood as antigens. In the context of the present invention, tumour antigens and pathogenic antigens as defined herein are particularly preferred.

Artificial nucleic acid molecule: An artificial nucleic acid molecule may typically be understood to be a nucleic acid molecule, e.g. a DNA or an RNA, that does not occur naturally. In other words, an artificial nucleic acid molecule may be understood as a non-natural nucleic acid molecule. Such nucleic acid molecule may be non-natural due to its individual sequence (which does not occur naturally) and/or due to other modifications, e.g. structural modifications of nucleotides which do not occur naturally. An artificial nucleic acid molecule may be a DNA molecule, an RNA molecule or a hybrid-molecule comprising DNA and RNA portions. Typically, artificial nucleic acid molecules may be designed and/or generated by genetic engineering methods to correspond to a desired artificial sequence of nucleotides (heterologous sequence). In this context an artificial sequence is usually a sequence that may not occur naturally, i.e. it differs from the wild type sequence by at least one nucleotide. The term "wild type" may be understood as a sequence occurring in nature. Further, the term "artificial nucleic acid molecule" is not restricted to mean "one single molecule" but is, typically, understood to comprise an ensemble of identical molecules. Accordingly, it may relate to a plurality of identical molecules contained in an aliquot.

Bicistronic RNA, multicistronic RNA: A bicistronic or multicistronic RNA is typically an RNA, preferably an mRNA, that typically may have two (bicistronic) or more (multicistronic) open reading frames (ORF). An open reading frame in this context is a sequence of codons that is translatable into a peptide or protein.

Carrier / polymeric carrier: A carrier in the context of the invention may typically be a compound that facilitates transport and/or complexation of another compound (cargo). A polymeric carrier is typically a carrier that is formed of a polymer. A carrier may be associated to its cargo by covalent or non-covalent interaction. A carrier may transport nucleic acids, e.g. RNA or DNA, to the target cells. The carrier may – for some embodiments – be a cationic component.

Cationic component: The term "cationic component" typically refers to a charged molecule, which is positively charged (cation) at a pH value typically from 1 to 9, preferably at a pH value of or below 9 (e.g. from 5 to 9), of or below 8 (e.g. from 5 to 8), of or below 7 (e.g. from 5 to 7), most preferably at a physiological pH, e.g. from 7.3 to 7.4. Accordingly, a cationic component may be any positively charged compound or polymer, preferably a cationic peptide or protein which is positively charged under physiological conditions, particularly under physiological conditions *in vivo*. A "cationic peptide or protein" may contain at least one positively charged amino acid, or more than one positively charged amino acid, e.g. selected from Arg, His, Lys or Orn. Accordingly, "polycationic" components are also within the scope exhibiting more than one positive charge under the conditions given.

5'-cap: A 5'-cap is an entity, typically a modified nucleotide entity, which generally "caps" the 5'-end of a mature mRNA. A 5'-cap may typically be formed by a modified nucleotide, particularly by a derivative of a guanine nucleotide. Preferably, the 5'-cap is linked to the 5'-terminus via a 5'-5'-triphosphate linkage. A 5'-cap may be methylated, e.g. m7GpppN, wherein N is the terminal 5' nucleotide of the nucleic acid carrying the 5'-cap, typically the 5'-end of an RNA. Further examples of 5'cap structures include glyceryl, inverted deoxy abasic residue (moiety), 4',5' methylene nucleotide, 1-(beta-D-erythrofuranosyl) nucleotide, 4'-thio nucleotide, carbocyclic nucleotide, 1,5-anhydrohexitol nucleotide, L-nucleotides, alpha-nucleotide, modified base nucleotide, threo-pentofuranosyl nucleotide, acyclic 3',4'-seco nucleotide, acyclic 3,4-dihydroxybutyl nucleotide, acyclic 3,5 dihydroxypentyl nucleotide, 3'-3'-inverted nucleotide moiety, 3'-3'-inverted abasic moiety, 3'-2'-inverted

nucleotide moiety, 3'-2'-inverted abasic moiety, 1,4-butanediol phosphate, 3'-phosphoramidate, hexylphosphate, aminohexyl phosphate, 3'-phosphate, 3'phosphorothioate, phosphorodithioate, or bridging or non-bridging methylphosphonate moiety.

Cellular immunity/cellular immune response: Cellular immunity relates typically to the activation of macrophages, natural killer cells (NK), antigen-specific cytotoxic T-lymphocytes, and the release of various cytokines in response to an antigen. In more general terms, cellular immunity is not based on antibodies, but on the activation of cells of the immune system. Typically, a cellular immune response may be characterized e.g. by activating antigen-specific cytotoxic T-lymphocytes that are able to induce apoptosis in cells, e.g. specific immune cells like dendritic cells or other cells, displaying epitopes of foreign antigens on their surface. Such cells may be virus-infected or infected with intracellular bacteria, or cancer cells displaying tumor antigens. Further characteristics may be activation of macrophages and natural killer cells, enabling them to destroy pathogens and stimulation of cells to secrete a variety of cytokines that influence the function of other cells involved in adaptive immune responses and innate immune responses.

The term "derived from" as used throughout the present specification in the context of a nucleic acid, i.e. for a nucleic acid "derived from" (another) nucleic acid, means that the nucleic acid, which is derived from (another) nucleic acid, shares at least 50%, preferably at least 60%, preferably at least 70%, more preferably at least 75%, more preferably at least 80%, more preferably at least 85%, even more preferably at least 90%, even more preferably at least 95%, and particularly preferably at least 98% sequence identity with the nucleic acid from which it is derived. The skilled person is aware that sequence identity is typically calculated for the same types of nucleic acids, i.e. for DNA sequences or for RNA sequences. Thus, it is understood, if a DNA is "derived from" an RNA or if an RNA is "derived from" a DNA, in a first step the RNA sequence is converted into the corresponding DNA sequence (in particular by replacing the uracils (U) by thymidines (T) throughout the sequence) or, vice versa, the DNA sequence is converted into the corresponding RNA sequence (in particular by replacing the thymidines (T) by uracils (U) throughout the sequence). Thereafter, the sequence identity of the DNA sequences or the sequence identity of the RNA sequences is determined. Preferably, a nucleic acid "derived from" a nucleic acid also refers to nucleic acid, which is modified in comparison to the nucleic acid from which it is derived, e.g. in

order to increase RNA stability even further and/or to prolong and/or increase protein production. It goes without saying that such modifications are preferred, which do not impair RNA stability, e.g. in comparison to the nucleic acid from which it is derived.

DNA: DNA is the usual abbreviation for deoxy-ribonucleic acid. It is a nucleic acid molecule, i.e. a polymer consisting of nucleotides. These nucleotides are usually deoxy-adenosine-monophosphate, deoxy-thymidine-monophosphate, deoxy-guanosine-monophosphate and deoxy-cytidine-monophosphate monomers which are – by themselves – composed of a sugar moiety (deoxyribose), a base moiety and a phosphate moiety, and polymerise by a characteristic backbone structure. The backbone structure is, typically, formed by phosphodiester bonds between the sugar moiety of the nucleotide, i.e. deoxyribose, of a first and a phosphate moiety of a second, adjacent monomer. The specific order of the monomers, i.e. the order of the bases linked to the sugar/phosphate-backbone, is called the DNA sequence. DNA may be single stranded or double stranded. In the double stranded form, the nucleotides of the first strand typically hybridize with the nucleotides of the second strand, e.g. by A/T-base-pairing and G/C-base-pairing.

Epitope: (also called "antigen determinant") can be distinguished in T cell epitopes and B cell epitopes. T cell epitopes or parts of the proteins in the context of the present invention may comprise fragments preferably having a length of about 6 to about 20 or even more amino acids, e.g. fragments as processed and presented by MHC class I molecules, preferably having a length of about 8 to about 10 amino acids, e.g. 8, 9, or 10, (or even 11, or 12 amino acids), or fragments as processed and presented by MHC class II molecules, preferably having a length of about 13 or more amino acids, e.g. 13, 14, 15, 16, 17, 18, 19, 20 or even more amino acids, wherein these fragments may be selected from any part of the amino acid sequence. These fragments are typically recognized by T cells in form of a complex consisting of the peptide fragment and an MHC molecule, i.e. the fragments are typically not recognized in their native form. B cell epitopes are typically fragments located on the outer surface of (native) protein or peptide antigens as defined herein, preferably having 5 to 15 amino acids, more preferably having 5 to 12 amino acids, even more preferably having 6 to 9 amino acids, which may be recognized by antibodies, i.e. in their native form.

Such epitopes of proteins or peptides may furthermore be selected from any of the herein mentioned variants of such proteins or peptides. In this context antigenic determinants can

be conformational or discontinuous epitopes which are composed of segments of the proteins or peptides as defined herein that are discontinuous in the amino acid sequence of the proteins or peptides as defined herein but are brought together in the three-dimensional structure or continuous or linear epitopes which are composed of a single polypeptide chain.

Fragment of a sequence: A fragment of a sequence may typically be a shorter portion of a full-length sequence of e.g. a nucleic acid molecule or an amino acid sequence. Accordingly, a fragment, typically, consists of a sequence that is identical to the corresponding stretch within the full-length sequence. A preferred fragment of a sequence in the context of the present invention, consists of a continuous stretch of entities, such as nucleotides or amino acids corresponding to a continuous stretch of entities in the molecule the fragment is derived from, which represents at least 5%, 10%, 20%, preferably at least 30%, more preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, and most preferably at least 80% of the total (i.e. full-length) molecule from which the fragment is derived.

G/C modified: A G/C-modified nucleic acid may typically be a nucleic acid, preferably an artificial nucleic acid molecule as defined herein, based on a modified wild-type sequence comprising a preferably increased number of guanosine and/or cytosine nucleotides as compared to the wild-type sequence. Such an increased number may be generated by substitution of codons containing adenosine or thymidine nucleotides by codons containing guanosine or cytosine nucleotides. If the enriched G/C content occurs in a coding region of DNA or RNA, it makes use of the degeneracy of the genetic code. Accordingly, the codon substitutions preferably do not alter the encoded amino acid residues, but exclusively increase the G/C content of the nucleic acid molecule.

Gene therapy: Gene therapy may typically be understood to mean a treatment of a patient's body or isolated elements of a patient's body, for example isolated tissues/cells, by nucleic acids encoding a peptide or protein. It typically may comprise at least one of the steps of a) administration of a nucleic acid, preferably an artificial nucleic acid molecule as defined herein, directly to the patient - by whatever administration route - or *in vitro* to isolated cells/tissues of the patient, which results in transfection of the patient's cells either *in vivo*/*ex vivo* or *in vitro*; b) transcription and/or translation of the introduced nucleic acid molecule;

and optionally c) re-administration of isolated, transfected cells to the patient, if the nucleic acid has not been administered directly to the patient.

Genetic vaccination: Genetic vaccination may typically be understood to be vaccination by administration of a nucleic acid molecule encoding an antigen or an immunogen or fragments thereof. The nucleic acid molecule may be administered to a subject's body or to isolated cells of a subject. Upon transfection of certain cells of the body or upon transfection of the isolated cells, the antigen or immunogen may be expressed by those cells and subsequently presented to the immune system, eliciting an adaptive, i.e. antigen-specific immune response. Accordingly, genetic vaccination typically comprises at least one of the steps of a) administration of a nucleic acid, preferably an artificial nucleic acid molecule as defined herein, to a subject, preferably a patient, or to isolated cells of a subject, preferably a patient, which usually results in transfection of the subject's cells either *in vivo* or *in vitro*; b) transcription and/or translation of the introduced nucleic acid molecule; and optionally c) re-administration of isolated, transfected cells to the subject, preferably the patient, if the nucleic acid has not been administered directly to the patient.

Heterologous sequence: Two sequences are typically understood to be 'heterologous' if they are not derivable from the same gene. I.e., although heterologous sequences may be derivable from the same organism, they naturally (in nature) do not occur in the same nucleic acid molecule, such as in the same mRNA.

Humoral immunity/humoral immune response: Humoral immunity refers typically to antibody production and optionally to accessory processes accompanying antibody production. A humoral immune response may be typically characterized, e.g., by Th2 activation and cytokine production, germinal center formation and isotype switching, affinity maturation and memory cell generation. Humoral immunity also typically may refer to the effector functions of antibodies, which include pathogen and toxin neutralization, classical complement activation, and opsonin promotion of phagocytosis and pathogen elimination.

Immunogen: In the context of the present invention an immunogen may be typically understood to be a compound that is able to stimulate an immune response. Preferably, an immunogen is a peptide, polypeptide, or protein. In a particularly preferred embodiment, an immunogen in the sense of the present invention is the product of translation of a provided

nucleic acid molecule, preferably an artificial nucleic acid molecule as defined herein. Typically, an immunogen elicits at least an adaptive immune response.

Immunostimulatory composition: In the context of the invention, an immunostimulatory composition may be typically understood to be a composition containing at least one component which is able to induce an immune response or from which a component which is able to induce an immune response is derivable. Such immune response may be preferably an innate immune response or a combination of an adaptive and an innate immune response. Preferably, an immunostimulatory composition in the context of the invention contains at least one artificial nucleic acid molecule, more preferably an RNA, for example an mRNA molecule. The immunostimulatory component, such as the mRNA may be complexed with a suitable carrier. Thus, the immunostimulatory composition may comprise an mRNA/carrier-complex. Furthermore, the immunostimulatory composition may comprise an adjuvant and/or a suitable vehicle for the immunostimulatory component, such as the mRNA.

Immune response: An immune response may typically be a specific reaction of the adaptive immune system to a particular antigen (so called specific or adaptive immune response) or an unspecific reaction of the innate immune system (so called unspecific or innate immune response), or a combination thereof.

Immune system: The immune system may protect organisms from infection. If a pathogen succeeds in passing a physical barrier of an organism and enters this organism, the innate immune system provides an immediate, but non-specific response. If pathogens evade this innate response, vertebrates possess a second layer of protection, the adaptive immune system. Here, the immune system adapts its response during an infection to improve its recognition of the pathogen. This improved response is then retained after the pathogen has been eliminated, in the form of an immunological memory, and allows the adaptive immune system to mount faster and stronger attacks each time this pathogen is encountered. According to this, the immune system comprises the innate and the adaptive immune system. Each of these two parts typically contains so called humoral and cellular components.

Immunostimulatory RNA: An immunostimulatory RNA (isRNA) in the context of the invention may typically be an RNA that is able to induce an innate immune response. It usually does not have an open reading frame and thus does not provide a peptide-antigen or immunogen but elicits an immune response e.g. by binding to a specific kind of Toll-like-

receptor (TLR) or other suitable receptors. However, of course also mRNAs having an open reading frame and coding for a peptide/protein may induce an innate immune response and, thus, may be immunostimulatory RNAs.

Innate immune system: The innate immune system, also known as non-specific (or unspecific) immune system, typically comprises the cells and mechanisms that defend the host from infection by other organisms in a non-specific manner. This means that the cells of the innate system may recognize and respond to pathogens in a generic way, but unlike the adaptive immune system, it does not confer long-lasting or protective immunity to the host. The innate immune system may be, e.g., activated by ligands of Toll-like receptors (TLRs) or other auxiliary substances such as lipopolysaccharides, TNF-alpha, CD40 ligand, or cytokines, monokines, lymphokines, interleukins or chemokines, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, IL-19, IL-20, IL-21, IL-22, IL-23, IL-24, IL-25, IL-26, IL-27, IL-28, IL-29, IL-30, IL-31, IL-32, IL-33, IFN-alpha, IFN-beta, IFN-gamma, GM-CSF, G-CSF, M-CSF, LT-beta, TNF-alpha, growth factors, and hGH, a ligand of human Toll-like receptor TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, a ligand of murine Toll-like receptor TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, TLR11, TLR12 or TLR13, a ligand of a NOD-like receptor, a ligand of a RIG-I like receptor, an immunostimulatory nucleic acid, an immunostimulatory RNA (isRNA), a CpG-DNA, an antibacterial agent, or an anti-viral agent. The pharmaceutical composition according to the present invention may comprise one or more such substances. Typically, a response of the innate immune system includes recruiting immune cells to sites of infection, through the production of chemical factors, including specialized chemical mediators, called cytokines; activation of the complement cascade; identification and removal of foreign substances present in organs, tissues, the blood and lymph, by specialized white blood cells; activation of the adaptive immune system; and/or acting as a physical and chemical barrier to infectious agents.

Cloning site: A cloning site is typically understood to be a segment of a nucleic acid molecule, which is suitable for insertion of a nucleic acid sequence, e.g., a nucleic acid sequence comprising an open reading frame. Insertion may be performed by any molecular biological method known to the one skilled in the art, e.g. by restriction and ligation. A cloning site typically comprises one or more restriction enzyme recognition sites (restriction sites). These one or more restrictions sites may be recognized by restriction enzymes which

cleave the DNA at these sites. A cloning site which comprises more than one restriction site may also be termed a multiple cloning site (MCS) or a polylinker.

Nucleic acid molecule: A nucleic acid molecule is a molecule comprising, preferably consisting of nucleic acid components. The term nucleic acid molecule preferably refers to DNA or RNA molecules. It is preferably used synonymous with the term "polynucleotide". Preferably, a nucleic acid molecule is a polymer comprising or consisting of nucleotide monomers which are covalently linked to each other by phosphodiester-bonds of a sugar/phosphate-backbone. The term "nucleic acid molecule" also encompasses modified nucleic acid molecules, such as base-modified, sugar-modified or backbone-modified etc. DNA or RNA molecules.

Open reading frame: An open reading frame (ORF) in the context of the invention may typically be a sequence of several nucleotide triplets which may be translated into a peptide or protein. An open reading frame preferably contains a start codon, i.e. a combination of three subsequent nucleotides coding usually for the amino acid methionine (ATG), at its 5'-end and a subsequent region which usually exhibits a length which is a multiple of 3 nucleotides. An ORF is preferably terminated by a stop-codon (e.g., TAA, TAG, TGA). Typically, this is the only stop-codon of the open reading frame. Thus, an open reading frame in the context of the present invention is preferably a nucleotide sequence, consisting of a number of nucleotides that may be divided by three, which starts with a start codon (e.g. ATG) and which preferably terminates with a stop codon (e.g., TAA, TGA, or TAG). The open reading frame may be isolated or it may be incorporated in a longer nucleic acid sequence, for example in a vector or an mRNA. An open reading frame may also be termed "protein coding region".

Peptide: A peptide or polypeptide is typically a polymer of amino acid monomers, linked by peptide bonds. It typically contains less than 50 monomer units. Nevertheless, the term peptide is not a disclaimer for molecules having more than 50 monomer units. Long peptides are also called polypeptides, typically having between 50 and 600 monomeric units.

Pharmaceutically effective amount: A pharmaceutically effective amount in the context of the invention is typically understood to be an amount that is sufficient to induce a pharmaceutical effect, such as an immune response, altering a pathological level of an expressed peptide or protein, or substituting a lacking gene product, e.g., in case of a pathological situation.

Protein A protein typically comprises one or more peptides or polypeptides. A protein is typically folded into 3-dimensional form, which may be required for to protein to exert its biological function.

Poly(A) sequence: A poly(A) sequence, also called poly(A) tail or 3'-poly(A) tail, is typically understood to be a sequence of adenosine nucleotides, e.g., of up to about 400 adenosine nucleotides, e.g. from about 20 to about 400, preferably from about 50 to about 400, more preferably from about 50 to about 300, even more preferably from about 50 to about 250, most preferably from about 60 to about 250 adenosine nucleotides. A poly(A) sequence is typically located at the 3'end of an mRNA. In the context of the present invention, a poly(A) sequence may be located within an mRNA or any other nucleic acid molecule, such as, e.g., in a vector, for example, in a vector serving as template for the generation of an RNA, preferably an mRNA, e.g., by transcription of the vector.

Polyadenylation: Polyadenylation is typically understood to be the addition of a poly(A) sequence to a nucleic acid molecule, such as an RNA molecule, e.g. to a premature mRNA. Polyadenylation may be induced by a so called polyadenylation signal. This signal is preferably located within a stretch of nucleotides at the 3'-end of a nucleic acid molecule, such as an RNA molecule, to be polyadenylated. A polyadenylation signal typically comprises a hexamer consisting of adenine and uracil/thymine nucleotides, preferably the hexamer sequence AAUAAA. Other sequences, preferably hexamer sequences, are also conceivable. Polyadenylation typically occurs during processing of a pre-mRNA (also called premature-mRNA). Typically, RNA maturation (from pre-mRNA to mature mRNA) comprises the step of polyadenylation.

Restriction site: A restriction site, also termed restriction enzyme recognition site, is a nucleotide sequence recognized by a restriction enzyme. A restriction site is typically a short, preferably palindromic nucleotide sequence, e.g. a sequence comprising 4 to 8 nucleotides. A restriction site is preferably specifically recognized by a restriction enzyme. The restriction enzyme typically cleaves a nucleotide sequence comprising a restriction site at this site. In a double-stranded nucleotide sequence, such as a double-stranded DNA sequence, the restriction enzyme typically cuts both strands of the nucleotide sequence.

RNA, mRNA: RNA is the usual abbreviation for ribonucleic-acid. It is a nucleic acid molecule, i.e. a polymer consisting of nucleotides. These nucleotides are usually adenosine-

monophosphate, uridine-monophosphate, guanosine-monophosphate and cytidine-monophosphate monomers which are connected to each other along a so-called backbone. The backbone is formed by phosphodiester bonds between the sugar, i.e. ribose, of a first and a phosphate moiety of a second, adjacent monomer. The specific succession of the monomers is called the RNA-sequence. Usually RNA may be obtainable by transcription of a DNA-sequence, e.g., inside a cell. In eukaryotic cells, transcription is typically performed inside the nucleus or the mitochondria. Typically, transcription of DNA usually results in the so-called premature RNA which has to be processed into so-called messenger-RNA, usually abbreviated as mRNA. Processing of the premature RNA, e.g. in eukaryotic organisms, comprises a variety of different posttranscriptional-modifications such as splicing, 5'-capping, polyadenylation, export from the nucleus or the mitochondria and the like. The sum of these processes is also called maturation of RNA. The mature messenger RNA usually provides the nucleotide sequence that may be translated into an amino-acid sequence of a particular peptide or protein. Typically, a mature mRNA comprises a 5'-cap, a 5'-UTR, an open reading frame, a 3'-UTR and a poly(A) sequence. Aside from messenger RNA, several non-coding types of RNA exist which may be involved in regulation of transcription and/or translation.

Sequence of a nucleic acid molecule: The sequence of a nucleic acid molecule is typically understood to be the particular and individual order, i.e. the succession of its nucleotides. The sequence of a protein or peptide is typically understood to be the order, i.e. the succession of its amino acids.

Sequence identity: Two or more sequences are identical if they exhibit the same length and order of nucleotides or amino acids. The percentage of identity typically describes the extent to which two sequences are identical, i.e. it typically describes the percentage of nucleotides that correspond in their sequence position with identical nucleotides of a reference-sequence. For determination of the degree of identity, the sequences to be compared are considered to exhibit the same length, i.e. the length of the longest sequence of the sequences to be compared. This means that a first sequence consisting of 8 nucleotides is 80% identical to a second sequence consisting of 10 nucleotides comprising the first sequence. In other words, in the context of the present invention, identity of sequences preferably relates to the percentage of nucleotides of a sequence which have the same position in two or more sequences having the same length. Gaps are usually regarded as non-identical positions, irrespective of their actual position in an alignment.

Stabilized nucleic acid molecule: A stabilized nucleic acid molecule is a nucleic acid molecule, preferably a DNA or RNA molecule that is modified such, that it is more stable to disintegration or degradation, e.g., by environmental factors or enzymatic digest, such as by an exo- or endonuclease degradation, than the nucleic acid molecule without the modification. Preferably, a stabilized nucleic acid molecule in the context of the present invention is stabilized in a cell, such as a prokaryotic or eukaryotic cell, preferably in a mammalian cell, such as a human cell. The stabilization effect may also be exerted outside of cells, e.g. in a buffer solution etc., for example, in a manufacturing process for a pharmaceutical composition comprising the stabilized nucleic acid molecule.

Transfection: The term "transfection" refers to the introduction of nucleic acid molecules, such as DNA or RNA (e.g. mRNA) molecules, into cells, preferably into eukaryotic cells. In the context of the present invention, the term "transfection" encompasses any method known to the skilled person for introducing nucleic acid molecules into cells, preferably into eukaryotic cells, such as into mammalian cells. Such methods encompass, for example, electroporation, lipofection, e.g. based on cationic lipids and/or liposomes, calcium phosphate precipitation, nanoparticle based transfection, virus based transfection, or transfection based on cationic polymers, such as DEAE-dextran or polyethylenimine etc. Preferably, the introduction is non-viral.

Vaccine: A vaccine is typically understood to be a prophylactic or therapeutic material providing at least one antigen, preferably an immunogen. The antigen or immunogen may be derived from any material that is suitable for vaccination. For example, the antigen or immunogen may be derived from a pathogen, such as from bacteria or virus particles etc., or from a tumor or cancerous tissue. The antigen or immunogen stimulates the body's adaptive immune system to provide an adaptive immune response.

Vector: The term "vector" refers to a nucleic acid molecule, preferably to an artificial nucleic acid molecule. A vector in the context of the present invention is suitable for incorporating or harboring a desired nucleic acid sequence, such as a nucleic acid sequence comprising an open reading frame. Such vectors may be storage vectors, expression vectors, cloning vectors, transfer vectors etc. A storage vector is a vector which allows the convenient storage of a nucleic acid molecule, for example, of an mRNA molecule. Thus, the vector may comprise a sequence corresponding, e.g., to a desired mRNA sequence or a part thereof, such

as a sequence corresponding to the open reading frame and the 3'-UTR and/or the 5'-UTR of an mRNA. An expression vector may be used for production of expression products such as RNA, e.g. mRNA, or peptides, polypeptides or proteins. For example, an expression vector may comprise sequences needed for transcription of a sequence stretch of the vector, such as a promoter sequence, e.g. an RNA polymerase promoter sequence. A cloning vector is typically a vector that contains a cloning site, which may be used to incorporate nucleic acid sequences into the vector. A cloning vector may be, e.g., a plasmid vector or a bacteriophage vector. A transfer vector may be a vector which is suitable for transferring nucleic acid molecules into cells or organisms, for example, viral vectors. A vector in the context of the present invention may be, e.g., an RNA vector or a DNA vector. Preferably, a vector is a DNA molecule. Preferably, a vector in the sense of the present application comprises a cloning site, a selection marker, such as an antibiotic resistance factor, and a sequence suitable for multiplication of the vector, such as an origin of replication. Preferably, a vector in the context of the present application is a plasmid vector.

Vehicle: A vehicle is typically understood to be a material that is suitable for storing, transporting, and/or administering a compound, such as a pharmaceutically active compound. For example, it may be a physiologically acceptable liquid which is suitable for storing, transporting, and/or administering a pharmaceutically active compound.

3'-untranslated region (3'-UTR): Generally, the term "3'-UTR" refers to a part of the artificial nucleic acid molecule, which is located 3' (i.e. "downstream") of an open reading frame and which is not translated into protein. Typically, a 3'-UTR is the part of an mRNA which is located between the protein coding region (open reading frame (ORF) or coding sequence (CDS)) and the poly(A) sequence of the mRNA. In the context of the invention, the term 3'-UTR may also comprise elements, which are not encoded in the template, from which an RNA is transcribed, but which are added after transcription during maturation, e.g. a poly(A) sequence. A 3'-UTR of the mRNA is not translated into an amino acid sequence. The 3'-UTR sequence is generally encoded by the gene which is transcribed into the respective mRNA during the gene expression process. The genomic sequence is first transcribed into pre-mature mRNA, which comprises optional introns. The pre-mature mRNA is then further processed into mature mRNA in a maturation process. This maturation process comprises the steps of 5'capping, splicing the pre-mature mRNA to excize optional introns and modifications of the 3'-end, such as polyadenylation of the 3'-end of the pre-mature mRNA and optional endo-/

or exonuclease cleavages etc.. In the context of the present invention, a 3'-UTR corresponds to the sequence of a mature mRNA which is located between the the stop codon of the protein coding region, preferably immediately 3' to the stop codon of the protein coding region, and the poly(A) sequence of the mRNA. The term "corresponds to" means that the 3'-UTR sequence may be an RNA sequence, such as in the mRNA sequence used for defining the 3'-UTR sequence, or a DNA sequence which corresponds to such RNA sequence. In the context of the present invention, the term "a 3'-UTR of a gene", is the sequence which corresponds to the 3'-UTR of the mature mRNA derived from this gene, i.e. the mRNA obtained by transcription of the gene and maturation of the pre-mature mRNA. The term "3'-UTR of a gene" encompasses the DNA sequence and the RNA sequence (both sense and antisense strand and both mature and immature) of the 3'-UTR. Preferably, the 3'UTRs have a length of more than 20, 30, 40 or 50 nucleotides.

5'-untranslated region (5'-UTR): Generally, the term "5'-UTR" refers to a part of the artificial nucleic acid molecule, which is located 5' (i.e. "upstream") of an open reading frame and which is not translated into protein. A 5'-UTR is typically understood to be a particular section of messenger RNA (mRNA), which is located 5' of the open reading frame of the mRNA. Typically, the 5'-UTR starts with the transcriptional start site and ends one nucleotide before the start codon of the open reading frame. Preferably, the 5'UTRs have a length of more than 20, 30, 40 or 50 nucleotides. The 5'-UTR may comprise elements for controlling gene expression, also called regulatory elements. Such regulatory elements may be, for example, ribosomal binding sites. The 5'-UTR may be posttranscriptionally modified, for example by addition of a 5'-CAP. A 5'-UTR of the mRNA is not translated into an amino acid sequence. The 5'-UTR sequence is generally encoded by the gene which is transcribed into the respective mRNA during the gene expression process. The genomic sequence is first transcribed into pre-mature mRNA, which comprises optional introns. The pre-mature mRNA is then further processed into mature mRNA in a maturation process. This maturation process comprises the steps of 5'capping, splicing the pre-mature mRNA to excize optional introns and modifications of the 3'-end, such as polyadenylation of the 3'-end of the pre-mature mRNA and optional endo-/ or exonuclease cleavages etc.. In the context of the present invention, a 5'-UTR corresponds to the sequence of a mature mRNA which is located between the start codon and, for example, the 5'-CAP. Preferably, the 5'-UTR corresponds to the sequence which extends from a nucleotide located 3' to the 5'-CAP, more preferably from the nucleotide located immediately 3' to the 5'-CAP, to a nucleotide located 5' to the start

codon of the protein coding region, preferably to the nucleotide located immediately 5' to the start codon of the protein coding region. The nucleotide located immediately 3' to the 5'-CAP of a mature mRNA typically corresponds to the transcriptional start site. The term "corresponds to" means that the 5'-UTR sequence may be an RNA sequence, such as in the mRNA sequence used for defining the 5'-UTR sequence, or a DNA sequence which corresponds to such RNA sequence. In the context of the present invention, the term "a 5'-UTR of a gene" is the sequence which corresponds to the 5'-UTR of the mature mRNA derived from this gene, i.e. the mRNA obtained by transcription of the gene and maturation of the pre-mature mRNA. The term "5'-UTR of a gene" encompasses the DNA sequence and the RNA sequence (both sense and antisense strand and both mature and immature) of the 5'-UTR.

5'Terminal Oligopyrimidine Tract (TOP): The 5'terminal oligopyrimidine tract (TOP) is typically a stretch of pyrimidine nucleotides located in the 5' terminal region of a nucleic acid molecule, such as the 5' terminal region of certain mRNA molecules or the 5' terminal region of a functional entity, e.g. the transcribed region, of certain genes. The sequence starts with a cytidine, which usually corresponds to the transcriptional start site, and is followed by a stretch of usually about 3 to 30 pyrimidine nucleotides. For example, the TOP may comprise 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 or even more nucleotides. The pyrimidine stretch and thus the 5' TOP ends one nucleotide 5' to the first purine nucleotide located downstream of the TOP. Messenger RNA that contains a 5'terminal oligopyrimidine tract is often referred to as TOP mRNA. Accordingly, genes that provide such messenger RNAs are referred to as TOP genes. TOP sequences have, for example, been found in genes and mRNAs encoding peptide elongation factors and ribosomal proteins.

TOP motif: In the context of the present invention, a TOP motif is a nucleic acid sequence which corresponds to a 5'TOP as defined above. Thus, a TOP motif in the context of the present invention is preferably a stretch of pyrimidine nucleotides having a length of 3-30 nucleotides. Preferably, the TOP-motif consists of at least 3 pyrimidine nucleotides, preferably at least 4 pyrimidine nucleotides, preferably at least 5 pyrimidine nucleotides, more preferably at least 6 nucleotides, more preferably at least 7 nucleotides, most preferably at least 8 pyrimidine nucleotides, wherein the stretch of pyrimidine nucleotides preferably starts

at its 5'end with a cytosine nucleotide. In TOP genes and TOP mRNAs, the TOP-motif preferably starts at its 5'end with the transcriptional start site and ends one nucleotide 5' to the first purin residue in said gene or mRNA. A TOP motif in the sense of the present invention is preferably located at the 5'end of a sequence which represents a 5'-UTR or at the 5'end of a sequence which codes for a 5'-UTR. Thus, preferably, a stretch of 3 or more pyrimidine nucleotides is called "TOP motif" in the sense of the present invention if this stretch is located at the 5'end of a respective sequence, such as the artificial nucleic acid molecule, the 5'-UTR element of the artificial nucleic acid molecule, or the nucleic acid sequence which is derived from the 5'-UTR of a TOP gene as described herein. In other words, a stretch of 3 or more pyrimidine nucleotides, which is not located at the 5'-end of a 5'-UTR or a 5'-UTR element but anywhere within a 5'-UTR or a 5'-UTR element, is preferably not referred to as "TOP motif".

TOP gene: TOP genes are typically characterised by the presence of a 5' terminal oligopyrimidine tract. Furthermore, most TOP genes are characterized by a growth-associated translational regulation. However, also TOP genes with a tissue specific translational regulation are known. As defined above, the 5'-UTR of a TOP gene corresponds to the sequence of a 5'-UTR of a mature mRNA derived from a TOP gene, which preferably extends from the nucleotide located 3' to the 5'-CAP to the nucleotide located 5' to the start codon. A 5'-UTR of a TOP gene typically does not comprise any start codons, preferably no upstream AUGs (uAUGs) or upstream open reading frames (uORFs). Therein, upstream AUGs and upstream open reading frames are typically understood to be AUGs and open reading frames that occur 5' of the start codon (AUG) of the open reading frame that should be translated. The 5'-UTRs of TOP genes are generally rather short. The lengths of 5'-UTRs of TOP genes may vary between 20 nucleotides up to 500 nucleotides, and are typically less than about 200 nucleotides, preferably less than about 150 nucleotides, more preferably less than about 100 nucleotides. Exemplary 5'-UTRs of TOP genes in the sense of the present invention are the nucleic acid sequences extending from the nucleotide at position 5 to the nucleotide located immediately 5' to the start codon (e.g. the ATG) in the sequences according to SEQ ID Nos. 1-1363 of the patent application WO2013/143700, whose disclosure is incorporated herewith by reference. In this context a particularly preferred fragment of a 5'-UTR of a TOP gene is a 5'-UTR of a TOP gene lacking the 5'TOP motif. The terms "5'-UTR of a TOP gene" or "5'-TOP UTR" preferably refer to the 5'-UTR of a naturally occurring TOP gene.

In a first aspect, the present invention relates to an artificial nucleic acid molecule comprising

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

b. at least one 3'-untranslated region element (3'-UTR element) and/or at least one 5'-untranslated region element (5'-UTR element), wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element prolongs and/or increases protein production from said artificial nucleic acid molecule and wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element is derived from a stable mRNA.

Preferably, the artificial nucleic acid molecule according to the present invention does not comprise a 3'-UTR (element) and/or a 5'-UTR (element) of ribosomal protein S6, of RPL36AL, of rps16 or of ribosomal protein L9. More preferably, the artificial nucleic acid molecule according to the present invention does not comprise a 3'-UTR (element) and/or a 5'-UTR (element) of ribosomal protein S6, of RPL36AL, of rps16 or of ribosomal protein L9 and the open reading frame of the artificial nucleic acid molecule according to the present invention does not code for a GFP protein. Even more preferably, the artificial nucleic acid molecule according to the present invention does not comprise a 3'-UTR (element) and/or a 5'-UTR (element) of ribosomal protein S6, of RPL36AL, of rps16 or of ribosomal protein L9 and the open reading frame of the artificial nucleic acid molecule according to the present invention does not code for a reporter protein, e.g., selected from the group consisting of globin proteins (particularly beta-globin), luciferase protein, GFP proteins, glucurinodase proteins (particularly beta- glucurinodase) or variants thereof, for example, variants exhibiting at least 70% sequence identity to a globin protein, a luciferase protein, a GFP protein, or a glucurinodase protein.

The term "3'-UTR element" refers to a nucleic acid sequence which comprises or consists of a nucleic acid sequence that is derived from a 3'-UTR or from a variant or a fragment of a 3'-UTR. A "3'-UTR element" preferably refers to a nucleic acid sequence which is comprised by a 3'-UTR of an artificial nucleic acid sequence, such as an artificial mRNA. Accordingly, in the sense of the present invention, preferably, a 3'-UTR element may be comprised by the 3'-UTR of an mRNA, preferably of an artificial mRNA, or a 3'-UTR element may be comprised by the 3'-UTR of the respective transcription template. Preferably, a 3'-UTR element is a

nucleic acid sequence which corresponds to the 3'-UTR of an mRNA, preferably to the 3'-UTR of an artificial mRNA, such as an mRNA obtained by transcription of a genetically engineered vector construct. Preferably, a 3'-UTR element in the sense of the present invention functions as a 3'-UTR or codes for a nucleotide sequence that fulfils the function of a 3'-UTR.

Accordingly, the term "5'-UTR element" refers to a nucleic acid sequence which comprises or consists of a nucleic acid sequence that is derived from a 5'-UTR or from a variant or a fragment of a 5'-UTR. A "5'-UTR element" preferably refers to a nucleic acid sequence which is comprised by a 5'-UTR of an artificial nucleic acid sequence, such as an artificial mRNA. Accordingly, in the sense of the present invention, preferably, a 5'-UTR element may be comprised by the 5'-UTR of an mRNA, preferably of an artificial mRNA, or a 5'-UTR element may be comprised by the 5'-UTR of the respective transcription template. Preferably, a 5'-UTR element is a nucleic acid sequence which corresponds to the 5'-UTR of an mRNA, preferably to the 5'-UTR of an artificial mRNA, such as an mRNA obtained by transcription of a genetically engineered vector construct. Preferably, a 5'-UTR element in the sense of the present invention functions as a 5'-UTR or codes for a nucleotide sequence that fulfils the function of a 5'-UTR.

The 3'-UTR element and/or the 5'-UTR element in the artificial nucleic acid molecule according to the present invention prolongs and/or increases protein production from said artificial nucleic acid molecule. Thus, the artificial nucleic acid molecule according to the present invention may in particular comprise:

- a 3'-UTR element which increases protein production from said artificial nucleic acid molecule,
- a 3'-UTR element which prolongs protein production from said artificial nucleic acid molecule,
- a 3'-UTR element which increases and prolongs protein production from said artificial nucleic acid molecule,
- a 5'-UTR element which increases protein production from said artificial nucleic acid molecule,
- a 5'-UTR element which prolongs protein production from said artificial nucleic acid molecule,

- a 5'-UTR element which increases and prolongs protein production from said artificial nucleic acid molecule,
- a 3'-UTR element which increases protein production from said artificial nucleic acid molecule and a 5'-UTR element which increases protein production from said artificial nucleic acid molecule,
- a 3'-UTR element which increases protein production from said artificial nucleic acid molecule and a 5'-UTR element which prolongs protein production from said artificial nucleic acid molecule,
- a 3'-UTR element which increases protein production from said artificial nucleic acid molecule and a 5'-UTR element which increases and prolongs protein production from said artificial nucleic acid molecule,
- a 3'-UTR element which prolongs protein production from said artificial nucleic acid molecule and a 5'-UTR element which increases protein production from said artificial nucleic acid molecule,
- a 3'-UTR element which prolongs protein production from said artificial nucleic acid molecule and a 5'-UTR element which prolongs protein production from said artificial nucleic acid molecule,
- a 3'-UTR element which prolongs protein production from said artificial nucleic acid molecule and a 5'-UTR element which increases and prolongs protein production from said artificial nucleic acid molecule,
- a 3'-UTR element which increases and prolongs protein production from said artificial nucleic acid molecule and a 5'-UTR element which increases protein production from said artificial nucleic acid molecule,
- a 3'-UTR element which increases and prolongs protein production from said artificial nucleic acid molecule and a 5'-UTR element which prolongs protein production from said artificial nucleic acid molecule, or
- a 3'-UTR element which increases and prolongs protein production from said artificial nucleic acid molecule and a 5'-UTR element which increases and prolongs protein production from said artificial nucleic acid molecule.

Preferably, the artificial nucleic acid molecule according to the present invention comprises a 3'-UTR element which prolongs protein production from said artificial nucleic acid

molecule and/or a 5'-UTR element which increases protein production from said artificial nucleic acid molecule.

Preferably, the artificial nucleic acid molecule according to the present invention comprises at least one 3'-UTR element and at least one 5'-UTR element, i.e. at least one 3'-UTR element which prolongs and/or increases protein production from said artificial nucleic acid molecule and which is derived from a stable mRNA and at least one 5'-UTR element which prolongs and/or increases protein production from said artificial nucleic acid molecule and which is derived from a stable mRNA.

"Prolonging and/or increasing protein production from said artificial nucleic acid molecule" in general refers to the amount of protein produced from the artificial nucleic acid molecule according to the present invention with the respective 3'-UTR element and/or the 5'-UTR element in comparison to the amount of protein produced from a respective reference nucleic acid lacking a 3'-UTR and/or a 5'-UTR or comprising a reference 3'-UTR and/or a reference 5'-UTR, such as a 3'-UTR and/or a 5'-UTR naturally occurring in combination with the ORF.

In particular, the at least one 3'-UTR element and/or the 5'-UTR element of the artificial nucleic acid molecule according to the present invention prolongs protein production from the artificial nucleic acid molecule according to the present invention, e.g. from an mRNA according to the present invention, compared to a respective nucleic acid lacking a 3'-UTR and/or 5'-UTR or comprising a reference 3'-UTR and/or 5'-UTR, such as a 3'- and/or 5'-UTR naturally occurring in combination with the ORF.

In particular, the at least one 3'-UTR element and/or 5'-UTR element of the artificial nucleic acid molecule according to the present invention increases protein production, in particular the protein expression and/or total protein production, from the artificial nucleic acid molecule according to the present invention, e.g. from an mRNA according to the present invention, compared to a respective nucleic acid lacking a 3'- and/or 5'-UTR or comprising a reference 3'- and/or 5'-UTR, such as a 3'- and/or 5'-UTR naturally occurring in combination with the ORF.

Preferably, the at least one 3'-UTR element and/or the at least one 5'-UTR element of the artificial nucleic acid molecule according to the present invention do not negatively influence translational efficiency of a nucleic acid compared to the translational efficiency of a respective nucleic acid lacking a 3'-UTR and/or a 5'-UTR or comprising a reference 3'-UTR and/or a reference 5'-UTR, such as a 3'-UTR and/or a 5'-UTR naturally occurring in combination with the ORF. Even more preferably, the translation efficiency is enhanced by the 3'-UTR and/or a 5'-UTR in comparison to the translation efficiency of the protein encoded by the respective ORF in its natural context.

The term "respective nucleic acid molecule" or "reference nucleic acid molecule" as used herein means that – apart from the different 3'-UTRs and/or 5'-UTRs – the reference nucleic acid molecule is comparable, preferably identical, to the inventive artificial nucleic acid molecule comprising the 3'-UTR element and/or the 5'-UTR element.

In order to assess the protein production in vivo or in vitro as defined herein (i.e. in vitro referring to ("living") cells and/or tissue, including tissue of a living subject; cells include in particular cell lines, primary cells, cells in tissue or subjects, preferred are mammalian cells, e.g. human cells and mouse cells and particularly preferred are the human cell lines HeLa, and U-937 and the mouse cell lines NIH3T3, JAWSII and L929, furthermore primary cells are particularly preferred, in particular preferred embodiments human dermal fibroblasts (HDF)) by the inventive artificial nucleic acid molecule, the expression of the encoded protein is determined following injection/transfection of the inventive artificial nucleic acid molecule into target cells/tissue and compared to the protein expression induced by the reference nucleic acid. Quantitative methods for determining protein expression are known in the art (e.g. Western-Blot, FACS, ELISA, mass spectrometry). Particularly useful in this context is the determination of the expression of reporter proteins like luciferase, Green fluorescent protein (GFP), or secreted alkaline phosphatase (SEAP). Thus, an artificial nucleic acid according to the invention or a reference nucleic acid is introduced into the target tissue or cell, e.g. via transfection or injection, preferably in a mammalian expression system, such as in mammalian cells, e.g. in HeLa or HDF cells. Several hours or several days (e.g. 6, 12, 24, 48 or 72 hours) post initiation of expression or post introduction of the nucleic acid molecule, a target cell sample is collected and measured via FACS and/or lysed. Afterwards the lysates can be used to detect the expressed protein (and thus determine the efficiency of protein

expression) using several methods, e.g. Western-Blot, FACS, ELISA, mass spectrometry or by fluorescence or luminescence measurement.

Therefore, if the protein expression from an artificial nucleic acid molecule according to the invention is compared to the protein expression from a reference nucleic acid molecule at a specific point in time (e.g. 6, 12, 24, 48 or 72 hours post initiation of expression or post introduction of the nucleic acid molecule), both nucleic acid molecules are introduced separately into target tissue/cells, a sample from the tissue/cells is collected after a specific point in time, protein lysates are prepared according to the particular protocol adjusted to the particular detection method (e.g. Western Blot, ELISA, fluorescence or luminescence measurement, etc. as known in the art) and the protein is detected by the chosen detection method. As an alternative to the measurement of expressed protein amounts in cell lysates - or, in addition to the measurement of protein amounts in cell lysates prior to lysis of the collected cells or using an aliquot in parallel - protein amounts may also be determined by using FACS analysis.

The term "prolonging protein production" from an artificial nucleic acid molecule such as an artificial mRNA preferably means that the protein production from the artificial nucleic acid molecule such as the artificial mRNA is prolonged compared to the protein production from a reference nucleic acid molecule such as a reference mRNA, e.g. comprising a reference 3'- and/or 5'-UTR or lacking a 3'- and/or 5'-UTR, preferably in a mammalian expression system, such as in HeLa or HDF cells. Thus, protein produced from the artificial nucleic acid molecule such as the artificial mRNA is observable for a longer period of time than what may be seen for a protein produced from a reference nucleic acid molecule. In other words, the amount of protein produced from the artificial nucleic acid molecule such as the artificial mRNA measured at a later point in time, e.g. 48 hours or 72 hours after transfection, is larger than the amount of protein produced from a reference nucleic acid molecule such as a reference mRNA at a corresponding later point in time. Such a "later point in time" may be, for example, any time beyond 24 hours post initiation of expression, such as post transfection of the nucleic acid molecule, e.g. 36, 48, 60, 72, 96 hours post initiation of expression, i.e. after transfection. Moreover, for the same nucleic acid, the amount of protein produced at a later point in time may be normalized to the amount produced an earlier (reference) point in time, for example

the amount of protein at a later point in time may be expressed as percentage of the amount of protein at 24 h after transfection.

Preferably, this effect of prolonging protein production is determined by (i) measuring protein amounts, e.g. obtained by expression of an encoded reporter protein such as luciferase, preferably in a mammalian expression system such as in HeLa or HDF cells, over time, (ii) determining the amount of protein observed at a "reference" point in time t_1, for example t_1 = 24h after transfection, and setting this protein amount to 100%, (iii) determining the amount of protein observed at one or more later points in time t_2, t_3, etc., for example t_2 = 48h and t_3 = 72h after transfection, and calculating the relative amount of protein observed at a later point in time as a percentage of the protein amount at a point in time t_1. For example, a protein which is expressed at t_1 in an amount of "80", at t_2 in an amount of "20", and at t_3 in an amount of "10", the relative amount of protein at t_2 would be 25%, and at t_3 12,5%. These relative amounts at a later point in time may then be compared in a step (iv) to relative protein amounts for the corresponding points in time for a nucleic acid molecule lacking a 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively. By comparing the relative protein amount produced from the artificial nucleic acid molecule according to the present invention to the relative protein amount produced from the reference nucleic acid molecule, i.e. the nucleic acid molecule lacking a 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively, a factor may be determined by which the protein production from the artificial nucleic acid molecule according to the present invention is prolonged compared to the protein production from the reference nucleic acid molecule.

Preferably, the at least one 3'- and/or 5'-UTR element in the artificial nucleic acid molecule according to the invention prolongs protein production from said artificial nucleic acid molecule at least 1.2 fold, preferably at least 1.5 fold, more preferably at least 2 fold, even more preferably at least 2.5 fold, compared to the protein production from a reference nucleic acid molecule lacking 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively. In other words, the (relative) amount of protein produced from in the artificial nucleic acid molecule according to the invention at a certain later point in time as described above is increased by a factor of at least 1.2, preferably at least 1.5, more preferably at least 2, even more preferably at least 2.5, compared to the (relative) amount of protein

produced from a reference nucleic acid molecule, which is e.g. lacking a 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively, for the same later point in time.

Alternatively, the effect of prolonging protein production may also be determined by (i) measuring protein amounts, e.g. obtained by expression of an encoded reporter protein such as luciferase, preferably in a mammalian expression system such as in HeLa or HDF cells, over time, (ii) determining the point in time at which the protein amount undercuts the amount of protein observed, e.g., at 1, 2, 3, 4, 5, or 6 hours post initiation of expression, e.g. 1, 2, 3, 4, 5, or 6 hours post transfection of the artificial nucleic acid molecule, and (iii) comparing the point in time at which the protein amount undercuts the protein amount observed at 1, 2, 3, 4, 5, or 6 hours post initiation of expression to said point in time determined for a nucleic acid molecule lacking a 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively.

For example, the protein production from the artificial nucleic acid molecule such as the artificial mRNA - in an amount which is at least the amount observed in the initial phase of expression, such as 1, 2, 3, 4, 5, or 6 hours post initiation of expression, such as post transfection of the nucleic acid molecule - is prolonged by at least about 5 hours, preferably by at least about 10 hours, more preferably by at least about 24 hours compared to the protein production from a reference nucleic acid molecule, such as a reference mRNA, in a mammalian expression system, such as in mammalian cells, e.g. in HeLa or HDF cells. Thus, the artificial nucleic acid molecule according to the present invention preferably allows for prolonged protein production in an amount which is at least the amount observed in the initial phase of expression, such as 1, 2, 3, 4, 5, or 6 hours post initiation of expression, such as post transfection, by at least about 5 hours, preferably by at least about 10 hours, more preferably by at least about 24 hours compared to a reference nucleic acid molecule lacking a 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively.

In preferred embodiments, the period of protein production from the artificial nucleic acid molecule according to the present invention is extended at least 1.2 fold, preferably at least 1.5 fold, more preferably at least 2 fold, even more preferably at least 2.5 fold, compared to

the protein production from a reference nucleic acid molecule lacking a 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively.

Preferably, this prolonging effect on protein production is achieved, while the total amount of protein produced from the artificial nucleic acid molecule according to the present invention, e.g. within a time span of 48 or 72 hours, corresponds at least to the amount of protein produced from a reference nucleic acid molecule lacking a 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively, such as a 3'-UTR and/or 5'-UTR naturally occurring with the ORF of the artificial nucleic acid molecule. Thus, the present invention provides an artificial nucleic acid molecule which allows for prolonged protein production in a mammalian expression system, such as in mammalian cells, e.g. in HeLa or HDF cells, as specified above, wherein the total amount of protein produced from said artificial nucleic acid molecule, e.g. within a time span of 48 or 72 hours, is at least the total amount of protein produced, e.g. within said time span, from a reference nucleic acid molecule lacking a 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively, such as a 3'- and/or 5'-UTR naturally occurring with the ORF of the artificial nucleic acid molecule.

Moreover, the term "prolonged protein expression" also includes "stabilized protein expression", whereby "stabilized protein expression" preferably means that there is more uniform protein production from the artificial nucleic acid molecule according to the present invention over a predetermined period of time, such as over 24 hours, more preferably over 48 hours, even more preferably over 72 hours, when compared to a reference nucleic acid molecule, for example, an mRNA comprising a reference 3'- and/or 5'-UTR, respectively, or lacking a 3'- and/or 5'-UTR, respectively.

Accordingly, the level of protein production, e.g. in a mammalian system, from the artificial nucleic acid molecule comprising a 3'- and/or 5'-UTR element according to the present invention, e.g. from an mRNA according to the present invention, preferably does not drop to the extent observed for a reference nucleic acid molecule, such as a reference mRNA as described above. To assess to which extent the protein production from a specific nucleic acid molecule drops, for example, the amount of a protein (encoded by the respective ORF) observed 24 hours after initiation of expression, e.g. 24 hours post transfection of the artificial

nucleic acid molecule according to the present invention into a cell, such as a mammalian cell, may be compared to the amount of protein observed 48 hours after initiation of expression, e.g. 48 hours post transfection. Thus, the ratio of the amount of protein encoded by the ORF of the artificial nucleic acid molecule according to the present invention, such as the amount of a reporter protein, e.g., luciferase, observed at a later point in time, e.g. 48 hours, post initiation of expression, e.g. post transfection, to the amount of protein observed at an earlier point in time, e.g. 24 hours, post initiation of expression, e.g. post transfection, is preferably higher than the corresponding ratio (including the same points in time) for a reference nucleic acid molecule comprising a reference 3'- and/or 5'-UTR, respectively, or lacking a 3'- and/or 5'-UTR, respectively.

Preferably, the ratio of the amount of protein encoded by the ORF of the artificial nucleic acid molecule according to the present invention, such as the amount of a reporter protein, e.g., luciferase, observed at a later point in time, e.g. 48 hours, post initiation of expression, e.g. post transfection, to the amount of protein observed at an earlier point in time, e.g. 24 hours, post initiation of expression, e.g. post transfection, is preferably at least 0.2, more preferably at least about 0.3, even more preferably at least about 0.4, even more preferably at least about 0.5, and particularly preferably at least about 0.7. For a respective reference nucleic acid molecule, e.g. an mRNA comprising a reference 3'- and/or 5'-UTR, respectively, or lacking a 3'- and/or 5'-UTR, respectively, said ratio may be, for example between about 0.05 and about 0.35.

Thus, the present invention provides an artificial nucleic acid molecule comprising an ORF and a 3'- and/or 5'-UTR element as described above, wherein the ratio of the protein amount, e.g. the amount of luciferase, observed 48 hours after initiation of expression to the protein amount observed 24 hours after initiation of expression, preferably in a mammalian expression system, such as in mammalian cells, e.g. in HDF cells or in HeLa cells, is preferably at least 0.2, more preferably at least about 0.3, more preferably at least about 0.4, even more preferably at least about 0.5, even more preferably at least about 0.6, and particularly preferably at least about 0.7. Thereby, preferably the total amount of protein produced from said artificial nucleic acid molecule, e.g. within a time span of 48 hours, corresponds at least to the total amount of protein produced, e.g. within said time span, from a reference nucleic acid molecule lacking a 3'- and/or 5'-UTR, respectively, or comprising a

reference 3'- and/or 5'-UTR, respectively, such as a 3'-UTR and/or 5'-UTR naturally occurring with the ORF of the artificial nucleic acid molecule.

Preferably, the present invention provides an artificial nucleic acid molecule comprising an ORF and a 3'-UTR element and/or a 5'-UTR element as described above, wherein the ratio of the protein amount, e.g. the amount of luciferase, observed 72 hours after initiation of expression to the protein amount observed 24 hours after initiation of expression, preferably in a mammalian expression system, such as in mammalian cells, e.g. in HeLa cells or HDF cells, is preferably above about 0.05, more preferably above about 0.1, more preferably above about 0.2, even more preferably above about 0.3, wherein preferably the total amount of protein produced from said artificial nucleic acid molecule, e.g. within a time span of 72 hours, is at least the total amount of protein produced, e.g. within said time span, from a reference nucleic acid molecule lacking a 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively, such as a 3'- and/or 5'-UTR naturally occurring with the ORF of the artificial nucleic acid molecule.

"Increased protein expression" or "enhanced protein expression" in the context of the present invention preferably means an increased/enhanced protein expression at one point in time after initiation of expression or an increased/enhanced total amount of expressed protein compared to the expression induced by a reference nucleic acid molecule. Thus, the protein level observed at a certain point in time after initiation of expression, e.g. after transfection, of the artificial nucleic acid molecule according to the present invention, e.g. after transfection of an mRNA according to the present invention, for example, 6, 12, 24, 48 or 72 hours post transfection, is preferably higher than the protein level observed at the same point in time after initiation of expression, e.g. after transfection, of a reference nucleic acid molecule, such as a reference mRNA comprising a reference 3'- and/or 5'-UTR, respectively, or lacking a 3'- and/or 5'-UTR, respectively. In a preferred embodiment, the maximum amount of protein (as determined e.g. by protein activity or mass) expressed from the artificial nucleic acid molecule is increased with respect to the protein amount expressed from a reference nucleic acid comprising a reference 3'- and/or 5'-UTR, respectively, or lacking a 3'- and/or 5'-UTR, respectively. Peak expression levels are preferably reached within 48 hours, more preferably within 24 hours and even more preferably within 12 hours after, for instance, transfection.

Preferably, the term "increased total protein production" or "enhanced total protein production" from an artificial nucleic acid molecule according to the invention refers to an increased/enhanced protein production over a time span, in which protein is produced from an artificial nucleic acid molecule, e.g. 48 hours or 72 hours, preferably in a mammalian expression system, such as in mammalian cells, e.g. in HeLa or HDF cells in comparison to a reference nucleic acid molecule lacking a 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively. According to a preferred embodiment, the cumulative amount of protein expressed over time is increased when using the artificial nucleic acid molecule according to the invention.

The total amount of protein for a specific time period may be determined by (i) collecting tissue or cells at several points in time after introduction of the artificial nucleic acid molecule (e.g. 6, 12, 24, 48 and 72 hours post initiation of expression or post introduction of the nucleic acid molecule), and the protein amount per point in time can be determined as explained above. In order to calculate the cumulative protein amount, a mathematical method of determining the total amount of protein can be used, e.g. the area under the curve (AUC) can be determined according to the following formula:

$$\text{AUC} = \int_a^b f(x)\, d(x)$$

In order to calculate the area under the curve for total amount of protein, the integral of the equation of the expression curve from each end point (a and b) is calculated.

Thus, "total protein production" preferably refers to the area under the curve (AUC) representing protein production over time.

Preferably, the at least one 3'- or 5'-UTR element according to the present invention increases protein production from said artificial nucleic acid molecule at least 1.5 fold, preferably at least 2 fold, more preferably at least 2.5 fold, compared to the protein production from a reference nucleic acid molecule lacking a 3'- and/or 5'-UTR, respectively. In other words, the total amount of protein produced from in the artificial nucleic acid molecule according to the

invention at a certain point in time, e.g. 48 hours or 72 hours post initiation of expression, e.g. post transfection, is increased by a factor of at least 1.5, preferably at least 2, more preferably at least 2.5, compared to the (relative) amount of protein produced from a reference nucleic acid molecule, which is e.g. lacking a 3'- and/or 5'-UTR, respectively, or comprising a reference 3'- and/or 5'-UTR, respectively, for the corresponding later point in time.

The mRNA and/or protein production prolonging effect and efficiency and/or the protein production increasing effect and efficiency of the variants, fragments and/or variant fragments of the 3'-UTR and/or the 5'-UTR as well as the mRNA and/or protein production prolonging effect and efficiency and/or the protein production increasing effect and efficiency of the at least one 3'-UTR element and/or the at least one 5'-UTR element of the artificial nucleic acid molecule according to the present invention may be determined by any method suitable for this purpose known to skilled person.

For example, artificial mRNA molecules may be generated comprising a coding sequence/open reading frame (ORF) for a reporter protein, such as luciferase, and a 3'-UTR element according to the present invention, i.e. which prolongs and/or increases protein production from said artificial mRNA molecule. In addition such an inventive mRNA molecule may further comprise a a 5'-UTR element according to the present invention, i.e. which prolongs and/or increases protein production from said artificial mRNA molecule, no 5'-UTR element or a 5'-UTR element which is not according to the present invention, e.g. a reference 5'-UTR. Accordingly, artificial mRNA molecules may be generated comprising a coding sequence/open reading frame (ORF) for a reporter protein, such as luciferase, and a 5'-UTR element according to the present invention, i.e. which prolongs and/or increases protein production from said artificial mRNA molecule. In addition such an inventive mRNA molecule may further comprise a a 3'-UTR element according to the present invention, i.e. which prolongs and/or increases protein production from said artificial mRNA molecule, no 3'-UTR element or a 3'-UTR element which is not according to the present invention, e.g. a reference 3'-UTR.

According to the present invention mRNAs may be generated, for example, by *in vitro* transcription of respective vectors such as plasmid vectors, e.g. comprising a T7 promoter and a sequence encoding the respective mRNA sequences. The generated mRNA molecules may

be transfected into cells by any transfection method suitable for transfecting mRNA, for example they may be lipofected into mammalian cells, such as HeLa cells or HDF cells, and samples may be analyzed certain points in time after transfection, for example, 6 hours, 24 hours, 48 hours, and 72 hours post transfection. Said samples may be analyzed for mRNA quantities and/or protein quantities by methods well known to the skilled person. For example, the quantities of reporter mRNA present in the cells at the sample points in time may be determined by quantitative PCR methods. The quantities of reporter protein encoded by the respective mRNAs may be determined, e.g., by Western Blot, ELISA assays, FACS analysisor reporter assays such as luciferase assays depending on the reporter protein used. The effect of stabilizing protein expression and/or prolonging protein expression may be, for example, analyzed by determining the ratio of the protein level observed 48 hours post transfection and the protein level observed 24 hours post transfection. The closer said value is to 1, the more stable the protein expression is within this time period. Such measurements may of course also be performed at 72 or more hours and the ratio of the protein level observed 72 hours post transfection and the protein level observed 24 hours post transfection may be determined to determine stability of protein expression.

Moreover, the at least one 3'-UTR element and/or the at least one 5'-UTR element in the artificial nucleic acid molecule according to the present invention, is derived from a stable mRNA. Thereby, "derived" from a stable mRNA means that the at least one 3'-UTR element and/or the at least one 5'-UTR element shares at least 50%, preferably at least 60%, preferably at least 70%, more preferably at least 75%, more preferably at least 80%, more preferably at least 85%, even more preferably at least 90%, even more preferably at least 95%, and particularly preferably at least 98% sequence identity with a 3'-UTR element and/or a 5'-UTR element of a stable mRNA. Preferably, the stable mRNA is a naturally occurring mRNA and, thus, a 3'-UTR element and/or a 5'-UTR element of a stable mRNA refers to a 3'-UTR and/or a 5'-UTR, or fragments or variants thereof, of naturally occurring mRNA. Moreover, a 3'-UTR element and/or a 5'-UTR element derived from a stable mRNA preferably also refers to a 3'-UTR element and/or a 5'-UTR element, which is modified in comparison to a naturally occurring 3'-UTR element and/or 5'-UTR element, e.g. in order to increase RNA stability even further and/or to prolong and/or increase protein production. It goes without saying that such modifications are preferred, which do not impair RNA stability, e.g. in comparison to a naturally occurring (non-modifed) 3'-UTR element and/or 5'-UTR element. In particular, the

term mRNA as used herein refers to an mRNA molecule, however, it may also refer to an mRNA species as defined herein.

Preferably, the stability of mRNA, i.e. mRNA decay and/or half-life, is assessed under standard conditions, for example standard conditions (standard medium, incubation, etc.) for a certain cell line used.

The term "stable mRNA" as used herein refers in general to an mRNA having a slow mRNA decay. Thus, a "stable mRNA" has typically a long half-life. The half-life of an mRNA is the the time required for degrading 50% of the *in vivo or in vitro* existing mRNA molecules. Accordingly, stability of mRNA is usually assessed *in vivo or in vitro*. Thereby, *in vitro* refers in particular to ("living") cells and/or tissue, including tissue of a living subject. Cells include in particular cell lines, primary cells, cells in tissue or subjects. In specific embodiments cell types allowing cell culture may be suitable for the present invention. Particularly preferred are mammalian cells, e.g. human cells and mouse cells. In particularly preferred embodiments the human cell lines HeLa, and U-937 and the mouse cell lines NIH3T3, JAWSII and L929 are used. Furthermore primary cells are particularly preferred, in particular preferred embodiments human dermal fibroblasts (HDF) may be used. Alternatively also a tissue of a subject may be used.

Preferably, the half-life of a "stable mRNA" is at least 5 h, at least 6 h, at least 7 h, at least 8 h, at least 9 h, at least 10 h, at least 11 h, at least 12 h, at least 13 h, at least 14 h, and/or at least 15 h. The half-life of an mRNA of interest may be determined by different methods known to the person skilled in the art. Typically, the half-life of an mRNA of interest is determined by determining the decay constant, whereby usually an ideal *in vivo* (or *in vitro* as defined above) situation is assumed, in which transcription of the mRNA of interest can be "turned off" completely (or at least to an undetectable level). In such an ideal situation it is usually assumed that mRNA decay follows first-order kinetics. Accordingly, the decay of an mRNA may usually be described by the following equation:

$$A(t) = A_0 * e^{-\lambda t}$$

with A_0 being the amount (or concentration) of the mRNA of interest at time 0, i.e. before the decay starts, A(t) being the amount (or concentration) of the mRNA of interest at a time t during decay and λ being the decay constant. Thus, if the amount (or concentration) of the mRNA of interest at time 0 (A_0) and the amount (or concentration) of the mRNA of interest at a certain time t during the decay process (A(t) and t) are known, the decay constant λ may be calculated. Based on the decay constant λ, the half-life $t_{1/2}$ can be calculated by the following equation:

$$t_{1/2} = \ln 2 / \lambda.$$

since per definition A(t)/A0 = 1/2 at $t_{1/2}$. Thus, to assess the half-life of an mRNA of interest, usually the amount or concentration of the mRNA is determined during the RNA decay process *in vivo* (or *in vitro* as defined above).

To determine the amount or concentration of mRNA during the RNA decay process *in vivo* (or *in vitro* as defined above), various methods may be used, which are known to the skilled person. Non-limiting examples of such methods include general inhibition of transcription, e.g. with a transcription inhibitor such as actinomycin D, use of inducible promotors to specifically promote transient transcription, e.g. c-fos serum-inducible promotor system and Tet-off regulatory promotor system, and kinetic labelling techniques, e.g. pulse labelling, for example by 4-Thiouridine (4sU), 5-Ethynyluridine (EU) or 5'-Bromo-Uridine (BrU). Further details and preferred embodiments regarding how to determine the amount or concentration of mRNA during the RNA decay are outlined below, in the context of a method for identifying a 3'-UTR element and/or the at least one 5'-UTR element, which is derived from a stable mRNA, according to the present invention. The respective description and preferred embodiments of how to determine the amount or concentration of mRNA during the RNA decay apply here as well.

Preferably, a "stable mRNA" in the sense of the present invention has a slower mRNA decay compared to average mRNA, preferably assessed *in vivo* (or *in vitro* as defined above). For example, "average mRNA decay" may be assessed by investigating mRNA decay of a plurality of mRNA species, preferably 100, at least 300, at least 500, at least 1000, at least 2000, at least 3000, at least 4000, at least 5000, at least 6000, at least 7000, at least 8000, at least

9000, at least 10000, at least 11000, at least 12000, at least 13000, at least 14000, at least 15000, at least 16000, at least 17000, at least 18000, at least 19000, at least 20000, at least 21000, at least 22000, at least 23000, at least 24000, at least 25000, at least 26000, at least 27000, at least 28000, at least 29000, at least 30000 mRNA species. It is particularly preferred that the whole transcriptome is assessed, or as many mRNA species of the transcriptome as possible. This may be achieved, for example, by using a micro array providing whole transcript coverage.

An "mRNA species", as used herein, corresponds to a genomic transcription unit, i.e. usually to a gene. Thus, within one "mRNA species" different transcripts may occur, for example, due to mRNA processing. For example, an mRNA species may be represented by a spot on a microarray. Accordingly, a microarray provides an advantageous tool to determine the amount of a plurality of mRNA species, e.g. at a certain point in time during mRNA decay. However, also other techniques known to the skilled person, e.g. RNA-seq, quantitative PCR etc. may be used.

In the present invention it is particularly preferred that a stable mRNA is characterized by an mRNA decay wherein the ratio of the amount of said mRNA at a second point in time to the amount of said mRNA at a first point in time is at least 0.5 (50%), at least 0.6 (60%), at least 0.7 (70%), at least 0.75 (75%), at least 0.8 (80%), at least 0.85 (85%), at least 0.9 (90%), or at least 0.95 (95%). Thereby, the second point in time is later in the decay process than the first point in time.

Preferably, the first point in time is selected such that only mRNA undergoing a decay process is considered, i.e. emerging mRNA – e.g. in ongoing transcription – is avoided. For example, if kinetic labelling techniques, e.g. pulse labelling, are used, the first point in time is preferably selected such that the incorporation of the label into mRNA is completed, i.e. no ongoing incorporation of the label into mRNA occurs. Thus, if kinetic labelling is used, the first point in time may be at least 10 min, at least 20 min, at least 30 min, at least 40 min, at least 50 min, at least 60 min, at least 70 min, at least 80 min, or at least 90 min after the end of the experimental labelling procedure, e.g. after the end of the incubation of cells with the label.

For example, the first point in time may be preferably from 0 to 6 h after the stop of transcription (e.g. by a transcriptional inhibitor), stop of promotor induction in case of inducible promotors or after stop of pulse or label supply, e.g. after end of labelling. More preferably, the first point in time may be 30 min to 5 h, even more preferably 1 h to 4 h and particularly preferably about 3 h after the stop of transcription (e.g. by a transcriptional inhibitor), stop of promotor induction in case of inducible promotors or after stop of pulse or label supply, e.g. after end of labelling.

Preferably, the second point in time is selected as late as possible during the mRNA decay process. However, if a plurality of mRNA species is considered, the second point in time is preferably selected such that still a considerable amount of the plurality of mRNA species, preferably at least 10% of the mRNA species, is present in a detectable amount, i.e. in an amount higher than 0. Preferably, the second point in time is at least 5 h, at least 6 h, at least 7 h, at least 8 h, at least 9 h, at least 10 h, at least 11 h, at least 12 h, at least 13 h, at least 14 h, or at least 15 h after the end of transcription or the end of the experimental labelling procedure.

Thus, the time span between the first point in time and the second point in time is preferably as large as possible within the above described limits. Therefore, the time span between the first point in time and the second point in time is preferably at least 4 h, at least 5 h, at least 6 h, at least 7 h, at least 8 h, at least 9 h, at least 10 h, at least 11 h, or at least 12 h.

Moreover, it is preferred that the at least one 3'-UTR element and/or the at least one 5'-UTR element in the artificial nucleic acid molecule according to the present invention, which is derived from a stable mRNA, is identified by a method for identifying a 3'-UTR element and/or a 5'-UTR element, which is derived from a stable mRNA, according to the present invention as described herein. It is particularly preferred that the at least one 3'-UTR element and/or the at least one 5'-UTR element in the artificial nucleic acid molecule according to the present invention, is identified by a method for identifying a 3'-UTR element and/or a 5'-UTR element, which prolongs and/or increases protein production from an artificial nucleic acid molecule and which is derived from a stable mRNA, according to the present invention as described herein.

Preferably, the at least one 3'-UTR element and/or the at least one 5'-UTR element in the artificial nucleic acid molecule according to the present invention comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a eukaryotic protein coding gene, preferably from the 3'-UTR and/or the 5'-UTR of a vertebrate protein coding gene, more preferably from the 3'-UTR and/or the 5'-UTR of a mammalian protein coding gene, e.g. from mouse and human protein coding genes, even more preferably from the 3'-UTR and/or the 5'-UTR of a primate or rodent protein coding gene, in particular the 3'-UTR and/or the 5'-UTR of a human or murine protein coding gene.

In general, it is understood that the at least one 3'-UTR element in the artificial nucleic acid molecule according to the present invention comprises or consists of a nucleic acid sequence which is preferably derived from a naturally (in nature) occurring 3'-UTR, whereas the at least one 5'-UTR element in the artificial nucleic acid molecule according to the present invention comprises or consists of a nucleic acid sequence which is preferably derived from a naturally (in nature) occurring 5'-UTR.

Preferably, the at least one open reading frame is heterologous to the at least one 3'-UTR element and/or to the at least one 5'-UTR element. The term "heterologous" in this context means that two sequence elements comprised by the artificial nucleic acid molecule, such as the open reading frame and the 3'-UTR element and/or the open reading frame and the 5'-UTR element, do not occur naturally (in nature) in this combination. They are typically recombinant. Preferably, the 3'-UTR element and/or the 5'-UTR element are/is derived from a different gene than the open reading frame. For example, the ORF may be derived from a different gene than the 3'-UTR element and/or to the at least one 5'-UTR element, e.g. encoding a different protein or the same protein but of a different species etc. I.e. the open reading frame is derived from a gene which is distinct from the gene from which the 3'-UTR element and/or to the at least one 5'-UTR element is derived. In a preferred embodiment, the ORF does not encode a human or plant (e.g., Arabidopsis) ribosomal protein, preferably does not encode human ribosomal protein S6 (RPS6), human ribosomal protein L36a-like (RPL36AL) or Arabidopsis ribosomal protein S16 (RPS16). In a further preferred embodiment, the open reading frame (ORF) does not encode ribosomal protein S6 (RPS6), ribosomal protein L36a-like (RPL36AL) or ribosomal protein S16 (RPS16).

In specific embodiments it is preferred that the open reading frame does not code for a reporter protein, e.g., selected from the group consisting of globin proteins (particularly beta-globin), luciferase protein, GFP proteins or variants thereof, for example, variants exhibiting at least 70% sequence identity to a globin protein, a luciferase protein, or a GFP protein. Thereby, it is particularly preferred that the open reading frame does not code for a GFP protein. It is also particularly preferred that the open reading frame (ORF) does not encode a reporter gene or is not derived from a reporter gene, wherein the reporter gene is preferably not selected from group consisting of globin proteins (particularly beta-globin), luciferase protein, beta-glucuronidase (GUS) and GFP proteins or variants thereof, preferably not selected from EGFP, or variants of any of the above genes, typically exhibiting at least 70% sequence identity to any of these reporter genes, preferably a globin protein, a luciferase protein, or a GFP protein.

Even more preferably, the 3'-UTR element and/or the 5'-UTR element is heterologous to any other element comprised in the artificial nucleic acid as defined herein. For example, if the artificial nucleic acid according to the invention comprises a 3'-UTR element from a given gene, it does preferably not comprise any other nucleic acid sequence, in particular no functional nucleic acid sequence (e.g. coding or regulatory sequence element) from the same gene, including its regulatory sequences at the 5' and 3' terminus of the gene's ORF. Accordingly, for example, if the artificial nucleic acid according to the invention comprises a 5'-UTR element from a given gene, it does preferably not comprise any other nucleic acid sequence, in particular no functional nucleic acid sequence (e.g. coding or regulatory sequence element) from the same gene, including its regulatory sequences at the 5' and 3' terminus of the gene's ORF.

Moreover, it is preferred that the artificial nucleic acid according to the present invention comprises at least one open reading frame, at least one 3'-UTR (element) and at least one 5'-UTR (element), whereby either the at least one 3'-UTR (element) is a 3'-UTR element according to the present invention and/or the at least one 5'-UTR (element) is a 5'-UTR element according to the present invention. In such a preferred artificial nucleic acid according to the present invention, which comprises at least one open reading frame, at least one 3'-UTR (element) and at least one 5'-UTR (element), it is particularly preferred that each of the at least one open reading frame, the at least one 3'-UTR (element) and the at least one

5'-UTR (element) are heterologous, i.e. neither the at least one 3'-UTR (element) and the at least one 5'-UTR (element) nor the the open reading frame and the 3'-UTR (element) or the 5'-UTR (element), respectively, are occurring naturally (in nature) in this combination. This means that the artificial nucleic acid molecule comprises an ORF, a 3'-UTR (element) and a 5'-UTR (element), all of which are heterologous to each other, e.g. they are recombinant as each of them is derived from different genes (and their 5' and 3' UTR's). In another preferred embodiment, the 3'-UTR (element) is not derived from a 3'-UTR (element) of a viral gene or is not of viral origin.

Preferably, the artificial nucleic acid molecule according to the present invention:

(i) comprises at least one 3'-UTR element and at least one 5'-UTR element, wherein preferably (each of) the at least one 3'-UTR element and at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR, or the 5'-UTR respectively, of a human or murine protein coding gene;

(ii) the at least one 3'-UTR element, the at least one 5'-UTR element and the at least one open reading frame of the artificial nucleic acid molecule according to the present invention are all heterologous to each other;

(iii) the at least one 3' UTR element is derived from a gene selected from the group consisting of: housekeeping genes, genes coding for a membrane protein, genes involved in cellular metabolism, genes involved in transcription, translation and replication processes, genes involved in protein modification and genes involved in cell division; and

(iv) the 3'UTR is not derived from a gene coding for a ribosomal protein or from the Fig4 gene.

Housekeeping genes are typically constitutive genes that are required for the maintenance of basic cellular function and that are typically expressed in all cells of an organism under normal and patho-physiological conditions. Although some housekeeping genes are expressed at relatively constant levels in most non-pathological situations, other housekeeping genes may vary depending on experimental conditions. Typically, housekeeping genes are expressed in at least 25 copies per cell and sometimes number in the thousands. Preferred examples of housekeeping genes in the context of the present invention are shown below in Table 10.

Acc	Definition	Symbol[a]	Length[b]	Abundance[c]
NM_001402	Eukaryotic translation elongation factor 1 alpha 1	EEF1A1	387	20011
NM_001614	Actin, gamma 1	ACTG1	718	16084
NM_002046	Glyceraldehyde-3-phosphate dehydrogenase	GAPD	201	15931
NM_001101	Actin, beta	ACTB	593	15733
NM_000967	Ribosomal protein L3	RPL3	74	10924
NM_006082	Tubulin, alpha, ubiquitous	K-ALPHA-1	174	10416
NM_001428	Enolase 1, (alpha)	ENO1	357	9816
NM_006098	Guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1	GNB2L1	45	8910
NM_002032	Ferritin, heavy polypeptide 1	FTH1	138	8861
NM_002654	Pyruvate kinase, muscle	PKM2	643	7413
NM_004048	Beta-2-microglobulin	B2M	568	7142
NM_006597	Heat shock 70kDa protein 8	HSPA8	258	6066
NM_000034	Aldolase A, fructose-bisphosphate	ALDOA	252	5703
NM_021009	Ubiquitin C	UBC	67	5579
NM_006013	Ribosomal protein L10	RPL10	1,503	5572
NM_012423	Ribosomal protein L13a	RPL13A	509	5552
NM_007355	Heat shock 90kDa protein 1, beta	HSPCB	309	5436
NM_004046	ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit, isoform 1, cardiac muscle	ATP5A1	164	5434
NM_000516	GNAS complex locus	GNAS	362	4677
NM_001743	Calmodulin 2 (phosphorylase kinase, delta)	CALM2	611	4306
NM_005566	Lactate dehydrogenase A	LDHA	566	4186
NM_000973	Ribosomal protein L8	RPL8	92	4042
NM_002948	Ribosomal protein L15	RPL15	1,368	3861
NM_000977	Ribosomal protein L13	RPL13	424	3774
NM_002952	Ribosomal protein S2	RPS2	86	3758
NM_005507	Cofilin 1 (non-muscle)	CFL1	508	3616
NM_004039	Annexin A2	ANXA2	294	3560
NM_021019	Myosin, light polypeptide 6, alkali, smooth muscle and non-muscle	MYL6	209	3512
NM_002300	Lactate dehydrogenase B	LDHB	230	3501
NM_003217	Testis enhanced gene transcript (BAX inhibitor 1)	TEGT	1,847	3438
NM_002568	Poly(A) binding protein, cytoplasmic 1	PABPC1	445	3241
NM_001015	Ribosomal protein S11	RPS11	85	3220
NM_003973	Ribosomal protein L14	RPL14	156	3198
NM_000969	Ribosomal protein L5	RPL5	78	3167
NM_007104	Ribosomal protein L10a	RPL10A	32	3079
NM_001642	Amyloid beta (A4) precursor-like protein 2	APLP2	1,364	3002
NM_001418	Eukaryotic translation initiation factor 4 gamma, 2	EIF4G2	791	2913
NM_002635	Solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 3	SLC25A3	197	2900
NM_001009	Ribosomal protein S5	RPS5	58	2897
NM_000291	Phosphoglycerate kinase 1	PGK1	1,016	2858
NM_001728	Basigin (OK blood group)	BSG	769	2827
NM_001658	ADP-ribosylation factor 1	ARF1	1,194	2772
NM_001003	Ribosomal protein, large, P1	RPLP1	39	2770
NM_018955	Ubiquitin B	UBB	144	2732
NM_005998	Chaperonin containing TCP1, subunit 3 (gamma)	CCT3	255	2709
NM_001967	Eukaryotic translation initiation factor 4A, isoform 2	EIF4A2	626	2693
NM_001469	Thyroid autoantigen 70kDa (Ku antigen)	G22P1	259	2682
NM_000918	Procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), beta polypeptide (protein disulfide isomerase; thyroid hormone binding protein p55)	P4HB	868	2659
NM_002574	Peroxiredoxin 1	PRDX1	323	2604
NM_001020	Ribosomal protein S16	RPS16	78	2573

NM_007363	Non-POU domain containing, octamer-binding	NONO	1,119	2557
NM_001022	Ribosomal protein S19	RPS19	63	2533
NM_001675	Activating transcription factor 4 (tax-responsive enhancer element B67)	ATF4	85	2479
NM_005617	Ribosomal protein S14	RPS14	78	2465
NM_001664	Ras homolog gene family, member A	RHOA	1,045	2426
NM_005801	Putative translation initiation factor	SUI1	836	2425
NM_000981	Ribosomal protein L19	RPL19	80	2381
NM_000979	Ribosomal protein L18	RPL18	49	2362
NM_001026	Ribosomal protein S24	RPS24	77	2355
NM_000975	Ribosomal protein L11	RPL11	53	2314
NM_002117	Major histocompatibility complex, class I, C	HLA-C	434	2278
NM_004068	Adaptor-related protein complex 2, mu 1 subunit	AP2M1	494	2230
NM_006429	Chaperonin containing TCP1, subunit 7 (eta)	CCT7	164	2216
NM_022551	Ribosomal protein S18	RPS18	5,538	2208
NM_001013	Ribosomal protein S9	RPS9	73	2113
NM_005594	Nascent-polypeptide-associated complex alpha polypeptide	NACA	133	2075
NM_001028	Ribosomal protein S25	RPS25	74	2066
NM_032378	Eukaryotic translation elongation factor 1 delta (guanine nucleotide exchange protein)	EEF1D	76	2051
NM_000999	Ribosomal protein L38	RPL38	50	2007
NM_000994	Ribosomal protein L32	RPL32	64	2003
NM_007008	Reticulon 4	RTN4	973	1969
NM_001909	Cathepsin D (lysosomal aspartyl protease)	CTSD	834	1940
NM_006325	RAN, member RAS oncogene family	RAN	892	1906
NM_003406	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide	YWHAZ	2,013	1892
NM_006888	Calmodulin 1 (phosphorylase kinase, delta)	CALM1	3,067	1880
NM_004339	Pituitary tumor-transforming 1 interacting protein	PTTG1IP	1,985	1837
NM_005022	Profilin 1	PFN1	289	1787
NM_001961	Eukaryotic translation elongation factor 2	EEF2	504	1754
NM_003091	Small nuclear ribonucleoprotein polypeptides B and B1	SNRPB	295	1735
NM_006826	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, theta polypeptide	YWHAQ	1,310	1726
NM_002140	Heterogeneous nuclear ribonucleoprotein K	HNRPK	1,227	1725
NM_001064	Transketolase (Wernicke-Korsakoff syndrome)	TKT	167	1721
NM_021103	Thymosin, beta 10	TMSB10	317	1714
NM_004309	Rho GDP dissociation inhibitor (GDI) alpha	ARHGDIA	1,206	1702
NM_002473	Myosin, heavy polypeptide 9, non-muscle	MYH9	1,392	1692
NM_000884	IMP (inosine monophosphate) dehydrogenase 2	IMPDH2	63	1690
NM_001004	Ribosomal protein, large P2	RPLP2	59	1688
NM_001746	Calnexin	CANX	2,302	1677
NM_002819	Polypyrimidine tract binding protein 1	PTBP1	1,561	1663
NM_000988	Ribosomal protein L27	RPL27	59	1660
NM_004404	Neural precursor cell expressed, developmentally down-regulated 5	NEDD5	2,090	1654
NM_005347	Heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa)	HSPA5	1,757	1651
NM_000175	Glucose phosphate isomerase	GPI	296	1635
NM_001207	Basic transcription factor 3	BTF3	300	1632
NM_003186	Transgelin	TAGLN	405	1612
NM_003334	Ubiquitin-activating enzyme E1 (A1S9T and BN75 temperature sensitivity complementing)	UBE1	199	1590
NM_001018	Ribosomal protein S15	RPS15	32	1574
NM_003404	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta polypeptide	YWHAB	2,088	1523
NM_003753	Eukaryotic translation initiation factor 3, subunit 7 zeta, 66/67kDa	EIF3S7	152	1509
NM_005762	Tripartite motif-containing 28	TRIM28	193	1507
NM_005381	Nucleolin	NCL	284	1501
NM_000995	Ribosomal protein L34	RPL34	450	1495
NM_002823	Prothymosin, alpha (gene sequence 28)	PTMA	720	1462
NM_002415	Macrophage migration inhibitory factor (glycosylation-inhibiting factor)	MIF	117	1459

NM_002128	High-mobility group box 1	HMGB1	1,527	1457
NM_006908	Ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)	RAC1	1,536	1437
NM_002070	Guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide 2	GNAI2	512	1435
NM_001997	Finkel-Biskis-Reilly murine sarcoma virus (FBR-MuSV) ubiquitously expressed (fox derived); ribosomal protein S30	FAU	68	1428
NM_014390	Staphylococcal nuclease domain containing 1	SND1	556	1422
NM_014764	DAZ associated protein 2	DAZAP2	1,322	1419
NM_005917	Malate dehydrogenase 1, NAD (soluble)	MDH1	208	1396
NM_001494	GDP dissociation inhibitor 2	GDI2	785	1395
NM_014225	Protein phosphatase 2 (formerly 2A), regulatory subunit A (PR 65), alpha isoform	PPP2R1A	472	1391
NM_001660	ADP-ribosylation factor 4	ARF4	858	1382
NM_001823	Creatine kinase, brain	CKB	206	1381
NM_003379	Villin 2 (ezrin)	VIL2	1,272	1380
NM_000182	Hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A hydratase (trifunctional protein), alpha subunit	HADHA	647	1379
NM_003746	Dynein, cytoplasmic, light polypeptide 1	DNCL1	281	1375
NM_007103	NADH dehydrogenase (ubiquinone) flavoprotein 1, 51kDa	NDUFV1	103	1352
NM_000992	Ribosomal protein L29	RPL29	164	1349
NM_007209	Ribosomal protein L35	RPL35	35	1345
NM_006623	Phosphoglycerate dehydrogenase	PHGDH	231	1340
NM_002796	Proteasome (prosome, macropain) subunit, beta type, 4	PSMB4	108	1340
NM_002808	Proteasome (prosome, macropain) 26S subunit, non-ATPase, 2	PSMD2	231	1326
NM_000454	Superoxide dismutase 1, soluble (amyotrophic lateral sclerosis 1 (adult))	SOD1	346	1323
NM_003915	RNA binding motif protein 12	RBM12	216	1323
NM_004924	Actinin, alpha 4	ACTN4	1,099	1316
NM_006086	Tubulin, beta 3	TUBB3	296	1314
NM_001016	Ribosomal protein S12	RPS12	56	1304
NM_003365	Ubiquinol-cytochrome c reductase core protein I	UQCRC1	126	1303
NM_003016	Splicing factor, arginine/serine-rich 2	SFRS2	1,059	1301
NM_007273	Repressor of estrogen receptor activity	REA	332	1281
NM_014610	Glucosidase, alpha; neutral AB	GANAB	1,652	1280
NM_001749	Calpain, small subunit 1	CAPNS1	514	1270
NM_005080	X-box binding protein 1	XBP1	1,003	1269
NM_005216	Dolichyl-diphosphooligosaccharide-protein glycosyltransferase	DDOST	616	1268
NM_004640	HLA-B associated transcript 1	BAT1	237	1262
NM_021983	Major histocompatibility complex, class II, DR beta 4	HLA-DRB1	313	1251
NM_013234	Eukaryotic translation initiation factor 3 subunit k	eIF3k	84	1251
NM_004515	Interleukin enhancer binding factor 2, 45kDa	ILF2	384	1249
NM_000997	Ribosomal protein L37	RPL37	50	1244
NM_000801	FK506 binding protein 1A, 12kDa	FKBP1A	1,149	1243
NM_000985	Ribosomal protein L17	RPL17	58	1243
NM_001014	Ribosomal protein S10	RPS10	57	1232
NM_001069	Tubulin, beta 2	TUBB2	194	1230
NM_004960	Fusion (involved in t(12;16) in malignant liposarcoma)	FUS	166	1197
NM_005165	Aldolase C, fructose-bisphosphate	ALDOC	432	1195
NM_004930	Capping protein (actin filament) muscle Z-line, beta	CAPZB	259	1193
NM_000239	Lysozyme (renal amyloidosis)	LYZ	1,016	1190
NM_007263	Coatomer protein complex, subunit epsilon	COPE	263	1179
NM_001861	Cytochrome c oxidase subunit IV isoform 1	COX4I1	129	1178
NM_003757	Eukaryotic translation initiation factor 3, subunit 2 beta, 36kDa	EIF3S2	408	1169
NM_005745	B-cell receptor-associated protein 31	BCAP31	438	1166
NM_002743	Protein kinase C substrate 80K-H	PRKCSH	337	1158
NM_004161	RAB1A, member RAS oncogene family	RAB1A	638	1115
NM_002080	Glutamic-oxaloacetic transaminase 2, mitochondrial (aspartate aminotransferase 2)	GOT2	1,039	1114
NM_005731	Actin related protein 2/3 complex, subunit 2, 34kDa	ARPC2	448	1113

NM_006445	PRP8 pre-mRNA processing factor 8 homolog (yeast)	PRPF8	173	1110
NM_001867	Cytochrome c oxidase subunit VIIc	COX7C	168	1106
NM_002375	Microtubule-associated protein 4	MAP4	1,164	1102
NM_003145	Signal sequence receptor, beta (translocon-associated protein beta)	SSR2	492	1099
NM_001788	CDC10 cell division cycle 10 homolog (S. cerevisiae)	CDC10	1,015	1094
NM_006513	Seryl-tRNA synthetase	SARS	323	1085
NM_003754	Eukaryotic translation initiation factor 3, subunit 5 epsilon, 47kDa	EIF3S5	152	1081
NM_005112	WD repeat domain 1	WDR1	845	1080
NM_004893	H2A histone family, member Y	H2AFY	635	1072
NM_004494	Hepatoma-derived growth factor (high-mobility group protein 1-like)	HDGF	1,339	1069
NM_001436	Fibrillarin	FBL	111	1069
NM_003752	Eukaryotic translation initiation factor 3, subunit 8, 110kDa	EIF3S8	201	1060
NM_003321	Tu translation elongation factor, mitochondrial	TUFM	207	1038
NM_001119	Adducin 1 (alpha)	ADD1	1,569	1037
NM_005273	Guanine nucleotide binding protein (G protein), beta polypeptide 2	GNB2	386	1030
NM_006755	Transaldolase 1	TALDO1	256	1026
NM_023009	MARCKS-like 1	MARCKSL 1	774	1014
NM_002799	Proteasome (prosome, macropain) subunit, beta type, 7	PSMB7	162	1012
NM_002539	Ornithine decarboxylase 1	ODC1	343	1009
NM_006801	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 1	KDELR1	742	1007
NM_014944	Calsyntenin 1	CLSTN1	1,481	1003
NM_007262	Parkinson disease (autosomal recessive, early onset) 7	PARK7	253	1002

Table 10. List of abundant housekeeping genes (cf. WO 2007/068265 A1, Table 1).

The above table was obtained from WO 2007/068265 A1, Table 1 and is based on the list of the accession numbers as provided by Eisenberg, E. and E. Y. Levanon (2003): Human housekeeping genes are compact; Trends Genet. 19(7): 362-365. The accession numbers were used as input for a PERL (Programmed Extraction Report Language) computer program that extracts EST data from the Unigene database. The Unigene database was downloaded as a text file from the NCBI website. The length of the 3'UTR was derived by computationally extracting the 3'UTR (Bakheet, T., Frevel, M., Williams, BR, and K.S. Khabar, 2001. ARED: Human AU-rich element-containing mRNA database reveals unexpectedly diverse functional repertoire of encoded proteins. Nucleic Acids Research. 29:246-254). <a> is a commonly used abbreviation of the gene product; <b> is the length of the 3 'UTR; <c> is the number of ESTs.

Preferred housekeeping genes include LDHA, NONO, PGK1 and PPIH.

A gene coding for a membrane protein typically refers to such a gene, which codes for a protein that interacts with biological membranes. In most genomes, about 20 – 30% of all genes encode membrane proteins. Common types of proteins include – in addition to membrane proteins – soluble globular proteins, fibrous proteins and disordered proteins.

Thus, genes coding for a membrane protein are typically different from genes coding for soluble globular proteins, fibrous proteins or disordered proteins. Membrane proteins include membrane receptors, transport proteins, membrane enzymes and cell adhesion molecules.

A gene involved in cellular metabolism typically refers to such a gene, which codes for a protein involved in cellular metabolism, i.e. in the set of life-sustaining chemical transformations within the cells of living organisms. These are typically enzyme-catalyzed reactions, which allow organisms to grow and reproduce, maintain their structures, and respond to their environments. Accordingly, preferred genes involved in cellular metabolism are such genes, which code for enzymes catalyzing a reaction, which allow organisms to grow and reproduce, maintain their structures, and respond to their environments. Other examples for a gene involved in cellular metabolism include genes coding for proteins having structural or mechanical function, such as those that form the cytoskeleton. Other proteins involved in cellular metabolism include proteins involved in cell signalling, immune responses, cell adhesion, active transport across membranes and in the cell cycle. Metabolism is usually divided into two categories: catabolism, the breaking down of organic matter by way of cellular respiration, and anabolism, the building up of components of cells such as proteins and nucleic acids.

A gene involved in transcription, translation and replication processes typically refers to such a gene, which codes for a protein involved in transcription, translation and replication processes. In particular, the term "replication", as used in this context, refers preferably to replication of nucleic acids, e.g. DNA replication. Preferred genes involved in transcription, translation and replication processes are genes coding for an enzyme involved in transcription, translation and/or (DNA) replication processes. Other preferred examples include genes coding for a transcription factor or for a translation factor. Ribosomal genes are other preferred examples of genes involved in transcription, translation and replication processes.

A gene involved in protein modification typically refers to such a gene, which codes for a protein involved in protein modification. Preferred examples of such genes code for enzymes involved in protein modification, in particular in post-translational modification processes. Preferred examples of enzymes involved in post-translational modification include (i)

enzymes involved in the addition of hydrophobic groups, in particular for membrane localization, e.g. enzymes involed in myristoylation, palmitoylation, isoprenylation or prenylation, farnesylation, geranylation or in glypiation; (ii) enzymes involved in the addition of cofactors for enhanced enzymatic activity, e.g. enzymes involved in lipoylation, in the attachment of a flavin moiety, in the attachment of heme C, in phosphopantetheinylation or in retinylidene Schiff base formation; (iii) enzymes involved in the modification of translation factors, e.g. in diphtamide formation, in ethanolamine phosphoglycerol attachment or in hypusine formation; and (vi) enzymes involved in the addition of smaller chemical groups, e.g. acylation, such as acetylation and formylation, alkylation such as methylation, amide bond formation, such as amidation at C-terminus and amino acid addition (e.g. arginylation, polyglutamylation and polyglycylation), butyrylation, gamma-carboxylation, glycosylation, malonylation, hydroxylation, iodination, nucleotide addition, oxidation, phosphate ester or phosphoramidate formation such as phosphorylation and adenylation, propionylation, pyroglutamate formation, S-glutathionylation, S-nitrosylation, succinylation and sulfation.

A gene involved in cell division processes typically refers to such a gene, which codes for a protein involved in cell division. Cell division is the process by which a parent cell divides into two or more daughter cells. Cell division usually occurs as part of a larger cell cycle. In eukaryotes, there are two distinct types of cell division: a vegetative division, whereby each daughter cell is genetically identical to the parent cell (mitosis), and a reductive cell division, whereby the number of chromosomes in the daughter cells is reduced by half, to produce haploid gametes (meiosis). Accordingly, preferred gene involved in cell division processes code for a protein involved in mitosis and/or meiosis.

Fig4 is an abbreviation for Factor-Induced Gene. The Fig4 gene codes for polyphosphoinositide phosphatase also known as phosphatidylinositol 3,5-bisphosphate 5-phosphatase or SAC domain-containing protein 3 (Sac3).

Preferably, the artificial nucleic acid molecule according to the present invention:

(i) comprises at least one 3′-UTR element and at least one 5′-UTR element, wherein preferably (each of) the at least one 3′-UTR element and at least one 5′-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3′-UTR, or the 5′-UTR respectively, of a human or murine protein coding gene;

(ii) the at least one 3'-UTR element, the at least one 5'-UTR element and the at least one open reading frame are all heterologous to each other;

(iii) the at least one 5'-UTR element is derived from a gene selected from the group consisting of: housekeeping genes, genes coding for a membrane protein, genes involved in cellular metabolism, genes involved in transcription, translation and replication processes, genes involved in protein modification and genes involved in cell division;

(iv) the 5'-UTR is preferably not a 5' TOP UTR; and

(v) the 3'-UTR is preferably not derived from a gene coding for a ribosomal protein or for albumin or from the Fig4 gene.

More preferably, such an artificial nucleic acid molecule according to the present invention:

(i) comprises at least one 3'-UTR element and at least one 5'-UTR element, wherein preferably (each of) the at least one 3'-UTR element and at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR, or the 5'-UTR respectively, of a human or murine protein coding gene;

(ii) the at least one 3'-UTR element, the at least one 5'-UTR element and the at least one open reading frame are all heterologous to each other;

(iii) the at least one 3' UTR element is derived from a human or a murine gene selected from the group consisting of: housekeeping genes, genes coding for a membrane protein, genes involved in cellular metabolism, genes involved in transcription, translation and replication processes, genes involved in protein modification and genes involved in cell division;

(iv) the 3'UTR is not derived from a gene coding for a ribosomal protein or for albumin or from the Fig4 gene;

(v) the at least one 5'-UTR element is derived from a human or a murine gene selected from the group consisting of: housekeeping genes, genes coding for a membrane protein, genes involved in cellular metabolism, genes involved in transcription, translation and replication processes, genes involved in protein modification and genes involved in cell division; and

(vi) the 5'-UTR is not a 5' TOP UTR.

Thereby, it is preferred in the artificial nucleic acid molecule according to the present invention that the 3'-UTR and the 5'-UTR are derived from a human or a murine housekeeping gene. It is also preferred that the 3'-UTR and the 5'-UTR are derived from a human or a murine gene coding for a membrane protein. It is also preferred that the 3'-UTR and the 5'-UTR are derived from a human or a murine gene involved in cellular metabolism. It is also preferred that the 3'-UTR and the 5'-UTR are derived from a human or a murine gene involved in transcription, translation and replication processes. It is also preferred that the 3'-UTR and the 5'-UTR are derived from a human or a murine gene involved in protein modification. It is also preferred that the 3'-UTR and the 5'-UTR are derived from a human or a murine gene involved in cell division. In this context, the skilled person is aware that if (i) the 3'-UTR and the 5'-UTR are derived from genes belonging to the same gene class and (ii) the at least one 3'-UTR and the at least one 5'-UTR are heterologous to each other, that the the 3'-UTR and the 5'-UTR are not derived from the same gene, but from distinct genes belonging to the same gene class. Accordingly, it is preferred that the at least one 3'-UTR and the at least one 5'-UTR are derived from distinct genes belonging to the same gene class.

As used herein the term "gene class" refers to the classification of genes. Examples of gene classes include (i) housekeeping genes, (ii) genes coding for a membrane protein, (iii) genes involved in cellular metabolism, (iv) genes involved in transcription, translation and replication processes, (v) genes involved in protein modification and (vi) genes involved in cell division. In other words, "housekeeping genes" is one gene class, whereas "genes involved in transcription" is another gene class, "genes involved in cellular metabolism" is a further gene class, etc..

It is also preferred in the artificial nucleic acid molecule according to the present invention as described herein, that the 3'-UTR and the 5'-UTR are derived from a human or a murine gene selected from the group consisting of: genes coding for a membrane protein, genes involved in cellular metabolism, genes involved in transcription, translation and replication processes, genes involved in protein modification and genes involved in cell division, wherein the 3'-UTR and the 5'-UTR are selected from distinct gene classes.

Preferably, the at least one 3′-UTR element and/or to the at least one 5′-UTR element is functionally linked to the ORF. This means preferably that the 3′-UTR element and/or to the at least one 5′-UTR element is associated with the ORF such that it may exert a function, such as an enhancing or stabilizing function on the expression of the encoded peptide or protein or a stabilizing function on the artificial nucleic acid molecule. Preferably, the ORF and the 3′-UTR element are associated in 5′→3′ direction and/or the 5′-UTR element and the ORF are associated in 5′→3′ direction. Thus, preferably, the artificial nucleic acid molecule comprises in general the structure 5′-[5′-UTR element]-(optional)-linker-ORF-(optional)-linker-[3′-UTR element]-3′, wherein the artificial nucleic acid molecule may comprise only a 5′-UTR element and no 3′-UTR element, only a 3′-UTR element and no 5′-UTR element, or both, a 3′-UTR element and a 5′-UTR element. Furthermore, the linker may be present or absent. For example, the linker may be one or more nucleotides, such as a stretch of 1-50 or 1-20 nucleotides, e.g., comprising or consisting of one or more restriction enzyme recognition sites (restriction sites).

Preferably, the at least one 3′-UTR element and/or the at least one 5′-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3′-UTR and/or the 5′-UTR of a transcript of a gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), CNTN1 (contactin 1), LTA4H, SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, SUPT3H, TMEM14A, GRAMD1C, C11orf80, C9orf46, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, NT5DC1, RAB7A, AGA, TPK1, MBNL3, HADHB, MCCC2, CAT, ANAPC4, PCCB, PHKB, ABCB7, PGCP, GPD2, TMEM38B, NFU1, OMA1, LOC128322/NUTF2, NUBPL, LANCL1, HHLA3, PIR, ACAA2, CTBS, GSTM4, ALG8, Atp5e, Gstm5, Uqcr11, Ifi27l2a, Anapc13, Atp5l, Tmsb10, Nenf, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufs5, 1810027O10Rik, Atp5o,

Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Hexa, Ndufb11, Map1lc3a, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Sepp1, Gaa, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1.

In a particularly preferred embodiment the at least one 3'-UTR element and/or the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a transcript of a gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, SUPT3H, TMEM14A, GRAMD1C, C11orf80, C9orf46, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, ITGA6, HERC5, NT5DC1, RAB7A, AGA, TPK1, MBNL3, HADHB, MCCC2, CAT, ANAPC4, PCCB, PHKB, ABCB7, PGCP, GPD2, TMEM38B, NFU1, OMA1, LOC128322/NUTF2, NUBPL, LANCL1, HHLA3, PIR, ACAA2, CTBS, GSTM4, ALG8, Atp5e, Gstm5, Uqcr11, Ifi27l2a, Anapc13, Atp5l, Nenf, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Ndufs5, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Hexa, Ndufb11, Map1lc3a,

Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Ybx1, Sepp1, Gaa, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1.

More preferably, the at least one 3′-UTR element and/or the at least one 5′-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3′-UTR and/or the 5′-UTR of a transcript of a gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), CNTN1 (contactin 1) and NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4).

Preferably, the at least one 3′-UTR element and/or the at least one 5′-UTR element of the artificial nucleic acid molecule according to the present invention comprises or consists of a "functional fragment", a "functional variant" or a "functional fragment of a variant" of the 3′-UTR and/or the 5′-UTR of a transcript of a gene.

Preferably, the at least one 3′-UTR element and/or the at least one 5′-UTR element comprises a nucleic acid sequence which is derived from the 3′-UTR and/or the 5′-UTR of a transcript of a human gene selected from the group consisting of GNAS (guanine nucleotide binding

protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, SUPT3H, TMEM14A, GRAMD1C, C11orf80, C9orf46, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, NT5DC1, RAB7A, AGA, TPK1, MBNL3, HADHB, MCCC2, CAT, ANAPC4, PCCB, PHKB, ABCB7, PGCP, GPD2, TMEM38B, NFU1, OMA1, LOC128322/NUTF2, NUBPL, LANCL1, HHLA3, PIR, ACAA2, CTBS, GSTM4, ALG8, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1.

Alternatively or additionally, it is also preferred that the at least one 3'-UTR element and/or the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a transcript of a murine gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Atp5e, Gstm5, Uqcr11, Ifi27l2a, Anapc13, Atp5l, Tmsb10, Nenf, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufs5, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Hexa, Ndufb11, Map1lc3a, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g,

2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Ybx1, Sepp1, and Gaa.

Preferably, the at least one 3'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, TMEM14A, GRAMD1C, C11orf80, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, HADHB, ANAPC4, PCCB, ABCB7, PGCP, NFU1, OMA1, HHLA3, ACAA2, GSTM4, ALG8, Atp5e, Gstm5, Uqcr11, Ifi27l2a, Cbr2, Atp5I, Tmsb10, Nenf, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Gnas, Snrpd2, Mgst3, Aldh2, Ss4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufa4, Ndufs5, Gstm1, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Ndufb11, Map1lc3a, Morn2, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Ybx1, Sepp1, Gaa, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3,

BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1. More preferably, the at least one 3'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

In a particularly preferred embodiment, the at least one 3'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, TMEM14A, GRAMD1C, C11orf80, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, HADHB, ANAPC4, PCCB, ABCB7, PGCP, NFU1, OMA1, HHLA3, ACAA2, GSTM4, ALG8, Atp5e, Gstm5, Uqcr11, Ifi27l2a, Cbr2, Atp5l, Tmsb10, Nenf, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Gnas, Snrpd2, Mgst3, Aldh2, Ss4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufa4, Ndufs5, Gstm1, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Ndufb11, Map1lc3a, Morn2, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Ybx1, Sepp1, Gaa, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2,

IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1. More preferably, the at least one 3'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

More preferably, the at least one 3'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a human gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, TMEM14A, GRAMD1C, C11orf80, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, HADHB, ANAPC4, PCCB, ABCB7, PGCP, NFU1, OMA1, HHLA3, ACAA2, GSTM4, ALG8, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1; preferably, the at least one 3'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a human gene

selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

Accordingly, it is also more preferable that the at least one 3'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a murine gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1), Ndufa1, Atp5e, Gstm5, Uqcr11, Ifi27l2a, Cbr2, Atp5l, Tmsb10, Nenf, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Gnas, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufa4, Ndufs5, Gstm1, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Ndufb11, Map1lc3a, Morn2, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Ybx1, Sepp1, and Gaa; preferably, the at least one 3'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a murine gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

Preferably, the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 5'-UTR of a transcript of a gene selected from the group consisting of MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha

subcomplex 4), LTA4H, DECR1, PIGK, TBC1D19, BRP44L, ACADSB, SUPT3H, TMEM14A, C9orf46, ANXA4, IFI6, C2orf34, ALDH6A1, CCDC53, CCDC104, CASP1, NDUFB6, BCKDHB, BBS2, HERC5, FAM175A, NT5DC1, RAB7A, AGA, TPK1, MBNL3, MCCC2, CAT, ANAPC4, PHKB, ABCB7, GPD2, TMEM38B, NFU1, LOC128322/NUTF2, NUBPL, LANCL1, PIR, CTBS, GSTM4, Ndufa1, Atp5e, Gstm5, Cbr2, Anapc13, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Ndufs6, Sec61b, Snrpd2, Mgst3, Prdx4; Pgcp; Myeov2; Ndufa4; Ndufs5; Gstm1; Atp5o; Tspo; Taldo1; Bloc1s1; and Hexa. More preferably, the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 5'-UTR of a transcript of MP68 (RIKEN cDNA 2010107E04 gene) or NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4).

In a particularly preferred embodiment, the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 5'-UTR of a transcript of a gene selected from the group consisting of MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, DECR1, PIGK, TBC1D19, BRP44L, ACADSB, SUPT3H, TMEM14A, C9orf46, ANXA4, IFI6, C2orf34, ALDH6A1, CCDC53, CASP1, NDUFB6, BCKDHB, BBS2, HERC5, FAM175A, NT5DC1, RAB7A, AGA, TPK1, MBNL3, MCCC2, CAT, ANAPC4, PHKB, ABCB7, GPD2, TMEM38B, NFU1, LOC128322/NUTF2, NUBPL, LANCL1, PIR, CTBS, GSTM4, Ndufa1, Atp5e, Gstm5, Cbr2, Anapc13, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Ndufs6, Sec61b, Snrpd2, Mgst3, Prdx4; Pgcp; Ndufa4; Ndufs5; Atp5o; Tspo; Taldo1; Bloc1s1; and Hexa. More preferably, the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 5'-UTR of a transcript of MP68 (RIKEN cDNA 2010107E04 gene) or NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4).

More preferably, the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 5'-UTR of a transcript of a human gene selected from the group consisting of MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, DECR1, PIGK, TBC1D19, BRP44L, ACADSB, SUPT3H, TMEM14A, C9orf46, ANXA4, IFI6, C2orf34, ALDH6A1, CCDC53, CCDC104, CASP1, NDUFB6, BCKDHB, BBS2, HERC5, FAM175A, NT5DC1, RAB7A, AGA, TPK1, MBNL3, MCCC2, CAT, ANAPC4, PHKB, ABCB7, GPD2, TMEM38B, NFU1, LOC128322/NUTF2, NUBPL, LANCL1, PIR, CTBS, and GSTM4; preferably, the at least one 5'-UTR element

comprises or consists of a nucleic acid sequence which is derived from the 5'-UTR of a human transcript of MP68 (RIKEN cDNA 2010107E04 gene) or NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4).

Accordingly, it is also more preferable that the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 5'-UTR of a transcript of a murine gene selected from the group consisting of MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ndufa1, Atp5e, Gstm5, Cbr2, Anapc13, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Ndufs6, Sec61b, Snrpd2, Mgst3, Prdx4; Pgcp; Myeov2; Ndufa4; Ndufs5; Gstm1; Atp5o; Tspo; Taldo1; Bloc1s1; and Hexa; preferably, the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 5'-UTR of a murine transcript of MP68 (RIKEN cDNA 2010107E04 gene) or NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4).

The phrase "nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a of a transcript of a gene" preferably refers to a nucleic acid sequence which is based on the 3'-UTR sequence and/or on the 5'-UTR sequence of a transcript of a gene or a fragment or part thereof, preferably a naturally occurring gene or a fragment or part thereof. This phrase includes sequences corresponding to the entire 3'-UTR sequence and/or the entire 5'-UTR sequence, i.e. the full length 3'-UTR and/or 5'-UTR sequence of a transcript of a gene, and sequences corresponding to a fragment of the 3'-UTR sequence and/or the 5'-UTR sequence of a transcript of a gene. Preferably, a fragment of a 3'-UTR and/or a 5'-UTR of a transcript of a gene consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in the full-length 3'-UTR and/or 5'-UTR of a transcript of a gene, which represents at least 5%, 10%, 20%, preferably at least 30%, more preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80%, and most preferably at least 90% of the full-length 3'-UTR and/or 5'-UTR of a transcript of a gene. Such a fragment, in the sense of the present invention, is preferably a functional fragment as described herein. Preferably, the fragment retains a regulatory function for the translation of the ORF linked to the 3'-UTR and/or 5'-UTR or fragment thereof.

The terms "variant of the 3'-UTR and/or variant of the 5'-UTR of a of a transcript of a gene" and "variant thereof" in the context of a 3'-UTR and/or a 5'-UTR of a transcript of a gene refers to a variant of the 3'-UTR and/or 5'-UTR of a transcript of a naturally occurring gene, preferably to a variant of the 3'-UTR and/or 5'-UTR of a transcript of a vertebrate gene, more preferably to a variant of the 3'-UTR and/or 5'-UTR of a transcript of a mammalian gene, even more preferably to a variant of the 3'-UTR and/or 5'-UTR of a transcript of a primate gene, in particular a human gene as described above. Such variant may be a modified 3'-UTR and/or 5'-UTR of a transcript of a gene. For example, a variant 3'-UTR and/or a variant of the 5'-UTR may exhibit one or more nucleotide deletions, insertions, additions and/or substitutions compared to the naturally occurring 3'-UTR and/or 5'-UTR from which the variant is derived. Preferably, a variant of a 3'-UTR and/or variant of the 5'-UTR of a of a transcript of a gene is at least 40%, preferably at least 50%, more preferably at least 60%, more preferably at least 70%, even more preferably at least 80%, even more preferably at least 90%, most preferably at least 95% identical to the naturally occurring 3'-UTR and/or 5'-UTR the variant is derived from. Preferably, the variant is a functional variant as described herein.

The phrase "a nucleic acid sequence which is derived from a variant of the 3'-UTR and/or from a variant of the 5'-UTR of a of a transcript of a gene" preferably refers to a nucleic acid sequence which is based on a variant of the 3'-UTR sequence and/or the 5'-UTR of a transcript of a gene or on a fragment or part thereof as described above. This phrase includes sequences corresponding to the entire sequence of the variant of the 3'-UTR and/or the 5'-UTR of a transcript of a gene, i.e. the full length variant 3'-UTR sequence and/or the full length variant 5'-UTR sequence of a transcript of a gene, and sequences corresponding to a fragment of the variant 3'-UTR sequence and/or a fragment of the variant 5'-UTR sequence of a transcript of a gene. Preferably, a fragment of a variant of the 3'-UTR and/or the 5'-UTR of a transcript of a gene consists of a continuous stretch of nucleotides corresponding to a continuous stretch of nucleotides in the full-length variant of the 3'-UTR and/or the 5'-UTR of a transcript of a gene, which represents at least 20%, preferably at least 30%, more preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80%, and most preferably at least 90% of the full-length variant of the 3'-UTR and/or the 5'-UTR of a transcript of a gene. Such a fragment of a variant, in the sense of the present invention, is preferably a functional fragment of a variant as described herein.

The terms "functional variant", "functional fragment", and "functional fragment of a variant" (also termed "functional variant fragment") in the context of the present invention, mean that the fragment of the 3'-UTR and/or the 5'-UTR, the variant of the 3'-UTR and/or the 5'-UTR, or the fragment of a variant of the 3'-UTR and/or the 5'-UTR of a transcript of a gene fulfils at least one, preferably more than one function of the naturally occurring 3'-UTR and/or 5'-UTR of a transcript of a gene of which the variant, the fragment, or the fragment of a variant is derived. Such function may be, for example, stabilizing mRNA and/or enhancing, stabilizing and/or prolonging protein production from an mRNA and/or increasing protein expression or total protein production from an mRNA, preferably in a mammalian cell, such as in a human cell. Preferably, the function of the 3'-UTR and/or the 5'-UTR concerns the translation of the protein encoded by the ORF. More preferably, the function comprises enhancing translation efficiency of the ORF linked to the 3'-UTR and/or the 5'-UTR or fragment or variant thereof. It is particularly preferred that the variant, the fragment, and the variant fragment in the context of the present invention fulfil the function of stabilizing an mRNA, preferably in a mammalian cell, such as a human cell, compared to an mRNA comprising a reference 3'-UTR and/or a reference 5'-UTR or lacking a 3'-UTR and/or a 5'-UTR, and/or the function of enhancing, stabilizing and/or prolonging protein production from an mRNA, preferably in a mammalian cell, such as in a human cell, compared to an mRNA comprising a reference 3'-UTR and/or a reference 5'-UTR or lacking a 3'-UTR and/or a 5'-UTR, and/or the function of increasing protein production from an mRNA, preferably in a mammalian cell, such as in a human cell, compared to an mRNA comprising a reference 3'-UTR and/or a reference 5'-UTR or lacking a 3'-UTR and/or a 5'-UTR. A reference 3'-UTR and/or a reference 5'-UTR may be, for example, a 3'-UTR and/or a 5'-UTR naturally occurring in combination with the ORF. Furthermore, a functional variant, a functional fragment, or a functional variant fragment of a 3'-UTR and/or a 5'-UTR of a transcript of a gene preferably does not have a substantially diminishing effect on the efficiency of translation of the mRNA which comprises such variant, fragment, or variant fragment of a 3'-UTR and/or a 5'-UTR compared to the wild type 3'-UTR and/or the wild-type 5'-UTR from which the variant, the fragment, or the variant fragment is derived. A particularly preferred function of a "functional fragment", a "functional variant" or a "functional fragment of a variant" of the 3'-UTR and/or the 5'-UTR of a transcript of a gene in the context of the present invention is the enhancement, stabilization and/or prolongation

of protein production by expression of an mRNA carrying the functional fragment, functional variant or functional fragment of a variant as described above.

Preferably, the efficiency of the one or more functions exerted by the functional variant, the functional fragment, or the functional variant fragment, such as mRNA and/or protein production stabilizing efficiency and/or the protein production increasing efficiency, is increased by at least 5%, more preferably by at least 10%, more preferably by at least 20%, more preferably by at least 30%, more preferably by at least 40%, more preferably by at least 50%, more preferably by at least 60%, even more preferably by at least 70%, even more preferably by at least 80%, most preferably by at least 90% with respect to the mRNA and/or protein production stabilizing efficiency and/or the protein production increasing efficiency exhibited by the naturally occurring 3'-UTR and/or 5'-UTR of a transcript of a gene from which the variant, the fragment or the variant fragment is derived.

In the context of the present invention, a fragment of the 3'-UTR and/or of the 5'-UTR of a transcript of a gene or of a variant of the 3'-UTR and/or of the 5'-UTR of a transcript of a gene preferably exhibits a length of at least about 3 nucleotides, preferably of at least about 5 nucleotides, more preferably of at least about 10, 15, 20, 25 or 30 nucleotides, even more preferably of at least about 50 nucleotides, most preferably of at least about 70 nucleotides. Preferably, such fragment of the 3'-UTR and/or of the 5'-UTR of a transcript of a gene or of a variant of the 3'-UTR and/or of the 5'-UTR of a transcript of a gene is a functional fragment as described above. In a preferred embodiment, the 3'-UTR and/or the 5'-UTR of a transcript of a gene or a fragment or variant thereof exhibits a length of between 3 and about 500 nucleotides, preferably of between 5 and about 150 nucleotides, more preferably of between 10 and 100 nucleotides, even more preferably of between 15 and 90, most preferably of between 20 and 70. Typically, the 5'-UTR element and/or the 3'-UTR element is characterized by less than 500, 400, 300, 200, 150 or less than 100 nucleotides.

Preferably, the at least one 3'-UTR element comprises or consists of a nucleic acid sequence which has an identity of at least about 1, 2, 3, 4, 5, 10, 15, 20, 30 or 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 the group consisting of SEQ ID NOs: 1 to 24 and SEQ ID NOs: 49 to 318 or the corresponding RNA sequence, respectively, 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 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 the group consisting of SEQ ID NOs: 1 to 24 and SEQ ID NOs: 49 to 318 or the corresponding RNA sequence, respectively:

Homo sapiens SLC38A6 3'-UTR
SLC38A6-001 ENST00000267488
AAGAAATATTTTCCTACTTCTTACAAGAATAATATACCCCTAGTTGCAAGAATGAATTATTCCGGA
AGACACCCTGGATGAAAAATAACATTTTAATAAAAATTATTAACAGAAAAGCAGAACAAAATGGCA
GTGGGTATGGGGAAGTAAGAGTGTGGCAGTTTTAATCAAAAAAAGAAACAAACTCGAAATGCTCTT
AAA
(SEQ ID NO:49)

Homo sapiens DECR1 3'-UTR
NM_001359.1
GACCACTTTGGCCTTCATCTTGGTTACAGAAAAGGGAATAGAAATGAAACAAATTATCTCTCATCT
TTTGACTATTTCAAGTCTAATAAATTCTTAATTAAC
(SEQ ID NO:50)

Homo sapiens PIGK 3'-UTR
ACTTGATGATGAATGAAGAATGCATGGAGGACTGCAAACTTGGATAATAATTTATGTCATTATATA
TTTTTAAAAATGTGTTTCTCTTGTATGAATTGGAAATAAGTATAAGGAAACTAAATTTGAATCAAC
TATTAATTTTATAACTTAAAGAAAAATAATTGTTAATGCAACTGCTTAATGGCACTAAATATATTC
CAGTTTTGTATTTTGTGTATTATAAAAGCGAATGAGACAGAGATCAGAATACATTGACTGTTTTTG
AAAATAGTAATTTCCCCTTATCCCCTTTTCATTTGGAAAAGAAACAATTGTGAAGACATTAAATTC
TCACTAACAGAAGTAACTTTGGTTAATTATTTTTTGTAT
(SEQ ID NO:51)

Homo sapiens FAM175A 3'-UTR
FAM175A-009 ENST00000506553
TCCTTTTAACCTTACAAGGAGATTTTTTTATTTGGCTGATGGGTAAAGCCAAACATTTCTATTGTT
TTTACTATGTTGAGCTACTTGCAGTAAGTTCATTTGTTTTTACTATGTTCACCTGTTTGCAGTAAT
ACACAGATAACTCTTAGTGCATTTACTTCACAAAGTACTTTTTCAAACATCAGATGCTTTTATTTC
CAAACCTTTTTTTCACCTTTCACTAAGTTGTTGAGGGGAAGGCTTACACAGACACATTCTTTAGAA
TTGGAAAAGTGAGACCAGGCACAGTGGCTCACACCTGTAATCCCAGCACTTAGGGAAGACAAGTCA
GGAGGATTGATTGAAGTTAGGAGTTAGAGACCAGCCTGGGCAACGTATTGAGACCATGTCTATTAA
AAAATAAAATGGAAAAGCAAGAATAGCCTTATTTTCAAAATATGGAAAGAAATTTATATGAAAA
(SEQ ID NO:52)

Homo sapiens PHYH 3'-UTR
PHYH-002 ENST00000396913
AATAGCCATCTGCTATAACTCTTTCAACAGAAAACCAAAACCAAACGAAATGTCTAAGGAAAATGT
TTTCTTAATGAGATGATGTAACCTTTTCTATCACTTGTTAAAAGCAGAAAACATGTATCAGGTACT
TAATTGCATAGAGTTAGTTTTGCAGCACAATGGTGTTGCTTTAATGGAAAAAAAAAACAGTAAAAG

TGAAATATTACTGTTTTAAGGAAAACTAATTTAGGGTGGCAGCCAATAAAGGTGGTTGGTGTCTAA
TTTAAGTGTTAAATCAATTTCTTTCATTCAGTTAGCTCTTTACCCAAGAAGAAGTGAATGATTTGG
AGCTTAGGGTATGTTTTGTATCCCCTTTCTGATAAACCCATTCCCTACCAATTTTATGTCATAAGA
GATTTTTTTCCCCCAAATCTAGAACAATGTATAATACATTCACATCTAGTCAAGGGCATAGGAACG
GTGTCATGGAGTCCAAATAAAGTGGATATTCCTGCTCGGACAA
(SEQ ID NO:53)

Homo sapiens TBC1D19 3'-UTR
TBC1D19-001 ENST00000264866
TCTTCTTCACAGTCACTGGCAACACATCTAGTTTTTCATTAGAAACAAATCATGAACTATGCAAAC
TCTGCATAAAACCAAAATGAAACTTTGCATATAAGCCAATAAAGATCATGTTCCCTCTTCAGTTAA
ACCTAAGTAGTTTCTCACTTTTTGAAACAATAACTCTGCACCAAATATTGCATCGCATGCTGCTGA
TTTTCAAGAGAGAAGCAATAAACACAACTTCTGCTAAATTGAGCATTATATATATAATATTATAAT
ATATATATAATCCTGACTTGTCAATGGCATGTAATAATATATGCAATAAGAACTAAAGATACTGTA
ATAAACTTCAAGAGGTAATGTAGCTTCTTGGATAATTCTTTTATGTCAGTTTATAAATTTATCTCT
AGATAATG
(SEQ ID NO:54)

Homo sapiens TBC1D19 NM_018317.2 3'-UTR
TCTTCTTCACAGTCACTGGCAACACATCTAGTTTTTCATTAGAAACAAATCATGAACTATGCAAAC
TCTGCATAAAACCAAAATGAAACTTTGCATATAAGCCAATAAAGATCATGTTCCCTCTTCAGTTAA
ACCTAAGTAGTTTCTCACTTTTTGAAACAATAACTCTGCACCAAATATTGCATCGCATGCTGCTGA
TTTTCAAGAGAGAAGCAATAAACACAACTTCTGCTAAATTGAGCATTATATATATAATATTATAAT
ATATATATAATCCTGACTTGTCAATGGCATGTAATAATATATGCAATAAGAACTAAAGATACTGTA
ATAAACTTCAAGAGGTAAAAAAA
(SEQ ID NO:55)

Homo sapiens PIGB 3'-UTR
PIGB-201 ENST00000539642
AAATTCAACATGAAGATGAAATTCTGAACTTTCCTAGATAAATTAACATTGCTGGGTGGAAATATT
CAGATGCTGCTTAAATACTTCGGTAAACACTGGGTAAGATTCATGGAACTTAGAAAAAAGCTGTAT
GAACTGCTTTACCAAATATCACTACTGAGGAAATGTATAAAATACCACATAGTATAAAATTACATG
TTAATACAATGCCAGATTTTAAATAAAGACCTTTAGTTTTCCTC
(SEQ ID NO:56)

Homo sapiens ALG6 3'-UTR
ALG6-006 ENST00000263440
CTGTATTCCTAAACAAATTGTTTCCTAAACAAATGTGAAAATGTGAACAGTGCTGAAAGGTTTTGT
GAACTTTTTGCTATGTATAAATGAAATTACCATTTTGAGAACCATGGAACCACAGGAAAGGAAATG
GTGAAAAGTCATTGTTGTCTACACA
(SEQ ID NO:57)

Homo sapiens CRYZ 3'-UTR
CRYZ-005 ENST00000370871
TGATTAATTCTTTCATGGATTTCCTATGTAATTAGAGGTACTGTCTTTCCCCCAGTTGTACTTACC
CTATCTTTTCTTTAATTAACATTCGATTCCATGAGCTTCTTATGTGAAAAAATAAGATTTTTCTTT
AGAGAGCAGAAGCAGAAGAGTAAAATTTATTGTATAGCTAGCAATATTTTTTTATGCCATCTGTCT
CAAATCAAAGAGTCATCATAGTAGGAAATAACATGTTAGTTGTCATTTGGCATGAGTGTGCATTCC
AGTAATTCTTAATTGATATTTGATTAATTCCATACCTTTGATTAAAACATGCTAGTTCAA
(SEQ ID NO:58)

Homo sapiens BRP44L 3'-UTR

BRP44L-001 ENST00000360961
CAATGGAAAAGGAAGAACAAGGTCTTGAAGGGACAGCATTGCCAGCTGCTGCTGAGTCACAGATTT
CATTATAAATAGCCTCCCTAAGGAAAATACACTGAATGCTATTTTTACTAACCATTCTATTTTTAT
AGAAATAGCTGAGAGTTTCTAAACCAACTCTCTGCTGCCTTACAAGTATTAAATATTTTACTTCTT
TCCATAAAGAGTAGCTCAAAATATGCAATTAATTTAATAATTTCTGATGATGGTTTTATCTGCAGT
AATATGTATATCATCTATTAGAATTTACTTAATGAAAAACTGAAGAGAACAAAATTTGTAACCACT
AGCACTTAAGTACTCCTGATTCTTAACATTGTCTTTAATGACCACAAGACAACCAACAGCTGGCCA
CGTACTTAAAATTTTGTCCCCACTGTTTAAAAATGTTACCTGTGTATTTCCATGCAGTGTATATAT
TGAGATGCTGTAACTTAATGGCAATAAATGATTTAAATATTTGTTAAA
(SEQ ID NO:59)

Homo sapiens ACADSB 3'-UTR
ACADSB-004
CGTCTATAGGAGTGGGACCCCTCCCTGGTGTCACTGCTGTAAAATTTTAAACGGTTGTGTCTTGTT
GGGAGTAAGTGCCTTGCGTGGGAATAAACTTCCACAGCATTCGAATATTTTAATGAAGCCCTTAGT
CAGGGTCCTGGTGTTGGCCTTTTTGGTTTTCTCTTTTCAGGCTGTTTAACTTAGGCACAGGAGATC
CACTTTTAAACTTGGGAAATAAGCACCTGTATTTTTTTCCAAAACTGTTTTTAAAGCTGTATACGC
ATACATATATATATTTTTACTCTGTCTTACTCTGTCACCCAGGCTAGAGTGCAGTGGCGCGATCTC
AGCTCACTGCAGCCTTGACCTCCT
(SEQ ID NO:60)

Homo sapiens TMEM14A 3'-UTR
NM_014051.3
GCATCTGGAGGAACAGAAAACTAAGTTCATGTCATCCTGCTGTAATGGGCAGAGCATATTTTTTTT
GTATTTAAAAGATAAACTTCAATATGGAATGCTAGAAACACAAATAGCACTGTCACCTCTAATATG
AACATTAGTTTGAGGTAGTTTTTTTCTAAAGCAAAAATTTTAACTGTTTTCTAATTGTCAAGCACT
ATTTTCATTAAAAGTGTCTAATGAATCATGATATACTCTTCCATTTGTTGTGTCTATTTTTTATAT
ATTTGGTATTTTTTGAAAATTCCAAATACTCATGTCTCAAGTAAGCTTAAACTACAACTTGTCACA
TAAAGGAAGTCTTAAGTGGAGTTCACAGAATGATAATGTATCTATTTGTCATTTGTGTTATATTTG
AAATTATTAGAAATTATGCTTTTTCCATTTTAATTGTATTGCTGCCAGTGCTATTTTTTTCTTTAA
AAAATTTTATTCTTAGCACACTGTTATGTCCTAACTGAATGTATTCAGTATTCAAATAAAAGACAT
TTTGGTTCAAA
(SEQ ID NO:61)

Homo sapiens GRAMD1C 3'-UTR
GRAMD1C-005 ENST00000472026
TGATCTGAAGGACTAAAACCGCAGAGATACTTGGAACTTAAAGAAAATACCTGGAAGAAAACCAGA
CGAATGAAGGATTTTGGCATAGAACATTTCTATGTTTTTTCATTATTGAGATTTCTAATATGAACA
TTTCTTTCAGTAACATTTATTTGATAATTAGTTTCTGCTGGCCTTAATAATCCATCCTTTCACTTC
TTATAGATATTTTTAAGCTGTGAATTTCTTCAGTGAACCATGAAATATATTATAGAACTGAATTTC
TCTGATACAAAAAGAAAATGACACACCC
(SEQ ID NO:62)

Homo sapiens C11orf80 3'-UTR
C11orf80-201 ENST00000360962
GCCGGGTCCCCTTCCGCAAGCGCCCACCGATCCGGAGGCTGCGGGCAGCCGTTATCCCGTGGTTTA
ATAAAGCTGCCGCGCGCTCACCAAGTCC
(SEQ ID NO:63)

Homo sapiens ANXA4 3'-UTR

ANXA4-002 ENST00000409920
AATAAAAATCCCAGAAGGACAGGAGGATTCTCAACACTTTGAATTTTTTTAACTTCATTTTTCTAC
ACTGCTATTATCATTATCTCAGAATGCTTATTTCCAATTAAAACGCCTACAGCTGCCTCCTAGAAT
ATAGACTGTCTGTATTATTATTCACCTATAATTAGTCATTATGATGCTTTAAAGCTGTACTTGCAT
TTCAAAGCTTATAAGATATAAATGGAGATTTTAAAGTAGAAATAAATATGTATTCCATGTTTTTAA
AA
(SEQ ID NO:64)

Homo sapiens TBCK 3'-UTR
TBCK-002 ENST00000361687
AGAACCAAGAGTGTGACTGCCAAAACTTAGTGTGGCATCAGCACCAACAGCACAGTTCTTCATATC
CACGCCACTCTCAGACAAAACTAGATGTCCAGATTGTTGCATTTCCGTAAAGTTTGTCACGAGACA
TTTTTTAAAATCTCATAACCCACATGTTCAGTTATCCATGCAAGAAACTTGACTCTACATGTATTG
CTGAAAGAATTTTCTTAACAGTGAAATCTGATCATATATTTTTACCACACTGCCACATAAAGCCCA
AGAAATTCAGCTGACAAGACAGATTTAGCATTATCAAGAAATCCCATTTGCCCTGAAAAAGCTGTC
CTCCATTGTACTGAACAGACAGTCCTGTCGATTGTGTTATTTAGAAACATACACTGAATGTGGGCT
GAAATCATCATCTTTCCATAATGAAAACTGAGAAACTATTCACAATGCATTCCTTATAAATAAATG
CTACATTTAGTAACTCATTTCACCCAAA
(SEQ ID NO:65)

Homo sapiens IFI6 3'-UTR
IFI6-001 ENST00000361157
CCAGCAGCTCCCAGAACCTCTTCTTCCTTCTTGGCCTAACTCTTCCAGTTAGGATCTAGAACTTTG
CCTTTTTTTTTTTTTTTTTTTTTTTGAGATGGGTTCTCACTATATTGTCCAGGCTAGAGTGCAGTG
GCTATTCACAGATGCGAACATAGTACACTGCAGCCTCCAACTCCTAGCCTCAAGTGATCCTCCTGT
CTCAACCTCCCAAGTAGGATTACAAGCATGCGCCGACGATGCCCAGAATCCAGAACTTTGTCTATC
ACTCTCCCCAACAACCTAGATGTGAAAACAGAATAAACTTCACCCAGAAAACACTT
(SEQ ID NO:66)

Homo sapiens CAMKMT 3'-UTR
(synonym C2orf34) ENST00000378494
AAGATTAAGCTTCTCAAAGACGAAGAAACGTATCAAGTGCATAGGGAATATTTTTACAAAAACGGA
AATCTGTAAGGGGTATAATCGCCTGCCTGCGCCCTTTGCAGCATTTCACGTGTGGGCTATGGACTC
CACCTGTCCTCACCCACGTTATTCCCCAGCTGCCCTCTCCAGCTCCCTCCCCGCCTCTTTTTACAC
TCTGCTTGTTGCTCGTCCTGCCCTAAACCTTTGTTTGTCTTTAAATGTGTATAAGCTGCCTGTCTG
TGACTTGAATTTGACTGGTGAACAAACTAAATATTTTTCCCTGTAATTGAGACAGAATTTCTTTTG
ATGATACCCATCCCTCCTTCATTTTTTTTTTTTTTTTGGTCTTTGTTCTGTTTTGGTGGTGGTAGT
TTTTAATCAGTAAACCCAGCAAATATCATGATTCTTTCCTGGTTAGAAAAATAAATAAAGTGTATC
TTTTTATCTCCCTCCAA
(SEQ ID NO:67)

Homo sapiens ALDH6A1 3'-UTR
NM_005589.2
AAACAAGTTTGTTTAAGACTGACTCCATCCTGAGTAATCTCCCTTTATTTTTGACCAGCTTCATTT
GTCAGCTTTGCTCAGATCAGATCGATGGGATTGGAATACATTGTAACTAAAATCTTCCTCAGGACT
ATTAACCCCCGCAAAGTTTCTATAGGGAACTGCCTAGTGTAACAATGAAACCAGATTTCTCACTTG
CTCTTCATACTTCTATTTTGAGGTAACTGTTGTAACTATGAAATGCTTATCTGAAAGTAGTGCTTA
AACCTGATTTCTAAAAATTATCCCATTTTCTGATGATTTGAAGGGGAGAAAAGCCAGTGTATGTAA
AGAAAATGTTCCAGCCAGGCGCGGTGGCTCACGCCTGTAATTCCATCATTTTGGGAGGCCACAGTG
GGCAGATTGCTTGAGCCCAGGAGTTGAAGAACGTGGCGAAACCCCGTATCTATTATTTAAAAAAAT
TGAAAAAGTAAAAA
(SEQ ID NO:68)

Homo sapiens AGTPBP1 3'-UTR
AGTPBP1-004 ENST00000357081
GCCCGCTGCCATCTCTTGTTAACTGCAAAGAATAAATGAAATATCTTGGTTTTTATTTCCCAGGAA
GCTTGAGAGAAATGAGTTTATACAGAGCTGACTCAAAAAGACAAAAAGTAACTTGGGCCAGTTTGG
TTTCAAGATAATAAATGTGTTATTAATTAATGATAAAATTGGCGCTTGTTTTATTTTCGATATTCA
ATGCACTTTATGTAGCATTGAATGATCAAATATTGGATTTACCTTTAAAAAAAAAACCTGAGTATC
ATTGCATGAATTTTTATCTCCCTATGGTTATATCCTGCATCAAGTGGATAATTTTGAAGTGTGTTC
AGAATATAAAATTGAAATTTTAGAGTTGTTGAAAATCCTGACTTGTTGAAAACTAATATATATGTA
CATGGATTTCTATAGATGTGTTTGTTTAGAAGTGGGTAGATATTGCAGATAAGACTGTTCTTCAGA
ATCATGTTAACTATTGGGTTGTGACTGAAGTAGTCCAGGGTTTGCCTTGAAACCATTACATTCTAC
ATTTACCAAATTAAACAAATAAAAACTGTATTAAATGTT
(SEQ ID NO:69)

Homo sapiens CCDC53 3'-UTR
CCDC53-001 ENST00000240079
GCTTAATTTTGATAAGAATTACATATGCATGCATAGGGGTACATTTACATTCTGTAAGAGATTGAG
CCTGAACTCTCTTAGTCATAAAAACATCAAATGGCCACATGTCCACTACCAAGCTTCTTCTATGTT
AAAAAAATAATAATAAAGCAGTTTTAACCTGCCAGTA
(SEQ ID NO:70)

Homo sapiens LRRC28 3'-UTR
LRRC28-002 ENST00000331450
TAAACACTCAAGAACCTCAGGAGCGCTGCCAGCTTGACACTGGGGAATCCAGCCAGTCCAGCACAC
TCTTCCATCCTGTCCTGTCCAATGCGGGGGCACTGCAGAACTCTCTAGAAATGTCATGATTGAGCT
TCAGAGCTAAAATGCCTTCACCCTTCCCCCAAGTTGGAATATATCCTCCCCCAAATTAAGGA
(SEQ ID NO:71)

Homo sapiens CCDC109B 3'-UTR
NM_017918.4
TCTTACAGTTTTAAATGTCGTCAGATTTTCCATTATGTATTGATTTTGCAACTTAGGATGTTTTTG
AGTCCCATGGTTCATTTTGATTGTTTAATCTTTGTTATTAAATTCTTGTAAAAC
(SEQ ID NO:72)

Homo sapiens PUS10 3'-UTR
PUS10-001 ENST00000316752
CTTTCAAATTTGGAGACAAAGAGTATGGTTTTCCTGGCATGATGTGGACATCCATGGAGCACATGC
CGTAAAATGGCTGTTTACCCACCATAACGGTGTCTTGAAAACTATTTGGATCATGTTGATCTATAT
AATTGTTAATTTGTTGTAACATCTCAGGATCTATATATGTGTATATTTTGTGTTAAATTGTTCCAA
GGATGTCTTAGGATTTTTCTCATTCCCTCTTTCACCCCCACAAACCAAACTATGAATAATGAAATA
ATTCTCCTTAATTCTTTCATTTAGAGAGGTGCACAAACAGGACACATTCTCTGTTAACCTAAGAAG
CTGTAATTTCAGCAAGATTTCCCTCCACAAGAGATATACCACCTTTAAAATCATGTTCTAATTTTT
GTAAATTATCTGAATAAAAGTTATATCTAG
(SEQ ID NO:73)

Homo sapiens CCDC104 3'-UTR
CCDC104-002 ENST00000339012
TAATTAAGAACAATTTAACAAAATGGAAGTTCAAATTGTCTTAAAAATAAATTATTTAGTCCTTAC
ACTGA
(SEQ ID NO:74)

Homo sapiens CASP1 3'-UTR

CASP1-007 ENST00000527979
AATAAGGAAACTGTATGAATGTCTGTGGGCAGGAAGTGAAGAGATCCTTCTGTAAAGGTTTTTGGA
ATTATGTCTGCTGAATAATAAACTTTTTTGAAATAATAAATCTGGTAGAAAAATGAAAA
(SEQ ID NO:75)

Homo sapiens SNX14 3'-UTR
SNX14-007 ENST00000513865
ACACTTGGATTTGGTATAGAATAACCCATTGAAATTTCTGCTGTGCGAGGGTGGTAGAAATTTACT
TTTTTGGGTATATTCTTATATATATTATGTACATCGCTGTCTGAAATTTTAGTTATTTTTTGTTTT
TAATAAAGACTAACACAAACTTAATGATTAAAAGTGATTGAG
(SEQ ID NO:76)

Homo sapiens SKAP2 3'-UTR
SKAP2-201 (part of SKAP2.001 ENST00000345317)
GAGTCCTGGAAAAGGAAAATTCTTCTGCTTGTCTGCAAATGCTTTGGATTTAGAAGCGTCATGAAA
GCACGAGTGACAGCTCCTAACCTCTCCTTGTTTTATTAAACATTACTTATCTTTGACTGTTATTTT
ATGCAGTCGCTCATTAAAATATTCCTCTGATGTGAAATTAAATGAAGGATATTAATGTAAATTAGA
TGCAACCAGTTAAGTTATACCTGTTGCTATTTTGCAAAG
(SEQ ID NO:77)

Homo sapiens NDUFB6 3'-UTR
NM_182739.2
AGATTATGTAAAAAGTTAAAAGGCTTATGAGCCTAAGTTTGTTCCTATATTACCATATTTACTGAA
TTTTCTGGAAAAGTAACTTTAATAAAGTTTAATCTCAGAAATTGTCATATCTGTTTTCAAGCATTG
TACAATTTGAGACTGAGTAATTTAACAATAAGTAAAAAGTGGACATGCTAAACAAATATGAGAGAC
TACCTACTTTTTCTGGTCATTCTTGACTTGGAAAACGGTATGGAAAAGTATTTAGTTACATGTTTG
TTTGTTTTTTTCTTACACAGTACTTACACTAATTTGGTATCAGGGTATGCAACAGTGAAATATCAC
AATAAACAAATGTAAGAACAAAAAAAAAAAAA
(SEQ ID NO:78)

Homo sapiens EFHA1 3'-UTR
EFHA1-001 ENST00000382374
TAAAAGATATAATAGTATGGCAATTATATTGTTCCAAATGTCAAAATTTGTGATTTTTTAGAAGTA
CTTGCTATTTATCTTCTTAAGTCTTCATTGATATTCTGTGTGAAATAAGCATGTCTTGTACTTGCT
TTCTGATTCATAATTTTATTAAAGAACTTAGTAGAAAGAAAAGTAAGTATAAAAATAGATATTGGA
TTCTGTCAGAAGGCCTAGATTTGAAATAATGTTTTGTACTTCGGTAAGATGGAAAACTTAGTGATT
CACTGATTTCTTAGACACTCTAATATGATATGCTTTCTGGAAGGATAAAACAAATACATATGGGAA
AAAGTACTTGAGACCAAGGCCAGCATCAATTCCAGACATCTTCATGTTCCTAATAGGCTAAATGAA
GTTAAAAACTTATTTCAGATTTTTCTCATCTGTACCTTATATCTCATAAATTTATTGCATATTTTA
TGTCAGTAGCTTAGCTGTTTATTGTCTTTAAAATAACATGTAAACTTCAATGTTCTATCTGGAAGC
AGAATAAAATATTTACATAGA
(SEQ ID NO:79)

Homo sapiens BCKDHB 3'-UTR
BCKDHB-005 ENST00000356489
CCATATAGAAAAGCTGGAAGATTATGACTAGATATGGAAATATTTTTTCTGAATTTTTTTTTATAT
TTCCTCCGACTTACCTCTTTTTGAAAAGAGAGTTTTTATTAAGTGAACCATCACGATATTGGCTGA
AAAGTTCTACATTCTATTATTGTATTGTAACACACATGTATTGATGATTTTCATTAAGAGTTTCAG
ATTAACTTTGAAAAATATTCCACATGGTAATCTTATAAATTCTGTTTAATTACATCTGTAAATATT
ATGTGTGTGATAGTATTCAATAAA
(SEQ ID NO:80)

Homo sapiens BCKDHB 3'-UTR
NM_001164783.1
GACCTGCTCAGCCCACCCCCACCCATCCTCAGCTACCCCGAGAGGTAGCCCCACTCTAAGGGGAGC
AGGGGGACCTGACAGCACACCACTGTCTTCCCCAGTCAGCTCCCTCTAAAATACTCAGCGGCCAGG
GCGGCTGCCACTCTTCACCCCTGCTCCTCCCGGCTGTTACATTGTCAGGGGACAGCATCTGCAGCA
GTTGCTGAGGCTCCGTCAGCCCCCTCTTCACCTGTTGTTACAGTGCCTTCTCCCAGGGGCTGGGTG
AGGGCACATTCAGGACTAGAAGCCCCTCTGGGCATGGGGTGGACATGGCAGGTCAGCCTGTGGAAC
TTGCGCAGGTGCGAGTGGCCAGCAGAGGTCACGAATAAACTGCATCTCTGCGCCTGGCTCTCTACC
AAAAAAAAAAAAAAAAAA
(SEQ ID NO:81)

Homo sapiens BBS2 3'-UTR
NM_031885.3
GTGAGGAAAATACAGGTCATGAAGTTCCTGGCAAAGATTTTCTGTTAAAAACCTATGCTGGTTTGC
TTTGGATCACACCCTGGTGAACCCCGGGTGCTAAGAATGAAAATAACCTTGGTGAGTTGTACAAAT
TAAAGACAAAGAACTACATGTGAAGATAGACTTGCTTTCTATTTTTAAATCAGTAGTAGTACTGTT
GCTGAATAATACTAGGTTTTTATGGAATAGGATGAATGCTTTTGAAGTATTAGGGCTTCAGAGTCC
AATTTTGCTTATTTATGGTATATAAATACATATTTTTTTCTTGAAATTGCAATTGAGTTTGTACTT
TTCAAATAGATTATCTACTTTTTCATTAAAATGTAAAGATGTTAAACTTTGTGTTGATTGATTATA
AAATCACCACCAAATCAG
(SEQ ID NO:82)

Homo sapiens LMBRD1 3'UTR
NM_018368.3
CAGCCTTCTGTCTTAAAGGTTTTATAATGCTGACTGAATATCTGTTATGCATTTTTAAAGTATTAA
ACTAACATTAGGATTTGCTAACTAGCTTTCATCAAAAATGGGAGCATGGCTATAAGACAACTATAT
TTTATTATATGTTTTCTGAAGTAACATTGTATCATAGATTAACATTTTAAATTACCATAATCATGC
TATGTAAATATAAGACTACTGGCTTTGTGAGGGAATGTTTGTGCAAAATTTTTTCCTCTAATGTAT
AATAGTGTTAAATTGATTAAAAATCTTCCAGAATTAATATTCCCTTTTGTCACTTTTTGAAAACAT
AATAAATCATCTGTATCTGTGCCTTAGGTTCTCCAGAGTGATGTGGAATTTTAAAGTGTCTCTCTC
TGATTGCCTCCAA
(SEQ ID NO:83)

Homo sapiens ITGA6 3'-UTR
ITGA6-003 ENST00000409532
TATTGATCTACTTCTGTAATTGTGTGGATTCTTTAAACGCTCTAGGTACGATGACAGTGTTCCCCG
ATACCATGCTGTAAGGATCCGGAAAGAAGAGCGAGAGATCAAAGATGAAAAGTATATTGATAACCT
TGAAAAAAAACAGTGGATCACAAAGTGGAACGAAAATGAAAGCTACTCATAGCGGGGGCCTAAAAA
AAAAAAGCTTCACAGTACCCAAACTGCTTTTTCCAACTCAGAAATTCAATTTGGATTTAAAAGCCT
GCTCAATCCCTGAGGACTGATTTCAGAGTGACTACACACAGTACGAACCTACAGTTTTAACTGTGG
ATATTGTTACGTAGCCTAAGGCTCCTGTTTTGCACAGCCAAATTTAAAACTGTTGGAATGGATTTT
TCTTTAACTGCCGTAATTTAACTTTCTGGGTTGCCTTTATTTTTGGCGTGGCTGACTTACATCATG
TGTT
(SEQ ID NO:84)

Homo sapiens HERC5 3'-UTR
HERC5-001 ENST00000264350
CCAGCTTGCTTGTCCAACAGCCTTATTTTGTTGTTGTTATCGTTGTTGTTGTTGTTGTTGTTGTTG
TTTCTCTACTTTGTTTTGTTTTAGGCTTTTAGCAGCCTGAAGCCATGGTTTTTCATTTCTGTCTCT
AGTGATAAGCAGGAAAGAGGGATGAAGAAGAGGGTTTACTGGCCGGTTAGAACCCGTGACTGTATT

CTCTCCCTTGGATACCCCTATGCCTACATCATATTCCTTACCTCTTTTGGGAAATATTTTTCAAAA
ATAAAATAACCGAAAAATTAA
(SEQ ID NO:85)

Homo sapiens HADHB 3'-UTR
HADHB-001 ENST00000317799
TAGATCCAGAAGAAGTGACCTGAAGTTTCTGTGCAACACTCACACTAGGCAATGCCATTTCAATGC
ATTACTAAATGACATTTGTAGTTCCTAGCTCCTCTTAGGAAAACAGTTCTTGTGGCCTTCTATTAA
ATAGTTTGCACTTAAGCCTTGCCAGTGTTCTGAGCTTTTCAATAATCAGTTTACTGCTCTTTCAGG
GATTTCTAAGCCACCAGAATCTCACATGAGATGTGTGGGTGGTTGTTTTTGGTCTCTGTTGTCACT
AAAGACTAAATGAGGGTTTGCAGTTGGGAAAGAGGTCAACTGAGATTTGGAAATCATCTTTGTAAT
ATTTGCAAATTATACTTGTTCTTATCTGTGTCCTAAAGATGTGTTCTCTATAAAATACAAACCAAC
GTGCCTAATTAATTATGGAAAAATAATTCAGAATCTAAACACCACTGAAAACTTATAAAAAATGTT
TAGATACATAAATATGGTGGTCAGCGTTAATAAAGTGGAGAAATATTGGAGAA
(SEQ ID NO:86)

Homo sapiens ANAPC4 3'-UTR
ANAPC4-001 ENST00000315368
TCTAGCTTGCCATTATTGTGTGTGTAATTATGGCCAAAAGGACATAGGAGATGGACTAAGATGTCT
TGGACCACCTTTGTGTAACAAAGAAATAAACAGTAAATTTTATTTTTTCA
(SEQ ID NO:87)

Homo sapiens PCCB 3'-UTR
NM_000532.4
ACAAATCAAAGGAAAAGAAACCAAGAACTGAATTACTGTCTGCCCATTCACATCCCATTCCTGCCT
TTTGCAATCATGAAACCTGGGAATCCAAATAGTTGGATAACTTAGAATAACTAAGTTTATTAAATT
CTAGAAAGATCTCAAAAAAAAA
(SEQ ID NO:88)

Homo sapiens ABCB7 3'-UTR
ABCB7-001 ENST00000253577
GTCACATAAGACATTTTCTTTTTTTGTTGTTTTGGACTACATATTTGCACTGAAGCAGAATTGTTT
TATTAAAAAAATCATACATTCCCA
(SEQ ID NO:89)

Homo sapiens PGCP 3'-UTR
CPQ-001 ENST00000220763
AAACAGTAAGAAAGAAACGTTTTCATGCTTCTGGCCAGGAATCCTGGGTCTGCAACTTTGGAAAAC
TCCTCTTCACATAACAATTTCATCCAATTCATCTTCAAAGCACAACTCTATTTCATGCTTTCTGTT
ATTATCTTTCTTGATACTTTCCAAATTCTCTGATTCTAGAAAAAGGAATCATTCTCCCCTCCCTCC
CACCACATAGAATCAACATATGGTAGGGATTACAGTGGGGGCATTTCTTTATATCACCTCTTAAAA
ACATTGTTTCCACTTTAAAAGTAAACACTTAATAAATTTTTGGAAGATCTCTGA
(SEQ ID NO:90)

Homo sapiens NFU1 3'-UTR
NM_001002755.2
AATAATCTGGATTTTCTTTGGGCATAACAGTCAGACTTGTTGATAATATATATCAAGTTTTTATTA
TTAATATGCTGAGGAACTTGAAGATTAATAAAATATGCTCTTCAGAGAATGATATATAAATATTGC
A
(SEQ ID NO:91)

Homo sapiens OMA1 3'-UTR

OMA1-001 ENST00000371226
ATTAAAATTTATGAGACACAAGATATATGAAGAATGTTGCAGTCCTTATCATTTTATGTTACTTTT
TAAAAAATGATGTTTGAAGTGAAAAAAAAAAGGATATTCAGGGTCAAATCATGTACATTACAGATA
TTATCTAAATTCTTCTAGAATTTATTTTTCATGAAATATTGATGTATTTTAATCTATGTTAAAATA
TCTTCAATGAGGAAAATGTCACAGAATAAATTTATATTACACATTTTA
(SEQ ID NO:92)

Homo sapiens HHLA3 3'-UTR
NM_001036646.1
GGCGAATCCATAGAGTAAGCTTAGTGATGTGTGTCAGACCTCTGAGCCCAAGCAAAGCCATCATAT
CCCCTGTGACCTGCATGTATACATCCAGATGGCCTGAAGCAAGTGAAGAATCACAAAAGAAGTGAA
AAGGGCCGGTTCCTGCCTTAACTGATGACATTCCACCATTGTGATTTGTTCCTGCCCCACCTTAAC
TGAGCGATTAACCTGTGAACTTCCTTCTCCTGGCTCAGAAGCTTCCCCACTGAGCACCTTGTGACC
CCCGCCCCTGCCTGCCATAGAACAACCCCCTTTGATTGTAATTTTCCTTTACCTACCCAAATCCTA
TAAAACGGCCCCACCCCTATCTCCCTTCGCTGACACTCTCTTTGGACTCAGCCTGCCTGCACCTAG
GTGATTAAAAAGCTTTATTGCTCACGC
(SEQ ID NO:93)

Homo sapiens HHLA3 3'-UTR
NM_001031693.2
AAAGGGCCGGTTCCTGCCTTAACTGATGACATTCCACCATTGTGATTTGTTCCTGCCCCACCTTAA
CTGAGCGATTAACCTGTGAACTTCCTTCTCCTGGCTCAGAAGCTTCCCCACTGAGCACCTTGTGAC
CCCCGCCCCTGCCTGCCATAGAACAACCCCCTTTGATTGTAATTTTCCTTTACCTACCCAAATCCT
ATAAAACGGCCCCACCCCTATCTCCCTTCGCTGACACTCTCTTTGGACTCAGCCTGCCTGCACCTA
GGTGATTAAAAAGCTTTATTGCTCACGC
(SEQ ID NO:94)

Homo sapiens ACAA2 3'-UTR
NM_006111.2
AGAGACCAGTGAGCTCACTGTGACCCATCCTTACTCTACTTGGCCAGGCCACAGTAAAACAAGTGA
CCTTCAGAGCAGCTGCCACAACTGGCCATGCCCTGCCATTGAAACAGTGATTAAGTTTGATCAAGC
CATGGTGACACAAAAATGCATTGATCATGAATAGGAGCCCATGCTAGAAGTACATTCTCTCAGATT
TGAACCAGTGAAATATGATGTATTTCTGAGCTAAAACTCAACTATAGAAGACATTAAAAGAAATCG
TATTCTTGCCAAGTAACCACCACTTCTGCCTTAGATAATATGATTATAAGGAAATCAAATAAATGT
TGCCTTAACTTC
(SEQ ID NO:95)

Homo sapiens GSTM4 3'-UTR
GSTM4-001 ENST00000369836
TGCCTTGAAGGCCAGGAGGTGGGAGTGAGGAGCCCATACTCAGCCTGCTGCCCAGGCTGTGCAGCG
CAGCTGGACTCTGCATCCCAGCACCTGCCTCCTCGTTCCTTTCTCCTGTTTATTCCCATCTTTACC
CCCAAGACTTTATTGGGCCTCTTCACTTCCCCTAAACCCCTGTCCCATGCAGGCCCTTTGAAGCCT
CAGCTACCCACTTTCCTTCATGAACATCCCCCTCCCAACACTACCCTTCCCTGCACTAAAGCCAGC
CTGACCTTCCTTCCTGTTAGTGGTTGTATCTGCTTTGAAGGGCCTACCTGGCCCCTCGCCTGTGGA
GCTCAGCCCTGAGCTGTCCCCGTGTTGCATGACAGCATTGACTGGTTTACAGGCCCTGCTCCTGCA
GCATGGCCCCTGCCTTAGGCCTACCTGATCAAAATAAAGCCTCAGCCACA
(SEQ ID NO:96)

Homo sapiens GSTM4 3'-UTR
GSTM4-003 ENST00000326729
TGGTCAATTTTCTGCATCAACTTGACTGGGCTAAGGGATGCTCAGATGGCAGGTAAAATCATTGTG
CTTGTGAGGGTGTTTCCAGAAGAGATTTGCCTTTGAATCAGAAGACAGCAAAGATTTCCTTCAGCA

ATGAAGGAGGCATCCACCAAACTGTCAGGGCCCAGAGAGAAGAAAAAGACAGGAAGGGTGAATTTG
ACCTCTCTGACTGGGACATCCATCTCTGCCTATCCTGGGACCTCCACACTCCTGGTTCTCTGGCCT
TCAGACTTGATCAGGGACTAACACCATCGCCTCCCACCCCCACCTTTGTTCTGAGGCCTTTAGCCT
CTGAATGATACCACTGGCTTTCCTGCTTCTCTATCCTGCAGTCGGCAGATCATGGGACTTCTTCAC
TCCAAAATTGTGTGAGCCAATTCCCATAACAGATAGATAAATTTATAAATAAACACACAAATTTCC
TAC
(SEQ ID NO:97)

Homo sapiens ALG8 3'-UTR
NM_001007027.2
CTGAAACCTCCGCCTCCCAGAAAAGAAAAACCTCTTTTTAATTGGATGGAAACTTTCTACCTGCTT
GGCCTGGGGCCTCTGGAAGTCTGCTGTGAATTTGTATTCCCTTTCACCTCCTGGAAGGTGAAGTAC
CCCTTCATCCCTTTGTTACTAACCTCAGTGTATTGTGCAGTAGGCATCACATATGCTTGGTTCAAA
CTGTATGTTTCAGTATTGATTGACTCTGCTATTGGCAAGACAAAGAAACAATGAATAAAGGAACTG
CTTAGATATG
(SEQ ID NO:98)

Homo sapiens C11orf74 3'UTR
TTCACAGAGGCATTTTGTGTGTGTGTGCTTATTTTAATTTTGTTCTTATTCTAGCAACATTAGAAT
AAAAGATAAACCTACTATAATTCCCTTTGTGGAAATTTAAAAAAAAAAAAAAAAAA
(SEQ ID NO:99)

Mus musculus Ndufa1 3'-UTR
Ndufa1-001 ENSMUST00000016571
GGAAGCATTTTCCTGGCTGATTAAAAGAAATTACTCAGCTATGGTCATCTGTTCCTGTTAGAAGGC
TATGCAGCATATTATATACTATGCGCATGTTATGAAATGCATAATAAAAAATTTTAAAAAATCTAA
A
(SEQ ID NO:100)

Mus musculus Atp5e 3'-UTR
NM_025983
CTGAATCTGAAGCCTGAAGTGCTGAGTCTTGAAGGTGAAGCATGTGGGCCCCTGTTCTGGCAGATG
GAAATCAACCTCACCTCCTGGGGGACAGGCTGCCCATCTCGTTGATAAATTGACTATGCCAATAAA
TTAACATGGTTCACTTTCAAAAA
(SEQ ID NO:101)

Mus musculus Gstm5 3'-UTR
NM_010360
GCCAGAGCTCGCTGCTGCTGAGCCATCTTGCCCTGAGGGGCCCACACTCTTAGCTCACTGTCAGTC
TTGTTCCATCCTGTCCTGAGGGCCCCCACTCTGTCTCCTCTGCTCTTTCTAATAAACAGCAGTTGC
ATTA
(SEQ ID NO:102)

Mus musculus Uqcr11 3'-UTR
NM_025650
GCAGCCCCTCCCCCACCACAGGCCTCGATGGTACCATGTGCCGAGGCCTCAGACACAGCGTAGTCC
TGTGGAAGACACTGAGGAAGCTGGACACTGGAGAGGTCTGCACCGCTCAGGGAGCTTCCATGTTGA
CAGACACTAGGGCTGCCTTGATGGGTGCAGCATTAAACCTTATTCTTATGCCTTGGA
(SEQ ID NO:103)

Mus musculus IFi27I2a 3'-UTR
IFi27I2a-001 ENSMUST00000055071; NM_029803

GCTTAGGAGATGACACTTCTATCAGCTCAACTCAAAGCCTGTACAGACTACGCAGGAGATGAAGTT
CCAAAAGGCACCTTCAGAACCCTCACTGATGTCAAAGAATGATGAAAACAACAAAGTATATGGGCT
GGTGTTCCTAA
(SEQ ID NO:104)

Mus musculus Cbr2 3'-UTR
NM_007621
TCTGCTCAGTTGCCGCGGACATCTGAGTGGCCTTCTTAGCCCCACCCTCAGCCAAAGCATTTACTG
ATCTCGTGACTCCGCCCTCATGCTACAGCCACGCCCACCACGCAGCTCACAGTTCCACCCCCATGT
TACTGTCGATCCCACAACCACTCCAGGCGCAGACCTTGTTCTCTTTGTCCACTTTGTTGGGCTCAT
TTGCCTAAATAAACGGGCCACCGCGTTACCTTTAACTAT
(SEQ ID NO:105)

Mus musculus Atp5l 3'-UTR
Atp5l-201 ENSMUST00000043675
AGACCAATCTTTAACTTCTGATTTGAGTTCTTATTTGAATGTTCTTGGACCATGTGTAACAGGACT
GCTATCTGAATAAAATACTAGGTGTTGAAAACACTGCTGTGTTTTCTCTGTC
(SEQ ID NO:106)

Mus musculus Tmsb10 3'-UTR
NM_025284
AAGCCTAGGAAGATTTCCCCACCCCACCCCACCCCGCCCCATCATCTCCAAGACCCCCTCGTGATG
TGGAGGAAGAGCCACCTGCAAGATGGACGCGAGCCACAAGCTGCACTGTGAAACCCGGGCACTCCG
AGCCGATGCCACCGGCCCGCGGGTCTCTGAAGGGGACCCCTCCACTAATCGGACTGCCAAATTTCA
CCGGTTTGCCCTGGGATATTATAGAAAATTATTTGTATGATTGATGAAAATAAAAACACCTCGTGG
CATGGTT
(SEQ ID NO:107)

Mus musculus Nenf 3'-UTR
NM_025424
TGTCTAGCTGAGAAGCAGCCGGTTCTAGGGAGAAGTGAGGGGACAGGAGTTAAGTGTCCCTCGGAA
CAAGCGGAGGAAGCCTCCGAGTGCCCTGCAGCTGAATAAAGCGAATGTTT
(SEQ ID NO:108)

Mus musculus Atp5k 3'-UTR
NM_007507
GGCGTCAGCGAGCTTGCTTTTCTCTAGTCGTTGAGAACGAATAAAGCTTCATTGTGTGAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:109)

Mus musculus 1110008P14Rik 3'-UTR
1110008P14Rik-001 ENSMUST00000048792
GTGCCGGGAGCCCCCATCCAGGCCCTACCCTCACCTCTCTAGGCCATGTTCTGGCCTGGGTAGATA
CTACTTGGCTTAGACACCATCTCGGGTACTGGCCTCCAGATCCTAGTGGGTCTACCAGCCTGGACC
AGTCCCCATTCACTGCCCATCACCCTTCCTGGAGTCAGGTGCAATCCTACAGTTCTCCCACTTGTC
TGTCTTCTTTCCCCTCCATCCAGACTGAGAGTCCGAATTAAAGATGTCTCCCACACCACTGC
(SEQ ID NO:110)

Mus musculus Cox4i1 3'-UTR
NM_009941
GAGCCCGCTGCCTGCCGGCTCCCTGCCTCCCTCACTCCCTCGGCATGCTGGAAGCTGCCGTATCCA
ATGGTCCATGCTAATAAAAGACCAGTTTACGTGGTG

(SEQ ID NO:111)

Mus musculus Cox6a1 3'-UTR
NM_007748
AGAGAACCTGGCCTCCCCCAGGCAACAAAGGGACCACAGCACTGGTTTTGGACCCTTACTCTGTGT
GGACCACGAAAACCCTTTGGATGCTAAGCTCGTGTCTCCTTTCCTCAGATGGCGACCATTACTCTG
ATCTTCCATCCCTTCTGCTTGTAAGAGGAGATGCCTTAAATAAATAACTTAAACTCA
(SEQ ID NO:112)

Mus musculus Ndufs6 3'-UTR
NM_010888
TGTGGGCTGTGTCCTGGTCCTCTGACTCCTATGGAACATCTCCACGCTGGGTGTTCTGTGTGAGGC
CACTGCTCTGTGAATGGTGTCCCTTGTTTTGAATAAAGGATGCTCCCACCATGAAAAAAAAAAAAA
AAAAAAA
(SEQ ID NO:113)

Mus musculus Sec61b 3'-UTR
NM_024171
ATTGGGCTACATCCATCTGTCATCTGAAGAAGAAGAAGAAGGAAAAAAACCCAACATATCTTGGAC
CAAAAGTGTAGTGATTTTCTGTTCACGTGTATTATTTTACAGAGAATAAGAATTGACTTTGAGAAA
TCAGTTTTTTCTATGGCTAATAAACTTTGGAATTGCTTT
(SEQ ID NO:114)

Mus musculus Romo1 3'-UTR
NM_025946
TTAGGGCTAGGATGCCCTGCAATACCTAAACTTCCCCATCCATTTCGACCCTTGTACAATAATAAA
GTTGTTTTCTTCTCGTTAAAAAAAAAAAAAAAAA
(SEQ ID NO:115)

Mus musculus Gnas 3'-UTR
NM_010309
GAAGGGAACACCCAAATTTAATTCAGCCTTAAGCACAATTAATTAAGAGTGAAACGTAATTGTACA
AGCAGTTGGTCACCCACCATAGGGCATGATCAACACCGCAACCTTTCCTTTTTCCCCCAGTGATTC
TGAAAAACCCCTCTTCCCTTCAGCTTGCTTAGATGTTCCAAATTTAGTAAGCTTAAGGCGGCCTAC
AGAAGAAAAAGAAAAAAAAGGCCACAAAAGTTCCCTCTCACTTTCAGTAAATAAAATAAAAGCAGC
AACAGAAATAAAGAAATAAATGAAATTCAAAATGAAATAAATATTGTGTTGTGCAGCATTAAAAAA
TCAATAAAAATTAAAAATGAGCAAAAAAAAAAAAAAAAA
(SEQ ID NO:116)

Mus musculus Snrpd2 3'-UTR
NM_026943
AGCCTGCTCCCTGCCCTGCGAAGGCCTGCAGAACCCTGCCCAGTGGGCGAGAAATAAAACCCTGTG
CTTTTTGGTTAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:117)

Mus musculus Mgst3 3'-UTR
NM_025569
GGTGTGGAGGGCCTTCCGACTCTCACTCACCTCCAGCGACTCACCCTGATTTCCAGTTGCACTGGT
TTTTTTTTTTTTTTTAATATAATAAAAACTTATCTGGCATCAGCCTCATACCT
(SEQ ID NO:118)

Mus musculus Aldh2 3'-UTR

NM_009656
AGCGGCATGCCTGCTTCCTCAGCCCGCACCCGAAAACCCAACAAGATATACTGAGAAAAACCGCCA
CACACACTGCGCCTCCAAAGAGAAACCCCTTCACCAAAGTGTCTTGGGTCAAGAAAGAATTTTATA
AACAGGGCGGGGCTGGTGGGGGGGAAAGCTCCTGATAAACTGGGTAGGGGATGAAGCTCAATGCAG
ACCGATCACGCGTCCAGATGTGCAGGATGCTGCCTTCAACCTGCAGTCCCTAAGCAGCAAATGAGC
AATAAAAATCAGCAGATCAAAGCCACGGGGTCAGTTCTCT
(SEQ ID NO:119)

Mus musculus Mp68 (2010107E04Rik) 3'-UTR
NM_027360
CTGCTCCGAATCCACAAGATGAAGACGTCGGCTAAACTTGAGCAAGCTTTGTTAGATGGGAACATG
GAACATCACTGTACACTTATCTAAGTACCATTTATAATGTGGCATTAATAAATGTATCTGTGAATA
CC
(SEQ ID NO:120)

Mus musculus Ssr4 3'-UTR
NM_001166480
GGGCAGCAACTTCAGCCGTCCATTGCTTCTTTCAATAAACAGTCACTATTTGACATGAGTACATTC
AAGAAAAAAAAAAAAAAAAAA
(SEQ ID NO:121)

Mus musculus Myl6 3'-UTR
NM_010860
GGACATTCTGTATCCCGAGTCTGTTCCTTGCCCAGTGTGATTTCTGTGTGGCTCCAGAGGCTCCCC
TGTCACAGCACCTTGCCCATTTGGTTTCTTTTGGATGATGTTTGCCTTCCCCAAATAAAATTTGCT
CTCTTTGCCCTCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:122)

Mus musculus Prdx4 3'-UTR
Prdx4-001, NM_016764
AAAGTACTTCAGTTATGATGTTTGGACCTTCTCAATAAAGGTCATTGTGTTATTACCA
(SEQ ID NO:123)

Mus musculus Ubl5 3'-UTR
NM_025401
AGGGGGATTCCTTCTCCTCCTCGCCCTGCTCTGCCCTGCCCTCCTCTCCCATCCTCATCTGACACT
GGTGTAGATGGTCATTTTTAACAGTTCACATGAATAAAAACTTGGCTGCTGCTTTGCTGCTGTC
(SEQ ID NO:124)

Mus musculus 1110001J03Rik 3'-UTR
NM_025363
TGCAGAGAGTCCTCAGATGTTCCTTCATTCAAGAGTTTAACCATTTCTAACAATATGTAGTTATCA
TTAAATCTTTTTTAAAGTGTG
(SEQ ID NO:125)

Mus musculus Ndufa13 3'-UTR
Ndufa13-201 ENSMUST00000110167
GGCCTGAGCCAACGCACATAATAAAGAGTGGTC
(SEQ ID NO:126)

Mus musculus Ndufa3 3'-UTR
NM_025348

ATGCCTCTGCTGATGGAAGAGGCCCCTTCCCTGTTGCTCTCCAATAAAAATGTGAAAACTAATAAC
CCC
(SEQ ID NO:127)

Mus musculus Gstp2 3'-UTR
NM_181796
TGGACTGAAGAGACAAGAGCTTCTTGTCCCCGTTTTCCCAGCACTAATAAAGTTTGTAAGACAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:128)

Mus musculus Tmem160 3'-UTR
NM_026938
ACAACAGGGCTGTGGGGACTGGCTGGGCCTGACGACTGGGACATTAAAACCTGACCCTTCCGCAAA
AAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:129)

Mus musculus Ergic3 3'-UTR
NM_025516
CTCTCTCCCTTCCCCACAGCTTGTCCTGCCCTCTCTTCCCCTGTGGGTTTACCCTCCAGCCTGTCA
ACTACCCATATCCTCTCCTCAGCCAGCCCAGCCCAGGGCAATAAATATGAATTGTGATAGGAA
(SEQ ID NO:130)

Mus musculus Pgcp 3'-UTR
NM_018755
GGAGAACAAGAAGAGAGGACCTTGTTCTCTGTAGTTGGGAATCCCAACTCTGAATCTTTACAACAT
CCATCGTCACAAAAGAGTGTTATACATTTAATCCACAGGGCATAGTTTTCTTTATACCTTCTGTTA
ATCATCTTTCCTTAATACTTTCTTATCTGTTTCTAGAATAAATCATGATCCCTACTGCACCACCTT
GAAAATGTTGTTTCCAGTTTTAAAATAAGCAATAAATATTTGAAATGCTTCTGATTTTTCATTTTC
ATTTAAAAACATTAAATTAAATGTAATGAGA
(SEQ ID NO:131)

Mus musculus Slpi 3'-UTR
NM_011414
GCCTGATCCCTGACATTGGCGCCGGCTCTGGACTCGTGCTCGGTGTGCTCTGGAAACTACTTCCCT
GCTCCCAGGCGTCCCTGCTCCGGGTTCCATGGCTCCCGGCTCCCTGTATCCCAGGCTTGGATCCTG
TGGACCAGGGTTACTGTTTTACCACTAACATCTCCTTTTGGCTCAGCATTCACCGATCTTTAGGGA
AATGCTGTTGGAGAGCAAATAAATAAACGCATTCATTTCTCTATGCAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:132)

Mus musculus Myeov2 3'-UTR
NM_001163425
GGCCGCCCGGTCCTATGTGCTCCATGTCTGTGATGTGTCTGGAGTCTCTCGGGACACGACCAGCTG
ATTGTAGACACCGTGTTGATATCACTAGAAATGAAGACCTTGTCAACCAATAGAGGAACTGTCTGA
ACCAACTGGGTACTGATGTCTCTGGGAATGCCAGCCCGTGTCCTTGTTTAAGTTAATAAAGAACAC
TGTAACACGCAGGGTGATTTTAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:133)

Mus musculus Ndufa4 3'-UTR
NM_010886
ACTATGAAGTTCACTGTAAAGCTGCTGATAATGAAGGTCTTTCAGAAGCCATCCGCACAATTTTCC
ACTTAAGCAGGAAATATGTCTCTGAATGCATGAAATCATGTTGATTTTTTTTTTTTTTGGAGTTTA
TTACACTGATGAATAAATCTCTGAAACTTG

(SEQ ID NO:134)

Mus musculus Ndufs5 3'-UTR
NM_001030274
GCGGGGCAGCTGGAGGCCGCTGTCATGCTCTGTTTTCCCCTGGAGAGAATATTTAAGGAAAGCTCC
TTCATTAAGTATTAAGTATGTGGAAATAAAGAATTACTCAGTCTTAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAA
(SEQ ID NO:135)

Mus musculus Gstm1 3'-UTR
NM_010358
GCCCTTGCTACACGGGCACTCACTAGGAGGACCTGTCCACACTGGGGATCCTGCAGGCCCTGGGTG
GGGACAGCACCCTGGCCTTCTGCACTGTGGCTCCTGGTTCTCTCTCCTTCCCGCTCCCTTCTGCAG
CTTGGTCAGCCCCATCTCCTCACCCTCTTCCCAGTCAAGTCCACACAGCCTTCATTCTCCCCAGTT
TCTTTCACATGGCCCCTTCTTCATTGGCTCCCTGACCCAACCTCACAGCCCGTTTCTGCGAACTGA
GGTCTGTCCTGAACTCACGCTTCCTAGAATTACCCCGATGGTCAACACTATCTTAGTGCTAGCCCT
CCCTAGAGTTACCCCGAAGGTCAATACTTGAGTGCCAGCCTGTTCCTGGTGGAGTAGCCTCCCCAG
GTCTGTCTCGTCTACAATAAAGTCTGAAACACACTTGCCATGAAAAAAAAAAAAAAAAA
(SEQ ID NO:136)

Mus musculus 1810027O10Rik 3'-UTR
1810027O10Rik-001 ENSMUST00000094065
AGTCTCTTGTTTAAGCGCCCAGTCCTGGCCTTTCTGGGTAATTGGGCGCAGAGGGAAGGAGCCAAT
GTTGAAGCAGAAAAGAAATTAAAAGAAAAAGGCATATAAAGAA
(SEQ ID NO:137)

Mus musculus 1810027O10Rik 3'-UTR
BC117077
AGTCTCTTGTTTAAGCGCCCAGTCCTGGCCTTTCTGGGTAATTGGGCGC
(SEQ ID NO:138)

Mus musculus Atp5o 3'-UTR
NM_138597
GAGACTGTCACCTGTGTGAGCTCTTGTCCTTGGAGCAACAATAAAATGCTTCCTG
(SEQ ID NO:139)

Mus musculus Shfm1 3'-UTR
NM_009169
CATCTGGGAATGTCCCAGGAACCTCAATCATGGACTCTACCACAGTCTAGGACAGAGAAAGCAGGA
CGGGATACTTTAAAGAACATGTTTATTTCATTATCTGCTTCAATTTATTTTTGTTTTATAACAAAA
AAAATAAGTAAATAAATGTTTTGATTTAATCTTTTTGGTTCA
(SEQ ID NO:140)

Mus musculus Tspo 3'-UTR
NM_009775
AGGCACCCAGCCATCAGGAATGCAGCCCTGCCAGCCAGGCACCATGGGTGGCAGCCATCATGCTTT
TATGACCATTGGGCCTGCTGGTCTACCTGGTCTTAGCCCAGGAAGCCACCAGGTAGGTTAGGGTGG
TCAGTGCCGAGTCTCCTGCAGACACAGTTATACCTGCCTTTCTGCACTGCTCCAGGCATGCCCTTA
GAGCATGGTGTTTTAAAGCTAAATAAAGTCTCTAACTTCATGTGTAAAAAAAAAAAAAAAAA
(SEQ ID NO:141)

Mus musculus S100a6 3'-UTR

NM_011313
AATGGGACCGTTGAGATGACTTCCGGGGGCCTCTCTCGGTCAAATCCAGTGGTGGGTAGTTATACA
ATAAATATTTCGTTTTTGTTATGCCT
(SEQ ID NO:142)

Mus musculus Taldo1 3'-UTR
NM_011528
TGCAACACCCGAGGCCCCAGTCCTGCACCGAGGCTGACCCCAGACCTGCACTGCCTTTGAGCTGGG
TCCTAATTGCACATGGCTTGTGACGAATGAATCTTGCATTTTTTAGTGATCGGAGAAGGGATGGAT
CATAGGATTCTGATTTTATGTGAAATTTTGTCTAATTCATTAAAGCAGTTGCTTTTCCTATGCTGT
TT
(SEQ ID NO:143)

Mus musculus Bloc1s1 3'-UTR
NM_015740
ACTAAAACCCACCCCTCTTACTTCACCCTCCTGGACAGGAGGGAAACTGGTGAGCCACGAATAAAA
ACACAAGCTTCCATTCT
(SEQ ID NO:144)

Mus musculus Ndufb11 3'-UTR
NM_019435
TGGCTTACCGAGCAGGGCCTAAGAAGCATTACTCATCCGCTGCTTGTTATTTACCTGGTTCCTCAG
AACACCTTATTAAAGGAATTGAAAGTA
(SEQ ID NO:145)

Mus musculus Map1lc3a 3'-UTR
NM_025735
GTCAAGAGGAGGGGAGGGGGGTGGCTGGGAGTTCTGGTCAGGTTCTCCCCAGGGAGGTCCTGGCTC
CTAAACTAAGCTATTTCAGTCCCCAGTGGATTAGGCAGAGATGTGACACCCACTCCCCCCCCCAGG
TAGGGGCCACCAGCCAGCCTACCACATCCTGGGTAGGTCCTGGGCCAGTCATGTTCGGGTTGCTCT
TTTGGGTGCTGGCTGGGTTGGGAGTGGGTGGGGAGCAGCATCCCTGCTCTGTGGGGTTTGTCATTT
TGTTAGGCCCTTGCCTGTCTGCCCATCTTGCCCCTCATCCACCTGAGGCTTTGCCTCCTGCCAGGA
CCTGCCCCACCCCTGAAAGGCTGGCTCCCCTTGTCCTGACTCGGTGTATGGATCTGTGGTCATTTC
CTCTGCAGAAAGAATAAAGACTGCTCAGGCCTGCCTGGCCAAAAAAAAAAAAAAAAAA
(SEQ ID NO:146)

Mus musculus Morn2 3'-UTR
NM_194269
ACCTGCTGCCTTAACGCTGAGATGTGGCCTCTGCAACCCCCCTTAGGCAAAGCAACTGAACCTTCT
GCTAAAGTGACCTGCCCTCTTCCGTAAGTCCAATAAAGTTGTCATGCACCCACAAAAAAAAAAAAA
AAA
(SEQ ID NO:147)

Mus musculus Gpx4 3'-UTR
NM_008162.2
CTAGCCCTACAAGTGTGTGCCCCTACACCGAGCCCCCCTGCCCTGTGACCCCTGGAGCCTTCCACC
CCGGCACTCATGAAGGTCTGCCTGAAAACCAGCCTGCTGGTGGGGCAGTCCTGAGGACCTGGCGTG
CATCCCTGCCGGAGGAAGGTCCAGAGGCCTGTGGCCCTGGGCTCGAGCTTCACCCTGGCTGCCTTG
TGGGAATAAAATGTAGAAATGTGAAAAAAAAAAAAAAAAA
(SEQ ID NO:148)

Mus musculus Mif 3'-UTR

NM_010798.2
GTCCTGGCCCCACTTACCTGCACCGCTGTTCTTTGAGCCTCGCTCCACGTAGTGTTCTGTGTTTAT
CCACCGGTAGCGATGCCCACCTTCCAGCCGGGAGAAATAAATGGTTTATAAGAGACCA
(SEQ ID NO:149)

Mus musculus Cox6b1 3'-UTR
NM_025628
CCTGGCTCCGCCCACCTCTCCTCTGTTCTTTGTCTTTCTCCCCGGATAGAAAAGGGGGACCTCAGC
ATATGATGGTCCTTACCCTGGGACCCTGAATCATGATGCAACTACTAATAAAAACTCACTGGAAAA
GTT
(SEQ ID NO:150)

Mus musculus RIKEN cDNA2900010J23 (Swi5) 3'-UTR
NM_175190
GCAGCTTCTTGGAGATTTTCATCTACAGCCCACAGGGACAGGAGGATGGGGGCATAAAAGGCAGAG
TCTAGACAGTATGTTCATATGGTTTTCAGATTTTAAAAGATGCTAGAAGCCCTCCAAAGTTTGGGG
TGGGTTCTAGAGAAGAGGAGTATTGGGAGGGGTGGGTATTGTCAATGTTAAGGTTCCTAAACATAC
TTGTGAGTAGGTGTGTGTGGTTGTCCCTTTTGTTAATAAACATATGAGCAGTCAAAAAAAAAAAAA
AAA
(SEQ ID NO:151)

Mus musculus Sec61g 3'-UTR
NM_011343.3
GTCCTTCTCATCATGGGACGAGTGAGCCAGAGCGGGGGAAAGGGCATGAAGTAAAGCGTTGCCTGA
ATGCTGTGTGGTGTTTTGTTTCTTCCTCCTTCCTATGAGGTTTTCTACTTCTCAATTAAAATAATT
TCAAAATAAACACTTTTTCCATAACAGA
(SEQ ID NO:152)

Mus musculus 2900010M23Rik 3'-UTR
BC_030629
CCGTGGGGTCTGATACTCATCAATAAAACTGCCTGGTTTCTCCCACAAAAAAAAAAAAAAAA
(SEQ ID NO:153)

Mus musculus Anapc5 3'-UTR
Anapc5-201 ENSMUST00000086216
CCAGGACTCCCTGCTTGATGGTGTGCATTTAGGGGTGGGTCATTACATGCTATCTTGTCAATAAAC
TGTTCTGATCAGTTTGTCTGAAGTGGGTTTTTTTTTATTTTTCTGGGTTGAATTGTCAGTATCTTT
GTTAAGAACTGTGTATCTAGGGGCTGGAGAGATGGCTTAGCAGTTAAGAGCACTAACTGTTCTTCT
AAAGGACCTGGGTTCAATTCCTAGCACCCTCATGACAGCTCACAGCTGTCTGTAACTCCTGTTCCA
GGGACTCTGACACCCTCAGGCAGACATAAAAGCAGTCAAAACACCGATGTACATAAAATTAAAATA
AATTATTT
(SEQ ID NO:154)

Mus musculus Mars2 3'-UTR
BC132343.1
GAACTCAGCTCTTACTGACTGGTAGTAAAAGATCAAATGTATTCTTTTTGCGTTTTTAAGTAAAGT
CATGC
(SEQ ID NO:155)

Mus musculus Phpt1 3'-UTR
NM_029293
AGCTCTGCCCCACCCCCCACCCCCCGGACTAAGTCAGGTCTCTGCTCTTGCTGTGTTCTGTTTTGA

GGGGCTGGCCCTGTGCTTTCCTTTTGTACCTTAGGCAGCATAGCACCTGCCAGGCCTTAGAGGCCA
GACCAATCTGGTCCATAGGAATTAAAAGCATTGATATGCCTACT
(SEQ ID NO:156)

Mus musculus Ndufb8 3'-UTR
NM_026061
GGAGGCTTGATGGGCTTTTTGCCCTCGTTCCTAGAGGCTTAACCATAATAAAATCCCTAATAAAGC
(SEQ ID NO:157)

Mus musculus Pfdn5 3'-UTR
NM_027044
GAGTGCACTGCAGAAATGAAGCAGAGTGAGGGACCCTTCTTCAAGGGGCCTGGGACTTTTTCCGGC
AATGGCCTCCTGGGAAAGTGGCCTGGGAAGAGAGTGTTTTGTGTTTAATGTTAATAAATGTGACCG
CTGCGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:158)

Mus musculus Arpc3 3'-UTR
NM_019824
GAGGAGCCTGGGCAGCACCATCACGTGGAGACACATCATAGGACACACAGGCCAATGTGTCTGTTC
ATACCTACCGTATCAAGGAGAGAAGAGAGCCTGTCTTTGCTGGAAAAGCTCTTGGTCAAGAATTGG
GAGGGTGGGTGTTGGGCGATTTCGATTTTTGGCAGTTTTAAGCTGGTACTTAATATATAATAAATG
TCACTGCTTATGTTAGACATTGAATTAAAACATTTTTGAGAAAAAGCTTTAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAA
(SEQ ID NO:159)

Mus musculus Ndufb7 3'-UTR
NM_025843
GGATTACCCGCCAGCCTGTGGACCTATCAGTGAAATAAAAGCTTTGGGTCACCTGCCT
(SEQ ID NO:160)

Mus musculus Atp5h 3'-UTR
NM_027862
AGCAGCCTGGGACGGAGCCCCGGCCGACATGAAATAAAACATTTAAATAGT
(SEQ ID NO:161)

Mus musculus Mrpl23 3'-UTR
NM_011288
CCTATGACAGCAGGATTTGGACCACAGACCCTAGTGAGCACAGTGGTTCTGACAAGCCCAAATAAA
AATTCTTTGTGGAG
(SEQ ID NO:162)

Mus musculus Tomm6 3'-UTR
NM_025365.3
CCAGAGAATGGAACTCCTGTGTATTCAGACTTTCCAAAGACAGCCTACTGTCTGTGACCACAAGAT
CCTACCTGAGTGGCAGCTGAAGTTGACTCCCTCTCCTTGCCTGAACCCCCCCCCACTGCCCCCCCA
TCCCCCAGTGTCGGCTGAGATGTTGCCTCTGCACGGTTCTGTGTGCAGTTCCCAACTTTCTGCAGA
AGATGGTCCTTGCCCTTGTCCTGAAGAGTAGTAATGGTTCTTGAAAAAGATTTCAAATAAAGCCTG
CACATAAAAGACAGGTATTTTATTCTTTTAATAAGAAACTTATTACAAAAACAAGGTGTAAAAAGT
CCGCTTACAAAAATCAAATAAACATGACTTGTATTTCAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:163)

Mus musculus Tomm6 3'-UTR

Tomm6-002 ENSMUST00000113301
CCAGGTGAGAGCAGTTCTCCTGTGTTTCCCCGTTTCTGATGCTGTTATCTGCTTACAGAGAATGGA
ACTCCTGTGTATTCAGACTTTCCAAAGACAGCCTACTGTCTGTGACCACAAGATCCTACCTGAGTG
GCAGCTGAAGTTGACTCCCTCTCCTTGCCTGAACCCCCCCCCCACTGCCCCCCCCATCCCCCAGTGTC
GGCTGAGATGTTGCCTCTGCACGGTTCTGTGTGCAGTTCCCAACTTTCTGCAGAAGATGGTCCTTG
CCCTTGTCCTGAAGAGTAGTAATGGTTCTTGAAAAAGATTTCAAATAAAGCCTGCACATAAAA
(SEQ ID NO:164)

Mus musculus Tomm6 3'-UTR
CCAGAGAATGGAACTCCTGTGTATTCAGACTTTCCAAAGACAGCCTACTGTCTGTGACCACAAGAT
CCTACCTGAGTGGCAGCTGAAGTTGACTCCCTCTCCTTGCCTGAACCCCCCCCCCACTGCCCCCCCA
TCCCCCAGTGTCGGCTGAGATGTTGCCTCTGCACGGTTCTGTGTGCAGTTCCCAACTTTCTGCAGA
AGATGGTCCTTGCCCTTGTCCTGAAGAGTAGTAATGGTTCTTGAAAAAGATTTCAAATAAAGCCTG
CACATAAAA
(SEQ ID NO:165)

Mus musculus Mtch1 3'-UTR
NM_019880
CCTAAGCTGCCCGACCAAACATTTATGGGGTCTTAGCCTACCCCTGGTGAGGACCCATCATCTCAG
ATGCCCAAGGGTGACTCCAGCCCAGCCTGGCTTCATGTCCATATTTGCCATGTGTCTGTCCAGATG
TGGGCTGGTGGAGGTGGGTCACCTGGGACCTGGGGAAGCCTGGGGGAGCAGTGTTGGGGTGGCATC
CCCTTCCTGCCTAGAGGTACTGGAGTCCATCTTGTACTCAGGCAGAGGCAGGCTGCAGAGGCAAAC
GTCACTCAGTGGCAAGGCTTCCCTGCACCTCTAGCCCAGCTCATCCTGCCAGTCAGCCAGAAGCAC
CCCCGCCCCCCACTTCCTGCTTTGTAAATTGGGCGCCATCACACCTGGGCCATGGGAGGCTGGAGC
TATGTTCCCAACACTAATTTTCTTATACAAGGGTGGTGCCTTCTCCTGAATAGGAAATCATGTTCT
CCTCAGACCATCCCCTCATCTGCTTGTCTGTGCTGGTGACGCCAGGTGTGAGGGTTCAGTCACTGT
GCTGGGTGCGAATACGCACAGGTTACATAGGCCGACATCTAGTCCTCCCCTCGTGGTAAGATAGAC
CCATCTCCTCGAATAAATGTATTGGTGGTGATTTGGA
(SEQ ID NO:166)

Mus musculus Pcbd2 3'-UTR
NM_028281
TCTGCGCCTGCCTTGTCTGCAGCGTTGTTTGCAAGCCACTTATGTTAATAAATTGTCATAAAGTAG
TTCATAGTTACATGTATACATTGTTGTATGATTGATGCTCAAATACAGAATGATTTGAAGCCAAAA
AAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:167)

Mus musculus Ecm1 3'-UTR
NM_007899
GTCACCCTGAGCCTCAGAGGATTAGATGGGGGAACTCCGCCCTACTCCACCCTCCTCGAACACTCA
TTACAATAAATGCCTCTTGGATTTGGC
(SEQ ID NO:168)

Mus musculus Hrsp12 3'-UTR
Hrsp12-001 ENSMUST00000022946
CTATAAGTAGCCATGCTGATGTTGACTCCGGAGGTTTTAGAATGTCTTTCACACTTTAATTTTTAC
AAATGATGCTGGGAAGTATAAAAATGACCAGAGTGGTTGAAGTTATTGTGGAAGTGATCAAATATG
TGGAGATTTGACATTAATTGGAGATTATTCAGTATAGTGACTGATGTTCTAATTTCACTTATGTTG
CTGGGTGTGAGAGAAGAGGTGCACAGCTACTGAGATGGGAAGCAGAAGGAAAGATGGGCTGTTGTA
CATGAGAAATAGTAAGGAGCACATCTACTTAAATCATATTAATTTGCTCATGTGAAATACTTAGTT
CTTATGTTAGATATAAGAAACTAAATTGAAATATTCAAACTTGAATAGTACCAGGAGAACAAGTGG
ACCAAAATCTTATACAGATAATATTACTTTAATTGAAATAAAAAATAGATGTGTAACTTTCC

(SEQ ID NO:169)

Mus musculus Mecr 3'-UTR
NM_025297
TTGCTCCAGAGGACCAGGAGGAAAGCAGGAGAGGCAAGACTGGCTGTCTGCTGGCCCCTCCATGAG
AACCCCAGCCTTCCCAGACTGCCTCACCCATATTGTCTCTTCCTACCAGGAGGGTGGGGGACCAAC
TCTAGGCTCCCTAATAAACCCTTAACTTCCCGAGTGGAGGATGAAGAGTAC
(SEQ ID NO:170)

Mus musculus Uqcrq 3'-UTR
NM_025352
ACGGCCTGCACCTGGGTGACAGTCCCCTGCCTCTGAAAGACCCTTCTCTGGGAGAGGAATCCACAC
TGTAGTCTTGAAGACAATAAACTACTTATGGACTTCCCTTTGAAAAAAAAAAAA
(SEQ ID NO:171)

Mus musculus Gstm3 3'-UTR
NM_010359
GCCCCTGCCATGCTGTCACTCAGAGTGGGGGACCTGTCCATACTGCGGATCCTGCAGGCTCTGGGT
GGGGACAGCACCCTGGCCTTCTGCACTGTGGCTCCCGGTTCTCTCTCCTTCCCGCTCCCTTCTGCA
GCTTGGTCAGCCCCATCTCCTCATCCTCACCCCAGTCAAGCCCATGCAGCCTTTATTCTCCCCATT
TTTTTTTCACATGGCCCCTTCTTCATTGGTGCCCAGACCCAACCTCACAGCCCTTTTCTGCAATCT
GAGGTCTGTCCTGAACTCAGGCTCCCTAGAGTTACCCCAATGGTCAACACTATCTTAGTGCCAGCC
CTCCCTAGAGATACCCTGATGGTCAATACTATCTTAGTGACGGCCCTCCCTAGAGTTACCCTGAAG
GTCAATACTCGAGTGCCAGCCTGTTCCTGTTTAAGGAGCTGCCCCAGGCCTGTCTCATGTACAATA
AAGCCTGAAACACACTTGAAACACAATAAACACTGAACACTTGCTGTGA
(SEQ ID NO:172)

Mus musculus Lsm4 3'-UTR
NM_015816
TCACTCCCTGCCTGAGCCGAGCCCAGAACGGTGGGTGAGGCCTCAGGGCACCTTTGTGTGAAGCCC
CACTTGGCGTCTGGTCCAGTGAAGTCCCTCGCTGGCCACTGACTCAGTTTCTGGAAGGTTCCGAGT
CTGAGGTGCCTGTGGAGCCTTAGATGCCCTTTGAAGGGCTGACTTCTTCCAGGCATGTTTGAGTTT
CAGTTGGAGCTGCAGGCTCAGCCCATGGCGGCTCACCTGTCCTTTACCAGCCATACCCTGTACATC
TTCTGTTTGAAAAATAAAAGCAAACACCATAGAAAGAAAAAAAAAAAA
(SEQ ID NO:173)

Mus musculus Park7 3'-UTR
NM_020569
AGCCCAAGCCCTGGGCCCCACGCTTGAGCAGGCATTGGAAGCCCACTGGTGTGTCCAGAGCCCAGG
GAACCTCAGCAGTAGTATGTGAAGCAGCCGCCACACGGGGCTCTCATCCCGGGTCTGTATGTTTCT
GAACCTTGCTAGTAGAATAAACAGTTTACCAAGCTCCTGCCAGCTAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:174)

Mus musculus Usmg5 3'-UTR
NM_023211
ATGGATTTTGAAATGTCTGACCTCACCTGTTAAGTCCCATGCCTGAAGAAGCTGATGTGAACTCAT
CATGTAATACTCAATTTGTACAATAAATTATGAACCCAAAAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:175)

Mus musculus Cox8a 3'-UTR
NM_007750
AGGGAGCAGTCTTCCCTCATCCTTTGACTAGACCACTTTTGCCAGCCCACCTTGATCATGTTGCCT

GCATTCCTGGCTGGCCTTCCCCGGGATCATGTTATTCAATTCCAGTCACCTCTTCTGCAATCATGA
CCTCTCGATGTCTCCATGGTGACAACTGGGACCACATGTATTGGCTCTGCTTGGTGGGGTCCCCCT
TTGTAACAATAAAGTCTATTTAAACCTTGCTCC
(SEQ ID NO:176)

Mus musculus Ly6c1 3'-UTR
NM_010741
TGGTCCTTCCAATGACCCCCACCCTTTTCCTTTTATCTTCATGTGCAACCACTCTTTCCTGGAGTC
CTCTAGTGACAAATTATATGTTATAGAAGGTCCAATGTGGGGATAGTGTGTGGAACACCCTGTTTC
ACCTTTATAGCCCCTGCTGGGTAAGTGCCCGACTCCTCTCTAGGGCTTTCAAATCTGTACTTCTTG
CAATGCCATTTAGTTGTGGATTTCTATTCTTGGCCCTGGAGGCATGTGGCCAGCACATGCAACAGG
CAGTATTCCAAGGTATTATAGTATCACCATCCACACATAAGTATCTGGGGTCCTGCAGGGTTCCCA
TGTATGCCTGTCAATGACCCCTGTTGAGTCCAATAAAAGCTTTGTTCTCCCAGCCAAAAAAAAAAA
AAAAAAA
(SEQ ID NO:177)

Mus musculus Ly6c1 3'-UTR
NM_001252058.1
ACTCATAAAAATGCTCCTGCCTCGGTCTTCCAAGTTCTAGGATTGCAAGTCTGACTTCAACATGCC
TTACAGACAACTCTGGGACATCCAGGCCTAGTGGCATGTTGCCCAGATATGGGGATGCTCTGTGGC
CCCTGCATAAGAAGTGAGTCACTCCCTGATTTCTTGCAGACTCTCAAAGAAGGAAACTAAAGACCC
GTCAGTGCCTTTCTTTCTGCCCTGCTGGTGTGCCAATCAGGGATCCTAACATCAGGGAGAGGACTT
CCTGTTGCAGCGAAGACCTCTGCAATGCAGCAGTTCCCACTGCAG
(SEQ ID NO:178)

Mus musculus Cox7b 3'-UTR
NM_025379
TCGTGCCAGCTGGTACAATAATCAAGGAATTGTTTAAAACCAACTTATAAGTGAATGCCAAGTCAA
AGAATCATGTACTCATTATACTATGGCAGATTGAAGAACAAATAAAGAAATAAAGTACCTTAACCT
TCATTCTAGGCTTTGTTTTTTTCCTTTGTAAATGAAGCCCAAGCATGGTGACTTCTCATTTATTTA
AGCTGTATTGTCTCTTAAAATGGCTTTTTACCCTATGAGGTGGTATGAGGGAAATCTATGATCAGG
AGGGCACCTTTATAGTAAGCTGAAATTACAGAGAATGAAGAAATAAGCACAGAGCTGTTTTAGGAG
CCCACTGGGTCATTGGCCATATAGGTTATGCTTACTGCCCTCTACCTCGTGGTTATATTTGGAATT
GCCATTAGCTCCCTTCTGCTTAGAGACTGGACTGTCACCAAACCCAAGGGGATAGTGATCCTGTAA
TGATCCTGTGTGAACTAGGTTTGCTAAAGACTACCACCTCCTTACACTGTATGGCATATTCATCTG
AAATAGGTGCTAATTTTTCAGCATAATCCTTAATCTTTAGGATCTGTCATACTTCCTAGTAATTTA
ACTGTTGCTGAAGAAATAAAGGCTATCTGTTAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAA
(SEQ ID NO:179)

Mus musculus Ppib 3'-UTR
NM_011149
AGAGCCTGGGGGACCTCATCCCTCTAAGCAGCTGTCTGTGTGGGTCCTGTCAATCCCCACACAGAC
GAAGGTAGCCAGTCACAAGGTTCTGTGCCACCCTGGCCCTAGTGCTTCCATCTGATGGGGTGACCA
CACCCCTCACATTCCACAGGCCTGATTTTTATAAAAAACTACCAATGCTGATCAATAAAGTGGGTT
TTTTTTATAGCTTGAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:180)

Mus musculus Bag1 3'-UTR

NM_009736
AGTGCAGTGGAGAGTGGCTGTACTGGCCTGAAGAGCAGCTTTACAGCCCTGCCCTCTCTGGAACAG
AAGTCGCCTGTTTCTCCATGGCTGCCAGGGGCAACTAGCCAAATGTCAATTTCCCTGCTCCTCCGT
CGGTTCTCAATGAAAAAGTCCTGTCTTTGCAACCTGAATTAGACTTGTGTTTTCTCAAAAAAAAAA
AAAAAAA
(SEQ ID NO:181)

Mus musculus S100a4 3'-UTR
S100a4-201 ENSMUST00000001046
AGACTCCTCAGATGAAGTGTTGGGGTGTAGTTTGCCAGTGGGGGATCTTCCCTGTTGGCTGTGAGC
ATAGTGCCTTACTCTGGCTTCTTCGCACATGTGCACAGTGCTGAGCAAATTCAATAAAAGGTTTTG
AAACTATT
(SEQ ID NO:182)

Mus musculus Bcap31 3'-UTR
NM_012060
AGGCTTGGTGTTTCCCTGCCTGCCGCTGGCTTCTACCTGACCCATGCTTACTGCTTCCTTGGAGCC
CAGACTATCCCTCTGGTACTTGGGTTTATTCCCTACTTCCCCAATTTTCTTCCATGGCTTATAGAT
CATTATTTTGGCACCATTACACATACTGCTCTTATACCAAAAGGGACCTGATTGTTGTTTATTCAG
AGTACTTTTGCCACTGTTCTGCCTGGCTAGGGCACTTTCCACTCCTGGAAGTGTAGAAAAGCACTG
GTGACCTGGCCTGCAGTTTGAACCCCTTTTTATTTTGCAATGTACCCTAAAGGAGGCTGCTGTGAA
GCAGGTCAACTGTTTTATCCTGAGGGGAATAAATGTTGTTATGT
(SEQ ID NO:183)

Mus musculus Tecr 3'-UTR
NM_134118
GCAGCTCCTCACGGCTCTGCCCAGTAATACTCTCCACCCCTCACTGCCCCTGTCCTGATGTGTGGC
TGGCCATGGCTCTCCAGCAGCAACAATAAAACCTGCTTACCCAAAAAAAAAAAAAAAAAA
(SEQ ID NO:184)

Mus musculus Rabac1 3'-UTR
NM_010261
AGTGTCCTCCAGGACCTGCCGGCCTCTCCTGCCGGCCGGCTGTCCCATCTCTGTCTGTTCTCGTCC
TACCTGGCCTTGCTGCTCAGCTCCGAGCCTTCCACCTGAGGCCTCAAACCCAGGGAGGGGCTTTTG
TCTTTGGAAATAAAGCTGTTACAATTGCTATTTGGCCAA
(SEQ ID NO:185)

Mus musculus Robld3 3'-UTR
NM_031248 (Lamtor2)
CAGCGTGATGGAGGCTGGAGTAGAAAAGGGATGATGATCTGGAGGGAGGGGCGGGGCCCTAGAAAC
GCCATATCGGGCGAGGTACAGGAAGGGGGGGTTGCTTTTTTCTGAATAAATTTTCAACTCTTAAAA
AAAAAAAAAAAA
(SEQ ID NO:186)

Mus musculus Sod1 3'-UTR
NM_011434
ACATTCCCTGTGTGGTCTGAGTCTCAGACTCATCTGCTACCCTCAAACCATTAAACTGTAATCTGA
AAAAAAAAAAAAAA
(SEQ ID NO:187)

Mus musculus Nedd8 3'-UTR
NM_008683

AGAAACTTGGTTCCGTTTACCTCCTTGCCCTGCCAATCATAATGTGGCATCACATATCCTCTCACT
CTCTGGGACACCAGAGCCACTGCCCCCTCTCTTGGATGCCCAATCTTGTGTGTCTACTGGTGGGAG
AATGTGAGGACCCCAGGGTGCAGTGTTCCTGGCCCAGATGGCCCCTGCTGGCTATTGGGTTTTAGT
TTGCAGTCATGTGTGCTTCCCTGTCTTATGGCTGTATCCTTGGTTATCAATAAAATATTTCCTG
(SEQ ID NO:188)

Mus musculus Higd2a 3'-UTR
NM_025933
GTATAGCCGGGTCTTAAAGCGCCATGGAAACCATTACAAAACCCAGGAACAACAGACATCCCTGTC
AGACTTGCTCCCTCCGTTTCAGACCGGACCTTATTGTCATTTGGGTGAGGAAGTGGCCGATTTTGT
AACTGATTTGCGCTTCCACCGCTGCCCCCTCCCGCTCCCAAAATCCCAGGTTCATTTCAGTTGGGT
TGCATGCTTCTATTTGTGATGCGTCCCCTTAATTACTTAATAAAAGCTTATTACACTTG
(SEQ ID NO:189)

Mus musculus Trappc6a 3'-UTR
Trappc6a-001 ENSMUST00000002112
GGACCCCAGACCCCAGGCTTGCCCTTCCCTAAGCTTAGCCTCGGAATGTGGCACCTGACCCTGCCT
CACTGCTCACCTTTGCAGGTCGCCTTGAAGCTGGAGCTCACAGGCTCTGGGGAGGTCACATGTGCT
TCAGACAAGGGAATGAAAGGGCCGGGAGGGTCCCGGGAGGTGGGACCATCCCCTGAGTTCCAAGTC
AGCATGGAGGGACATTAGGGCATCACCCAGATGACAGATGTTCAGTAAAGGTTCTTTATGTGCAAA
CAGA
(SEQ ID NO:190)

Mus musculus Ldhb 3'-UTR
Ldhb-001 ENSMUST00000032373
CTGCCAGTCTCTAGGCTGTAGAACACAAACCTCCAATGTGACCATGAACCTTTAGTCTTCAGCCAT
GTATGTAGGTCACAGTTTGCTTCTTCCCTGACATGTGATATGAGCTCACAGATCAAAGCCCAGGCT
TGTTTGATGTTTGCACTAGGAGCTCCTGATCAAATAAAGTTAGCAATTGCAGCATA
(SEQ ID NO:191)

Mus musculus Nme2 3'-UTR
Nme2-001 ENSMUST00000021217
ACATGAAGAAACCAGAATCCTTTTCAGCACTACTGATGGGTTTCTGGACAGAGCTCTTCATCCCAC
TGACAGGATGGATCATCTTTTCTAAAACAATAAAGACTTTGGAACT
(SEQ ID NO:192)

Mus musculus Snrpg 3'-UTR
NM_026506
CCTGTGCTCAGCAAGCAGTGTCCACATCCCTCCCCAAAGGCCTGTTTGATTGTGATGTAGAATTAG
GTCATGTACATTTTCATATGGAACTTTTTACTAAATAAACTTTTGTGATACTC
(SEQ ID NO:193)

Mus musculus Ndufa2 3'-UTR
NM_010885
AGGTCTCCACTGAGGACTGTGAGCGAGAGCAGCTGAACCTGCTGGACTGAAGACAGTGTGGGGAAA
TGTGTGCTTTGGGTCCTTATAAAGCTTACGCTGTACAGTGTCCCTTCAGAATGTCCTCTTCATTAC
CTTCTCCCTCTTACTGCGCAACACTGAGGCAAAGTAGTTTTATATAAAAATACTCCTTTATTTCTC
CTCAAAAAAAAAAAAAAAAAAAACCCACCAGGTGCCA
(SEQ ID NO:194)

Mus musculus Serf1 3'-UTR
Serf1-003 ENSMUST00000142155
TGACTGGCTTTTTGGAAAACCTGGGTGCTATTGCCAGTGGGTGCATCATACGCTCTAAGATTAAAA
TTTCACAGTGACTAATCATTATATGTGTTATAACTTGTCCTTATAAAACTATTTTAAACTTTACTC
TTCAGCCTATCTTAATGTGATGTTTTAAGACCATCAAAAAATAAAGTACTGACCTTGCATGTAA
(SEQ ID NO:195)

Mus musculus Oaz1 3'-UTR
Oaz1-001 ENSMUST00000180036
GTGCCAGCCCTGCCCAGTGTCCCTGTGCCCTCTCCTGGGTTAGTCCACATGTCGTGATTGTGCAGA
ATAAACGCTCACTCCATTAGCGGGGTGCTTCTTCGAGCTGAATGCTGTGTTTGTCACACTCAAGTG
TTGGCTTTAATTCTAAATAAAGGTTTCTATTTTACTTTTTTATTGCTGTTTAAGATGGTCAGGTGA
CCTATGCTATAGCAGTCTCCTTTGAAGTCTGGAAAAATAGTGTCACCTCCCCTGGCTCAAATCCAA
TAAAGTGATCTCGTTCATTGGC
(SEQ ID NO:196)

Mus musculus Ybx1 3'-UTR
Ybx1-001 ENSMUST00000079644
ATGCCGGCTTACCATCTCTACCATCATCCGGTTTGGTCATCCAACAAGAAGAAATGAATATGAAAT
TCCAGCAATAAGAAATGAACAAAGATTGGAGCTGAAGACCTTAAGTGCTTGCTTTTTGCCCTCTGA
CCAGATAACATTAGAACTATCTGCATTATCTATGCAGCATGGGGTTTTTATTATTTTTACCTAAAG
ATGTCTCTTTTTGGTAATGACAAACGTGTTTTTTAAGAAAAAAAAAAAAAAAGGCCTGGTTTTTCTC
AATACACCTTTAACGGTTTTTAAATTGTTTCATATCTGGTCAAGTTGAGATTTTTAAGAACTTCAT
TTTTAATTTGTAATAAAGTTTACAACTTGATTTTTTCAAAAAAGTCAACAAACTGCAAGCACCTGT
TAATAAAGGTCTTAAATAATAA
(SEQ ID NO:197)

Mus musculus Ybx1(v2) 3'-UTR
with mutation T128bpG and deletion del236-237bp
*TTT*TTATGCCGGCTTACCATCTCTACCATCA
TCCGGTTTGGTCATCCAACAAGAAGAAATGAATATGAAATTCCAGCAATAAGAAATGAAC
AAAGATTGGAGCTGAAGACCTTAAGTGCTTGCTTTTTGCCCGCTGACCAGATAACATTAG
AACTATCTGCATTATCTATGCAGCATGGGGTTTTTATTATTTTTACCTAAAGATGTCTCT
TTTTGGTAATGACAAACGTGTTTTTTTAAGAAAAAAAAAAAAAGGCCTGGTTTTTCTCAATA
CACCTTTAACGGTTTTTTAAATTGTTTCATATCTGGTCAAGTTGAGATTTTTAAGAACTTC
ATTTTTAATTTGTAATAAAGTTTACAACTTGATTTTTTCAAAAAAGTCAACAAACTGCAA
GCACCTGTTAATAAAGGTCTTAAATAATAA
(SEQ ID NO:198)

Mus musculus Sepp1 3'-UTR
NM_009155
ATTATTTAAAACAAGGCATACCTCTCCCCAACTCAGTCTAAAGACACAATTTCATTTTGAGAATGT
TTACAGCCCATTTAATTAATCAGTGAACTAAAAGTCATAGAAATTGGATTTGTGCAAATGTAGAGA
AATCTACCATATTGGCTTCCAAAATTTAAAAATTTTATGCCACAGAACATTTCATCCAAATCAGAT
TTGTACAATAGGGCACCTGAAAAGTGACTGCAGCCTTTGGTTAATATGTCTTTCTTTTTCCTTTTT
CCAGTGTTCTAGTTACATTAATGAGAACAGAAACATAAACTATGACCTAGGGGTTTCTGTTGGATA
GCTTGTAATTAAGAACGGAGAAAGAACAACAAAGACATATTTTCCAGTTTTTTTTTTCTTTACTTA
AACTCTGAAAACAACAGAAACTTTGTCTTCCTACTCTTACATTCTAAACCGATGAAATCTTTAACA
GATTACACTTTAAATATCTACTCATCATTTTCTCTCTCAGAGTCCTAGCTTGAGTTGCACTGCATG
TATCTGTGCATCTTGTTCTCTTCATTTAATGCTGTACTGTTCTGCTGAGCTCTGAGGGACTATCTT
GAGAGATGTAATGGAAGGAAAGCGTGGTGTTAATCTGCGTACTGCTTAAGACAGTATTTCCATAAT
CAATGATGGTTTCATAGAGAAACTAAGTCCTATGAACCTGACCTCTTTTATGGCTAATACGACTAA

GCAAGAATGGAGTACAGAATTAAGTGGCTACAGTACACACTTATCAAAATAAATGCAATTTTAAAA
CCTTTC
(SEQ ID NO:199)

Mus musculus Gaa 3'-UTR
Gaa-001 ENSMUST00000106259
GAGAGTCCGTCGTTTACAGAGGCCTCCAGGGAGGCAGAGGGAGCTTGAGCTGGCTCTGGCTGGTGG
CTCCTGTAAGGACCTGCGTCCTGCTCTCCTGACACATCTTTGAGCTTTTCCCACCGTGTTACTGCA
TGCGCCCCTGAAGCTCTGTGTTCTTAGGAGAGTGAGGCTCGCCTCACCTGCCCCACCCCAGCTGTC
TGTCCCTCACCTGGCACTAGAGAATGTGGAGCTCGGCGTGGGGACATCGTGTCTGCACCAACATCA
GGCTGTGCAGCCACTGCAGCCGCAACCCTGCAGAGACAGAGCTGGTGCCTTCACCAGGTTCCCAAG
ACTCGAGAAACTTACTGTGAAGTGTACTTACTTTTAATAAAAAGGATATTGTTTGGAAGC
(SEQ ID NO:200)

Homo sapiens ACTR10 3'-UTR
ACTR10-002 ENST00000254286
AAGTTTGATTAAAAATCAACCTTGCTTCATATCAAATATTTAACCAATTATAAGCAAATTGTACAA
AGTATGTAGGATGTTTTGTTATAGAGGACTATAGTGGAAGTGAAAGCATTCTGTGTTTACTCTTTG
CATTAATATATAATTCTTTTGACTTTGTTTCTCTTGTGTAGTGGTAAAATGGTAGCTGGTGCTTAT
TGAGATTTGCTGTATTTATATCAATAAAGTATAGTAAAGCAGTTTGATTTTGGAAGTTTGTTATGT
GGCTTTTTTTTTTTTTTTTTTTTTGAGACGGAGTCTCGCTCTGTCACTTAGGCTGGAGTGCAGTGG
CACAATCTCTACTCATTGCAAGCTCCGCCTCCCGGGTTTACGCCATTCTGTCTCAGCCTCCTGAGT
AGCTGGGACTATAGGCATACGCCACCCCGCCCGGCTAATTTTTTGTATATTTAGTAGAGACGGGGT
TTCACCATGTTAGCCAGGA
(SEQ ID NO:201)

Homo sapiens PIGF 3'-UTR
NM_173074
GTAACTTAATCCTGACAACCGTAGTGCAAGGTATGGCCCATCTCCTGTACGCTTGGAGCGACCTTT
GGCTACGTGGCTGGCCTTGTTATTTCACCACTCTGGATATACTGGAATAGAAAGCAACTTACATAC
AAGAACAATTAACTGGAGCAAAGGGAGATATTTCTTTGTGCAGATTCTGTAAGGGCTGGGCAGAAA
TGTGTATGGTCAAAGCCAAGCAGTTCCATTTACAGCTCTGTTTTTTACGTAGTTACAACATGATGT
GATTGTAGCTTTTTAAACTATGAAACCCCTGAGAGATTGTACCTTCTAGTTGAAATAAAGTATTTA
TAATAGATTGTGGCTTC
(SEQ ID NO:202)

Homo sapiens PIGF 3'-UTR
NM_002643.3
CTGGAGCAAAGGGAGATATTTCTTTGTGCAGATTCTGTAAGGGCTGGGCAGAAATGTGTATGGTCA
AAGCCAAGCAGTTCCATTTACAGCTCTGTTTTTTACGTAGTTACAACATGATGTGATTGTAGCTTT
TTAAACTATGAAACCCCTGAGAGATTGTACCTTCTAGTTGAAATAAAGTATTTATAATAGATTGTG
GCTTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:203)

Homo sapiens MGST3 3'-UTR
MGST3-001 ENST00000367889
AGAATTATAGGGGTTTAAAAACTCTCATTCATTTTAAATGACTTACCTTTATTTCCAGTTACATTT
TTTTTCTAAATATAATAAAAACTTACCTGGCATCAGCCTCATACCTAAAA
(SEQ ID NO:204)

Homo sapiens SCP2 3'-UTR
NM_001193599
AGAACTCCCTTTGGCTACTTTTGAAAATCAAGATGAGATATATAGATATATATCCATACATTTTAT
TGTCAGAATTTAGACTGAAACTACACATTGGCAAATAGCGTGGGATAGATTTGTTTCTTAATGGGT
GTGACCAATCCTGTTTTTCCTATGCTCTGGGTGAATAGAGCCTGATGGTATACTACTGCTTTGCGG
AATTGCATACAACTGTGCATTACAAAGTTAATATGGTAATTATGGTCTGGGGTAAAATTGAGTTTC
AGAATAAAATTAGGAACAGTAAAATCCAAAGAACTATGTAAACAAAAAAGCTTTTGTTTTGCTTAC
AAAGTATATTTAAGGATTATTCTGCTGAAGATTCAGTTTAAGAGTTTTCCTTGGGAGAACTAAGTA
AGAAACACAATGCCAACAGCTGGCCAGTAATTAGTGTTGTGCACTTCATGTCATTAATCAATTTCT
CAATAGTTCTTAAAATTAGTGAGATTAAAAATCTAAAAATTTTGCATTTCATGCTATCAGAAACAG
TATTTTCTTCCCAAATCAAAATAAAAGAAATATGATCAGAGCTTGAACACAGGCTTATTTTTAAAA
TAAAAATATTTTTAACATGGGTTTCCTTATTGAAAAATCAGTGTATTAGTCATAAAACACCATCAT
TAAGAATAATTGAACAATAAAGTTTGCTTTCAGATGCAGTTTTCAAATTATAATCTCATTTCAATT
TATAACGTTCTCAGTCCTTTGTTATAATTTTCCTTTTTCATGTAAGTTTAATTATCTGCATTTATC
TTTTTTCCTAGTTTTTCTAATACTAATGTTATTTCTTAAAATTCAGTGAGATATAGGATAAAATAA
TGCTTTGAGAAGAATGTTTAATAGAAAATTAAAATAACTTTTTCTGGCCTCTCTT
(SEQ ID NO:205)

Homo sapiens SCP2 3'-UTR
SCP2-015 ENST00000435345
AGAACTCCCTTTGGCTACTTTTGAAAATCAAGATGAGATATATAGATATATATCCATACATTTTAT
TGTCAGAATTTAGACTGAAACTACACATTGGCAAATAGCGTGGGATAGATTTGTTTCTTAATGGGT
GTGACCAATCCTGTTTTTCCTATGCTCTGGGTGAATAGAGCCTGATGGTATACTACTGCTTTGCGG
AATTGCATACAACTGTGCATTACAAAGTTAATATGGTAATTATGGTCTGGGGTAAAATTGAGTTTC
AGAATAAAATTAGGAACAGTAAAATCCAAAGAACTATGTAAACAAAAAAGCTTTTGTTTTGCTTAC
AAAGTATATTTAAGGATTATTCTGCTGAAGATTCAGTTTAAGAGTTTTCCTTGGGAGAACTAAGTA
AGAAACACAATGC
(SEQ ID NO:206)

Homo sapiens HPRT1 3'-UTR
HPRT1-001 ENST00000298556
GATGAGAGTTCAAGTTGAGTTTGGAAACATCTGGAGTCCTATTGACATCGCCAGTAAAATTATCAA
TGTTCTAGTTCTGTGGCCATCTGCTTAGTAGAGCTTTTTGCATGTATCTTCTAAGAATTTTATCTG
TTTTGTACTTTAGAAATGTCAGTTGCTGCATTCCTAAACTGTTTATTTGCACTATGAGCCTATAGA
CTATCAGTTCCCTTTGGGCGGATTGTTGTTTAACTTGTAAATGAAAAAATTCTCTTAAACCACAGC
ACTATTGAGTGAAACATTGAACTCATATCTGTAAGAAATAAAGAGAAGATATATTAGTTTTTTAAT
TGGTATTTTAATTTTTATATATGCAGGAAAGAATAGAAGTGATTGAATATTGTTAATTATACCACC
GTGTGTTAGAAAAGTAAGAAGCAGTCAATTTTCACATCAAAGACAGCATCTAAGAAGTTTTGTTCT
GTCCTGGAATTATTTTAGTAGTGTTTCAGTAATGTTGACTGTATTTTCCAACTTGTTCAAATTATT
ACCAGTGAATCTTTGTCAGCAGTTCCCTTTTAAATGCAAATCAATAAATTCCCAAAAATTTAA
(SEQ ID NO:207)

ACSF2
Homo sapiens
ATAAAGCAGCAGGCCTGTCCTGGCCGGTTGGCTTGACTCTCTCCTGTCAGAATGCAACCTGGCTTT
ATGCACCTAGATGTCCCCAGCACCCAGTTCTGAGCCAGGCACATCAAATGTCAAGGAATTGACTGA
ACGAACTAAGAGCTCCTGGATGGGTCCGGGAACTCGCCTGGGCACAAGGTGCCAAAAGGCAGGCAG
CCTGCCCAGGCCCTCCCTCCTGTCCATCCCCCACATTCCCCTGTCTGTCCTTGTGATTTGGCATAA
AGAGCTTCTGTTTTCTTTG
(SEQ ID NO:208)

Homo sapiens VPS13A 3'-UTR
NM_033305
AATTCATATGTTCTTTATTTTACTTGGAATGTTTCATTAACATGTTTTGTATGACTTATACCATAA
TGCCCATATGTCCATTTATAGGGAGGTAAAACACATTTTCTTTTAAAATGTTTTCCTACACATTTT
CATAAAGCAAAATAATTGTATTATTTAAGCACAGAAAAAAATGTATCTTACATCCAAAGTAGGGAG
GGCATCCAACATATTATAGATTTGCTTTTATATATTTTATAGCTTTGTATTGCATAGTTTGTCTTT
AAGAGTTCAAGTTAGACTTAAATATAATTTTGATGTTCACTGGTTTTATTTTAAATTGCCTTCTTA
TTTGTTAGCAAAATGCCTTTTTTTTAATGGTCTCTGTAAATTTTCTGGGCTTTAATGTAATGCCACT
GTGTAAAAAAAAAGGAAGAAAATAGTAATAGCCATTTAATGTTTTATATTTATCATTTTAAAGATA
TTTTTGTCAAATTTCTTTTAATAATAATAAACATATGTAATCTAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:209)

Homo sapiens CTH 3'-UTR
NM_001190463.1
TATTCCAGAGCTGCTATTAGAAGCTGCTTCCTGTGAAGATCAAATCTTCCTGAGTAATTAAATGGA
CCAACAATGAGCCTTTGCAAAATTTTCAAGCGGAAATTTTAAGGCACCTCATTATCTTTCATAACT
GTAATTTTCTTAGGGATCATCTCTGTTAAAAAGTTTTCTGTATGTCATGTTATAATTACAGGTCAA
TTCTGTTAATATCTTTTTGTTAATTTTGCTCTATGTTTGCCTCTGAAGGAGGTGAGATTTGTGCTA
CTTTGGGAGATTATGTTCTTTTTTCATGTCTAAGATTTATTTTGATCATGTTTATAATATAATGGT
AATTCATTTTTGATGTTTTGTGAAGAATTTAAATTTAAACGAATGTTCTTAAATCAAGTGTGATTT
TTTTGCATATCATTGAAAAGAACATTAAAAGCAATGGTTTACACTTAGTTACCATAAGCCGAAAAT
CAAATACTTGAAAAGTTTACTGTGAAATTCTACTGATTTAAGACTATACTTAATATTTTTAAAAAA
ATAAATCAGCTGGGCGCGGTGGCTCACGCATGTAATGCCAGCACTTTTGGAGGATAAGGCGGGCGG
ATCACGAGGTCAGGAGATTGAGACCATCCTGGCTAGCGCAGTGAAACCCCCATCTCTACTAAAAAT
GCAAAAAAAATTAGACGGACGTGGTGGCGGGTGCCTGTAGTCCCAGCTACTTGGGAGGCTGAGG
(SEQ ID NO:210)

Homo sapiens CTH 3'-UTR
CTH-001 ENST00000370938
TATTCCAGAGCTGCTATTAGAAGCTGCTTCCTGTGAAGATCAAATCTTCCTGAGTAATTAAATGGA
CCAACAATGAGCCTTTGCAAAATTTTCAAGCGGAAATTTTAAGGCACCTCATTATCTTTCATAACT
GTAATTTTCTTAGGGATCATCTCTGTTAAAAAGTTTTCTGTATGTCATGTTATAATTACAGGTCAA
TTCTGTTAATATCTTTTTGTTAATTTTGCTCTATGTTTGCCTCTGAAGGAGGTGAGATTTGTGCTA
CTTTGGGAGATTATGTTCTTTTTTCATGTCTAAGATTTATTTTGATCATGTTTATAATATAATGGT
AATTCATTTTTGATGTTTTGTGAAGAATTTAAATTTAAACGAATGTTCTTAAATCAAGTGTGATTT
TTTTGCATATCATTGAAAAGAACATTAAAAGCAATGGTTTACACTTA
(SEQ ID NO:211)

Homo sapiens CTH 3'-UTR
CTH-002 ENST00000346806
TATTCCAGAGCTGCTATTAGAAGCTGCTTCCTGTGAAGATCAAATCTTCCTGAGTAATTAAATGGA
CCAACAATGAG
(SEQ ID NO:212)

Homo sapiens NXT2 3'-UTR
NXT2-004 ENST00000372107
AGGGGCAAAAGTCCATTCTCATTTGGTCCATTAGTTCCAGCAATTGAAATTTATGTGAATTATTTT
GATTGTAGAAGCACTATAATATGTGCTGAAACTAAATTTCTTTAATATTTTCTATTCCTGTCAGCA
CCTTTTCTAGCAGCTGCCAGTTTGGAGCATTGCCCTCTAAGAGCTTTAAAACTATTTTTTTACATG
CCTTATATACATTCCACTAATGACATTCTTATAATAATATTAAACACATGATCTTGGTACTAACAT
ACTCACTGTGAACCCAGCCTAT

(SEQ ID NO:213)

Homo sapiens MGST2 3'-UTR
NM_002413
CTTTTTCTCTTCCCTTTAATGCTTGCAGAAGCTGTTCCCACCATGAAGGTAATATGGTATCATTTG
TTAAATAAAAATAAAGTCTTTATTCTGTTTTTCTTGAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:214)

Homo sapiens MGST2 3'-UTR
NM_001204366.1
CTTTTTCTCTTCCCTTTAATGCTTGCAGAAGCTGTTCCCACCATGAAGGCTTGAAGCCACAGTGCA
TGGCCAGAACCAGCCAGACCTTTGGAGTTCAAGAACTCGAGAGGTGGGTGAAAACTGCCATTGCCT
CCACAGACTGTCTTCTCCGTGGAAAGAAGACCTGAGTCACCAGGGCTGGGAAACCTGCACCACTGA
GACGAGCACAGCCTCTGCCGGCATGCAAGTGGCCGCTGTCAGGACACATGGACTGAAAGTGGTTTG
TCAGCTGCTCCATTAGGTTTTTTTTACCCATATGTTTGCTACCTTTCTTTCCTTGATTTAAAAATA
GGGAGGGGGAGCAGTCTCAGCTGTCTTCAGCTGCTAGGGAGATTTTTTTCCCCCTCCTGAGCTACT
GTTTCCCCCAACCCGAGCCTTTCTCTCTTATTGTACCCACCCTTTCTGATGAAGTCATCAAAGCAA
AGATTGCATAACTGATGCATAGGCCTATCTTGTGTTATACTGGGAGACAGGCCAATGTTTCCATTA
ATAGACAAGAGCACCACCACGCTGCCAAATGGAGCTCTCTGCTGCAACCACTAC
(SEQ ID NO:215)

Homo sapiens C11orf67 3'-UTR
AAMDC-005 ENST00000526415
TGGAGCCTTAAGAGGAGAATAAATCACTAAGTGCCTA
(SEQ ID NO:216)

Homo sapiens PCCA 3'-UTR
NM_000282
AGGATTTATAACCTTTCAGTCATCACCCAATTTAATTAGCCATTTGCATGATGCTTTCACACACAA
TTGATTCAAGCATTATACAGGAACACCCCTGTGCAGCTACGTTTACGTCGTCATTTATTCCACAGA
GTCAAGACCAATATTCTGCCAAAAAATCACCAATGGAAATTTTCATTGATATAAATACTTGTACAT
ATGATTTGTACTTCTGCTGTGAGATTCCCTAGTGTCAAAATTAAATCAATAAAACTGAGCATTTGT
CT
(SEQ ID NO:217)

Homo sapiens GLMN 3'-UTR
NM_053274
AAGTTCCATTTCCTAAATAAAAACTAATAAAATATAGTACTTTCCATTATGATTCATTTAATACCT
TTATAAAAAATTTTTCTGTAAAAATTTACTGCTTGAAAAATAAATGTAGCTTTTCTCATTTATCAA
AAAAAAAAAA
(SEQ ID NO:218)

Homo sapiens DHRS1 3'-UTR
NM_001136050
CCCTCCTGGTCTGACACTACGTCTCTGCTTGTCTTCTCATTTGGACTTGGTGGTTCGTCCTGTCTC
AGTGAAACAGCAGCCTTTCTTGTTTACCCATACCCTTGATATGAAGAGAAGCCCTCTGCTGTGTGT
CCGTGGTGAGTTCTGGGGTGCGCCTAGGTCCCTTCTTTGTGCCTTGGTTTTCCTTGTCCTTCTTTT
TACTTTTTGCCTTAGTATTGAAAAATGCTCTTGGAGCTAATAAAAGTCTCATTTCTCTTTCAAAAA
AAAAAAAAAAAA
(SEQ ID NO:219)

Homo sapiens PON2 3'-UTR
PON2-001 ENST00000433091
ATTGTACTTTTGGCATGAAAGTGCGATAACTTAACAATTAATTTTCTATGAATTGCTAATTCTGAG
GGAATTTAACCAGCAACATTGACCCAGAAATGTATGGCATGTGTAGTTAATTTTATTCCAGTAAGG
AACGGCCCTTTTAGTTCTTAGAGCACTTTTAACAAAAAAGGAAAATGAACAGGTTCTTTAAAATGC
CAAGCAAGGGACAGAAAAGAAAGCTGCTTTCGAATAAAGTGAATACATTTTGCACAAAGTAAGCCT
CACCTTTGCCTTCCAACTGCCAGAACATGGATTCCACTGAAATAGAGTGAATTATATTTCCTTAAA
ATGTGAGTGACCTCACTTCTGGCACTGTGACTACTATGGCTGTTTAGAACTACTGATAACGTATTT
TGATGTTTTGTACTTACATCTTTGTTTACCATTAAAAAGTTGGAGTTATATTAA
(SEQ ID NO:220)

Homo sapiens NME7 3'-UTR
NM_013330
TGGTGTGGAAAGTAAAGAAGTCACAGGTTGGGACATTTAGACAAGAGTGAATCACACACGAGGAAT
GTGTTCATTCTTTTATTGTCCGTTGTTTTAACCTGACTGAATACAAGATCAACAAGAGCACTGTAC
TCCTGGCAATTATTACATATGTTAGAACATGGATTTTGCACTGTAGACAACATTTAACACCAGTCT
ATGGGGTACTGCATTGCTTTTTTATAAAGTTCAAAATAAAGATTTATTTTCAAACAAAAAAAAAAAA
AAAAAAAAAAAAA
(SEQ ID NO:221)

Homo sapiens ETFDH 3'-UTR
NM_004453
ACTGCAGCTAGCCAGTTTCTTTCAAGTATGGCAAGCTAACGTTAAAATGTTTAGAGATTAACAGAT
TTCAGAATGTCTTTCTGCATATTACTGAACAGAATAGTCACAAAATGATTATCAAATAAAAATTTT
ATACTATATGTAAGATTGTCCCATAAAGAAA
(SEQ ID NO:222)

Homo sapiens ALG13 3'-UTR
BC117377
GATCCAGCAGTATGAAGTATTCTTGCACTGCCATTTTCTTGCTGTTTTTGTTTTTAAAAAGTATTT
TATGTTAGTGGTTAAATGATTTAGGTGATTAGTGTTTACTATTGTATTTGTCTTTAAAATTATTTT
ATCTTTTGATTTAAAATAGTACTTTAAAATTAAGGGGTATTATTTTGGGCTGTGACTAAGGAAATT
GAGATGGATGTACAACTAGCCCCATATTGAGCATACTTCATTGTATTCAGCTGTTTTCCTGTCAGC
CATTTGTCAGC
(SEQ ID NO:223)

Homo sapiens ALG13 3'-UTR
NM_001099922.2
GATCCAGCAGTATGAAGTATTCTTGCACTGCCATTTTCTTGCTGTTTTTGTTTTTAAAAAGTATTT
TATGTTAGTGGTTAAATGATTTAGGTGATTAGTGTTTACTATTGTATTTGTCTTTAAAATTATTTT
ATCTTTTGATTTAAAATAGTACTTTAAAATTAAGGGGTATTATTTTGGGCTGTGACTAAGGAAATT
GAGATGGATGTACAACTAGCCCCATATTGAGCATACTTCATTGTATTCAGCTGTTTTCCTGTCAGC
CATTTGTCAGCTTTATATTAGCTGATGGTACCAATTGATAAAATGAATATAAAGTATTTCATTGGT
TCAAAAATCACACATCATATTAAACCATGCAGAATTGGAGTAACTTCCACTTTTTTCTAGAAAGTA
AAACCAAGAGCCTTTGCTTCTGGATAACTCACTTAATATTAAATTAAAGAGCTCTTCACGTTTCTT
GAGAATTATCTGAAGCCAGTTGCATTCTGTGATATCAGTTTTGAAGGCACATGGTTCTCTGCTTTA
GATTTATCCCATATGCTATTGTTTAATACTGGATGTATGTAAGTGTTTTACTGCACTGTATTGAAT
TGGTGTCTTTTGCACAGTTAGCAGTAAATAAAAATTAGCATTTAAAATTGCCAAAAAAAAAAAAAA
AAAA
(SEQ ID NO:224)

Homo sapiens DDX60 3'-UTR
DDX60-001 ENST00000393743
AAACAAAGTCTATGCAAACCACTTAAAAATAATTCCATAGTAGTTTTTCAGGTCACGTTTTTGATT
CTTATGCTTCTTGCCAGAAATACATTATGATAAAGTGGAAATACATTACGATGAAGTGGAAAGAGC
AAACACTTTGGAATCAAACAGAGTTGCAATCAAACCTGCCATGTTCTGTCATGAATACTCACAAAT
TATTTAGTATACCTGAATCTTGGTTTCTTTTTATAACTGAGTAATAATGGTTACATCTCAGGTAGT
TTGAGGATTGACTAAAAAAATGCGAGAATGTTGTATGTGACTGAATAACAATTTTTACTCTGCGAA
GCCAAAGTAAATATAATATTATCAGTAACTTTATCCCCAGTGTCAGTATTTATAAAATGTTTATTA
AGGCTAGAAAAAATGAATACAATATCCTGAAGGTGAAATATATTCTCTTCAATTAGCATAAATATG
ATTTACATAAGTTAGCTATACAGCTATTGAGATAGTACTTTCTAGTAAACTTAAACTACTTTTTAA
ACATACATTTTGTGATGATTTAACAAAAATATAGAGAATGATTTGCTTTATTGTAATTGTATATAA
GTGACTGGAAAAGCACAAAGAAATAAAGTGGGTTCGATCTGTTTAC
(SEQ ID NO:225)

Homo sapiens DYNC2LI1 3'-UTR
NM_015522.3
AATTCATTTGATGTAGATGAACCTGTTCACTGGAAAATTACAGCAATTTATTAAAACCTCAGTAAG
AGCAAAACAAGGAAGAAGATTCCTTATATCTTCTTGTTAGACATCTTCTGTGATTGTTATGGCATA
TTACACCAATCAGAGAAATAGAGTTTTAAAGTAGTGGTTTGATATTGATTTTATAATCTCTGTAAA
AATGAAGATAAAAAGCCAGATTGTACAAAAGTCACCTGACAAAGACTAGATGAAGCTACAACTTTA
AGCAAGGGGTAGAGTTGTAATAGCCTTCACCATCACTCTGTATTTTACATTCATTTCGTTTCTGTC
ACTTATTCAGTATCTTTTTATCATCTGACAGCTAATTAAATTATAAAGTTGCTATGATGGTAACAC
AAGTTCTTCAAATACAATAATAAATATCATCATCTGGAAAAAAAAAAAAAAAAAA
(SEQ ID NO:226)

Homo sapiens VPS8 3'-UTR
NM_001009921, NM_015303
TGACTCCATGGAGCCTGGCCCAGGAGAACCAGAGATGATCCCGAGGCAGCTGGGGAGAGGCCCCGC
CTCTGGTGGGCTTGGCCTCCACCACCTCCCACGCTTCTGAGAAGAGGTTCCAAATTGGGCTTCTGT
GCCCAGAGCGTCCACAGCACCATTCCCAGTGTAGACTCCCAGTCTTCTCCACATTGCTGTCATGGC
GTCAGTTCACCAGACTCATTGATTTTGTTTTGCTTGTTAAGCAAAGGAATGTCACATACCTCTGTC
CAGCTTTTTAGGAAATACATTTCGCCTATTGCGACTTTTTCCATTTACCCTGAAGCCTAGAAAGTA
GGTGGAACTCACACAAATGGCATTCCAGAGTCTGCCATACTCCGTCTCCTCCAGCTGCTGGATAAT
ACAGAGGAACTTCAACTTCTACAGGGAACAGTGGTTGGCCAGGCTGCAGTATAACTGAAGCATGCC
TTGGAGAGAGCAGACACTGTGGGGGCCAGGGCCATCTCCCTTTAATGTGTTCATGTTAAAACCTAT
TTGAGTGTAAGACTTGCCCTTTCTAACAATAAATGCTCCGTGTTTAAGTTCTGCAGGTCTCAAAAA
AAAAAAAAAAAA
(SEQ ID NO:227)

Homo sapiens ITFG1 3'-UTR
NM_030790
CTTGCCTTTAATATTACATAATGGAATGGCTGTTCACTTGATTAGTTGAAACACAAATTCTGGCTT
GAAAAAATAGGGGAGATTAAATATTATTTATAAATGATGTATCCCATGGTAATTATTGGAAAGTAT
TCAAATAAATATGGTTTGAATATGTCACAAGGTCTTTTTTTTTAAAGCACTTTGTATATAAAAATT
TGGGTTCTCTATTCTGTAGTGCTGTACATTTTTGTTCCTTTGTGGAATGTGTTGCATGTACTCCAG
TGTTTGTGTATTTATAATCTTATTTGCATCATGATGATGGAAAAAGTTGTGTAAATAAAAATAATT
AAAAAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:228)

Homo sapiens CDK5 3'-UTR
NM_004935

GCCCCGGGACCCCCGGCCTCCAGGCTGGGGCCTGGCCTATTTAAGCCCCCTCTTGAGAGGGGTGAG
ACAGTGGGGGTGCCTGGTGCGCTGTGCTCCAGCAGTGCTGGGCCCAGCCGGGGTGGGGTGCCTGAG
CCCGAATTTCTCACTCCCTTTGTGGACTTTATTTAATTTCATAAATTGGCTCCTTTCCCACAGTCA
AAAAAAAAAAAAAAAAA
(SEQ ID NO:229)

Homo sapiens C1orf112 3'-UTR
BC091516
AACTTATCACTAGGCAGAACTGGGTTTGATGCTTTGTCAACTGAAAATACTTATGTCTGTACATTT
TCTAACAGATATAAAACAAATTTTGTAAAGTTGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAA
(SEQ ID NO:230)

Homo sapiens IFT52 3'-UTR
NM_016004
AGACCATGCCTCTTGAAGCTTTTTCTGCCTCCTGATTCTCTCTTTGTAAACTATTTTCAAATTGTT
TTTCAACTCCTTATCAAAATTGTTTATACACTCTTTCCTCCATGAGCTCTGGAAGGTATATGCATC
TTCTGTAATACTCAGATAGGTATAAGATTTTTCACAAAATCCTTATGTAAGATACATTCCATTTTT
AAAAATTAAATGTATGGTTGCATCTGTCTTTTTATACCCTA
(SEQ ID NO:231)

Homo sapiens CLYBL 3'-UTR
CLYBL-003 ENST00000339105
TCTGTTAAATGAAGCTGTCATCAGGCTAAAGGGTATTGAAGCTGCAGAGGGATCAACTTGTGCTTG
CCAGAGGACGCCAATGAAGTTTGAAACACCAACAATCAGAGATTTTGTTTCTGTTCCTCATTAAAT
CATGAGCTTTTGTG
(SEQ ID NO:232)

Homo sapiens FAM114A2 3'-UTR
FAM114A2-006 ENST00000520667
AGAATGGAGACGTTTTGACCTGGGACTTGTGACGGCCAAGGAATGCCACCTTATTCTGGCTACTCC
TGCAGAAATGAAGGAGTGGGGTTATTTTAGTATATAAAAATTCAGGCAGGAGAGATGGTTTAAAGA
GGAAGATTGTTGCCTTCAGTGTTTGATTGAAGTATTCAGGTTCTCACAGTATTCTTTCCAGTTGTT
GTAATTCATAAATTATTTGAAAAGAAACTTTTGTAGAAAGTCCAAGAATAATAACTCTAGATAAAG
ATTAGTGGGACACTCAGGCAAAAATGTTGGTCTTTCTTTGACATGTTGCAAAATGTTATCAATTTT
GTCATGGATATAATTTGCAGCCCATGGATATAACTGGTTGATAAGCCAGAGAAAAATAATTTAGTG
TTCTAAAATTCATGGCATGTGTGGTTTATTAATGCCATGTACTTTCTCCTTTCTGGAATAAAATCT
ATGGCTTTAAGAAAA
(SEQ ID NO:233)

Homo sapiens NUDT7 3'-UTR
NM_001243661
TTTACTAGAGCAAGAGACAAAGAACTATTCACGAGGATTCTGTGTGTGCTTATTCGTAGAACAACA
ACAATGCCAGCTGTTGGAATTTGACAGGTGTGAATATTTTTTCTGCAGTATGTAGTTAGAATCCTT
GCCTCTTTTCCAGTTGCCTTCTATTGTCTGAAAAAGTAAAAGCCATTCAAAAATGAAAACTATGTT
CATAGTGTTGCATATTTTCACCCACAATATGTTAATAATATTTTTCTTACACATATAATAAAGAAT
ATCTGGCACATACTAGGCCCTTAATAAAGATTTTTTGAATATATAA
(SEQ ID NO:234)

Homo sapiens AKD1 3'-UTR
NM_001145128

TTTACTTAGGTGATAGCAGCCTGAATCTCAAGAGTTATCTGAAAGTGATAGAGGGAAACTGAGAGA
AGTAGATTGAAAATCTGGGCCTCTTGGAAGTACTTTTGCCTCCTGAGCAAGGTACCATGGCTGCCA
GACTTCAGGTGAACTCAAAGGTCTGCCAGCCAGGAAGGAGCACTCTTATGGAAACAAGTTTTAATA
CAATTTTAAAATGTATTGCTCTTTGCCTGAACTTTGATGCTTTAACAAAATAAACATTCTATTTAT
AATTCCATATAGAAAAGTTAAGTGACTTATTTAATAAATGTATTATTTTCCTTTTTAACATTTTCA
GTAGAAAAGTCAGTCTCTGTTAAAATTACTCATTAAATGTTAGAAAGCTTTAAGACATTTAACATT
GTTATAAATGAAACCAAAATATGGGTTATACATTTTACATACAAAACTGTTTGTGAACTTTGTGAA
CATAAGATACTATCATTTTCCCAATAAAATAAATGGATTTTGCAACAACTT
(SEQ ID NO:235)

Homo sapiens MAGED2 3′-UTR
NM_014599
GATTTTAGATATTGTTAATCCTGCCAGTCTTTCTCTTCAAGCCAGGGTGCATCCTCAGAAACCTAC
TCAACACAGCACTCTAGGCAGCCACTATCAATCAATTGAAGTTGACACTCTGCATTAAATCTATTT
GCCATTTCAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:236)

Homo sapiens HRSP12 3′-UTR
HRSP12-001 ENST00000254878
GTGGGCCCAGTGCTGTGTAGTCTGGAATTGTTAACATTTTAATTTTTACAATTGATGTAACATCTT
AATTAACCTTTTAATTTTCACAATTGATGACAGTGTGAGTTTGATGAAAATATCTGAAGCTATTAT
GGAAATACCATGTAATAGGGAGAGTTGAACATGAATATTAGAGAAGGAATCCAGTTACTTTTTTAA
ATTACACCTGTGTGCACCTGTATTACTGAATATAGGAAAGAGATACCCATTACATAGTTACTCAGT
AAACAAAAGAGAAATACCAGGTAGGAAAGAAGAGTTACTATTCCTGAGAAATAATCAAGAACATAT
TTAATTTAAACTAATGATGTGAACTATTTAGTTTTGATGTCCGTTATGTGATTCTGCTTTTACTTG
AGTAAAATTAAAGTGTTTAAATTTGAGATCAAGGAGAAGATAGTGGAACAAAATGTTATATAGATA
ATATTTTTCTAATGGAAATAAAATAGGCAGATTTCC
(SEQ ID NO:237)

Homo sapiens STX8 NM_004853 3′-UTR
TGGCAGTAAAGAGACCACCAGCAGTGACACCTGCCAATGACAGATGCAAGCCCAACACCCTTTTGG
TACGCAAAACCTGCTCTCAATAAATTCCCCCAAAGCTCTGAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:238)

Homo sapiens ACAT1 3′-UTR
ACAT1-001 ENST00000265838
ACAACCTCTGCTATTTAAGGAGACAACCCTATGTGACCAGAAGGCCTGCTGTAATCAGTGTGACTA
CTGTGGGTCAGCTTATATTCAGATAAGCTGTTTCATTTTTTATTATTTTCTATGTTAACTTTTAAA
AATCAAAATGATGAAATCCCAAAACATTTTGAAATTAAAAATAAATTTCTTCTTCTGCTTTTTTCT
TGGTAACCTTGAAAAGTTTGATACATTTTTGCATTCTGAGTCTATACTTATCGAAATATGGTAGAA
ATACCAATGTGTAATATTAGTGACTTACATAAGTAGCTAGAAGTTTCCATTTGTGAGAACACATTT
ATATTTTTGAGGATTGTTAAAGGTCAAGTGAATGCTCTTTATAGGTAATTTACATT
(SEQ ID NO:239)

Homo sapiens IFT74 3′-UTR
IFT74-201 ENST00000433700
GTTTAAGTCCACTGAAAGTCTCTAAGGAAGTATCCTCTTGCTGCTAAACTTGGTACAAGTTGACTA
CCAAAAAAAAAAAAAGCTTACTTTTGGAGTTTACCTAAAATTTCTGAATGTTATAATTTTTGTGGC
CTCTTTTAAGAATGATATTTTAAAATAGTAAATAGTTCAATAAATGGTTTGCATATT
(SEQ ID NO:240)

Homo sapiens KIFAP3 3'-UTR
NM_014970
TAAAGTATCTGTTTCCATGTGTAATCTCAGCTTAGAAGAAATCTGTGTGGGTTGGGTTAATTTTGG
ATCTTTGCCTAATAATGCATGTTGATGTTATTGTGGGTCTGTGTTTGTTTTTATTTTTATATGTTG
TTAGCTGCAGATTAACCCCAGCCCCTCTGTCTTCTGTTAAGTACAGTTGATACTGACATTGTTCAC
TCATCAAACCACATCTTGATGCTAAGTAACATTTCCCATGAGCCACAAAACTGAATGCTGAAAAGC
TACTAGACTGGAAAACAAACACTGCATTATGTATGTTAAGTGACTAATTTAATTTCAATTAAAAAG
CGTAAAGTGAAAATGAAAAAAAAAAAAAAAA
(SEQ ID NO:241)

Homo sapiens CAPN1 3'-UTR
NM_005186
GGCAGGGACTCGGTCCCCCTTGCCGTGCTCCCCTCCCTCCTCGTCTGCCAAGCCTCGCCTCCTACC
ACACCACACCAGGCCACCCCAGCTGCAAGTGCCTTCCTTGGAGCAGAGAGGCAGCCTCGTCCTCCT
GTCCCCTCTCCTCCCAGCCACCATCGTTCATCTGCTCCGGGCAGAACTGTGTGGCCCCTGCCTGTG
CCAGCCATGGGCTCGGGATGGACTCCCTGGGCCCCACCCATTGCCAAGCCAGGAAGGCAGCTTTCG
CTTGTTCCTGCCTCGGGACAGCCCCGGGTTTCCCCAGCATCCTGATGTGTCCCCTCTCCCCACTTC
AGAGGCCACCCACTCAGCACCACCGGCCTGGCCTTGCCTGCAGACTATAAACTATAACCACTAGCT
CGACACAGTCTGCAGTCCAGGCGTGTGGAGCCGCCTCCCGGCTCGGGGAGGCCCCGGGGCTGGGAA
CGCCTGTGCCTTCCTGCGCCGAAGCCAACGCCCCCTCTGTCCTTCCCTGGCCCTGCTGCCGACCAG
GAGCTGCCCAGCCTGTGGGCGGTCGGCCTTCCCTCCTTCGCTCCTTTTTTATATTAGTGATTTTAA
AGGGGACTCTTCAGGGACTTGTGTACTGGTTATGGGGGTGCCAGAGGCACTAGGCTTGGGGTGGGG
AGGTCCCGTGTTCCATATAGAGGAACCCCAAATAATAAAAGGCCCCACATCTGTCTGTGAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:242)

Homo sapiens COX11 3'-UTR
NM_001162861
AGAGTTGGCACCTTTGATGTGGTAGTGAGCTGATCATCCACTTTCTTCTAAAATAAAGAGAAGAAA
ATGGCCAGTAAAAAAAAAAAAA
(SEQ ID NO:243)

Homo sapiens GLT8D4 3'-UTR
BC127733
ATATTTTGTCTTGTTGCAAGTCAATTAGGTGTCTTGTGAACAAGGAAATACTAATCTCTAAGCTGC
CTGGGTCTTTT
(SEQ ID NO:244)

Homo sapiens GLT8D4 3'-UTR
NM_001080393
ATATTTTGTCTTGTTGCAAGTCAATTAGGTGTCTTGTGACCAAGGAAATACTAATCTCTAAGCTGC
CTGGGTCTTTTTGTGTGAATATTTAATGGTGCTCCATGACTGTTGAGTTTTAAAAACCTCGTTAAA
TTTTGCCAAATCAGTTGCCCCCAAAAGGGAATATGCTTTTCCTTATTTTTTTTTCTAAAATGCTAT
TTATCTCTAAGGAAAAA
(SEQ ID NO:245)

Homo sapiens HACL1 3'-UTR
NM_012260
ATAAAGACGCCAGTTGGTGGTCTTGAGTTTTCTCTTTCTTGCAAGATGAAATTTTATTTTCCACAG
CAAAATTACTCTACTGTTAAAATTGTGCAAAATAAAATAAACATTTAAAATGACATTTTACAGTAA
AAAAAAAA
(SEQ ID NO:246)

Homo sapiens IFT88 3'-UTR
NM_175605
TATTCACTTTAATATTTATTAAAGGAAAGAAATTGCCTTATGAGATCATCCTCATGTTAAACCTTG
GATTAAATATCTAACCTGTAATTATTTTTTTTCACTGTCAAAACTTAAGTAAGTGTATTCTATTCT
GTATGTATGCATTTAAGTTGTTTTTTTCTTTTAAGGAATAAAAACAGGTAAAACTAATACTTTAGG
CCAGTGACTTCCTTAGCTTTTTGAAAACATTGACACACAGGAAGAAATAAATTTCATAACACAAAA
AAAAAAAAA
(SEQ ID NO:247)

Homo sapiens IFT88 3'-UTR
IFT88-001 ENST00000351808
TATTCACTTTAATATTTATTAAAGGAAAGAAATTGCCTTATGAGATCATCCTCATGTTAAACCTTG
GATTAAATATCTAACCTGTAATTATTTTTTTTCACTGTCAAAACTTAAGTAAGTGTATTCTATTCT
GTATGTATGCATTTAAGTTGTTTTTTTCTTTTAAGGAATAAAAACAGGTAAAACT
(SEQ ID NO:248)

Homo sapiens NDUFB3 3'-UTR
NM_002491
AGATAATACCTGGAAGCATCATAGTGGTTTCTTAACTCTCCAAAATAAGATTTCTTCTCTGTAGCC
TACTTGTCTGGTTTATCCCTTACAGAATATTAGTAAGATTTAATCAATTAAAATATATATATATGC
CAAAAAAAAAAAAAAAAA
(SEQ ID NO:249)

Homo sapiens ANO10 3'-UTR
NM_018075
GTGCCCAGCGTGCCCAGCTGCCCTGTTGGCAGAGGCCTGTGTCTGTGCCACACCTGCCACGGTGGC
AGGGGGGGTACCCGGGGCAGCATCGTGGCTCCTGAACCCAGACCCAATGCTTAGCCAAACGAAGTG
GCTCCCATGTGGCAAGCACCCTTCTCAGTTTCGCAGTGGCTTGGCTCGGGATCCTTGGCAGTTCCC
CCAGCCCCACCCTGTCTGCTCCTTCCCAGTTCCTTCCCGGGCCCCACACGCTGCTCCAGCTGCCAA
CTTTGCTGCAGAGCCACTGCCGCCCTTGAGCCTCTCACCATGAGTGAGCCACCAGCTCTCCACGTT
CCCCTCATAGCAGTGTCACTCCCAACCCCACCATGGCCCAGGGACCCGTGGACAGGTTGGGGATGG
GGTGTGTGCCCACTGTGCTCATCACAGGAGCCTCAGTTGAGAGTGAGCGGGGTACAGTAAGGCAGT
GCTTCCCACACTGGACCTCTTTCCTGGTTCTCTTTTGCAATACATTAACAGACCCTTTATCAACAT
AAACAATAGTAACTGAGCTATTAAAGGCAACCTCTCTGACTCCTTCTGCCTAAAAAAAAAA
(SEQ ID NO:250)

Homo sapiens ANO10 3'-UTR
ANO10-005 ENST00000451430
GTGCCCAGCGTGCCCAGCTGCCCTGTTGGCAGAGGCCTGTGTCTGTGCCACACCTGCCACGGTGGC
AGGGGGGGTACCCGGGGCAGCATCGTGGCTCCTGAACCCAGACCCAATGCTTAGCCAAACGAAGTG
GCTCCCATGTGGCAAGCACCCTTCTCAGTTTCGCAGTGGCTTGGCTCGGGATCCTTGGCAGTTCCC
CCAGCCCCACCCTGTCTGCTCCTTCCCAGTTCCTTCCCGGGCCCCACACGCTGCTCCAGCTGCCA
(SEQ ID NO:251)

Homo sapiens ARL6 3'-UTR
NM_032146
AAAGATAATAGTTGGAAACCTCAGCAATTTTCAATTCAAGGAATCTATCTAAGACAAATAGAATAC
ATTTTGTAAAAGATGTTTATGCATCAAAAAATATAATTTTCTGCTTGCATTTATGGACTCTGACCT
TTTTAAGAACATAGGACTTCAGGTATGCTAATTTGGCCATTAATTATTTAAAAACTAAATATTCCC
TCAAAAGGGCTCCCTAGAATTATCAAGTTCTTAGTGAAGGTCTACATTTGATTGTACGTAGAATGT
TTAAAAGTCAGTTATAAGCCATCTCATCCCATCATAATTTATGATATGTTTAATATATTTTATTTT

TTAATTGTCTTTTTAAAAAATTTAGTTTATGACTTTGCAGTATGAATTGTGCTTGTGAAAAAGAAC
TTTAAATATTTATAAGGGACCATGGGTAATTAATATATATTCAATTTTTACTATGTGTCACTGTCA
ATAAAATGTAAAATATAATGTGCC
(SEQ ID NO:252)

Homo sapiens LPCAT3 3'-UTR
NM_005768
TCCATTTCCCTGGTGGCCTGTGCGGGACTGGTGCAGAAACTACTCGTCTCCCTTTTCACAGCACTC
CTTTGCCCCAGAGCAGAGAATGGAAAAGCCAGGGAGGTGGAAGATCGATGCTTCCAGCTGTGCCTC
TGCTGCCAGCCAAGTCTTCATTTGGGGCCAAAGGGGAAACTTTTTTTTGGAGAAGGCGTCTTGCTT
TGTCACCCACGCTGGAATGCAGTGGCGGGATCTCAGCTCACCGCAACCTCCACCTCCTGGGTTCAA
GTGATTTTCCTGCCTCAGCCTCCCAAGTAGCTGGGAATACAGGCACGCCACCATGCCCAGCTAATT
TTTGTATTTTCAGTAGAAACGGGATTTCACCACGTTGGCCAGGCTGGTCTCGAACTCCTGACCGCA
AGTGATCCACCCGCCTCCGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGTGCCCGGCCC
AAAGGGGAAACTCTTGTGGGAGGAGCAGAGGGGCTCACATCTCCCCTCTGATTCCCCCATGCACAT
TGCCTTATCTCTCCCCATCTAGCCAGGAATCTATTGTGTTTTTCTTCTGCCAATTTACTATGATTG
TGTATGTGCCGCTACCACCACCCCCCCCATGGGGGGGTGGAGAGGGGTGCAAGGCCCTGCCTGCTC
CACTTTTTCTACCTTGGAACTGTATTAGATAAAATCACTTCTGTTTGTTCAGTTTTTCA
(SEQ ID NO:253)

Homo sapiens ABCD3 3'-UTR
NM_001122674
AAACCAGACAAATGTATTGGCCAGGCGTGGTGGCTCATGCCTGTAATCCCAGCACTTTGGGAGGCT
GAGATGGGAGGATCGCTTGAATCCAGGAGTTCGAGACAAGCCTGGACAAAAAGCGAGACCCGCTTC
TTTAAAAAATAATAATAAAACA
(SEQ ID NO:254)

Homo sapiens COPG2 3'-UTR
NM_012133
ATGCTTACTGGACAAGAGGAAACTGATGCACACTACATGGTCAGTGGGCTTTTAGGCTAGTGGCAT
CAGTTTCCCAGAATCAGACTTTTGAAGATGAATGACTTTGGAGAAGCAAATTAAACATTTGGCCCT
GAGCCAGCAGATCAAGCAAATGTCTATCTTTGCGCATGGGTTGTTTTTTTTTTTTTTCTTTTTATT
CTACTTGGTCAGCTTTGGGACGATAGTGCAGCTTTGGGTGATCTTGAAAATCAAATACTATCCTAT
ACTCCAGCTGCTTAACTTCATTTTATTCTTTAATGTGTACCTGAAAGCTCCTGGCAATGCTGGAAA
ATTTTTATCCCAGAGGGGTGGGGGGGAGGGGGGAGGGGAAGCCAGAGTCCACTTTTGTCACAATTC
ATTTTTATTAATAGAAAATAAACACTTATTCCAGTTTCAAAAAAAAAAAAAA
(SEQ ID NO:255)

Homo sapiens MIPEP 3'-UTR
NM_005932
AAGAAACACTCTACACCTCTTAAATCAAGGTCATGTAGATAATGACTTTGTTATAAATGCTACAGC
TGTGAGAGCTTGTTTCTGATTTCATTGTTCGCTTCTGTAATTCTGAAAAACTTTAAACTGGTAGAA
CTTGGAATAAATAATTTGTTTTAATTAAAAAAAAAAAAAAAAA
(SEQ ID NO:256)

Homo sapiens LEPR 3'-UTR
NM_002303
TTTCACTGAAGAAACCTTCAGATTTGTGTTATAATGGGTAATATAAAGTGTAATAGATTATAGTTG
TGGGTGGGAGAGAGAAAAGAAACCAGAGTCAAATTTGAAAATAATTGTTCCAAATGAATGTTGTCT
GTTTGTTCTCTCTTAGTAACATAGACAAAAAATTTGAGAAAGCCTTCATAAGCCTACCAATGTAGA
CACGCTCTTCTATTTTATTCCCAAGCTCTAGTGGGAAGGTCCCTTGTTTCCAGCTAGAAATAAGCC
CAACAGACACCATCTTTTGTGAGATGTAATTGTTTTTTCAGAGGGCGTGTTGTTTTACCTCAAGTT

TTTGTTTTGTACCAACACACACACACACACACATTCTTAACACATGTCCTTGTGTGTTTTGAGAGT
ATATTATGTATTTATATTTTGTGCTATCAGACTGTAGGATTTGAAGTAGGACTTTCCTAAATGTTT
AAGATAAACAGAATTC
(SEQ ID NO:257)

Homo sapiens LEPR 3'-UTR
NM_001198688
GAAATGCTTGTAGACTACGTCCTACCTCGCTGCCGCACCTGCTCTCCCTGAGGTGTGCACAATG
(SEQ ID NO:258)

Homo sapiens C2orf76 3'-UTR
NM_001017927
AAACATCTCGAGGGCTTCCTTTTTGCAT
(SEQ ID NO:259)

Homo sapiens C2orf76 3'-UTR
C2orf76-001 ENST00000409466
AAACATCTCGAGGGCTTCCTTTTTGCATACCTGTATTAAGCTCTTTATTCCACTGCTGAATTTTTG
AAATTGACAAACAAATCTTAAAAAATTAATCCCAGGCTATACTCTTTGAGCTAAAATCTGGTTATT
TCTTTCTCTTCAGGTCTTTCCTTCTCTCTTTCTTTTTCTTTGTTGTTGTAAAATAATATATTATGA
GAAAAACATTTGATCTTTTTAAAGGGAAATAAATTGTTATTAAAAA
(SEQ ID NO:260)

Homo sapiens ABCA6 3'-UTR
NM_080284.2
AACCTCAAACCTAGTAATTTTTTGTTGATCTCCTATAAACTCATGTTTTATGTAATAATTAATAGT
ATGTTTAATTTTAAAGATCATTTAAAATTAACATCAGGTATATTTTGTAAATTTAGTTAACAAATA
CATAAATTTTAAAATTATTCTTCCTCTCAAACATAGGGGTGATAGCAAACCTGTGATAAAGGCAAT
ACAAAATATTAGTAAAGTCACCCAAAGAGTCAGGCACTGGGTATTGTGGAAATAAAACTATATAAA
CTT
(SEQ ID NO:261)

Homo sapiens LY96 3'-UTR
NM_015364.4
AATAAATTGAGTATTTAAAAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:262)

Homo sapiens CROT 3'-UTR
NM_ 001243745.1
TGATGATGTTTAAAGAATGATAAATAAAAAGTGCATAGTTTTTATTTTTAAATTATTGCTGTAAAA
ATTTTTACAGTTATTATTGTTATTTTCATAATCCAAAAGAAGGAATGAATCACTTAACTTTGGGAG
TTTTCAGTGGGTGGATTCGGGAACTTGTTAAAATGCAGATTTGCTGGGATAAGTGATTCTGATTCA
CATGGCTGGAATGAGGCCCAGAGATTCTTATTTTAACAATCACTTCATGTGGTTTGGCTGCAGGTA
ATCTGTAGACCATGCTGAAGGAAAACATTTTGTCCAGGTGACTAGCTTGAAAAATCAGAAACACTA
AAATAGACATGTCACATAGGTGGCATAGAAATATTTTCGTAGTACAATGGAGAAAGGGAATCATTA
AAAATCAGAGTGGAGAATGGTTATGTATATTGTATATTTCAGTTAGATAAATTGAGGAAGCTAGTA
TAATAATTATTGAAGGTCTCAATAATTTTCCACAAAATTCTTTAACTTCTTCAGCTCAACCATTTC
TGTACTTCTCTACTATGAATCAGAGGATGAGGTTGTATAATTCAAAAGCATTGCCTTAGTCTAGAA
ATAATTATTGTACCTATCATTTAGTTTTAGAAATAAAAAGCAAGCTGATTTTTTTTGATGAACCAT
TTATATCTGTGATGGAATAATAAAATTTCACACTTCCGGATTCCTTTGTTCTCAATTTTGAGCCTT
GAGTTGTTTTAATTAAAGAGGGGTAAAGG
(SEQ ID NO:263)

Homo sapiens ENPP5 3'-UTR
ENPP5-002 ENST00000230565
TGTTACTTTGAAGTGGATTTGCATATTGAAGTGGAGATTCCATAATTATGTCAGTGTTTAAAGGTT
TCAAATTCTGGGAAACCAGTTCCAAACATTTGCAGAAACCATTAAGCAGTTACATATTTAGGTATA
CACACACACACACACACACACATACACACACACGGACCAAAATACTTACACCTGCAAAGGAATAAAGA
TGTGAGAGTATGTCTCCATTGTTCACTGTAGCATAGGGATAGATAAGATCCTGCTTTATTTGGACT
TGGCGCAGATAATGTATATATTTAGCAACTTTGCACTATGTAAAGTACCTTATGTATTGCACTTTA
AATTTCTCTCCTGATGGGTACTTTAATTTGAAATGCACTTTATGCACAGTTATGTCTTATAACTTG
ATTGAAAATGACAACTTTTTGCACCCATGTCACAGAATACTTGTTACGCATTGTTCAAACTGAAGG
AAATTTCTAATAATCCCGAATAATGAACGTAGAAATCTATCTCCATAAATTGAGAGAAGAAGAAGG
TGATAAGTGTTGAAAATTAAATGTGATAACCTTTGAACCTTGAATTTTGGAGATGTATTCCCAACA
GCAGAATGCAACTGTGGGCATTTCTTGTCTTATTTCTTTCCAGAGAACGTGGTTTTCATTTATTTT
TCCCTCAAAAGAGAGTCAAATACTGACAGATTCGTTCTAAATATATTGTTTCTGTCATAAAATTAT
TGTGATTTCCTGATGAGTCATATTACTGTGATTTTCATAATAATGAAGACACCATGAATATACTTT
TTTTCTATATAGTTCAGCAATGGCCTGAATAGAAGCAACCAGGCACCATCTCAGCAATGTTTTCTC
TTGTTTGTAATTATTTGCTCCTTTGAAAATTAAATCACTATTAATTACATTAA
(SEQ ID NO:264)

Homo sapiens SERPINB7 3'-UTR
SERPINB7-203 ENST00000546027
AAATCCAATTGGTTTCTGTTATAGCAGTCCCCACAACATCAAAGAACCACCACAAGTCAATAGATT
TGAGTTTAATTGGAAAAATGTGGTGTTTCCTTTGAGTTTATTTCTTCCTAACATTGGTCAGCAGAT
GACACTGGTGACTTGACCCTTCCTAGACACCTGGTTGATTGTCCTGATCCCTGCTCTTAGCATTCT
ACCACCATGTGTCTCACCCATTTCTAATTTCATTGTCTTTCTTCCCACGCTCATTTCTATCATTCT
CCCCCATGACCCGTCTGGAAATTATGGAGAGTGCTC
(SEQ ID NO:265)

Homo sapiens TCP11L2 3'-UTR
NM_152772
AGAAGAACTGACATTGGACGAGAGATTGGAAATCCAGTACTTTGGTATCCAGTCCACTTCCATTGA
TGGCATTAGAGATCCAGCACATTCTCAGTACTGTGGTGCAGTATTAGCCCAAATCTGTGTAATGGG
TAATATTAGCATTACAGAAGACACACACATCACATAGACCCTCAGAAGACGTAAACATCACATAGA
CCCTATTTGTGCATCATTTTCAAGTTTAAAACAGATATTTGTAATGAACAGAAAACAATTTGTAAT
TAATTATATTACCTATATAATACTTGTAAATGTTTTCTTAACCATTTATATTTGGCTTATGACATT
TAACCCCTAAGGAGTTGTTTTTCTCACTTGTTATTATCAAACCTAATGGTTTTTAATTTTGGTACA
ACTCCTTAAAGGGTTGAAGGTTGTGACAATAACTGAGGGAACTGATGTTCTGAATAAATGATGTGA
AGTAAACACAATTGTATTTGAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:266)

Homo sapiens IRAK1BP1 3'-UTR
NM_001010844
AATTCCAAACAAATTATATTGTACTTGTATCTTTTTACCTATTTTTATACTTTTTATAATGTTTAC
GTTTGTCCTGAATATATA
(SEQ ID NO:267)

Homo sapiens CDKL2 3'-UTR
CDKL2-002 ENST00000307465
GAACCATTTTGGTTCTGAACTGGATGATGCTCTTGCACTTGAGATGACATCTTCTTGCAGCAAGAG
TGCTGATATCCCAAGAGGAGAGATTCATGGTTTTGATCATTTCCTTCTGAACTGCCTGCATTTTCT
GAGGAAGGCCTTCTAGAAGAAGGAAAGACAAAGACTTCCAAATGTTTCAAAGGAAGATTGAACAAA
TGGCCCTCCCCAACTGTTATCCCATTACCTTTCACGTCCACCGATGCTATTTCAAGACATATCCAG

TGGAATAACAGTGATATGGTTCTTGTTACATGAATGTGTATTTACTGTTAGGAGATTGTATATTTT
AAGTTACC
(SEQ ID NO:268)

Homo sapiens GHR 3'-UTR
GHR-202 ENST00000537449
CCTTTCTTTGGTTTCCCAAGAGCTACGTATTTAATAGCAAAGAATTGACTGGGGCAATAACGTTTA
AGCCAAAACAATGTTTAAACCTTTTTTGGGGGAGTGACAGGATGGGGTATGGATTCTAAAATGCCT
TTTCCCAAAATGTTGAAATATGATGTTAAAAAAATAAGAAGAATGCTTAATCAGATAGATATTCCT
ATTGTGCAATGTAAATATTTTAAAGAATTGTGTCAGACTGTTTAGTAGCAGTGATTGTCTTAATAT
TGTGGGTGTTAATTTTTGATACTAAGCATTGAATGGCTATGTTTTTAATGTATAGTAAATCACGCT
TTTTGAAAAAGCGAAAAAATCAGGTGGCTTTTGCGGT
(SEQ ID NO:269)

Homo sapiens KIAA1107 3'-UTR
NM_015237
GTGTTAACATTTTGGAAAAATTTATGCCACTCCTTTATTTTTTGATGCCTATATTATATCCAAATG
ATAATTGCATTAGCCGGATATAAACTTTCTTTAATATTGAGTCTTTCCAATTTAATGAGGTAAACA
TAGTTTATTTATTAATATATCACATATAGAAAAATGTTTTTCTAAAGTTTTTGAGCATGTTTTCTC
TAATTATTAGAGAAATTAGAAGACTTATAAGGAAACCCTAGCTTCAGTTTTCCTTTCCTAGCTGAT
GATTTGTTCACTTAATCATTATTCAAGAATTTAAAATGTGAATGCAGAAGTAGATCAGTCCCTTTA
CTTTTTGCTCTGCATAGGGTAACATAGTAATTTAACAATAAAAACTTACCGTGCTTGTGTCCAAAA
AAAAAAAAAA
(SEQ ID NO:270)

Homo sapiens RPS6KA6 3'-UTR
RPS6KA6-001 ENST00000262752
GATTTGTGGTGTTCCTAGGCCAAACTGGATGAAGATGAAATTAAATGTGTGGCTTTTTTCCTATTC
TTATCAAAGGCATCGTTGTCTGCTAAATTACTTGAATATTAAGTAATATTAAATCCCCATTTTTAG
GGGAAGTGAGATTTAAAAAACCATTCACAGGTCCACAATATTCATACTATGTGTTTGCAGTAGTGT
TCAAGTGTTTATTTAAGCATATAATTGGTGTCCACCAGGTCCTCACAACTTCTCTGCACACAAGCT
TCTAAAATTCCTTTCAAATAAAGTTACTTTAATATTT
(SEQ ID NO:271)

Homo sapiens CLGN 3'-UTR
NM_004362, NM_001130675
ACTAGATTGAAATATTTTTAATTCCCGAGAGGGATGTTTGGCATTGTAAAAATCAGCATGCCAGAC
CTGAACTTTAATCAGTCTGCACATCCTGTTTCTAATATCTAGCAACATTATATTCTTTCAGACATT
TATTTTAGTCCTTCATTTCAGAGGAAAAAGAAGCAACTTTGAAGTTACCTCATCTTTGAATTTAGA
ATAAAAGTGGCACATTACATATCGGATCTAAGAGATTAATACCATTAGAAGTTACACAGTTTTAGT
TGTTTGGAGATAGTTTTGGTTTGTACAGAACAAAATAATATGTAGCAGCTTCATTGCTATTGGAAA
AATCAGTTATTGGAATTTCCACTTAAATGGCTATACAACAATATAACTGGTAGTTCTATAATAAAA
ATGAGCATATGTTCTGTTGTGAAGAGCTAAATGCAATAAAGTTTCTGTATGGTTGTTTGATTCTAT
CAACAATTGAAAGTGTTGTATATGACCCACATTTACCTAGTTTGTGTCAAATTATAGTTACAGTGA
GTTGTTTGCTTAAATTATAGATTCCTTTAAGGACATGCCTTGTTCATAAAATCACTGGATTATATT
GCAGCATATTTTACATTTGAATACAAGGATAATGGGTTTTATCAAAACAAAATGATGTACAGATTT
TTTTTCAAGTTTTTATAGTTGCTTTATGCCAGAGTGGTTTACCCCATTCACAAAATTTCTTATGCA
TACATTGCTATTGAAAATAAAATTTAAATATTTTTTCATCCTGAAAAAAAA
(SEQ ID NO:272)

Homo sapiens CLGN-202 3'-UTR
NM_004362, NM_001130675
ENST00000325617
ACTAGATTGAAATATTTTTAATTCCCGAGAGGGATGTTTGGCATTGTAAAAATCAGCATGCCAGAC
CTGAACTTTAATCAGTCTGCACATCCTGTTTCTAATATCTAGCAACATTATATTCTTTCAGACATT
TATTTTAGTCCTTCATTTCAGAGGAAAAAGAAGCAACTTTGAAGTTACCTCATCTTTGAATTTAGA
ATAAAAGTGGCACATTACATATCGGATCTAAGAGATTAATACCATTAGAAGTTACACAGTTTTAGT
TGTTTGGAGATAGTTTTGGTTTGTACAGAACAAAATAATATGTAGCAGCTTCATTGCTATTGGAAA
AATCAGTTATTGGAATTTCCACTTAAATGGCTATACAACAATATAACTGGTAGTTCTATAATAAAA
ATGAGCATATGTTCTGTTGTGAAGAGCTAAATGCAATAAAGTTTCTGTATGGTTGTTTGATTCTAT
CAAC
(SEQ ID NO:273)

Homo sapiens TMEM45A 3'-UTR
NM_018004
CTTTGATGAGCTTCCAGTTTTTCTAGATAAACCTTTTCTTTTTTACATTGTTCTTGGTTTTGTTTC
TCGATCTTTTGTTTGGAGAACAGCTGGCTAAGGATGACTCTAAGTGTACTGTTTGCATTTCCAATT
TGGTTAAAGTATTTGAATTTAAATATTTTCTTTTTAGCTTTGAAAATATTTTGGGTGATACTTTCA
TTTTGCACATCATGCACATCATGGTATTCAGGGGCTAGAGTGATTTTTTTCCAGATTATCTAAAGT
TGGATGCCCACACTATGAAAGAAATATTTGTTTTATTTGCCTTATAGATATGCTCAAGGTTACTGG
GCTTGCTACTATTTGTAACTCCTTGACCATGGAATTATACTTGTTTATCTTGTTGCTGCAATGAGA
AATAAATGAATGTATGTATTTTGGTGC
(SEQ ID NO:274)

Homo sapiens TBC1D8B 3'-UTR
TBC1D8B-007 ENST00000276175
ATCCCTAGGAATTGCCTATCATAGACAAGTTTACTAACATTCCTGTAGCTGTCAGTTTGATTCCTG
TGAGTAGGGCTCAGGGATTTATCTTGTTACCAATGTGTCTGAAGGCCAAAATATATATCCAGAAGC
ACAATGCATCATTCCTTTGT
(SEQ ID NO:275)

Homo sapiens ACP6 3'-UTR
NM_016361
CTGATTTATAAAAGCAGGATGTGTTGATTTTAAAATAAAGTGCCTTTATACAATGCCAAAAAAAAA
AAAAAAAAAAAAAAA
(SEQ ID NO:276)

Homo sapiens RP6-213H19.1 3'-UTR
MST4-003 (RBM4B-003 ENST00000496850)
GAAACTTATTATTGGCTTCTGTTTCATATGGACCCAGAGAGCCCCACCAAACCTACGTCAAGATTA
ACAATGCTTAACCCATGAGCTCCATGTGCCTTTTGGATCTTTGCA
(SEQ ID NO:277)

Homo sapiens SNRPN 3'-UTR
NM_022807
CATACTGTTGATCCATCTCAGTCACTTTTTCCCCTGCAATGCGTCTTGTGAAATTGTGTAGAGTGT
TTGTGAGCTTTTTGTTCCCTCATTCTGCATTAATAATAGCTAATAATAAATGCATAGAGCAATTAA
ACTGTG
(SEQ ID NO:278)

Homo sapiens GLRB 3'-UTR
GLRB-005 ENST00000512619
GATCTAATGACTTCAGCATTGTTGGAAGCTTACCAAGAGATTTTGAACTATCCAATTATGACTGCT
ATGGAAAACCCATTGAAGTTAACAACGGACTTGGGAAATCTCAGGCTAAGAACAACAAGAAGCCTC
CCCCTGCGAAACCTGTTATTCCAACAGCAGCAAAGCGAATTGATCTTTATGCAAGAGCATTGTTTC
CTTTCTGCTTCTTGTTCTTCAATGTTATATATTGGTCTATATATTTATGATAAATCTTTTCCATTT
GTACAAAATAAAATTCCATTTCATTGTGACCTACTCCTTTCATAAATGCCAATCTGTGAGAACTTT
TGAATTTTCATAGCAACATTGCATTTTGGATGCCATTTGATTGTAATAAAACTGTGGCACCTTAAT
TTTGAATGGCAGCATGATCATGTAATATC
(SEQ ID NO:279)

Homo sapiens HERC6 3'-UTR
NM_017912
TCACCTCTGAGAGACTCAGGGTGGGCTTTCTCACACTTGGATCCTTCTGTTCTTCCTTACACCTAA
ATAATACAAGAGATTAATGAATAGTGGTTAGAAGTAGTTGAGGGAGAGATTGGGGGAATGGGGAGA
TGATGATGATGGTCAAAGGGTGCAAAATCTCACACAAGACTGAGGCAGGAGAATAGGGTACAGAGA
TAGGGATCTAAGGATGACTTGGACACACTCCCTGGCACTGAAGAGTCTGAACACTGGCCTGTGATT
GGTCCATTCCAGGACCTTCATTTGCATAAGGTATCAAACCACATCAGCCTCTGATTGGCCATGGGC
CAGACCTGCACTCTGGCCAATGATTGGTTCATTCCAGGACATTCATTTGCATAAGGAGTCAAACCA
CACCAGTCTTGGATTGGCTGTGAGCCAATTCACCTCAGTCTCTAATTGGCTGTGAGTCAGTCTTTC
ATTTACATAGGGTGTAACCATCAAGAAACCTCTACAGGGTACTTAAGCCCCAGAAGATTTTGCTAC
CAGGGCTCTTGAGCCACTTGCTCTAGCCCACTCCCACCCTGTGGAATGTACTTTCACTTTTGCTGC
TTCACTGCCTTGTGCTCCAATAAATCCACTCCTTCACCACCCAAAAAAAAAAAAAAA
(SEQ ID NO:280)

Homo sapiens CFH 3'-UTR
NM_000186
AATCAATCATAAAGTGCACACCTTTATTCAGAACTTTAGTATTAAATCAGTTCTCAATTTCATTTT
TTATGTATTGTTTTACTCCTTTTTATTCATACGTAAAATTTTGGATTAATTTGTGAAAATGTAATT
ATAAGCTGAGACCGGTGGCTCTCTTCTTAAAAGCACCATATTAAATCCTGGAAAACTAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:281)

Homo sapiens GALC 3'-UTR
GALC-002 ENST00000393569
TACTTAACAGGGCATCATAGAATACTCTGGATTTTCTTCCCTTCTTTTTGGTTTTGGTTCAGAGCC
AATTCTTGTTTCATTGGAACAGTATATGAGGCTTTTGAGACTAAAAATAATGAAGAGTAAAAGGGG
AGAGAAATTTATTTTTAATTTACCCTGTGGAAGATTTTATTAGAATTAATTCCAAGGGGAAAACTG
GTGAATCTTTAACATTACCTGGTGTGTTCCCTAACATTCAAACTGTGCATTGGCCATACCCTTAGG
AGTGGTTTGAGTAGTACAGACCTCGAAGCCTTGCTGCTAACACTGAGGTAGCTCTCTTCATCTTAT
TTGCAAGCGGTCCTGTAGATGGCAGTAACTTGATCATCACTGAGATGTATTTATGCATGCTGACCG
TGTGT
(SEQ ID NO:282)

Homo sapiens GALC 3'-UTR
GALC-005 ENST00000393568
TACTTAACAGGGCATCATAGAATACTCTGGATTTTCTTCCCTTCTTTTTGG
(SEQ ID NO:283)

Homo sapiens PDE1A 3'-UTR
NM_001003683.2

ACACCTTTAAGTAAAACCTCGTGCATGGTGGCAGCTCTAATTTGACCAAAAGACTTGGAGATTTTG
ATTATGCTTGCTGGAAATCTACCCTGTCCTGTGTGAGACAGGAAATCTATTTTTGCAGATTGCTCA
ATAAGCATCATGAGCCACATAAATAACAGCTGTAAACTCCTTAATTCACCGGGCTCAACTGCTACC
GAACAGATTCATCTAGTGGCTACATCAGCACCTTGTGCTTTCAGATATCTGTTTCAATGGCATTTT
GTGGCATTTGTCTTTACCGAGTGCCAATAAATTTTCTTTGAGCAGCTAATTGCTAATTTTGTCATT
TCTACAATAAAGCTTGGTCCACCTGTTTTC
(SEQ ID NO:284)

Homo sapiens PDE1A 3'-UTR
PDE1A-003 ENST00000410103
ACACCTTTAAGTAAAACCTCGTGCATGGTGGCAGCTCTAATTTGACCAAAAGACTTGGAGATTTTG
ATTATGCTTGCTGGAAATCTACCCTGTCCTGTGTGAGACAGGAAATCTATTTTTGCAGATTGCTCA
ATAAGCATCATGAGCCACATAAATAACAGCTGTAAACTCCTTAATTCACCGGGCTCAACTGCTACC
GAACAGATTCATCTAGTGGCTACATCAGCACCTTGTGCTTTCAGATATCTGTTTCAATGGCATTTT
GTGGCATTTGTCTTTACCGAGTGCCAATAAATTTTCTTTGAGCA
(SEQ ID NO:285)

Homo sapiens GSTM5 3'-UTR
NM_000851
GGCCCAGTGATGCCAGAAGATGGGAGGGAGGAGCCAACCTTGCTGCCTGCGACCCTGGAGGACAGC
CTGACTCCCTGGACCTGCCTTCTTCCTTTTTCCTTCTTTCTACTCTCTTCTCTTCCCCAAGGCCTC
ATTGGCTTCCTTTCTTCTAACATCATCCCTCCCCGCATCGAGGCTCTTTAAAGCTTCAGCTCCCCA
CTGTCCTCCATCAAAGTCCCCCTCCTAACGTCTTCCTTTCCCTGCACTAACGCCAACCTGACTGCT
TTTCCTGTCAGTGCTTTTCTCTTCTTTGAGAAGCCAGACTGATCTCTGAGCTCCCTAGCACTGTCC
TCAAAGACCATCTGTATGCCCTGCTCCCTTTGCTGGGTCCCTACCCCAGCTCCGTGTGATGCCCAG
TAAAGCCTGAACCATGCCTGCCATGTCTTGTCTTATTCCCTGAGGCTCCCTTGACTCAGGACTGTG
CTCGAATTGTGGGTGGTTTTTTGTCTTCTGTTGTCCACAGCCAGAGCTTAGTGGATGGGTGTGTGT
GTGTGTGTGTTGGGGGTGGTGATCAGGCAGGTTCATAAATTTCCTTGGTCATTTCTGCCCTCTAGC
CACATCCCTCTGTTCCTCACTGTGGGGATTACTACAGAAAGGTGCTCTGTGCCAAGTTCCTCACTC
ATTCGCGCTCCTGTAGGCCGTCTAGAACTGGCATGGTTCAAAGAGGGGCTAGGCTGATGGGGAAGG
GGGCTGAGCAGCTCCCAGGCAGACTGCCTTCTTTCACCCTGTCCTGATAGACTTCCCTGATCTAGA
TATCCTTCGTCATGACACTTCTCAATAAAACGTATCCCACCGTATTGTAAAAAAAAAAAAAAA
(SEQ ID NO:286)

Homo sapiens CADPS2 3'-UTR
CADPS2-002 ENST00000412584
TATCACACAGCTTTGCAGAAGGAAGGAAGACCTTGATCGACATTGTTTTTTATTTTTTTAACCTTG
TCCTTGTAATTACATTCATTGTTTGTTTTGGCCAAATAAAAATGCTTGTATTTCTTTAAAAAGTAA
GCCTGAATGTAGAGTAAAAGGGGAAATGCCAAGATTTTGGGGTTTTTTTGTTTCCTTTTTTTGTTT
GTTTGTTTGTTTGTTTTTTTGGAGAAGAGCATCCTCTTTTGTGTAGTTTGACCTAAAAATGAACCT
TGGCTCTGCTTGTGATCAGAACATGAACTTTTTTTTTTAAAGAAGATTTGAGCATTTTTCTGTAAT
CACATCAAAATGATGTTTTCTGTGTAAAGCGAGATACATATTTCTCATAATGCAGCATTGTGAGAA
GTCAGTTCGGACCACTGCACCAA
(SEQ ID NO:287)

Homo sapiens CADPS2 3'-UTR
CADPS2-001 ENST00000449022
TATCACACAGCTTTGCAGAAGGAAGGAAGACCTTGATCGACATTGTTTTTTATTTTTTTAACCTTG
TCCTTGTAATTACATTCATTGTTTGTTTTGGCCAAATAAAAATGCTTGTATTTCTTTAAAAAGTAA
GCCTGAATGTAGAGTAAAAGGGGAAATGCC
(SEQ ID NO:288)

Homo sapiens AASS 3'-UTR
AASS-001 ENST00000417368
TTGGGAATTATATTTTGTTTTTTTCTTCCCAGGCAATACACCTCTGAACATGTGTGTGATAAATGG
GTTTGCTAATGTGCTGTTTTAAAGTATAAAGCATAATATGTTTTGGTTAACACAATGTACTTTTTG
AACTATAAATCTTTATTTTAATATGGAAATGTTTGGAACAGGAGATGCAAGCCACTAACAGAGAAC
TTTAATAATTCTACCCTGTATTTTATAAATACGTATGTGAAAGTGATGA
(SEQ ID NO:289)

Homo sapiens TRIM6-TRIM34 3'-UTR
NM_001003819
ATTTTCTCATTTCTTCACCTACAACCCTTTGTCTTGACTTATCTCCTGCAACTGACTCATCTGCAA
CATTCACACCATTGCTTCCTTGTGGTTTCCCTTCTTTAGAACTTTTACTCATCCTTGAGATGTATG
GTGTATTTGGCTTGAGTTATGAGAGATGCTTATTTATTCATTTACTCTTTTTCATATTTTCAGAGA
AAGTTACCTAATCCCTCCTAAAGACACAGCAGTATGGGTATAACATCCTTGCCTTCCCATTTATCC
ATGTTTCACTTTATCACTGATATGAAGAGGCCCAAAGCCTGTTAGCCACCATCCATGCTACCTAGG
TAGTCCATAGGAACCACCCCCATGACCACCACCAACATCAACTAAAGGTTCTTGGAGGGTATGTCA
GTGTGTTGCTCAGGATACCCCAGGTACATCAAGGAATCAAGGAGAGGAAAATATGAGCAATATGTG
TATTCAGAGTGAAGATTTTATGTCCAGAGTATTTGAGCTCAAACCTTGCCTGTTGTTTTCTAATCA
TGATGAATACTTTCTCAGTTTCTTTTTCCTGAAATATAAATTGGGATTTAAGACTGTACCTAACTA
TTAAGATCACTGTGTAAAACTAAGTGTCTCTAAATGTAATGCATCGATTTAGTGTCTGGAACATAA
TAAATATTTGCTCTCATGATTGCTAAAAAAAAAAA
(SEQ ID NO:290)

Homo sapiens SEPP1 3'-UTR
NM_005410
ATATTTAAAATAGGACATACTCCCCAATTTAGTCTAGACACAATTTCATTTCCAGCATTTTTATAA
ACTACCAAATTAGTGAACCAAAAATAGAAATTAGATTTGTGCAAACATGGAGAAATCTACTGAATT
GGCTTCCAGATTTTAAATTTTATGTCATAGAAATATTGACTCAAACCATATTTTTTATGATGGAGC
AACTGAAAGGTGATTGCAGCTTTTGGTTAATATGTCTTTTTTTTTCTTTTTCCAGTGTTCTATTTG
CTTTAATGAGAATAGAAACGTAAACTATGACCTAGGGGTTTCTGTTGGATAATTAGCAGTTTAGAA
TGGAGGAAGAACAACAAAGACATGCTTTCCATTTTTTTCTTTACTTATCTCTCAAAACAATATTAC
TTTGTCTTTTCAATCTTCTACTTTTAACTAATAAAATAAGTGGATTTTGTATTTTAAGATCCAGAA
ATACTTAACACGTGAATATTTTGCTAAAAAAGCATATATAACTATTTTAAATATCCATTTATCTTT
TGTATATCTAAGACTCATCCTGATTTTTACTATCACACATGAATAAAGCCTTTGTATCTTTCTTTC
TCTAATGTTGTATCATACTCTTCTAAAACTTGAGTGGCTGTCTTAAAAGATATAAGGGGAAAGATA
ATATTGTCTGTCTCTATATTGCTTAGTAAGTATTTCCATAGTCAATGATGGTTTAATAGGTAAACC
AAACCCTATAAACCTGACCTCCTTTATGGTTAATACTATTAAGCAAGAATGCAGTACAGAATTGGA
TACAGTACGGATTTGTCCAAATAAATTCAATAAAAACCTTAAAGCTGAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:291)

Homo sapiens SEPP1 3'-UTR
SEPP1-004 ENST00000506577
ATATTTAAAATAGGACATACTCCCCAATTTAGTCTAGACACAATTTCATTTCCAGCATTTTTATAA
ACTACCAAATTAGTGAACCAAAAATAGAAATTAGATTTGTGCAAACATGGAGAAATCTACTGAATT
GGCTTCCAGATTTTAAATTTTATGTCATAGAAATATTGACTCAAACCATATTTTTTATGATGGAGC
AACTGAAAGGTGATTGCAGCTTTTGGTTAATATGTCTTTTTTTTTCTTTTTCCAGTGTTCTATTTG
CTTTAATGAGAATAGAAACGTAAACTATGACCTAGGGGTTTCTGTTGGATAATTAGCAGTTTAGAA
TGGAGGAAGAACAACAAAGACATGCTTTCCATTTTTTTCTTTACTTATCTCTCAAAACAATATTAC
TTTGTCTTTTCAATCTTCTACTTTTAACTAATAAAATAAGTGGATTTTGTATTTTAAGATCCAGAA
ATACTTAACACGTGAATATTTTGCTAAAAAAGCATATATAACTATTTTAAATATCCATTTATCTTT
TGTATATCTAAGACTCATCCTGATTTTTACTATCACACATGAATAAAGCCTTTGTATCTTT

(SEQ ID NO:292)

Homo sapiens PDE5A 3'-UTR
PDE5A-002 ENST00000264805
GTGGCCTATTTCATGCAGAGTTGAAGTTTACAGAGATGGTGTGTTCTGCAATATGCCTAG
(SEQ ID NO:293)

Homo sapiens SATB1 3'-UTR
SATB1-004 ENST00000417717
GATAAAAGTATTTGTTTCGTTCAACAGTGCCACTGGTATTTACTAACAAAATGAAAAGTCCACCTT
GTCTTCTCTCAGAAAACCTTTGTTGTTCATTGTTTGGCCAATGAATCTTCAAAAACTTGCACAAAC
AGAAAAGTTGGAAAAGGATAATACAGACTGCACTAAATGTTTTCCTCTGTTTTACAAACTGCTTGG
CAGCCCCAGGTGAAGCATCAAGGATTGTTTGGTATTAAAATTTGTGTTCACGGGATGCACCAAAGT
GTGTACCCCGTAAGCATGAAACCAGTGTTTTTTGTTTTTTTTTTAGTTCTTATTCCGGAGCCTCAA
ACAAGCATTATACCTTCTGTGATTATGATTTCCTCTCCTATAATTATTTCTGTAGCACTCCACACT
GATCTTTGGAAACTTGCCCCTTATTT
(SEQ ID NO:294)

Homo sapiens CCPG1 3'-UTR
CCPG1-002 ENST00000442196
TTCACAATTGAGTTAAATTAGACAACTGTAAGAGAAAAATTTATGCTTTGTATAATGTTTGGTATT
GAAACTAATGAAATTACCAAGATGACAATGTCTTTTCTTTTGTTTCTAAGTATCAGTTTGATAACT
TTATATTATTCCTCAGAAGCATTAGTTAAAAGTCTACTAACCTGCATTTTCCTGTAGTTTAGCTTC
GTTGAATTTTTTTTGACACTGGAAATGTTCAACTGTAGTTTTATTAAGGAAGCCAGGCATGCAACA
GATTTTGTGCATGAAATGAGACTTCCTTTCAGTGTAAGAGCTTAAAGCAAGCTCAGTCATACATGA
CAAAGTGTAATTAACACTGATGTTTGTGTTAAATTTGCAGCAGAGCTTGAGAAAAGTACATTGTTC
TGGAATTTCATCATTAACATTTTATAATCTTACACTCACTTCTTGTCTTTTTGTGGGTTCAAGAGC
CCTCTGACTTGTGAAGAATTTGCTGCCCTCTTAAGAGCTTGCTGACTTGTTTTCTTGTGAAATTTT
TTGCACATCTGAATATCGTGGAAGAAACAATAAAACTACACCATGAGGAAAACTAAAGGTCTTTAT
TTAAAATCTGGCATTGTATTAACATGTAATTTTATACTATGTGGTATTTTATACATTTCCTCAGTA
GTGATATTTGGTAAAGCAGTTCATACAGCTTTTTTCTAAGTTCCATGAATCTTACCCAGTGTTTAC
CGAAGTATTTAAGCAGCATCTGAATATTTCCACCCAGCAATGTTAATTTATCTAGGAAAGTTCAGA
ATTTCATCTTCATGTTGAATTTCCCTTTTAACTTCCGTTCATAGACATATATGTGACTTCCAATTC
GACCCTCTGGCAAGTGAGTGTGGAAGAAAACAGCAGTTCTTTTATAATTGCTTGAAATTAGGAAAG
CGCTTATTTCCTAGAAGCAAATAAATGTTTAAGTAAATAAAGGCTACATTTTGCTGA
(SEQ ID NO:295)

Homo sapiens CCPG1 3'-UTR
CCPG1-004 ENST00000425574
TTCACAATTGAGTTAAATTAGACAACTGTAAGAGAAAAATTTATGCTTTGTATAATGTTTGGTATT
GAAACTAATGAAATTACCAAGATGACAATGTCTTTTCTTTTGTTTCTAAGTATCAGTTTGATAACT
TTATATTATTCCTCAGAAGCATTAGTTAAAAGTCTACTAACCTGCATTTTCCTGTAGTTTAGCTTC
GTTGAATTTTTTTTGACACTGGAAATGTTCAACTGTAGTTTTATTAAGGAAGCCAGGCATGCAACA
GATTTTGTGCATGAAATGAGACTTCCTTTCAGTGTAAGAGCTTAAAGCAAGCTCAGTCATACATGA
CAAAGTGTAATTAACACTGATGTTTGTGTTAAATTTGCAGCAGAGCTTGAGAAAAGTACATTGTTC
TGGAATTTCATCATTAACATTTTATAATCTTACACTCACTTCTTGTCTTTTTGTGGGTTCAAGAGC
CCTCTGACTTGTGAAGAATTTGCTGCCCTCTTAAGAGCTTGCTGACTTGTTTTCTTGTGAAATTTT
TTGCACATCTGAATATCGTGGAAGAAACAATAAAACTACACCATGAG
(SEQ ID NO:296)

Homo sapiens CNTN1 3'-UTR
CNTN1-002 ENST00000348761
ATGTGTTGTGACAGCTGCTGTTCCCATCCCAGCTCAGAAGACACCCTTCAACCCTGGGATGACCAC
AATTCCTTCCAATTTCTGCGGCTCCATCCTAAGCCAAATAAATTATACTTTAACAAACTATTCAAC
TGATTTACAACACACATGATGACTGAGGCATTCGGGAACCCCTTCATCCAAAAGAATAAACTTTTA
AATGGATATAAATGATTTTTAACTCGTTCCAA
(SEQ ID NO:297)

Homo sapiens CNTN1 3'-UTR
CNTN1-004 ENST00000547849
TCGTTGACACTCACCATTTCTGTGAAAGACTTTTTTTTTTTTAACATATTATACTAGATTTGACTA
ACTCAATCTTGTAGCTTCTGCAGTTCTCCCCACCCCCAACCTAGTTCTTAGAGTATGTTTCCCCTT
TTGAAACATGTAAACATACTTTGGGCATAAATATTTTTTAAAATATAACTATAATGCTTCACTAAT
ACCTTAAAAATGCCTAGTGAACTAACTCAGTACATTATATAATGGCCAAGTGAAAGTTTTGTGTTT
TCATGTCCTGTTTTTCTTTGAAATTATATAGCCCAGAAATTAGCTCATTATCTGAAAAACGTATGA
AGAACTGATGAATTGTATAATACAGGAGTATTGCCATTGAATGTACTGTTTGATTTATTCAAGCAG
GTAATGAACAATGTTGTCAAACTCTCTAATGAGACATCATAATTAGGACATAAGCTAAAAGGGGCA
TTACTCCGGCAGTCTTTTTTTCTTAATCCTAGTACCATACATATTCTTTGGCATGAAAGAATGAAA
AGCATTAGTAAACAACTGAAGTCCTACCATGGCTCTGTAGGGTTTTTGGAACAATTCCTGGAATTG
GAAAGTGAAAATGGATAGCATGTGGGGGAAACCCTCATCTGAGTAGCAAGATTTTAGTAAAGATGA
CTAAGCCATTAACAGCATGCATTCATATTTAATTTTATTGACTCCTGCCATCAGCTTTTGTAGATC
GTTTGGGTGGAAGGTTGTGATTTTTACTGGGAGGACTTGAGTAGAAGTGGATGATTAAAATTGAGG
AGTATATAATTCTTTCTGGGACTGCTTAAATGTTATTGTTTGAAAATACCTTCACTTTCCCCCTTT
GGTCAAAGAGATGTGCTTAAAATTCTTATTCCTTCACAATAAATAATTTTGATTTTCTTAGACA
(SEQ ID NO:298)

Homo sapiens CNTN1 3'-UTR
CNTN1-004 ENST00000547849
+T at pos. 30bp, mutations G727bpT, A840bpG
*TTT*TTTCGTTGACACTCACCATTTCTGTGAA
AGACTTTTTTTTTTTTTAACATATTATACTAGATTTGACTAACTCAATCTTGTAGCTTCT
GCAGTTCTCCCCACCCCCAACCTAGTTCTTAGAGTATGTTTCCCCTTTTGAAACATGTAA
ACATACTTTGGGCATAAATATTTTTTAAAATATAACTATAATGCTTCACTAATACCTTAA
AAATGCCTAGTGAACTAACTCAGTACATTATATAATGGCCAAGTGAAAGTTTTGTGTTTT
CATGTCCTGTTTTTCTTTGAAATTATATAGCCCAGAAATTAGCTCATTATCTGAAAAACG
TATGAAGAACTGATGAATTGTATAATACAGGAGTATTGCCATTGAATGTACTGTTTGATT
TATTCAAGCAGGTAATGAACAATGTTGTCAAACTCTCTAATGAGACATCATAATTAGGAC
ATAAGCTAAAAGGGGCATTACTCCGGCAGTCTTTTTTTCTTAATCCTAGTACCATACATA
TTCTTTGGCATGAAAGAATGAAAAGCATTAGTAAACAACTGAAGTCCTACCATGGCTCTG
TAGGGTTTTTGGAACAATTCCTGGAATTGGAAAGTGAAAATGGATAGCATGTGGGGGAAA
CCCTCATCTGAGTAGCAAGATTTTAGTAAAGATGACTAAGCCATTAACAGCATGCATTCA
TATTTAATTTTATTGACTCCTGCCATCAGCTTTTGTAGATCTTTTGGGTGGAAGGTTGTG
ATTTTTACTGGGAGGACTTGAGTAGAAGTGGATGATTAAAATTGAGGAGTATATAATTCT
TTCTGGGACTGCTTAAATGTTATTGTTTGAAAATGCCTTCACTTTCCCCCTTTGGTCAAA
GAGATGTGCTTAAAATTCTTATTCCTTCACAATAAATAATTTTGATTTTCTTAGACA
(SEQ ID NO:299)

Homo sapiens LMBRD2 3'-UTR
AGTCTGAAAAAGTTTGTGGGACCACTAACCAAGGTCAACACATCAGTTCAGTCTTGATGAACATCT
GTGTACCCTAGAATTTCCTCTATACACAGTGAAAAGTGTCAAGATAACAAAAAAGGCACTGAGAAT
TAATTATATCTTAGGAATAATAGTTTAATGTGCATTGAATAGAGTATCACCTTTTTCAACAAGATT
TATTACATATCATTTCCTAAGCATCTGCCTTAGAAATACAGTTACAGTGGAAGGACTTTAAGAAAG

ATCAACATATGTTAAGAACATGCAGTTCAGTTTGTTTCAGATTAATTTTTTTTCAAGAGAGTTATT
TTAAAGATTCAAGGAAGCCATAAGTCATACTAAATAATATTATATACAGTTTTGTTATTGTGACTT
ACATTTTTGTTACTTCTAAAAAGTATATTCAACCTGTATTTCCCAAAGAAATGTAAGTGAATGGAG
ACCTCAAATAATAACTGTATTCATAAAACTCGTGTCTTAAAACAAGGCTTACTTACTAGACATAAC
TGAATGTAAAAAGTGCTTTTTCAAATCTGTTTGCAAACTCGTGGGGGATTTTTGCATGTATAAGAT
TAAGATTATACTTCAAGTGATGCGTGTCTGTGTATTTAGCATGTGTACTATAATCAGGTGATATAG
TATTCCTTCAGTCTTTGTAGTAACTGGATTTTTTTATGCTTCTGGTATTGCTTTATAAAAGATTTT
CATTTCAG
(SEQ ID NO:300)

Homo sapiens TLR3 3'-UTR
NM_003265
ATTTATTTAAATATTCAATTAGCAAAGGAGAAACTTTCTCAATTTAAAAAGTTCTATGGCAAATTT
AAGTTTTCCATAAAGGTGTTATAATTTGTTTATTCATATTTGTAAATGATTATATTCTATCACAAT
TACATCTCTTCTAGGAAAATGTGTCTCCTTATTTCAGGCCTATTTTTGACAATTGACTTAATTTTA
CCCAAAATAAAACATATAAGCACGTAAAAAAAAAAAAAAAAAA
(SEQ ID NO:301)

Homo sapiens BCAT1 3'-UTR
BCAT1-002 ENST00000342945
ATGGAAAATAGAGGATACAATGGAAAATAGAGGATACCAACTGTATGCTACTGGGACAGACTGTTG
CATTTGAATTGTGATAGATTTCTTTGGCTACCTGTGCATAATGTAGTTTGTAGTATCAATGTGTTA
CAAGAGTGATTGTTTCTTCATGCCAGAGAAAATGAATTGCAATCATCAAATGGTGTTTCATAACTT
GGTAGTAGTAACTTACCTTACCTTACCTAGAAAAACATTAATGTAAGCCATATAACATGGGATTTT
CCTCAATGATTTTAGTGCCTCCTTTTGTACTTCACTCAGATACTAAATAGTAGTTTATTCTTTAAT
ATAAGTTACATTCTGCTCCTCAAACAAATGCAATTTTTTGTGTGTGTTTGAAAGCTAATTTGAGAA
AATTTCATAGGTTACATTTCCTGCAGCCTATCTTTATCCACAGAAAGTGTTTTCTTTTTTTTAAAT
CAAGACTTTTAAAACTGGATTTCCTCCCATCACTGTTTTTTGAAGGTCCTCCAAGTCCGTGTTAA
(SEQ ID NO:302)

Homo sapiens BCAT1 3'-UTR
ATGGAAAATAGAGGATACAATGGAAAATAGAGGATACCAACTGTATGCTACTGGGACAGACTGTTG
CATTTGAATTGTGATAGATTTCTTTGGCTACCTGTGCATAATGTAGTTTGTAGTATCAATGTGTTA
CAAGAGTGATTGTTTCTTCATGCCAGAGAAAATGAATTGCAATCATCAAATGGTGTTTCATAACTT
G
(SEQ ID NO:303)

Homo sapiens TOM1L1 3'-UTR
TOM1L1-001 ENST00000575882
GAAGAAAGTGGATGATCAGCTCACTACCACATCAAAGGTGCCAACTCTCTAAAACGTAGACTCTGT
GCAGCTTTGAAGCCTGGAAGACAATACCTACCAACATGTCAAAGCCATGGTGGCACATTTCTGCTA
TAATGAAGATTAAATAGAATAACAGTTCCAGGATAACACTGATTCCTGACAACAGCGTGAGATTTC
AACAGAACTTGTTTGGAACAAATACTCACTTAAAACTTCAGCAGAAGAAAAATTACTTAGTCCTTA
GGCCAACCAATTTAACTGCAGTGTCATGTTTCACAGGCCTTCCTACATTTAGAAATCGTCACACAG
CTGTGATAAGAGTAGATTATTTTACTATGAAATAATTCTGAATAGATGAAAGCATAAAATGTGAGA
AACTGAATGTATTATTCAGGAAGAATACTGAGTGCCTTCATTTAACTAAAGTTGAATGTAAAAGTC
AATTTGCACTTCTTTATAATCCTCTGGTTTAGAATTATAAATTGTTAAAACCTTGATAATTGTCAT
TTAATTATATTTCAGGTGTCCTGAACAGGTCACTAGACTCTACATTGGGCAGCCTTTAAATATGAT
TCTTTGTAATGCTAAATAGCCTTTTTTTCTCTTTTTACTGCAACTTAATATTTCTATTTAGAACAC
AGAAAATGAAAATATTTAGAATAAGTTGTACATTTGATGACAAATAAATCACTATT
(SEQ ID NO:304)

Homo sapiens SLC35A1 3′-UTR
SLC35A1-201 ENST00000369556
TTTTAGCCTCACGTGAGACTCCTTTTAAGACTAAACCATTTGCATTAAACTAGAGCCTTAAGTCAA
TCTCAGAAGGTAGCATAAACAAATAAAAATTAACTGTATGGCATGATCAGTGCGGTTATGTGGAAA
CAACAACAAACAAACGAAGCTATCTGAGTGAACTGCTAATACAGAAACTTAATGTAGACCTGTTTG
GGGTCTACTATTGTTTTAGAATGAAGGAATTGTATTATTGTGTGTATATATAATTTGTAAATAAAA
AGTATGGAGATGATACGGTGTTAAAAAAAATCATGGTAAGGCTACAATACTCAAGTAACAAGGTTT
GGGACAATGTCTAAGGGTTAAAGTGCCAAAGCCATTTCTGTACTAACTGTTCTCTTGTTCCGGTAC
CGGGGAGAAGGATGACCCCTCCTTATTCTCCAATTCATGTACAGTATTTTGTCCTAGCAGCATAAA
GACCTAGCTCTTTTCTTACAAGAGGCAGAAACAAGACAGGCTAGTTCATAAACAAACTGTGTAACT
TCTCAAAATGAATCTATTTCATAACTCGGACAATTTCTGGGTGGTGACTGAGTACCCCTTTAGTGA
GTACCCCTTTAGTGCTATATTTGTGCCATTCATTATCTGGTTCATATTTCTTTTCTGTTAGATGAT
ACACATTTCTTCAAAAAAATTTCTAATGTCACTTTTGTACTTTTTTAAATAAAGTATGTTTAACTG
TTGGGCTCTCAATAATTTGTGAAATTTCAGTGTTTTCTATAATGTTAATGGGGAAATTCAGCAATA
AACTTTATTTGT
(SEQ ID NO:305)

Homo sapiens GLYATL2 3′-UTR
GLYATL2-003 ENST00000532258
TTGATTCCACTGTCCATTTCAAATCTTTCTTATCAGTAAAAAAACATTAATTCAAACACAAGCATT
GTGATCTACATTAGCACAAAATGCAACTGATTATCTAGGATCTGTGTATTACTTAAGCTCACCCTT
AACAGTTTTACCTTCCTTCTCCTCTGTATTCTTACAGAAAATTAGAAGCTCAATTTTATGGTCTCA
TAATTTCCTTTATGACAGACATCTCAGAATTAAAATCACCCAAAGCCAATCATTAGTGCCAAGATA
ACCCTTTAACGGCAACACTTTCTTAAATGAAGACTATTTCTTTCATGAAAAAATTCACTTTTATGA
CT
(SEQ ID NO:306)

Homo sapiens STAT4 3′-UTR
STAT4-002 ENST00000392320
CAGGATAAACTCTGACGCACCAAGAAAGGAAGCAAATGAAAAAGTTTAAAGACTGTTCTTTGCCCA
ATAACCACATTTTATTTCTTCAGCTTTGTAAATACCAGGTTCTAGGAAATGTTTGACATCTGAAGC
TCTCTTCACACTCCCGTGGCACTCCTCAATTGGGAGTGTTGTGACTGAAATGCTTGAAACCAAAGC
TTCAGATAAACTTGCAAGATAAGACAACTTTAAGAAACCAGTGTTAATAACAATATTAACAG
(SEQ ID NO:307)

Homo sapiens GULP1 3′-UTR
GULP1-002 ENST00000409609
CATCAAGAACAAGAAATCCTGATTCATGTTAAATGTGTTTGTATACACATGTCATTTATTATTATT
ACTTTAAGATAGGTATTATTCATGTGTCAATGTTTTTGAATATTTTAATATTTTGAAAATTTTCTC
AGTTAAATTTCCTCACCTTCACTATTGATCTGTAATTTTTATTTTAAAAACAGCTTACTGTAAAGT
AGATCATACTTTTATGTTCCTTTCTGTTTCTACTGTAGATGAATTTGTAATTGAAAGACATATTAT
ACAAAT
(SEQ ID NO:308)

Homo sapiens GULP1 3′-UTR
GULP1-010 ENST00000409805
CATCAAGAACAAGAAATCCTGATTCATGTTAAATGTGTTTGTATACACATGTCATTTATTATTATT
ACTTTAAGATAGG
(SEQ ID NO:309)

Homo sapiens EHHADH 3'-UTR
EHHADH-002 ENST00000456310
TTCAGTCTTCCAGATTATGCCTCACATGCTAGCATCAGGTAATGCTGACTGAATTTCAGTGAAATT
AAATCAAAAATCCAAAGTAAGATTGTTCTGAAATACAAAGCAAAATAAATAATCATTAGAATCTTC
TGTGTAACGACTCTAATGGTCAAATCTTTAGGAATGTGCTTCCTATGCCTCTGAATCTGTCCTTAT
CAGATAAATTCAATGCATGAACTTGTGTGAATATAATACCATAATAGCTAATGAAAGA
(SEQ ID NO:310)

Homo sapiens NBEAL1 3'-UTR
NM_001114132.1
TTGTTATTTCCATTTTCTGTTATGATTACTGAAACCTGATTTATTGCTTTGTCACTTTAACCACAT
CTCTCAACTCTCTGCAATGTTGCAAGGCTTTTATCCCTGAAAATCATTTACAGATAACCACAATTT
GCTGTGGTATATAAACTAATTCTTGGTCTATACTAAGATGTATTTGAGAAAATACATTTGATTTGA
TTTTGTGGCCCATTCCTAAAGGTCATTGTATCCATTTTTAAAACAAACTAAAATGAGAACATTAGG
TTCAATTTTCTTATTATTCCAAATGATAAAATTTAAGATTTTTCTAATAAAAGAGTACAGATAATG
GGACAGTTGAGAGAGATGGCTTTAAATACATTCTTAAGTAATCATTTTCCTATTTACTGACCACTG
TAATGAAAATATATCAATTTATTTATGGAACTCCTGATTGGGGATAATATTTTAAAGGTATCTGTT
GCACACTTGGATTTTCAAAACTCGGTGAAAGTTACAAGTTTGCATGGTAAGAATAAAATAAGAATA
TTGAAACTGGTACATTAGCTAATTCTATTACTACTTAGCGTGTTTCTAATGAGAAGTTACTGAAAT
CTATTACTGTCCTTAATAAAAATTGAGTAGAAAAAAGTGGAACTAG
(SEQ ID NO:311)

Homo sapiens KIAA1598 3'-UTR
NM_001258299.1
TCTGAATCAGAAAATACTGCAACTCCTTCCTCCTTTTGTCTGCCTTTTGTTCTCCAAAAGTAAGTG
GAAATTACATTTCCAAGAAAGGAAATGAAATAATTGCAGGCCCAAGGTCTGCAAAATATGTGTTGA
ATTGACAGTGAAAAGGATCCATGTGTTGACAGACACAGTTGTTAGATGCCATAAAGGCAGATGTGA
AGCTCAATTTATTTCTCATCTTGCTTG
(SEQ ID NO:312)

Homo sapiens HFE 3'-UTR
HFE-006 ENST00000317896
CACGCAGCCTGCAGACTCACTGTGGGAAGGAGACAAAACTAGAGACTCAAAGAGGGAGTGCATTTA
TGAGCTCTTCATGTTTCAGGAGAGAGTTGAACCTAAACATAGAAATTGCCTGACGAACTCCTTGAT
TTTAGCCTTCTCTGTTCATTTCCTCAAAAAGATTTCCCCATTTAGGTTTCTGAGTTCCTGCATGCC
GGTGATCCCTAGCTGTGACCTCTCCCCTGGAACTGTCTCTCATGAACCTCAAGCTGCATCTAGAGG
CTTCCTTCATTTCCTCCGTCACCTCAGAGACATACACCTATGTCATTTCATTTCCTATTTTTGGAA
GAGGACTCCTTAAATTTGGGGGACTTACATGATTCATTTTAACATCTGAGAAAAGCTTTGAACCCT
GGGACGTGGCTAGTCATAACCTTACCAGATTTTTACACATGTATCTATGCATTTTCTGGACCCGTT
CAACTTTTCCTTTGAATCCTCTCTCTGTGTTACCCAGTAACTCATCTGTCACCAAGCCTTGGGGAT
TCTTCCATCTGATTGTGATGTGAGTTGCACAGCTATGAAGGCTGTACACTGCACGAATGGAAGAGG
CACCTGTCCCAGAAAAAGCATCATGGCTATCTGTGGGTAGTATGATGGGTGTTTTTAGCAGGTAGG
AGGCAAATATCTTGAAAGGGGTTGTGAAGAGGTGTTTTTTCTAATTGGCATGAAGGTGTCATACAG
ATTTGCAAAGTTTAATGGTGCCTTCATTTGGGATGCTACTCTAGTATTCCAGACCTGAAGAATCAC
AATAATTTTCTACCTGGTCTCTCCTTGTTCTGATAATGAAAATTATGATAAGGATGATAAAAGCAC
TTACTTCGTGTCCGACTCTTCTGAGCACCTACTTACATGCATTACTGCATGCACTTCTTACAATAA
TTCTATGAGATAGGTACTATTATCCCCATTTCTTTTTTAAATGAAGAAAGTGAAGTAGGCCGGGCA
C
(SEQ ID NO:313)

Homo sapiens HFE 3'-UTR
HFE-004 ENST00000349999
CACGCAGCCTGCAGACTCACTGTGGGAAGGAGACAAAACTAGAGACTCAAAGAGGGAGTGCATTTA
TGAGCTCTTCATGTTTCAGGAGAGAGTTGAACCTAAACATAGAAATTGCCTGACGAACTCCTTGAT
TTTAGCCTTCTCTGTTCATTTCCTCAAAAAGATTTCCCCATTTAGGTTTCTGAGTTCCTGCATGCC
GGTGATCCCTAGCTGTGACCTCTCCCCTGGAACTGTCTCTCATGAACCTCAAGCTGCATCTAGAGG
CTTCCTTCATTTCCTCCGTCACCTCAGAGACATACACCTATGTCATTTCATTTCCTATTTTTGGAA
GAGGACTCCTTAAATTTGGGGGACTTACATGATTCATTTTAACATCTGAGAAAAGCTTTGAACCCT
GGGACGTGGCTAGTCATAACCTTACCAGATTTTTACACATGTATCTATGCATTTTCTGGACCCGTT
CAACTTTTCCTTTGAATCCTCTCTCTGTGTTACCCAGTAACTCATCTGTCACCAAGCCTTGGGGAT
TCTTCCATCTGATTGTGATGTGAGTTGCACAGCTATGAAGGCTGTACACTGCACGAATGGAAGAGG
CACCTGTCCCAGAAAAAGCATCATGGCTATCTGTGGGTAGTATGATGGGTGTTTTTAGCAGGTAGG
AGGCAAATATCTTGAAAGGGGTTGTGAAGAGGTGTTTTTTCTAATTGGCATGAAGGTGTCATACAG
ATTTGCAAAGTTTAATGGTGCCTTCATTTGGGATG
(SEQ ID NO:314)

Homo sapiens HFE 3'-UTR
HFE-005 ENST00000397022
CACGCAGCCTGCAGACTCACTGTGGGAAGGAGACAAAACTAGAGACTCAAAGAGGGAGTGCATTTA
TGAGCTCTTCATGTTTCAGGAGAGAGTTGAACCTAAACATAGAAATTGCCTGACGAACTCCTTGAT
TTTAGCCTTC
(SEQ ID NO:315)

Homo sapiens HFE 3'-UTR
HFE-012 ENST00000336625
CACGCAGCCTGCAGACTCACTGTGGGAAGGA
(SEQ ID NO:316)

Homo sapiens KIAA1324L 3'-UTR
KIAA1324L-005 ENST00000416314
AGAGACAGTGCTGTAGCCTTGAGACTAATGAACAAAGAAACCTGCTCTAGTTTTACAGGACCATAT
TTTAGGGTCTGTCCTCATACCTGTCACATTGGTGATCTCACAGAGGAGGGCCATGCCGCTGAAAAG
GGAAGGAGATTGAAACATTTGATTGCCTTATCACATGGTCAAGTACCTTGCCAAATAAAGGAAAGC
AAATGATTTGGGTCTCAACTGAAGATGAAGCTCAACTCAGGAAGAGATTTATCTGTATATACACAT
AACTGAAAACCAAGTTTAAGCCCACCAATGCACTGCTGATGCATGCCATATAATTAATGGGTAACT
TTTATTCTTTATGATGTCTACATAACAAGTGTGATTTGGAAGGCACATGTGAGCATATGCATTA
(SEQ ID NO:317)

Homo sapiens MANSC1 NM_018050 3'-UTR
GGATGGAACTCGGTGTCTCTTAATTCATTTAGTAACCAGAAGCCCAAATGCAATGAGTTTCTGCTG
ACTTGCTAGTCTTAGCAGGAGGTTGTATTTTGAAGACAGGAAAATGCCCCCTTCTGCTTTCCTTTT
TTTTTTTTGGAGACAGAGTCTTGCTTTGTTGCCCAGGCTGGAGTGCAGTAGCACGATCTCGGCTCT
CACCGCAACCTCCGTCTCCTGGGTTCAAGCGATTCTCCTGCCTCAGCCTCCTAAGTATCTGGGATT
ACAGGCATGTGCCACCACACCTGGGTGATTTTTGTATTTTTAGTAGAGACGGGGTTTCACCATGTT
GGTCAGGCTGGTCTCAAACTCCTGACCTAGTGATCCACCCTCCTCGGCCTCCCAAAGTGCTGGGAT
TACAGGCATGAGCCACCACAGCTGGCCCCCTTCTGTTTTATGTTTGGTTTTTGAGAAGGAATGAAG
TGGGAACCAAATTAGGTAATTTTGGGTAATCTGTCTCTAAAATATTAGCTAAAAACAAAGCTCTAT
GTAAAGTAATAAAGTATAATTGCCATATAAATTTCAAAATTCAACTGGCTTTTATGCAAAGAAACA
GGTTAGGACATCTAGGTTCCAATTCATTCACATTCTTGGTTCCAGATAAAATCAACTGTTTATATC
AATTTCTAATGGATTTGCTTTTCTTTTTATATGGATTCCTTTAAAACTTATTCCAGATGTAGTTCC
TTCCAATTAAATATTTG
(SEQ ID NO:318)

Preferably, the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which has an identity of at least about 1, 2, 3, 4, 5, 10, 15, 20, 30 or 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 the group consisting of SEQ ID NO: 25 or SEQ ID NO: 30 and SEQ ID NOs: 319 to 382 or the corresponding DNA or RNA sequence, respectively, 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 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 the group consisting of SEQ ID NO: 25 or SEQ ID NO: 30 and SEQ ID NOs: 319 to 382 or the corresponding DNA or RNA sequence, respectively:

Homo sapiens LTA4H 5'-UTR
LTA4H-001 ENST00000228740
AAGAAACTTCCTTTCCCGGCGTGCACCGCGAATCCCTCCTCCTCTTCTTTACCTCTCTCCCTCCTC
CTCAGGTTCTCTATCGACGAGTCTGGTAGCTGAGCGTTGGGCTGTAGGTCGCTGTGCTGTGTGATC
CCCCAGAGCC
(SEQ ID NO:319)

Homo sapiens DECR1 5'-UTR
DECR1-001 ENST00000220764
TCCAGCCCCGAGAACTTTGTTCTTTTTGTCCCGCCCCCTGCGCCCAACCGCCTGCGCCGCCTTCCG
GCCCGAGTTCTGGAGACTCAAC
(SEQ ID NO:320)

Homo sapiens PIGK 5'-UTR
ACTGCCTCCGCCCCTTCAGGTGCGGGAAGTCTGAAGCCGGTAAAC
(SEQ ID NO:321)

Homo sapiens BRP44L 5'-UTR
BRP44L-001
GTCGTGAGGCGGGCCTTCGGGCTGGCTCGCCGTCGGCTGCCGGGGGGTTGGCCGGGGTGTCATTGG
CTCTGGGAAGCGGCAGCAGAGGCAGGGACCACTCGGGGTCTGGTGTCGGCACAGCC
(SEQ ID NO:322)

Homo sapiens ACADSB 5'-UTR
ACADSB-004 NM_001609.3 ENST00000368869
AGGGATTAAGGGGGGGTGTGTGCGGGGCGGGTACTGAGTGGGCGGGGCCTTGCTCGGGTAACTCCC
AGGGGCTGGCTAGAGACCCAGAGGCGCAGAGCGGAGAGGCCTGCGGCGAGG

(SEQ ID NO:323)

Homo sapiens SUPT3H 5'-UTR
SUPT3H-006 ENST00000371459
CACAGCCGAGTCACCTTTTCCCTTTCTACACTCCACACTCTCAGTCCCCCACCCCGCCCCTTTCCA
AGCGTGTCCCGGGCCGCAGCAGCAGAAACCGCACCATCTCCACCCCCACATTCTCCTCGCGGGAAG
CGCAGCAGTGCCTCCAAGGGTTCTTAAAGCAGAG
(SEQ ID NO:324)

Homo sapiens TMEM14A 5'-UTR
NM_014051.3
GTTTCCAGGAGGGAGCGGCCTTTGCTCAGCGCGAGACGGCTGGGCGCCGAGTGGGACAGCGCTGGT
GCGGAGACTGCTTCCGGACTCCAGGTACCGCGCTTGGCGGCAGCTGGCCCCAGACTTCTGTCTTTT
CAGCTGCAGTGAAGGCTCGGGGCTGCAGAATTGCAACCTTGCCA
(SEQ ID NO:325)

Homo sapiens C9orf46 5'-UTR
AF225420.1
GAGCGAGGCCCGGTCCCTGCAGCGGGCGAAAGGAGCCCGGGCCTGGAGGTTTGCGTACCGGTCGCC
TGGTCCCGGCACCAGCGCCGCCCAGTGTGGTTTCCCATAAGGAAGCTCTTCTTCCTGCTTGGCTTC
CACCTTTAACCCTTCCACCTGGGAGCGTCCTCTAACACATTCAGACTACAAGTCCAGACCCAGGAG
AGCAAGGCCCAGAAAGAGGTCAAA
(SEQ ID NO:326)

Homo sapiens ANXA4 5'-UTR
NM_001153.3
GCCCCAGGTGCGCTTCCCCTAGAGAGGGATTTTCCGGTCTCGTGGGCAGAGGAACAACCAGGAACT
TGGGCTCAGTCTCCACCCCACAGTGGGGCGGATCCGTCCCGGATAAGACCCGCTGTCTGGCCCTGA
GTAGGGTGTGACCTCCGCAGCCGCAGAGGAGGAGCGCAGCCCGGCCTCGAAGAACTTCTGCTTGGG
TGGCTGAACTCTGATCTTGACCTAGAGTC
(SEQ ID NO:327)

Homo sapiens IFI6 5'-UTR
NM_022873.2
CCAGCCTTCAGCCGGAGAACCGTTTACTCGCTGCTGTGCCCATCTATCAGCAGGCTCCGGGCTGAA
GATTGCTTCTCTTCTCTCCTCCAAGGTCTAGTGACGGAGCCCGCGCGCGGCGCCACC
(SEQ ID NO:328)

Homo sapiens C2orf34 5'-UTR
CAMKMT -008 ENST00000402247
TCCTGGCAGGGGACGAGCTGCGGCGGTGGCACCTCCGGGTGTGGAAGGCTCCAGTGAG
(SEQ ID NO:329)

Homo sapiens C2orf34 5'-UTR
NM_024766.3
GAGGGTGCCGGGCGTCACAGGTCCTGACAGGGAAGAAGTTGGCAGGTCCTGGCAGGGGACGAGCTG
CGGCGGTGGCACCTCCGGGTGTGGAAGGCTCCAGTGAG
(SEQ ID NO:330)

Homo sapiens ALDH6A1 5'-UTR
ALDH6A1-002 ENST00000350259
AGTGCTTCTGGGCAGTAGAGGCGCGGGGTGCGGAGCTAGGGCGGCCGAGAGCC

(SEQ ID NO:331)

Homo sapiens CCDC53 5'-UTR
CCDC53-002 ENST00000545679
GGAAGGGCCCCGGAGGCGGGCACTTGGGGGGAAAGTTGAGACGTGATTACCGGGTTGGGCGGGCCC
CATCTGGGAGGGGTTTGTGGGTGAACTCGGGGTCCACCGCCCGCTGAGGAG
(SEQ ID NO:332)

Homo sapiens CASP1 5'-UTR
NM_001257119.1
ATACTTTCAGTTTCAGTCACACAAGAAGGGAGGAGAGAAAAGCC
(SEQ ID NO:333)

Homo sapiens NDUFB6 5'-UTR
NM_182739.2
GTAATAACCGCGCGCGGCGCTCGGCGTTCCCGCAAGGTCGCTTTGCAGAGCGGGAGCGCGCTTAAG
TAACTAGTCCGTAGTTCGAGGGTGCGCCGTGTCCTTTTGCGTTGGTACCAGCGGCGAC
(SEQ ID NO:334)

Homo sapiens BCKDHB 5'-UTR
BCKDHB-002 ENST00000369760
AGGCGGCGTGCGGCTGCATAGCCTGAGAATCCCGGTGGTGAGCGGGG
(SEQ ID NO:335)

Homo sapiens BCKDHB 5'-UTR
NM_001164783.1
CTACGTGAGTGCCGGACCGCTGAGTGGTTGTTAGCCAAG
(SEQ ID NO:336)

Homo sapiens BBS2 5'-UTR
NM_031885.3
CACAGAAGGCGCCGAGGCTCCACCGCGCAGCCGCAAAAAGAGCGGACGGGTCTGCGCCGCCGCAGG
AGGAGCAGGCGGTACCTGGACGGGTTCGTCCCGGGCTGTTTCGCGTCCGGCCTGAGGCGGCTGGGG
CCGCGCAGGTAGTGTCCCTGCACTTCTTGCCCGGGCGCGTGAGGCCAGCTCCGCTGCGCTTGTCTC
CAGCTTCCAGCCCTCCTCCCCTAAGCCGCCGCCATC
(SEQ ID NO:337)

Homo sapiens HERC5 5'-UTR
HERC5-001 ENST00000264350
TCAGTAGCTGAGGCTGCGGTTCCCCGACGCCACGCAGCTGCGCGCAGCTGGTTCCCGCTCTGCAGC
GCAACGCCTGAGGCAGTGGGCGCGCTCAGTCCCGGGACCAGGCGTTCTCTCCTCTCGCCTCTGGGC
CTGGGACCCCGCAAAGCGGCG
(SEQ ID NO:338)

Homo sapiens FAM175A 5'-UTR
NM_139076.2
ACCACAGGGTCTTGCCTCCGCGCGCCCCGCCCTCGTCCTCTTGTGTAGCCTGAGGCGGCGGTAGC
(SEQ ID NO:339)

Homo sapiens NT5DC1 5'-UTR

NT5DC1-002 ENST00000319550
CGGTCCTGTCCCGCAGCGTCCCGCCAGCCAGCTCCTTGCACCCTTCGCGGCCGAGGCGCTCCCTGG
TGCTCCCCGCGCAGCC
(SEQ ID NO:340)

Homo sapiens RAB7A 5'-UTR
RAB7A-001 ENST00000265062
GTCTCGTGACAGGTACTTCCGCTCGGGGCGGCGGCGGTGGCGGAAGTGGGAGCGGGCCTGGAGTCT
TGGCCATAAAGCCTGAGGCGGCGGCAGCGGCGGAGTTGGCGGCTTGGAGAGCTCGGGAGAGTTCCC
TGGAACCAGAACTTGGACCTTCTCGCTTCTGTCCTCCGTTTAGTCTCCTCCTCGGCGGGAGCCCTC
GCGACGCGCCCGGCCCGGAGCCCCCAGCGCAGCGGCCGCGTTTGAAGG
(SEQ ID NO:341)

Homo sapiens AGA 5'-UTR
AGA-001 ENST00000264595
AGGGACGCCTGAGCGAACCCCCGAGAGAGCGGGCGTGGGCGCCAGGCGGGCGGGGCACTGGGGATT
AATTGTTCGGCGATCGCTGGCTGCCGGGACTTTTCTCGCGCTGGTCTCTTCGGTGGTCAGGG
(SEQ ID NO:342)

Homo sapiens TPK1 5'-UTR
TPK1-001 ENST00000360057
AAGGCTCCTCAGCCGAGCGCCGAGCGGTCGATCGCCGTAGCTCCCGCAGCCTGCGATCTCCAGTCT
GTGGCTCCTACCAGCCATTGTAGGCCAATAATCCGTT
(SEQ ID NO:343)

Homo sapiens MBNL3 5'-UTR
MBNL3-001 ENST00000370839
AATTCATTTTTAATCCTTTAATAGTCCACAGTAATATTGTCCTAAAGAGGGTACATTGGATTTTAA
TTTTGCTTTCAAT
(SEQ ID NO:344)

Homo sapiens MCCC2 5'-UTR
MCCC2-001 ENST00000340941
AGAATCAGAGAAACCTTCTCTGGGGCTGCAAGGACCTGAGCTCAGCTTCCGCCCCAGCCAGGGAAG
CGGCAGGGGAAAGCACCGGCTCCAGGCCAGCGTGGGCCGCTCTCTCGCTCGGTGCCCGCCGCC
(SEQ ID NO:345)

Homo sapiens CAT 5'-UTR
CAT-001 ENST00000241052
ACTCGGGGCAACAGGCAGATTTGCCTGCTGAGGGTGGAGACCCACGAGCCGAGGCCTCCTGCAGTG
TTCTGCACAGCAAACCGCACGCT
(SEQ ID NO:346)

Homo sapiens ANAPC4 5'-UTR
ANAPC4-001 ENST00000315368
CCCGACGCCGGAAGTGCCTGGAGCGCGCGACAGCGGCGGGGCGGGGCGGCCTGGAGGCTGTGGCGC
GCGGCCGGCAGAGGGAGGGGAGAGGCCACTGGGGCCGTGTTAGTCTGCCGGTGGGGACTCTTGCAG
GGCCGTCCCC
(SEQ ID NO:347)

Homo sapiens PHKB 5'-UTR
PHKB-002 ENST00000323584
GGCCAAGGCGGCGACCGGAGCGCG
(SEQ ID NO:348)

Homo sapiens ABCB7 5'-UTR
ABCB7-001 ENST00000253577
CTCGGTTCCTCTTTCCTCGCTCAAG
(SEQ ID NO:349)

Homo sapiens GPD2 5'-UTR
GPD2-002 ENST00000438166
CCCGCGCGCCTCGCTGGGAGCACCCGGGCCGAGGCTCTGATTCTGGGGGGAGGCCGACTCCACCCT
GGCTGGAGGAACTGGGTGCTCCTGCCCGCTGGCCCCTCGCGCGTGAGGATCTATCTCAGGCTAAGA
A
(SEQ ID NO:350)

Homo sapiens TMEM38B 5'-UTR
TMEM38B-001 ENST00000374692
GCTGGAGCCGGCGCGGAGGAGCGGGCGGCCGCGGCTGTGCCCTCTCCTACTCCTCACCGCGCGAGC
GCGGGGAACCAGTAGCCGCGGCTGCTTCGGTTGCCGCGGTCGGTGGTCGTT
(SEQ ID NO:351)

Homo sapiens NFU1 5'-UTR
NM_001002755.2
GGGAAAGGTTCCCCGGCCTCTCTTGGTCAGGGTGACGCAGTAGCCTGCAAACCTCGGCGCGTAGGC
CACCGCACTTATCCGCAGCAGGACCGCCCGCAGCCGGTAGGGTGGGCTCTTCCCAGTGCCCGCCCA
GCTACCGGCCAGCCTGCGGCTGCGCAGATCTTTCGTGGTTCTGTCAGGGAGACCCTTAGGCACTCC
GGACTAAG
(SEQ ID NO:352)

Homo sapiens LOC128322/NUTF2 5'-UTR
NM_005796.1
GGAAGGGACAGTCGGCCGCAGACCGCGCTGGGTTGCCGCTGCCGCTGCCGCCATCGTGCCAGCCCC
TCGGGTCTCCGTGAGGCCGGGTGACGCTCCAGA
(SEQ ID NO:353)

Homo sapiens NUBPL 5'-UTR
NM_025152.2
ACTCCGCGCCACCCGCGACAGTTTCCCAGCAGGGCTCACAGCAGCGTTCCGCGTC
(SEQ ID NO:354)

Homo sapiens LANCL1 5'-UTR
LANCL1-004 ENST00000233714
GAGAAGGGCTTCAGGACGCGGGAGGCGCACTTGCTTCAAGTCGCGGGCGTGGGAACGGGGCTTGCT
TCCGGCGTC
(SEQ ID NO:355)

Homo sapiens PIR 5'-UTR
PIR-002 ENST00000380420
CCTCCCGCCTCCTCTAGGCCGCCGGCCGCGAAGCGCTGAGTCACGGTGAGGCTACTGGACCCACAC
TCTCTTAACCTGCCCTCCCTGCACTCGCTCCCGGCGGCTCTTCGCGTCACCCCCGCCGCTAAGGCT

CCAGGTGCCGCTACCGCAGCCCCTCCATCCTCTACAGCTCAGCATCAGAACACTCTCTTTTTAGAC
TCCGAT
(SEQ ID NO:356)

Homo sapiens CTBS 5'-UTR
NM_004388.2
GACGCGCAGCAGGCCCCGCCCACCCAGGCGGTAGGAACCCACTCCGGCCCGCTAGACCTGCTGCT
(SEQ ID NO:357)

Homo sapiens GSTM4 5'-UTR
NM_000850.4
AAGCTGGCGAGGCCGAGCCCCTCCTAGTGCTTCCGGACCTTGCTCCCTGAACACTCGGAGGTGGCG
GTGGATCTTACTCCTTCCAGCCAGTGAGGATCCAGCAACCTGCTCCGTGCCTCCCGCGCCTGTTGG
TTGGAAGTGACGACCTTGAAGATCGGCCGGTTGGAAGTGACGACCTTGAAGATCGGCGGGCGCAGC
GGGGCCGAGGGGGCGGGTCTGGCGCTAGGTCCAGCCCCTGCGTGCCGGGAACCCCAGAGGAGGTCG
CAGTTCAGCCCAGCTGAGGCCTGTCTGCAGAATCGACACCAACCAGCATC
(SEQ ID NO:358)

Mus musculus Ndufa1 5'-UTR
Ndufa1-001 ENSMUST00000016571
GCCGGAAGAGAGGTAAAGCCGGGTCACCTCTGAGGAGCCGGTGACGGGTTGGCGTGCGAGTAACGG
TGCGGAG
(SEQ ID NO:359)

Mus musculus Atp5e 5'-UTR
NM_025983
CCCACCCCTTCCGCTACTCAGGCCTGACCTTCCTGCTGCCGGGCCGGTTTGAGGCTACTCTGAAGC
GACCCAGCGGTTCTGCCCGACGCGCCCGCTCGAGACACC
(SEQ ID NO:360)

Mus musculus Gstm5 5'-UTR
NM_010360
GAGACAGTTCGGTCGCGTCAGCCCGGCCCACAGCGTCCAGTATAAAGTTAGCCGCCCACAGTCCAT
CGCTGTATCCCCGAAGGGGCTAAGATCGCCCAAA
(SEQ ID NO:361)

Mus musculus Cbr2 5'-UTR
NM_007621
ATAAAAGCTGAGCCCATCTCTTGCTTCGGAAGAAGCTGGTGTCAGCAGC
(SEQ ID NO:362)

Mus musculus Anapc13 5'-UTR
NM_181394
GTGACCCAGAAGAAGGGCGGGGCCGGGAGGAAGCCGACGCGCGCGCAGTGGGCCTGACAAGATCAA
AGCTGCAGGAGG
(SEQ ID NO:363)

Mus musculus Ndufa7 5'-UTR
NM_023202
TCGGAGCGGAAGGAAT
(SEQ ID NO:364)

Mus musculus Atp5k 5'-UTR
NM_007507
CGAAGGTCACGGACAAA
(SEQ ID NO:365)

Mus musculus Cox4i1 5'-UTR
NM_009941
CTTCCGGTCGCGAGCACCCCAGGGTGTAGAGGGCGGTCGCGGCGGTCGCCTGGGCAGCGGTGGCAG
A
(SEQ ID NO:366)

Mus musculus Ndufs6 5'-UTR
NM_010888
TTGGTACGACGCGTGGGGTCAAGGGTCACCGGCAAG
(SEQ ID NO:367)

Mus musculus Sec61b 5'-UTR
NM_024171
AGAGCCTGTATCTACGAGAGTTCTGAGTGCTCGGCAACTTCACGACTTCCCTCTTCCTGCCTCCTG
TGCCCACCGTTCTTAGGCATCAGC
(SEQ ID NO:368)

Mus musculus Snrpd2 5'-UTR
NM_026943
AAGGCTGGAGCAACGCGCTTGGAGGCGGGAGTGATCTGCGAGCGAAACCTACACC
(SEQ ID NO:369)

Mus musculus Mgst3 5'-UTR
NM_025569
ACTGCTGTGCTTCTCAGGTCTGTACCAGGCGCACGAAGGTGAGCCAGAGCCAAG
(SEQ ID NO:370)

Mus musculus Mp68 (2010107E04Rik) 5'-UTR
NM_027360
CTTTCCCATTCTGTAGCAGAATTTGGTGTTGCCTGTGGTCTTGGTCCCGCGGAG
(SEQ ID NO:371)

Mus musculus Prdx4-001, 5'-UTR
NM_016764
GCGCGGTCTCCAGCGCGCCGTTTTAGCTGGCTGCCTGGCGGCAGGGGACTCTGTGCTTTAGCAGAG
GGACGTGTTTTCGCGCTTGCTTGGTC
(SEQ ID NO:372)

Mus musculus Pgcp 5'-UTR
NM_176073
GCTGTCCTGGCACACAAAGAAGCCAGGCCTGCAGACTACTGGGGCTCCGGGCTGTTCCTGAGGCCT
CTGGAGGCCCGCCCTGTGGCTCCAGTGCGCTCTGAGGACCTTCCTGGTCCCGCCCCCGAACGTGCC
TGTGGTCTGCAGGCCTCACCGGGTGTTGTGGCCGCTGCTGCTCCGCAGAGCCTCGTGATCAGGAAG
AAAAGCAACTAGGAACA
(SEQ ID NO:373)

Mus musculus Myeov2 5'-UTR
NM_001163425
AGAAGGGGCTGGCCGGAAGTGAGCGCAACGCCGCCTTGTCGAG
(SEQ ID NO:374)

Mus musculus Ndufa4 5'-UTR
NM_010886
GTCCGCTCAGCCAGGTTGCAGAAGCGGCTTAGCGTGTGTCCTAATCTTCTCTCTGCGTGTAGGTAG
GCCTGTGCCGCAAAC
(SEQ ID NO:375)

Mus musculus Ndufs5 5'-UTR
NM_001030274
ACGGCAGGCGTCTGCGTCCTCCCGCAGCCGGCGGTCGGGAATTGCACCAGGGACCTGACAAGGGCA
CTGCAGAGCC
(SEQ ID NO:376)

Mus musculus Gstm1 5'-UTR
NM_010358
CTGCCTTCCGCTTTAGGGTCTGCTGCTCTGGTTACAGACCTAGGAAGGGGAGTGCCTAATTGGGAT
TGGTGCAGGGTTGGGAGGGACCCGCTGTTTTGTCCTGCCCACGTTTCTCTAGTAGTCTGTATAAAG
TCACAACTCCAAACACACAGGTCAGTCCTGCTGAAGCCAGTTTGAGAAGACCACAGCACCAGCACC
(SEQ ID NO:377)

Mus musculus Atp5o 5'-UTR
NM_138597
CTGGCGCGCGCGCGTGCGCTCTGGCGCCAGTAGTCTCTTTTCATTTGGGTTTGACCTACAGCCGCC
CGGGAAAAG
(SEQ ID NO:378)

Mus musculus Tspo 5'-UTR
NM_009775
GTCAGCGGCTACCAACCTCTGTGCGCAGTGTCCTTCACGGAACAACCAGCGACTGCGTGAGCGGGG
CTGTGGATCTTTCCAGAACATCAGTTGCAATCACC
(SEQ ID NO:379)

Mus musculus Taldo1 5'-UTR
NM_011528
GACGCGCGGGGCATTGTGGGTTAGCACGCACCGGCTACCGCCTCAGCTGTTCGCGTTTCGCC
(SEQ ID NO:380)

Mus musculus Bloc1s1 5'-UTR
NM_015740
GTGACGCCTTCCGGGTGAGCCAAGGCATAGTCCAGTTCCTGCAGCCTTAGGGAGGGGTCCGCCGTG
CCCACACCCAGCCAGACTCGACC
(SEQ ID NO:381)

Mus musculus Hexa 5'-UTR
NM_010421
AGCTGACCGGGGCTCACGTGGGCTCAGCCTGCTGGAAGGGGAGCTGGCCGGTGGGCC
(SEQ ID NO:382)

Preferably, the at least one 3'-UTR element of the artificial nucleic acid molecule according to the present invention comprises or consists of a nucleic acid sequence which has an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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%, most preferably of 100% to the 3'-UTR sequence of a transcript of a gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1; whereby CNTN1-004 is particularly preferred). Most preferably, the at least one 3'-UTR element of the artificial nucleic acid molecule according to the present invention comprises or consists of a nucleic acid sequence which has an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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%, most preferably of 100% to a sequence selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 24, or the corresponding RNA sequences, respectively:

SEQ ID NO: 1

GAAGGGAACACCCAAATTTAATTCAGCCTTAAGCACAATTAATTAAGAGTGAAACGTAATGTACAA
GCAGTTGGTCACCCACCATAGGGCATGATCAACACCGCAACCTTTCCTTTTTCCCCCAGTGATTCT
GAAAAACCCCTCTTCCCTTCAGCTTGCTTAGATGTTCCAAATTTAGTAAGCTTAAGGCGGCCTACA
GAAGAAAAAGAAAAAAAAGGCCACAAAAGTTCCCTCTCACTTTCAGTAAATAAAATAAAAGCAGCA
ACAGAAATAAAGAAATAAATGAAATTCAAAATGAAATAAATATTGTTTGTGCAGCATTAAAAAATC
AATAAAAATTAAAAATGAGCA
(Mus musculus GNAS 3'-UTR)

SEQ ID NO: 2

GAAGGGAACACCCAAATTTAATTCAGCCTTAAGCACAATTAATTAAGAGTGAAACGTAATTGTACA
AGCAGTTGGTCACCCACCATAGGGCATGATCAACACCGCAACCTTTCCTTTTTCCCCCAGTGATTC
TGAAAAACCCCTCTTCCCTTCAGCTTGCTTAGATGTTCCAAATTTAGTAAGCTTAAGGCGGCCTAC
AGAAGAAAAAGAAAAAAAAGGCCACAAAAGTTCCCTCTCACTTTCAGTAAATAAAATAAAAGCAGC
AACAGAAATAAAGAAATAAATGAAATTCAAAATGAAATAAATATTGTGTTGTGCAGCATTAAAAAA
TCAATAAAAATTAAAAATGAGCA
(Mus musculus GNAS 3'-UTR)

SEQ ID NO: 3

GAAGGGAACCCCCAAATTTAATTAAAGCCTTAAGCACAATTAATTAAAAGTGAAACGTAATTGTAC
AAGCAGTTAATCACCCACCATAGGGCATGATTAACAAAGCAACCTTTCCCTTCCCCCGAGTGATTT
TGCGAAACCCCCTTTTCCCTTCAGCTTGCTTAGATGTTCCAAATTTAGAAAGCTTAAGGCGGCCTA
CAGAAAAAGGAAAAAAGGCCACAAAAGTTCCCTCTCACTTTCAGTAAAAATAAATAAAACAGCAGC
AGCAAACAAATAAAATGAAATAAAAGAAACAAATGAAATAAATATTGTGTTGTGCAGCATTAAAAA
AAATCAAAATAAAAATTAAATGTGAGCAAAGAATGAAAAAAAAAAAAAAAAAAAA
(Homo sapiens GNAS 3'-UTR)

SEQ ID NO: 4

TGGAGGACGCCGTCCAGATTCTCCTTGTTTTCATGGATTCAGGTGCTGGAGAATCTGGTAAAAGCA
CCATTGTGAAGCAGATGAGGATCCTGCATGTTAATGGGTTTAATGGAGAGGGCGGCGAAGAGGACC
CGCAGGCTGCAAGGAGCAACAGCGATGGCAGTGAGAAGGCAACCAAAGTGCAGGACATCAAAAACA
ACCTGAAAGAGGCGATTGAAACCATTGTGGCCGCCATGAGCAACCTGGTGCCCCCCGTGGAGCTGG
CCAACCCCGAGAACCAGTTCAGAGTGGACTACATCCTGAGTGTGATGAACGTGCCTGACTTTGACT
TCCCTCCCGAATTCTATGAGCATGCCAAGGCTCTGTGGGAGGATGAAGGAGTGCGTGCCTGCTACG
AACGCTCCAACGAGTACCAGCTGATTGACTGTGCCCAGTACTTCCTGGACAAGATCGACGTGATCA
AGCAGGCTGACTATGTGCCGAGCGATCAGGACCTGCTTCGCTGCCGTGTCCTGACTTCTGGAATCT
TTGAGACCAAGTTCCAGGTGGACAAAGTCAACTTCCACATGTTTGACGTGGGTGGCCAGCGCGATG
AACGCCGCAAGTGGATCCAGTGCTTCAACGATGTGACTGCCATCATCTTCGTGGTGGCCAGCAGCA
GCTACAACATGGTCATCCGGGAGGACAACCAGACCAACCGCCTGCAGGAGGCTCTGAACCTCTTCA
AGAGCATCTGGAACAACAGATGGCTGCGCACCATCTCTGTGATCCTGTTCCTCAACAAGCAAGATC
TGCTCGCTGAGAAAGTCCTTGCTGGGAAATCGAAGATTGAGGACTACTTTCCAGAATTTGCTCGCT
ACACTACTCCTGAGGATGCTACTCCCGAGCCCGGAGAGGACCCACGCGTGACCCGGGCCAAGTACT
TCATTCGAGATGAGTTTCTGAGGATCAGCACTGCCAGTGGAGATGGGCGTCACTACTGCTACCCTC
ATTTCACCTGCGCTGTGGACACTGAGAACATCCGCCGTGTGTTCAACGACTGCCGTGACATCATTC
AGCGCATGCACCTTCGTCAGTACGAGCTGCTCTAAGAAGGGAACCCCCAAATTTAATTAAAGCCTT
AAGCACAATTAATTAAAAGTGAAACGTAATTGTACAAGCAGTTAATCACCCACCATAGGGCATGAT
TAACAAAGCAACCTTTCCCTTCCCCCGAGTGATTTTGCGAAACCCCCTTTTCCCTTCAGCTTGCTT
AGATGTTCCAAATTTAGAAAGCTTAAGGCGGCCTACAGAAAAAGGAAAAAAGGCCACAAAAGTTCC
CTCTCACTTTCAGTAAAAATAAATAAAACAGCAGCAGCAAACAAATAAAATGAAATAAAAGAAACA
AATGAAATAAATATTGTGTTGTGCAGCATTAAAAAAAATCAAAATAAAAATTAAATGTGAGCAAAG
AATGAAAAAAAAAAAAAAAAAAAA
(Homo sapiens GNAS 3'-UTR)

SEQ ID NO: 5

ACCTGCTGCCTTAACGCTGAGATGTGGCCTCTGCAACCCCCCTTAGGCAAAGCAACTGAACCTTCT
GCTAAAGTGACCTGCCCTCTTCCGTAAGTCCAATAAAGTTGTCATGCACCC
(Mus musculus MORN2 3'-UTR)

SEQ ID NO: 6

ACCTGCTGCCTTAACGCTGAGATGTGGCCTCTGCAACCCCCCTTAGGCAAAGCAACTGAACCTTCT
GCTAAAGTGACCTGCCCTCTTCCGTAAGTCCAATAAAGTTGTCATGCACCCACAAAAAAAAAAAAA
AAA
(Mus musculus MORN2 3'-UTR)

SEQ ID NO: 7

CATGTAGATGTGATGTTAAATTAAAGTTGAAATGTAGTAATTGAAGCTTTTAGTTGTAAGGAAAGC
AACTTAATCTGTTATTTGAAATGACTTCATACACTACCCCTATAAGTTTGCCAATAAAACCATCAC
CTGCTTACACCTTTTTGAACTTTATATTCATTGTCTTACAATTAGTTTAAAATAAATGACATGATT
CAAAAAAAAAAA
(Homo sapiens MORN2 3'-UTR)

SEQ ID NO: 8

GCCCTTGCTACACGGGCACTCACTAGGAGGACCTGTCCACACTGGGGATCCTGCAGGCCCTGGGTG
GGGACAGCACCCTGGCCTTCTGCACTGTGGCTCCTGGTTCTCTCTCCTTCCCGCTCCCTTCTGCAG
CTTGGTCAGCCCCATCTCCTCACCCTCTTCCCAGTCAAGTCCACACAGCCTTCATTCTCCCCAGTT
TCTTTCACATGGCCCCTTCTTCATTGGCTCCCTGACCCAACCTCACAGCCCGTTTCTGCGAACTGA
GGTCTGTCCTGAACTCACGCTTCCTAGAATTACCCCGATGGTCAACACTATCTTAGTGCTAGCCCT
CCCTAGAGTTACCCCGAAGGTCAATACTTGAGTGCCAGCCTGTTCCTGGTGGAGTAGCCTCCCCAG
GTCTGTCTCGTCTACAATAAAGTCTGAAACACACTTGCCATG
(Mus musculus GSTM1 3'-UTR)

SEQ ID NO: 9

GCCCTTGCTACACGGGCACTCACTAGGAGGACCTGTCCACACTGGGGATCCTGCAGGCCCTGGGTG
GGGACAGCACCCTGGCCTTCTGCACTGTGGCTCCTGGTTCTCTCTCCTTCCCGCTCCCTTCTGCAG
CTTGGTCAGCCCCATCTCCTCACCCTCTTCCCAGTCAAGTCCACACAGCCTTCATTCTCCCCAGTT
TCTTTCACATGGCCCCTTCTTCATTGGCTCCCTGACCCAACCTCACAGCCCGTTTCTGCGAACTGA
GGTCTGTCCTGAACTCACGCTTCCTAGAATTACCCCGATGGTCAACACTATCTTAGTGCTAGCCCT
CCCTAGAGTTACCCCGAAGGTCAATACTTGAGTGCCAGCCTGTTCCTGGTGGAGTAGCCTCCCCAG
GTCTGTCTCGTCTACAATAAAGTCTGAAACACACTTGCCATGAAAAAAAAAAAAAAAAAA
(Mus musculus GSTM1 3'-UTR)

SEQ ID NO: 10

GGCCTTGAAGGCCAGGAGGTGGGAGTGAGGAGCCCATACTCAGCCTGCTGCCCAGGCTGTGCAGCG
CAGCTGGACTCTGCATCCCAGCACCTGCCTCCTCGTTCCTTTCTCCTGTTTATTCCCATCTTTACT
CCCAAGACTTCATTGTCCCTCTTCACTCCCCCTAAACCCCTGTCCCATGCAGGCCCTTTGAAGCCT
CAGCTACCCACTATCCTTCGTGAACATCCCCTCCCATCATTACCCTTCCCTGCACTAAAGCCAGCC
TGACCTTCCTTCCTGTTAGTGGTTGTGTCTGCTTTAAAGGGCCTGCCTGGCCCCTCGCCTGTGGAG
CTCAGCCCCGAGCTGTCCCCGTGTTGCATGAAGGAGCAGCATTGACTGGTTTACAGGCCCTGCTCC
TGCAGCATGGTCCCTGCCTTAGGCCTACCTGATGGAAGTAAAGCCTCAACCACAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAA
(Homo sapiens GSTM1 3'-UTR)

SEQ ID NO: 11

GGAAGCATTTTCCTGGCTGATTAAAAGAAATTACTCAGCTATGGTCATCTGTTCCTGTTAGAAGGC
TATGCAGCATATTATATACTATGCGCATGTTATGAAATGCATAATAAAAAATTTTAAAAAATCTAA
A
(Mus musculus NDUFA1 3'-UTR)

SEQ ID NO: 12

GGAAGCATTTTCCTGATTGATGAAAAAAATAACTCAGTTATGGCCATCTACCCCTGCTAGAAGGTT
ACAGTGTATTATGTAGCATGCAATGTGTTATGTAGTGCTTAATAAAAATAAAATGAAAAAAATGCA
AAAAAAAAAAAAAAAA
(Homo sapiens NDUFA1 3'-UTR)

SEQ ID NO: 13

TCTGCTCAGTTGCCGCGGACATCTGAGTGGCCTTCTTAGCCCCACCCTCAGCCAAAGCATTTACTG
ATCTCGTGACTCCGCCCTCATGCTACAGCCACGCCCACCACGCAGCTCACAGTTCCACCCCCATGT
TACTGTCGATCCCACAACCACTCCAGGCGCAGACCTTGTTCTCTTTGTCCACTTTGTTGGGCTCAT
TTGCCTAAATAAACGGGCCACCGCGTTACCTTTAACTAT
(Mus musculus CBR2 3'-UTR)

SEQ ID NO: 14

ATGCCGGCTTACCATCTCTACCATCATCCGGTTTGGTCATCCAACAAGAAGAAATGAATATGAAAT
TCCAGCAATAAGAAATGAACAAAGATTGGAGCTGAAGACCTTAAGTGCTTGCTTTTTGCCCGCTGA
CCAGATAACATTAGAACTATCTGCATTATCTATGCAGCATGGGGTTTTTATTATTTTTACCTAAAG
ATGTCTCTTTTTGGTAATGACAAACGTGTTTTTTAAGAAAAAAAAAAAAAGGCCTGGTTTTTCTCAA
TACACCTTTAACGGTTTTTAAATTGTTTCATATCTGGTCAAGTTGAGATTTTTAAGAACTTCATTT
TTAATTTGTAATAAAGTTTACAACTTGATTTTTTCAAAAAAGTCAACAAACTGCAAGCACCTGTTA
ATAAAGGTCTTAAATAATAA
(Mus musculus YBX1 3'-UTR)

SEQ ID NO: 15

ATGCCGGCTTACCATCTCTACCATCATCCGGTTTGGTCATCCAACAAGAAGAAATGAATATGAAAT
TCCAGCAATAAGAAATGAACAAAGATTGGAGCTGAAGACCTTAAGTGCTTGCTTTTTGCCCTCTGA
CCAGATAACATTAGAACTATCTGCATTATCTATGCAGCATGGGGTTTTTATTATTTTTACCTAAAG
ATGTCTCTTTTTGGTAATGACAAACGTGTTTTTTAAGAAAAAAAAAAAAAGGCCTGGTTTTTCTC
AATACACCTTTAACGGTTTTTAAATTGTTTCATATCTGGTCAAGTTGAGATTTTTAAGAACTTCAT
TTTTAATTTGTAATAAAGTTTACAACTTGATTTTTTCAAAAAAGTCAACAAACTGCAAGCACCTGT
TAATAAAGGTCTTAAATAATAA
(Mus musculus YBX1 3'-UTR)

SEQ ID NO: 16

ATGCCGGCTTACCATCTCTACCATCATCCGGTTTAGTCATCCAACAAGAAGAAATATGAAATTCCA
GCAATAAGAAATGAACAAAAGATTGGAGCTGAAGACCTAAAGTGCTTGCTTTTTGCCCGTTGACCA
GATAAATAGAACTATCTGCATTATCTATGCAGCATGGGGTTTTTATTATTTTTACCTAAAGACGTC
TCTTTTTGGTAATAACAAACGTGTTTTTTAAAAAAGCCTGGTTTTTCTCAATACGCCTTTAAAGGT
TTTTAAATTGTTTCATATCTGGTCAAGTTGAGATTTTTAAGAACTTCATTTTTAATTTGTAATAAA
AGTTTACAACTTGATTTTTTCAAAAAAGTCAACAAACTGCAAGCACCTGTTAATAAAGGTCTTAAA
TAATAAAAAAAAAAAAAAA
(Homo sapiens YBX1 3'-UTR)

SEQ ID NO: 17

GGAGGCTTGATGGGCTTTTTGCCCTCGTTCCTAGAGGCTTAACCATAATAAAATCCCTAATAAAGC

(Mus musculus Ndufb8 3'-UTR)

SEQ ID NO: 18

GGAGGCTTCGTGGGCTTTTGGGTCCTCTAACTAGGACTCCCTCATTCCTAGAAATTTAACCTTAAT
GAAATCCCTAATAAAACTCAGTGCTGTGTTATTTGTGCCTCAAAAAAAAAAAAAAAAAA
(Homo sapiens Ndufb8 3'-UTR)

SEQ ID NO: 19

GTGAGGAAGAGGAGTGCTGTTCCTGCCTTCCTAGCCCAGCTGGGTCTGACCAGAGGCTACTGTGTA
CCCATTTACCATGCGTGATTGTTAACTCAGAGTGGGGTGTAGCCAGGTATTGACTGAATGTATGTT
CTTGCTGACCTGTGTTTTTTTCTGTAGGGACCAAAGCAGTATCCTTACAATAATCTGTACCTGGAA
CGAGGCGGTGATCCCTCCAAAGAACCAGAGCGGGTGGTTCACTATGAGATCTGAGGAGGCTTCGTG
GGCTTTTGGGTCCTCTAACTAGGACTCCCTCATTCCTAGAAATTTAACCTTAATGAAATCCCTAAT
AAAACTCAGTGCTGTGTTATTTGTGCCTCAAAAAAAAAAAAAAAAAA
(Homo sapiens Ndufb8 3'-UTR)

SEQ ID NO: 20

TCGTTGACACTCACCATTTCTGTGAAAGACTTTTTTTTTTTTTAACATATTATACTAGATTTGACT
AACTCAATCTTGTAGCTTCTGCAGTTCTCCCCACCCCCAACCTAGTTCTTAGAGTATGTTTCCCCT
TTTGAAACATGTAAACATACTTTGGGCATAAATATTTTTTAAAATATAACTATAATGCTTCACTAA
TACCTTAAAAATGCCTAGTGAACTAACTCAGTACATTATATAATGGCCAAGTGAAAGTTTTGTGTT
TTCATGTCCTGTTTTTCTTTGAAATTATATAGCCCAGAAATTAGCTCATTATCTGAAAAACGTATA
AGAACTGATGAATTGTATAATACAGGAGTATTGCCATTGAATGTACTGTTTGATTTATTCAAGCAG
GTAATGAACAATGTTGTCAAACTCTCTAATGAGACATCATAATTAGGACATAAGCTAAAAGGGGCA
TTACTCCGGCAGTCTTTTTTTCTTAATCCTAGTACCATACATATTCTTTGGCATGAAAGAATGAAA
AGCATTAGTAAACAACTGAAGTCCTACCATGGCTCTGTAGGGTTTTTGGAACAATTCCTGGAATTG
GAAAGTGAAAATGGATAGCATGTGGGGGAAACCCTCATCTGAGTAGCAAGATTTTAGTAAAGATGA
CTAAGCCATTAACAGCATGCATTCATATTTAATTTTATTGACTCCTGCCATCAGCTTTTGTAGATC
TTTTGGGTGGAAGGTTGTGATTTTTACTGGGAGGACTTGAGTAGAAGTGGATGATTAAAATTGAGG
AGTATATAATTCTTTCTGGGACTGCTTAAATGTTATTGTTTGAAAATGCCTTCACTTTCCCCCTTT
GGTCAAAGAGATGTGCTTAAAATTCTTATTCCTTCACAATAAATAATTTTGATTTTCTTAGACA
(Homo sapiens CNTN1-004 3'-UTR)

SEQ ID NO: 21

TCGTTGACACTCACCATTTCTGTGAAAGACTTTTTTTTTTTTTAACATATTATACTAGATTTGACTA
ACTCAATCTTGTAGCTTCTGCAGTTCTCCCCACCCCCAACCTAGTTCTTAGAGTATGTTTCCCCTT
TTGAAACATGTAAACATACTTTGGGCATAAATATTTTTTAAAATATAACTATAATGCTTCACTAAT
ACCTTAAAAATGCCTAGTGAACTAACTCAGTACATTATATAATGGCCAAGTGAAAGTTTTGTGTTT
TCATGTCCTGTTTTTCTTTGAAATTATATAGCCCAGAAATTAGCTCATTATCTGAAAAACGTATGA
AGAACTGATGAATTGTATAATACAGGAGTATTGCCATTGAATGTACTGTTTGATTTATTCAAGCAG
GTAATGAACAATGTTGTCAAACTCTCTAATGAGACATCATAATTAGGACATAAGCTAAAAGGGGCA
TTACTCCGGCAGTCTTTTTTTCTTAATCCTAGTACCATACATATTCTTTGGCATGAAAGAATGAAA
AGCATTAGTAAACAACTGAAGTCCTACCATGGCTCTGTAGGGTTTTTGGAACAATTCCTGGAATTG
GAAAGTGAAAATGGATAGCATGTGGGGGAAACCCTCATCTGAGTAGCAAGATTTTAGTAAAGATGA
CTAAGCCATTAACAGCATGCATTCATATTTAATTTTATTGACTCCTGCCATCAGCTTTTGTAGATC
GTTTGGGTGGAAGGTTGTGATTTTTACTGGGAGGACTTGAGTAGAAGTGGATGATTAAAATTGAGG

AGTATATAATTCTTTCTGGGACTGCTTAAATGTTATTGTTTGAAAATACCTTCACTTTCCCCCTTT
GGTCAAAGAGATGTGCTTAAAATTCTTATTCCTTCACAATAAATAATTTTGATTTTCTTAGACA
(Homo sapiens CNTN1-004 3'-UTR)

SEQ ID NO: 22

*TTT*TTTCGTTGACACTCACCATTTCTGTGAAAGACTTTTTTTTTTTTTAACATATTATACTAGATT
TGACTAACTCAATCTTGTAGCTTCTGCAGTTCTCCCCACCCCCAACCTAGTTCTTAGAGTATGTTT
CCCCTTTTGAAACATGTAAACATACTTTGGGCATAAATATTTTTTAAAATATAACTATAATGCTTC
ACTAATACCTTAAAAATGCCTAGTGAACTAACTCAGTACATTATATAATGGCCAAGTGAAAGTTTT
GTGTTTTCATGTCCTGTTTTTCTTTGAAATTATATAGCCCAGAAATTAGCTCATTATCTGAAAAAC
GTATGAAGAACTGATGAATTGTATAATACAGGAGTATTGCCATTGAATGTACTGTTTGATTTATTC
AAGCAGGTAATGAACAATGTTGTCAAACTCTCTAATGAGACATCATAATTAGGACATAAGCTAAAA
GGGGCATTACTCCGGCAGTCTTTTTTTCTTAATCCTAGTACCATACATATTCTTTGGCATGAAAGA
ATGAAAAGCATTAGTAAACAACTGAAGTCCTACCATGGCTCTGTAGGGTTTTTGGAACAATTCCTG
GAATTGGAAAGTGAAAATGGATAGCATGTGGGGGAAACCCTCATCTGAGTAGCAAGATTTTAGTAA
AGATGACTAAGCCATTAACAGCATGCATTCATATTTAATTTTATTGACTCCTGCCATCAGCTTTTG
TAGATCTTTTGGGTGGAAGGTTGTGATTTTTACTGGGAGGACTTGAGTAGAAGTGGATGATTAAAA
TTGAGGAGTATATAATTCTTTCTGGGACTGCTTAAATGTTATTGTTTGAAAATGCCTTCACTTTCC
CCCTTTGGTCAAAGAGATGTGCTTAAAATTCTTATTCCTTCACAATAAATAATTTTGATTTTCTTA
GACA
(Homo sapiens CNTN1-004 3'-UTR)

SEQ ID NO: 23

ATGTGTTGTGACAGCTGCTGTTCCCATCCCAGCTCAGAAGACACCCTTCAACCCTGGGATGACCAC
AATTCCTTCCAATTTCTGCGGCTCCATCCTAAGCCAAATAAATTATACTTTAACAAACTATTCAAC
TGATTTACAACACACATGATGACTGAGGCATTCGGGAACCCCTTCATCCAAAAGAATAAACTTTTA
AATGGATATAAATGATTTTTAACTCGTTCCAATATGCCTTATAAACCACTTAACCTGATTCTGTGA
CAGTTGCATGATTTAACCCAATGGGACAAGTTACAGTGTTCAATTCAATACTATAGGCTGTAGAGT
GAAAGTCAAATCACCATATACAGGTGCTTTAAATTTAATAACAAGTTGTGAAATATAATAGAGATT
GAAATGTTGGTTGTATGTGGTAAATGTAAGAGTAATACAGTCTCTTGTACTTTCCTCACTGTTTTG
GGTACTGCATATTATTGAATGGCCCCTATCATTCATGACATCTTGAGTTTTCTTGAAAAGACAATA
GAGTGTAACAAATATTTTGTCAGAAATCCCATTATCAAATCATGAGTTGAAAGATTTTGACTATTG
AAAACCAAATTCTAGAACTTACTATCAGTATTCTTATTTTCAAAGGAAATAATTTTCTAAATATTT
GATTTTCAGAATCAGTTTTTTAATAGTAAAGTTAACATACCATATAGATTTTTTTTTACTTTTATA
TTCTACTCTGAAGTTATTTTATGCTTTTCTTATCAATTTCAAATCTCAAAAATCACAGCTCTTATC
TAGAGTATCATAATATTGCTATATTTGTTCATATGTGGAGTGACAAATTTTGAAAAGTAGAGTGCT
TCCTTTTTTATTGAGATGTGACAGTCTTTACATGGTTAGGAATAAGTGACAGTTAAGTGAATATCA
CAATTACTAGTATGTTGGTTTTTCTGCTTCATTCCTAAGTATTACGTTTCTTTATTGCAGATGTCA
GATCAAAAAGTCACCTGTAGGTTGAAAAAGCTACCGTATTCCATTTTGTAAAAATAACAATAATAA
TAATAATAATAATTAGTTTTAAGCTCATTTCCCACTTCAATGCAATACTGAAAACTGGCTAAAAAT
ACCAAATCAATATACTGCTAATGGTACTTTGAAGAGTATGCAAAACTGGAAGGCCAGGAGGAGGCA
AATAATATGTCTTTCCGATGGTGTCTCCCAAGTGTTGGTGCTTTGGGTTTTTATAAGTTGTGAAAA
GGAAGATGCACATTTCTTCATTCTCCATGGTGTGCATGGAAATGTGTTTGAGTGTGGATGTAAAAG
AAATCGAGTAATAAAGAATTAGCTGGCTTGTGAAATAGTGCAGTGTTGGATGCTTCAAGAGGTATA
ATCCTATTTTATTAGCACAAACTTGCTAGCTAATTAGAGTTTATCTTTTTAGAAAGGACACCGTAT
AGGTTCGTAAAAAATATTTACAGGAAGCAAAATAGATCTATTACTACTTTACCGACTTTACCCCCT
TTCTTTAATTTGTATAATTTTTGTACTATATATCGATGTGTAAATGTTTAGAGTCTTCATTATGAA
AATATCAATAAATATTTCATTAGTTTACATTTAACTCTGGTATAAAATGAAACTTTTAAAAATAAG
TGAAATGGATGATTTCCCAGTGGAAGTATGTCAACAGTCTTAAGATCATTGCCAGATTTCATAAAA
TATTTAAGTATTTGAAAAAGAAACAAAATGTCTTCATACTTTAGGGAAACGAATACCCTGTATACC

TTCTGTACAAATGTTTGTGTTTTCATTGTTACACTTTGGGGTTTTACTTTTGCAATGTGACCCATG
TTGGGCATTTTTATATAATCAACAACTAAATCTTTTGCCAAATGCATGCTTGCCTTTTATTTTCTA
ATATATGATAATAACGAGCAAAACTGGTTAGATTTTGCATGAAATGGTTCTGAAAGGTAAGAGGAA
AACAGACTTTGGAGGTTGTTTAGTTTTGAATTTCTGACAGAGATAAAGTAGTTTAAAATCTCTCGT
ACACTGATAACTCAAGCTTTTCATTTTCTCATACAGTTGTACAGATTTAACTGGGACCATCAGTTT
TAAACTGTTGTCAAGCTAACTAATAATCATCTGCTTTAAGACGCAAGATTCTGAATTAAACTTTAT
ATAGGTATAGATACATCTGTTGTTTCTTTGTATTTCAGGAAAGGTGATAGTAGTTTTATTTGATAC
TGATAAATATTGAATTGATTTTTTAGTTATTTTTTATCATTTTTTCAATGGAGTAGTATAGGACTG
TGCTTTGTCCTTTTTATGAATGAAAAAATTAGTATAAAGTAATAAATGTCTTATGTTACCCAAGAA
AAAA
(Homo sapiens CNTN1-004 3'-UTR)

SEQ ID NO: 24

TCGTTGACACTCACCATTTCTGTGAAAGACTTTTTTTTTTTTAACATATTATACTAGATTTGACTA
ACTCAATCTTGTAGCTTCTGCAGTTCTCCCCACCCCCAACCTAGTTCTTAGAGTATGTTTCCCCTT
TTGAAACATGTAAACATACTTTGGGCATAAATATTTTTTAAAATATAACTATAATGCTTCACTAAT
ACCTTAAAAATGCCTAGTGAACTAACTCAGTACATTATATAATGGCCAAGTGAAAGTTTTGTGTTT
TCATGTCCTGTTTTTCTTTGAAATTATATAGCCCAGAAATTAGCTCATTATCTGAAAAACGTATGA
AGAACTGATGAATTGTATAATACAGGAGTATTGCCATTGAATGTACTGTTTGATTTATTCAAGCAG
GTAATGAACAATGTTGTCAAACTCTCTAATGAGACATCATAATTAGGACATAAGCTAAAAGGGGCA
TTACTCCGGCAGTCTTTTTTTCTTAATCCTAGTACCATACATATTCTTTGGCATGAAAGAATGAAA
AGCATTAGTAAACAACTGAAGTCCTACCATGGCTCTGTAGGGTTTTTGGAACAATTCCTGGAATTG
GAAAGTGAAAATGGATAGCATGTGGGGGAAACCCTCATCTGAGTAGCAAGATTTTAGTAAAGATGA
CTAAGCCATTAACAGCATGCATTCATATTTAATTTTATTGACTCCTGCCATCAGCTTTTGTAGATC
GTTTGGGTGGAAGGTTGTGATTTTTACTGGGAGGACTTGAGTAGAAGTGGATGATTAAAATTGAGG
AGTATATAATTCTTTCTGGGACTGCTTAAATGTTATTGTTTGAAAATACCTTCACTTTCCCCCTTT
GGTCAAAGAGATGTGCTTAAAATTCTTATTCCTTCACAATAAATAATTTTGATTTTCTTAGACAGG
TTTGTGTTTAGGTATGAGTTTCTCTTTTACTTCATCTAGCAATTCTCTCTGTGGTCAGAAGAACTC
TGAAGAAAGCTTTGAGGGAAATGAATATAACTCTTAAATTATTATATGTGTGTGTATATATATAGT
TTAACTTTAAAAATAATTTATTAGTCATCATAAAGAAATAAATGTCTCTGGCTCAAGATGTTACTT
ATTTCCTTCTTTTATATTTTCTAGTCTCAATTACTGTTCCAAAAGGAGCTATCTTAGAACTTAGAC
TAGAGATCCAGATTAA
(Homo sapiens CNTN1-004 3'-UTR)

Preferably, the at least one 5'-UTR element of the artificial nucleic acid molecule according to the present invention comprises or consists of a nucleic acid sequence which has an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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%, most preferably of 100% to the 5'-UTR sequence of a transcript of MP68 (RIKEN cDNA 2010107E04 gene), or NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4). Most preferably, the at least one 5'-UTR element of the artificial nucleic acid molecule according to the present invention comprises or consists of a nucleic acid sequence which has an identity of at least about 40%, preferably of at least about 50%, preferably of at

least about 60%, preferably of at least about 70%, more preferably 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%, most preferably of 100% to a sequence according to SEQ ID NO: 25 or SEQ ID NO: 30, or the corresponding RNA sequence, respectively:

SEQ ID NO: 25

CTTTCCCATTCTGTAGCAGAATTTGGTGTTGCCTGTGGTCTTGGTCCCGCGGAG
(Mus musculus MP68 5'-UTR)

SEQ ID NO: 26

CTTCCCGGCATCCCCTGCGCGCGCCTGCGCGCTCGGTGACCTTTCCGAGTTGGCTGCAGATTTGTG
GTGCGTTCTGAGCCGTCTGTCCTGCGCCAAG
(Homo sapiens MP68 5'-UTR)

SEQ ID NO: 27

CTTCCCGGCATCCCCTGCGCGCGCCTGCGCGCTCGGTGACCTTTCCGAGTTGGCTGCAGATTTGTG
GTGCGTTCTGAGCCGTCTGTCCTGCGCCAAGGGAGCGTACCTTGGCCTTGAGAGGTTCAGCTGCCT
AACCCAGAGGCTACGCAGAGTTAGAGAAGCCAGAGTCCAAGCCAAGAACTCTGACTCCACATCCAG
TCCCTTCTCTCCTTTATAACTCAAGTTTCCTTGCGCCACACTGCCCTCCACGTTATGCTGTACATG
ACAACTTGGGTGAGGCAACAGGGAAGCTGAAAAGAGATCATACGGTGCTGA
(Homo sapiens MP68 5'-UTR)

SEQ ID NO: 28

GTCCGCTCAGCCAGGTTGCAGAAGCGGCTTAGCGTGTGTCCTAATCTTCTCTCTGCGTGTAGGTA
GGCCTGTGCCGCAAAC
(Mus musculus NDUFA4 5'-UTR)

SEQ ID NO: 29

GUCCGCUCAGCCAGGUUGCAGAAGCGGCUUAGCGUGUGUCCUAAUCUUCUCUCUGCGUGUAGGUA
GGCCUGUGCCGCAAAC
(Homo sapiens NDUFA4 5'-UTR)

SEQ ID NO: 30

GGGTCCTTCAGGTAGGAGGTCCTGGGTGACTTTGGAAGTCCGTAGTGTCTCATTGCAGATAATTTT
TAGCTTAGGGCCTGGTGGCTAGGTCGGTTCTCTCCTTTCCAGTCGGAGACCTCTGCCGCAAAC
(Homo sapiens NDUFA4 5'-UTR)

The at least one 3'-UTR element of the artificial nucleic acid molecule according to the present invention may also comprise or consist of a fragment of a nucleic acid sequence

which has an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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%, most preferably of 100% to the nucleic acid sequence of the 3'-UTR of a transcript of a gene, such as to the 3'-UTR of a sequence according to SEQ ID NOs: 1 to 24 and SEQ ID NOs: 49 to 318, wherein the fragment is preferably a functional fragment or a functional variant fragment as described above. Such fragment preferably exhibits a length of at least about 3 nucleotides, preferably of at least about 5 nucleotides, more preferably of at least about 10, 15, 20, 25 or 30 nucleotides, even more preferably of at least about 50 nucleotides, most preferably of at least about 70 nucleotides. In a preferred embodiment, the fragment or variant thereof exhibits a length of between 3 and about 500 nucleotides, preferably of between 5 and about 150 nucleotides, more preferably of between 10 and 100 nucleotides, even more preferably of between 15 and 90, most preferably of between 20 and 70. Preferably, said variants, fragments or variant fragments are functional variants, functional fragments, or functional variant fragments of the 3'-UTR, prolong protein production from the artificial nucleic acid molecule according to the invention with an efficiency of at least 30%, preferably with an efficiency of at least 40%, more preferably of at least 50%, more preferably of at least 60%, even more preferably of at least 70%, even more preferably of at least 80%, most preferably of at least 90% of the protein production prolonging efficiency exhibited by an artificial nucleic acid molecule comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 24.

The at least one 5'-UTR element of the artificial nucleic acid molecule according to the present invention may also comprise or consist of a fragment of a nucleic acid sequence which has an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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%, most preferably of 100% to the nucleic acid sequence of the 5'-UTR of a transcript of a gene, such as to the 5'-UTR of a sequence according to SEQ ID NO: 25 or SEQ ID NO: 30 and SEQ ID NOs: 319 to 382, wherein the fragment is preferably a functional fragment or a functional variant fragment as described above. Such fragment preferably exhibits a length of at least about 3 nucleotides, preferably of at least about 5 nucleotides, more preferably of at least about 10, 15, 20, 25 or 30 nucleotides, even more

preferably of at least about 50 nucleotides, most preferably of at least about 70 nucleotides. In a preferred embodiment, the fragment or variant thereof exhibits a length of between 3 and about 500 nucleotides, preferably of between 5 and about 150 nucleotides, more preferably of between 10 and 100 nucleotides, even more preferably of between 15 and 90, most preferably of between 20 and 70. Preferably, said variants, fragments or variant fragments are functional variants, functional fragments, or functional variant fragments of the 5'-UTR, increase protein production from the artificial nucleic acid molecule according to the invention with an efficiency of at least 30%, preferably with an efficiency of at least 40%, more preferably of at least 50%, more preferably of at least 60%, even more preferably of at least 70%, even more preferably of at least 80%, most preferably of at least 90% of the protein production increasing efficiency exhibited by an artificial nucleic acid molecule comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 25 to SEQ ID NO: 30.

Preferably, the at least one 3'-UTR element and/or the at least one 5'-UTR element of the artificial nucleic acid molecule according to the present invention exhibits a length of at least about 3 nucleotides, preferably of at least about 5 nucleotides, more preferably of at least about 10, 15, 20, 25 or 30 nucleotides, even more preferably of at least about 50 nucleotides, most preferably of at least about 70 nucleotides. The upper limit for the length of the at least one 3'-UTR element and/or the at least one 5'-UTR element may be 500 nucleotides or less, e.g. 400, 300, 200, 150 or 100 nucleotides. For other embodiments the upper limit may be chosen within the range of 50 to 100 nucleotides. For example, the fragment or variant thereof may exhibit a length of between 3 and about 500 nucleotides, preferably of between 5 and about 150 nucleotides, more preferably of between 10 and 100 nucleotides, even more preferably of between 15 and 90, most preferably of between 20 and 70.

Furthermore, the artificial nucleic acid molecule according to the present invention may comprise more than one 3'-UTR elements and/or more than one 5'-UTR elements as described above. For example, the artificial nucleic acid molecule according to the present invention may comprise one, two, three, four or more 3'-UTR elements, and/or one, two, three, four or more 5'-UTR elements, wherein the individual 3'-UTR elements may be the same or they may be different, and similarly, the individual 5'-UTR elements may be the same or they may be different. For example, the artificial nucleic acid molecule according to the

present invention may comprise two essentially identical 3'-UTR elements as described above, e.g. two 3'-UTR elements comprising or consisting of a nucleic acid sequence, which is derived from the 3'-UTR of a transcript of a gene, such as from a sequence according to SEQ ID NOs: 1 to 24 and SEQ ID NO: 49 to 318, or from a fragment or variant of the 3'-UTR of a transcript of a gene, functional variants thereof, functional fragments thereof, or functional variant fragments thereof as described above. Accordingly, for example, the artificial nucleic acid molecule according to the present invention may comprise two essentially identical 5'-UTR elements as described above, e.g. two 5'-UTR elements comprising or consisting of a nucleic acid sequence, which is derived from the 5'-UTR of a transcript of a gene, such as from a sequence according to SEQ ID NOs: 25 to 30 and SEQ ID NO: 319 to 382, or from a fragment or variant of the 5'-UTR of a transcript of a gene, functional variants thereof, functional fragments thereof, or functional variant fragments thereof as described above.

Surprisingly, the inventors found that an artificial nucleic acid molecule comprising a 3'-UTR element as described above and/or a 5'-UTR element as described above may represent or may provide an mRNA molecule, which allows for increased, prolonged and/or stabilized protein production. Thus, a 3'-UTR element as described herein and/or a 5'-UTR element as described herein may improve stability of protein expression from an mRNA molecule and/or improve translational efficiency.

In particular, the artificial nucleic acid molecule according to the invention may comprise (i) at least one 3'-UTR element and at least one 5'-UTR element, which prolongs and/or increases protein production; (ii) at least one 3'-UTR element, which prolongs and/or increases protein production, but no 5'-UTR element, which prolongs and/or increases protein production; or (iii) at least one 5'-UTR element, which prolongs and/or increases protein production, but no 3'-UTR element, which prolongs and/or increases protein production.

However, in particular in case (ii) and (iii), but possibly also in case (i), the artificial nucleic acid molecule according to the present invention may further comprise one or more "further 3'-UTR elements and/or 5'-UTR elements", i.e. 3'-UTR elements and/or 5'-UTR elements which do not fulfil the requirements as described above. For example, an artificial nucleic acid molecule according to the invention, which comprises a 3'-UTR element according to

the present invention, i.e. a 3'-UTR element which prolongs and/or increases protein production from said artificial nucleic acid molecule, may additionally comprise any further 3'-UTR and/or any further 5'-UTR, in particular a further 5'-UTR, e.g. a 5'-TOP UTR, or any other 5'-UTR or 5'-UTR element. Similarly for example, an artificial nucleic acid molecule according to the invention, which comprises a 5'-UTR element according to the present invention, i.e. a 5'-UTR element which prolongs and/or increases protein production from said artificial nucleic acid molecule, may additionally comprise any further 3'-UTR and/or any further 5'-UTR, in particular a further 3'-UTR, e.g. a 3'-UTR derived from a 3'-UTR of an albumin gene, particularly preferably a 3'-UTR comprising a sequence according to SEQ ID NO. 31 or 32, in particular to SEQ ID NO. 32, or any other 3'-UTR or 3'-UTR element.

If additionally to the inventive at least one 5'-UTR element and/or to the inventive at least one 3'-UTR element, which prolongs and/or increases protein production, a further 3'-UTR (element) and/ or a further 5'-UTR (element) are present in the artificial nucleic acid molecule according to the invention, the further 5'-UTR (element) and/or the further 3'-UTR (element) may interact with the inventive 3'-UTR element and/or inventive 5'-UTR element and, thus, support the increasing and/or prolonging effect of the inventive 3'-UTR element and/or of the inventive 5'-UTR element, respectively. Such further 3'-UTR and/or 5'-UTR (elements) may further support stability and translational efficiency. Moreover, if both, an inventive 3'-UTR element and an inventive 5'-UTR element are present in the artificial nucleic acid molecule according to the invention, the prolonging and/or increasing effect of the inventive 5'-UTR element and the inventive 3'-UTR element result preferably in enhanced and prolonged protein production in a synergistic way.

Preferably, the further 3'-UTR comprises or consists of a nucleic acid sequence which is 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, such as a collagen alpha 1(I) gene, or from a variant of 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, such as a collagen alpha 1(I) gene according to SEQ ID No. 1369-1390 of the patent application WO2013/143700 whose disclosure is incorporated herein by reference. In a particularly preferred embodiment, the further 3'-UTR comprises or consists of a nucleic acid sequence

which is derived from a 3'-UTR of an albumin gene, preferably a vertebrate albumin gene, more preferably a mammalian albumin gene, most preferably a human albumin gene according to SEQ ID NO. 31:

SEQ ID NO. 31:

CATCACATTT AAAAGCATCT CAGCCTACCA TGAGAATAAG AGAAAGAAAA TGAAGATCAA AAGCTTATTC ATCTGTTTTT CTTTTTCGTT GGTGTAAAGC CAACACCCTG TCTAAAAAAC ATAAATTTCT TTAATCATTT TGCCTCTTTT CTCTGTGCTT CAATTAATAA AAAATGGAAA GAATCT

(Human albumin 3'-UTR; corresponding to SEQ ID No: 1369 of the patent application WO2013/143700)

In this context it is particularly preferred that the inventive nucleic acid molecule comprises a further 3'-UTR element derived from the nucleic acids according to SEQ ID No. 1369-1390 of the patent application WO2013/143700 or a fragment, homolog or variant thereof.

Most preferably the further 3'-UTR comprises the nucleic acid sequence derived from a fragment of the human albumin gene according to SEQ ID NO. 32:

SEQ ID NO. 32:

CATCACATTTAAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAGAAAATGAAGATCAATAGCTT ATTCATCTCTTTTTCTTTTTCGTTGGTGTAAAGCCAACACCCTGTCTAAAAAACATAAATTTCTTT AATCATTTTGCCTCTTTTCTCTGTGCTTCAATTAATAAAAAATGGAAAGAACCT

(albumin7 3'-UTR; corresponding to SEQ ID No: 1376 of the patent application WO2013/143700)

In this context it is particularly preferred that the further 3'-UTR of the inventive artificial nucleic acid molecule comprises or consists of the nucleic acid sequence according to SEQ ID NO. 32, or a corresponding RNA sequence.

The further 3'-UTR may also comprise or consist of a nucleic acid sequence derived from a ribosomal protein coding gene, whereby ribosomal protein coding genes from which a further 3'-UTR may be derived include, but are not limited to, ribosomal protein L9 (RPL9), ribosomal protein L3 (RPL3), ribosomal protein L4 (RPL4), ribosomal protein L5 (RPL5), ribosomal protein L6 (RPL6), ribosomal protein L7 (RPL7), ribosomal protein L7a (RPL7A), ribosomal protein L11 (RPL11), ribosomal protein L12 (RPL12), ribosomal protein L13

(RPL13), ribosomal protein L23 (RPL23), ribosomal protein L18 (RPL18), ribosomal protein L18a (RPL18A), ribosomal protein L19 (RPL19), ribosomal protein L21 (RPL21), ribosomal protein L22 (RPL22), ribosomal protein L23a (RPL23A), ribosomal protein L17 (RPL17), ribosomal protein L24 (RPL24), ribosomal protein L26 (RPL26), ribosomal protein L27 (RPL27), ribosomal protein L30 (RPL30), ribosomal protein L27a (RPL27A), ribosomal protein L28 (RPL28), ribosomal protein L29 (RPL29), ribosomal protein L31 (RPL31), ribosomal protein L32 (RPL32), ribosomal protein L35a (RPL35A), ribosomal protein L37 (RPL37), ribosomal protein L37a (RPL37A), ribosomal protein L38 (RPL38), ribosomal protein L39 (RPL39), ribosomal protein, large, P0 (RPLP0), ribosomal protein, large, P1 (RPLP1), ribosomal protein, large, P2 (RPLP2), ribosomal protein S3 (RPS3), ribosomal protein S3A (RPS3A), ribosomal protein S4, X-linked (RPS4X), ribosomal protein S4, Y-linked 1 (RPS4Y1), ribosomal protein S5 (RPS5), ribosomal protein S6 (RPS6), ribosomal protein S7 (RPS7), ribosomal protein S8 (RPS8), ribosomal protein S9 (RPS9), ribosomal protein S10 (RPS10), ribosomal protein S11 (RPS11), ribosomal protein S12 (RPS12), ribosomal protein S13 (RPS13), ribosomal protein S15 (RPS15), ribosomal protein S15a (RPS15A), ribosomal protein S16 (RPS16), ribosomal protein S19 (RPS19), ribosomal protein S20 (RPS20), ribosomal protein S21 (RPS21), ribosomal protein S23 (RPS23), ribosomal protein S25 (RPS25), ribosomal protein S26 (RPS26), ribosomal protein S27 (RPS27), ribosomal protein S27a (RPS27a), ribosomal protein S28 (RPS28), ribosomal protein S29 (RPS29), ribosomal protein L15 (RPL15), ribosomal protein S2 (RPS2), ribosomal protein L14 (RPL14), ribosomal protein S14 (RPS14), ribosomal protein L10 (RPL10), ribosomal protein L10a (RPL10A), ribosomal protein L35 (RPL35), ribosomal protein L13a (RPL13A), ribosomal protein L36 (RPL36), ribosomal protein L36a (RPL36A), ribosomal protein L41 (RPL41), ribosomal protein S18 (RPS18), ribosomal protein S24 (RPS24), ribosomal protein L8 (RPL8), ribosomal protein L34 (RPL34), ribosomal protein S17 (RPS17), ribosomal protein SA (RPSA), ubiquitin A-52 residue ribosomal protein fusion product 1 (UBA52), Finkel-Biskis-Reilly murine sarcoma virus (FBR-MuSV) ubiquitously expressed (FAU), ribosomal protein L22-like 1 (RPL22L1), ribosomal protein S17 (RPS17), ribosomal protein L39-like (RPL39L), ribosomal protein L10-like (RPL10L), ribosomal protein L36a-like (RPL36AL), ribosomal protein L3-like (RPL3L), ribosomal protein S27-like (RPS27L), ribosomal protein L26-like 1 (RPL26L1), ribosomal protein L7-like 1 (RPL7L1), ribosomal protein L13a pseudogene (RPL13AP), ribosomal protein

L37a pseudogene 8 (RPL37AP8), ribosomal protein S10 pseudogene 5 (RPS10P5), ribosomal protein S26 pseudogene 11 (RPS26P11), ribosomal protein L39 pseudogene 5 (RPL39P5), ribosomal protein, large, P0 pseudogene 6 (RPLP0P6) and ribosomal protein L36 pseudogene 14 (RPL36P14).

Preferably, the further 5'-UTR comprises or consists of a nucleic acid sequence which is derived from the 5'-UTR of a TOP gene or which is derived from a fragment, homolog or variant of the 5'-UTR of a TOP gene.

It is particularly preferred that the 5'-UTR element does not comprise a TOP-motif or a 5'TOP, as defined above. In particular, it is preferred that a 5'-UTR of a TOP gene is a 5'-UTR of a TOP gene lacking the TOP motif.

The nucleic acid sequence which is derived from the 5'-UTR of a TOP gene is derived from a eukaryotic TOP gene, preferably a plant or animal TOP gene, more preferably a chordate TOP gene, even more preferably a vertebrate TOP gene, most preferably a mammalian TOP gene, such as a human TOP gene.

For example, the further 5'-UTR is preferably selected from 5'-UTR elements comprising or consisting of a nucleic acid sequence which is derived from a nucleic acid sequence selected from the group consisting of SEQ ID NOs. 1-1363, SEQ ID NO. 1395, SEQ ID NO. 1421 and SEQ ID NO. 1422 of the patent application WO2013/143700 whose disclosure is incorporated herein by reference, from the homologs of SEQ ID NOs. 1-1363, SEQ ID NO. 1395, SEQ ID NO. 1421 and SEQ ID NO. 1422 of the patent application WO2013/143700, from a variant thereof, or preferably from a corresponding RNA sequence. The term "homologs of SEQ ID NOs. 1-1363, SEQ ID NO. 1395, SEQ ID NO. 1421 and SEQ ID NO. 1422 of the patent application WO2013/143700" refers to sequences of other species than homo sapiens, which are homologous to the sequences according to SEQ ID NOs. 1-1363, SEQ ID NO. 1395, SEQ ID NO. 1421 and SEQ ID NO. 1422 of the patent application WO2013/143700.

In a preferred embodiment, the further 5'-UTR comprises or consists of a nucleic acid sequence which is derived from a nucleic acid sequence extending from nucleotide position

5 (i.e. the nucleotide that is located at position 5 in the sequence) to the nucleotide position immediately 5′ to the start codon (located at the 3′ end of the sequences), e.g. the nucleotide position immediately 5′ to the ATG sequence, of a nucleic acid sequence selected from SEQ ID NOs. 1-1363, SEQ ID NO. 1395, SEQ ID NO. 1421 and SEQ ID NO. 1422 of the patent application WO2013/143700, from the homologs of SEQ ID NOs. 1-1363, SEQ ID NO. 1395, SEQ ID NO. 1421 and SEQ ID NO. 1422 of the patent application WO2013/143700, from a variant thereof, or a corresponding RNA sequence. It is particularly preferred that the further 5′-UTR is derived from a nucleic acid sequence extending from the nucleotide position immediately 3′ to the 5′TOP to the nucleotide position immediately 5′ to the start codon (located at the 3′ end of the sequences), e.g. the nucleotide position immediately 5′ to the ATG sequence, of a nucleic acid sequence selected from SEQ ID NOs. 1-1363, SEQ ID NO. 1395, SEQ ID NO. 1421 and SEQ ID NO. 1422 of the patent application WO2013/143700, from the homologs of SEQ ID NOs. 1-1363, SEQ ID NO. 1395, SEQ ID NO. 1421 and SEQ ID NO. 1422 of the patent application WO2013/143700, from a variant thereof, or a corresponding RNA sequence.

In a particularly preferred embodiment, the further 5′-UTR comprises or consists of a nucleic acid sequence which is derived from a 5′-UTR of a TOP gene encoding a ribosomal protein or from a variant of a 5′-UTR of a TOP gene encoding a ribosomal protein. For example, the 5′-UTR element comprises or consists of a nucleic acid sequence which is derived from a 5′-UTR of a nucleic acid sequence according to any of SEQ ID NOs: 170, 232, 244, 259, 1284, 1285, 1286, 1287, 1288, 1289, 1290, 1291, 1292, 1293, 1294, 1295, 1296, 1297, 1298, 1299, 1300, 1301, 1302, 1303, 1304, 1305, 1306, 1307, 1308, 1309, 1310, 1311, 1312, 1313, 1314, 1315, 1316, 1317, 1318, 1319, 1320, 1321, 1322, 1323, 1324, 1325, 1326, 1327, 1328, 1329, 1330, 1331, 1332, 1333, 1334, 1335, 1336, 1337, 1338, 1339, 1340, 1341, 1342, 1343, 1344, 1346, 1347, 1348, 1349, 1350, 1351, 1352, 1353, 1354, 1355, 1356, 1357, 1358, 1359, or 1360 of the patent application WO2013/143700, a corresponding RNA sequence, a homolog thereof, or a variant thereof as described herein, preferably lacking the 5′-TOP motif. As described above, the sequence extending from position 5 to the nucleotide immediately 5′ to the ATG (which is located at the 3′end of the sequences) corresponds to the 5′-UTR of said sequences.

Preferably, the further 5'-UTR 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) or from a homolog or variant of a 5'-UTR of a TOP gene encoding a ribosomal Large protein (RPL). For example, the 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from a 5'-UTR of a nucleic acid sequence according to any of SEQ ID NOs: SEQ ID NOs: 67, 259, 1284-1318, 1344, 1346, 1348-1354, 1357, 1358, 1421 and 1422 of the patent application WO2013/143700, a corresponding RNA sequence, a homolog thereof, or a variant thereof as described herein, preferably lacking the 5'TOP motif.

In a particularly preferred embodiment, the 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 5'-UTR of a ribosomal protein Large 32 gene, preferably from a vertebrate ribosomal protein Large 32 (L32) gene, more preferably from a mammalian ribosomal protein Large 32 (L32) gene, most preferably from a human ribosomal protein Large 32 (L32) gene, or from a variant of the 5'-UTR of a ribosomal protein Large 32 gene, preferably from a vertebrate ribosomal protein Large 32 (L32) gene, more preferably from a mammalian ribosomal protein Large 32 (L32) gene, most preferably from a human ribosomal protein Large 32 (L32) gene, wherein preferably the further 5'-UTR does not comprise the 5'TOP of said gene.

Accordingly, in a particularly preferred embodiment, the further 5'-UTR comprises or consists of a nucleic acid sequence which has an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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. 33 (5'-UTR of human ribosomal protein Large 32 lacking the 5' terminal oligopyrimidine tract:
GGCGCTGCCTACGGAGGTGGCAGCCATCTCCTTCTCGGCATC (SEQ ID NO. 33);
corresponding to SEQ ID NO. 1368 of the patent application WO2013/143700) or preferably to a corresponding RNA sequence, or wherein the further 5'-UTR comprises or consists of a fragment of a nucleic acid sequence which has an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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. 33 or more preferably to a corresponding RNA sequence, wherein, preferably, the fragment is as described above, i.e. being a continuous stretch of nucleotides representing at least 20% etc. of the full-length 5'-UTR. Preferably, the fragment exhibits a length of at least about 20 nucleotides or more, preferably of at least about 30 nucleotides or more, more preferably of at least about 40 nucleotides or more. Preferably, the fragment is a functional fragment as described herein.

In some embodiments, the artificial nucleic acid molecule comprises a further 5'-UTR which comprises or consists of a nucleic acid sequence which is derived from the 5'-UTR of a vertebrate TOP gene, such as a mammalian, e.g. a human TOP gene, selected from RPSA, RPS2, RPS3, RPS3A, RPS4, RPS5, RPS6, RPS7, RPS8, RPS9, RPS10, RPS11, RPS12, RPS13, RPS14, RPS15, RPS15A, RPS16, RPS17, RPS18, RPS19, RPS20, RPS21, RPS23, RPS24, RPS25, RPS26, RPS27, RPS27A, RPS28, RPS29, RPS30, RPL3, RPL4, RPL5, RPL6, RPL7, RPL7A, RPL8, RPL9, RPL10, RPL10A, RPL11, RPL12, RPL13, RPL13A, RPL14, RPL15, RPL17, RPL18, RPL18A, RPL19, RPL21, RPL22, RPL23, RPL23A, RPL24, RPL26, RPL27, RPL27A, RPL28, RPL29, RPL30, RPL31, RPL32, RPL34, RPL35, RPL35A, RPL36, RPL36A, RPL37, RPL37A, RPL38, RPL39, RPL40, RPL41, RPLP0, RPLP1, RPLP2, RPLP3, RPLP0, RPLP1, RPLP2, EEF1A1, EEF1B2, EEF1D, EEF1G, EEF2, EIF3E, EIF3F, EIF3H, EIF2S3, EIF3C, EIF3K, EIF3EIP, EIF4A2, PABPC1, HNRNPA1, TPT1, TUBB1, UBA52, NPM1, ATP5G2, GNB2L1, NME2, UQCRB or from a homolog or variant thereof, wherein preferably the further 5'-UTR does not comprise a TOP-motif or the 5'TOP of said genes, and wherein optionally the further 5'-UTR 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 5'terminal oligopyrimidine tract (TOP) and wherein further optionally the further 5'-UTR which is derived from a 5'-UTR of a TOP gene 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 (A(U/T)G) of the gene it is derived from.

The artificial nucleic acid molecule according to the present invention may be RNA, such as mRNA or viral RNA or a replicon, DNA, such as a DNA plasmid or viral DNA, or may be a modified RNA or DNA molecule. It may be provided as a double-stranded molecule having a sense strand and an anti-sense strand, for example, as a DNA molecule having a sense strand and an anti-sense strand.

The artificial nucleic acid molecule according to the present invention may further comprise optionally a 5'-cap. The optional 5'-cap is preferably located 5' to the ORF, more preferably 5' to the at least one 5'-UTR or to any further 5'-UTR within the artificial nucleic acid molecule according to the present invention.

Preferably, the artificial nucleic acid molecule according to the present invention further comprises a poly(A) sequence and/or a polyadenylation signal. Preferably, the optional poly(A) sequence is located 3' to the at least one 3'-UTR element or to any further 3'-UTR, more preferably the optional poly(A) sequence is connected to the 3'-end of an 3'-UTR element. The connection may be direct or indirect, for example, via a stretch of 2, 4, 6, 8, 10, 20 etc. nucleotides, such as via a linker of 1-50, preferably of 1-20 nucleotides, e.g. comprising or consisting of one or more restriction sites. However, even if the artificial nucleic acid molecule according to the present invention does not comprise a 3'-UTR, for example if it only comprises at least one 5'-UTR element, it preferably still comprises a poly(A) sequence and/or a polyadenylation signal.

In one embodiment, the optional polyadenylation signal is located downstream of the 3' of the 3'-UTR element. Preferably, 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. Such consensus sequence may be recognised by most animal and bacterial cell-systems, for example by the polyadenylation-factors, such as cleavage/polyadenylation specificity factor (CPSF) cooperating with CstF, PAP, PAB2, CFI and/or CFII. Preferably, the polyadenylation signal, preferably the consensus sequence NNUANA, is located less than about 50 nucleotides, more preferably less than about 30 bases, most preferably less than about 25 bases, for example 21 bases, downstream of the 3'-end of the 3'-UTR element or of the ORF, if no 3'-UTR element is present.

Transcription of an artificial nucleic acid molecule according to the present invention, e.g. of an artificial DNA molecule, comprising a polyadenylation signal downstream of the 3'-UTR element (or of the ORF) will result in a premature-RNA containing the polyadenylation signal downstream of its 3'-UTR element (or of the ORF).

Using an appropriate transcription system will then lead to attachment of a poly(A) sequence to the premature-RNA. For example, the inventive artificial nucleic acid molecule may be a DNA molecule comprising a 3'-UTR element as described above and a polyadenylation signal, which may result in polyadenylation of an RNA upon transcription of this DNA molecule. Accordingly, a resulting RNA may comprise a combination of the inventive 3'-UTR element followed by a poly(A) sequence.

Potential transcription systems are *in vitro* transcription systems or cellular transcription systems etc. Accordingly, transcription of an artificial nucleic acid molecule according to the invention, e.g. transcription of an artificial nucleic acid molecule comprising an open reading frame, a 3'-UTR element and/or a 5'-UTR element and optionally a polyadenylation-signal, may result in an mRNA molecule comprising an open reading frame, a 3'-UTR element and optionally a poly(A) sequence.

Accordingly, the invention also provides an artificial nucleic acid molecule, which is an mRNA molecule comprising an open reading frame, a 3'-UTR element as described above and/or a 5'-UTR element as described above and optionally a poly(A) sequence.

In another embodiment, the 3'-UTR of the artificial nucleic acid molecule according to the invention does not comprise a polyadenylation signal or a poly(A) sequence. Further preferably, the artificial nucleic acid molecule according to the invention does not comprise a polyadenylation signal or a poly(A) sequence. More preferably, the 3'-UTR of the artificial nucleic acid molecule, or the inventive artificial nucleic acid molecule as such, does not comprise a polyadenylation signal, in particular it does not comprise the polyadenylation signal AAU/TAAA.

In a preferred embodiment, the invention provides an artificial nucleic acid molecule which is an artificial RNA molecule comprising an open reading frame and an RNA sequence corresponding to a DNA sequence selected from the group consisting of sequences according to SEQ ID NOs: 1 to 30, preferably from the group consisting of sequences according to SEQ ID NO. 1, SEQ ID NO. 5, SEQ ID NO. 8, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 14, SEQ ID NO. 17, SEQ ID NO. 20, SEQ ID NO. 25 and SEQ ID NO. 28, or sequences having an identity of at least about 40 % or more to SEQ ID NOs: 1 to 30,

preferably to SEQ ID NO. 1, SEQ ID NO. 5, SEQ ID NO. 8, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 14, SEQ ID NO. 17, SEQ ID NO. 20, SEQ ID NO. 25 and SEQ ID NO. 28 or a fragment thereof as described above. Moreover, a corresponding artificial DNA molecule is also provided.

In another preferred embodiment, the invention provides an artificial nucleic acid molecule which is an artificial DNA molecule comprising an open reading frame and a sequence selected from the group consisting of sequences according to SEQ ID NOs: 1 to 30, preferably from the group consisting of sequences according to SEQ ID NO. 1, SEQ ID NO. 5, SEQ ID NO. 8, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 14, SEQ ID NO. 17, SEQ ID NO. 20, SEQ ID NO. 25 and SEQ ID NO. 28, or sequences having an identity of at least about 40 % or more to SEQ ID NOs: 1 to 30, preferably to SEQ ID NO. 1, SEQ ID NO. 5, SEQ ID NO. 8, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 14, SEQ ID NO. 17, SEQ ID NO. 20, SEQ ID NO. 25 and SEQ ID NO. 28.

Accordingly, the invention provides an artificial nucleic acid molecule which may serve as a template for an RNA molecule, preferably for an mRNA molecule, which is stabilised and optimized with respect to translation efficiency. In other words, the artificial nucleic acid molecule may be a DNA which may be used as a template for production of an mRNA. The obtainable mRNA, may, in turn, be translated for production of a desired peptide or protein encoded by the open reading frame. If the artificial nucleic acid molecule is a DNA, it may, for example, be used as a double-stranded storage form for continued and repetitive *in vitro* or *in vivo* production of mRNA. Thereby, *in vitro* refers in particular to ("living") cells and/or tissue, including tissue of a living subject. Cells include in particular cell lines, primary cells, cells in tissue or subjects. In specific embodiments cell types allowing cell culture may be suitable for the present invention. Particularly preferred are mammalian cells, e.g. human cells and mouse cells. In particularly preferred embodiments the human cell lines HeLa, and U-937 and the mouse cell lines NIH3T3, JAWSII and L929 are used. Furthermore primary cells are particularly preferred, in particular preferred embodiments human dermal fibroblasts (HDF) may be used. Alternatively also a tissue of a subject may be used.

In one embodiment, the artificial nucleic acid molecule according to the present invention further comprises a poly(A) sequence. For example, a DNA molecule comprising an ORF, optionally followed by a 3' UTR, may contain a stretch of thymidine nucleotides which can

be transcribed into a poly(A) sequence in the resulting mRNA. The length of the poly(A) sequence may vary. For example, the poly(A) sequence may have a length of about 20 adenine nucleotides up to about 300 adenine nucleotides, preferably of about 40 to about 200 adenine nucleotides, more preferably from about 50 to about 100 adenine nucleotides, such as about 60, 70, 80, 90 or 100 adenine nucleotides. Most preferably, the inventive nucleic acid comprises a poly(A) sequence of about 60 to about 70 nucleotides, most preferably 64 adenine nucleotides.

Artificial RNA-molecules may also be obtainable *in vitro* by common methods of chemical-synthesis without being necessarily transcribed from a DNA-progenitor.

In a particularly preferred embodiment, the artificial nucleic acid molecule according to the present invention is an RNA molecule, preferably an mRNA molecule comprising in 5'-to-3'-direction an open reading frame, a 3'-UTR element as described above and a poly(A) sequence or comprising in 5'-to-3'-direction a 5'-UTR element as described above, an open reading frame and a poly(A) sequence.

In a preferred embodiment, the open reading frame is derived from a gene, which is distinct from the gene from which the 3'-UTR element and/or the 5'-UTR element of the inventive artificial nucleic acid is derived. In some further preferred embodiments, the open reading frame does not code for a gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), CNTN1 (contactin 1), preferably CNTN1-004 or variants thereof, provided that the 3'-UTR element and/or the 5'-UTR element is a sequence which is selected from the group consisting of sequences according to SEQ ID NO. 1 to SEQ ID NO. 30.

In a preferred embodiment, the ORF does not encode human or plant, in particular Arabidopsis, ribosomal proteins, in particular does not encode human ribosomal protein S6 (RPS6), human ribosomal protein L36a-like (RPL36AL) or Arabidopsis ribosomal protein S16

(RPS16). In a further preferred embodiment, the open reading frame (ORF) does not encode ribosomal protein S6 (RPS6), ribosomal protein L36a-like (RPL36AL) or ribosomal protein S16 (RPS16) of whatever origin.

In one embodiment, the invention provides an artificial DNA molecule comprising an open reading frame, preferably an open reading frame derived from a gene, which is distinct from the gene from which the 3'-UTR element and/or the 5'-UTR element is derived; a 3'-UTR element comprising or consisting of a sequence which has at least about 60%, preferably at least about 70%, more preferably at least about 80%, more preferably at least about 90%, even more preferably at least about 95%; even more preferably at least 99%; even more preferably 100% sequence identity to a DNA sequence selected from the group consisting of sequences according to SEQ ID NO. 1 to 24, and/or a 5'-UTR element comprising or consisting of a sequence which has at least about 60%, preferably at least about 70%, more preferably at least about 80%, more preferably at least about 90%, even more preferably at least about 95%; even more preferably at least 99%; even more preferably 100% sequence identity to a DNA sequence selected from the group consisting of sequences according to SEQ ID NO. 25 to 30; and a polyadenylation signal and/or a poly(A) sequence.

In a further embodiment there is provided a composition comprising a plurality of RNA molecules of the embodiments in pharmaceutically acceptable carrier, wherein at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or greater of the RNA in the composition comprises a poly(A) sequence that differs in length by no nor that 10 nucleotides. In a preferred embodiment at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or greater of the RNA in the composition comprises a poly(A) sequence of identical length. In certain embodiments, the poly(A) sequence is positioned at the 3' end of the RNA, with no other nucleotides positioned 3' relative the poly(A) sequence. In still a further embodiment, there is provided a composition comprising a plurality of RNA molecules of the embodiments in pharmaceutically acceptable carrier, wherein said plurality of RNA molecules comprise both capped and uncapped RNAs. For example, in some aspects, a composition comprises a plurality of RNA molecules wherein no more than 95%, 90%, 80%, 70% or 60% of the RNAs comprise a cap and the remaining RNA molecules are uncapped.

Furthermore, the invention provides an artificial RNA molecule, preferably an artificial mRNA molecule or an artificial viral RNA molecule, comprising an open reading frame, preferably an open reading frame is derived from a gene, which is distinct from the gene from which the 3'-UTR element and/or the 5'-UTR element is derived; a 3'-UTR element comprising or consisting of a sequence which has at least about 60%, preferably at least about 70%, more preferably at least about 80%, more preferably at least about 90%, even more preferably at least about 95%; even more preferably at least 99%; even more preferably 100% sequence identity to an RNA sequence corresponding to a DNA sequence selected from the group consisting of sequences according to SEQ ID NO. 1 to 24, and/or a 5'-UTR element comprising or consisting of a sequence which has at least about 60%, preferably at least about 70%, more preferably at least about 80%, more preferably at least about 90%, even more preferably at least about 95%; even more preferably at least 99%; even more preferably 100% sequence identity to an RNA sequence corresponding to a DNA sequence selected from the group consisting of sequences according to SEQ ID NO. 25 to 30; and a polyadenylation signal and/or a poly(A) sequence.

The invention provides an artificial nucleic acid molecule, preferably an artificial mRNA, which may be characterized by increased and/or prolonged expression of the encoded peptide or protein. Without being bound by any theory, enhanced stability of protein expression and thus prolonged protein expression may result from reduction in degradation of the artificial nucleic acid molecule, such as an artificial mRNA molecule according to the present invention. Accordingly, the inventive 3'-UTR element and/or the inventive 5'-UTR element may prevent the artificial nucleic acid from degradation and decay.

Preferably, the artificial nucleic acid molecule may additionally comprise a histone stem-loop. Thus, an artificial nucleic acid molecule according to the present invention may, for example, comprise in 5'-to-3'-direction an ORF, a 3'-UTR element, an optional histone stem-loop sequence, an optional poly(A) sequence or polyadenylation signal and an optional poly(C) sequence or in 5'-to-3'-direction an 5'-UTR element, an ORF, an optional histone stem-loop sequence, an optional poly(A) sequence or polyadenylation signal and an optional poly(C) sequence or in 5'-to-3'-direction an 5'-UTR element, an ORF, a 3'-UTR element, an optional histone stem-loop sequence, an optional poly(A) sequence or polyadenylation signal and an optional poly(C) sequence. It may also comprise in 5'-to-3'-direction an ORF, an 3'-UTR element, an optional poly(A) sequence, an optional poly (C) sequence and an optional

histone stem-loop sequence, or in 5'-to-3'-direction an 5'-UTR element, an ORF, an optional poly(A) sequence, an optional poly(C) sequence and an optional histone stem-loop sequence, or in 5'-to-3'-direction an 5'-UTR element, an ORF, a 3'-UTR element, an optional poly(A) sequence, an optional poly(C) sequence and an optional histone stem-loop sequence.

In a preferred embodiment, the artificial nucleic acid molecule according to the invention further comprises at least one histone stem-loop sequence.

Such histone stem-loop sequences are preferably selected from histone stem-loop sequences as disclosed in WO 2012/019780, whose disclosure is incorporated herewith by reference.

A histone stem-loop sequence, suitable to be used within the present invention, is preferably selected from at least one of the 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):

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

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 or 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 nucleoside 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, e.g.

by Watson-Crick base pairing of nucleotides A and U/T or G and C or by non-Watson-Crick base pairing e.g. wobble base pairing, reverse Watson-Crick base pairing, Hoogsteen base pairing, reverse Hoogsteen base pairing or are capable of base pairing with each other forming a partially reverse complementary sequence, wherein an incomplete base pairing may occur between stem1 and stem2, on the basis that one ore more bases in one stem do not have a complementary base in the reverse complementary sequence of the other stem.

According to a further preferred embodiment the histone stem-loop sequence may be selected according to at least one of the following specific formulae (Ia) or (IIa):

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

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

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

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

wherein:

N, C, G, T and U	are as defined above.

According to a further more particularly preferred embodiment of the first aspect, the artificial nucleic acid molecule sequence may comprise at least one histone stem-loop sequence according to at least one of the following specific formulae (Ib) or (IIb):

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

$$\underbrace{[N_1GN_4]}_{\text{stem1}}\ \underbrace{[N_2(U/T)N_1]}_{\text{loop}}\ \underbrace{[N_4CN_1]}_{\text{stem2}}$$

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

$$\underbrace{N_{4\text{-}5}}_{\text{stem1 bordering element}}\ \underbrace{[N_1GN_4]}_{\text{stem1}}\ \underbrace{[N_2(U/T)N_1]}_{\text{loop}}\ \underbrace{[N_4CN_1]}_{\text{stem2}}\ \underbrace{N_{4\text{-}5}}_{\text{stem2 bordering element}}$$

wherein:

N, C, G, T and U	are as defined above.

A particular preferred histone stem-loop sequence is the sequence according to SEQ ID NO: 34: CAAAGGCTCTTTTCAGAGCCACCA or more preferably the corresponding RNA sequence of the nucleic acid sequence according to SEQ ID NO: 34.

As an example, the single elements may be present in the artificial nucleic acid molecule in the following order:

5'-cap – 5'-UTR (element) – ORF – 3'-UTR (element) – histone stem-loop – poly(A)/(C) sequence;

5'-cap – 5'-UTR (element) – ORF – 3'-UTR (element) – poly(A)/(C) sequence – histone stem-loop;

5'-cap - 5'-UTR (element) – ORF – IRES – ORF – 3'-UTR (element) - histone stem-loop - poly(A)/(C) sequence;

5'-cap - 5'-UTR (element) – ORF – IRES – ORF – 3'-UTR (element) - histone stem-loop - poly(A)/(C) sequence – poly(A)/(C) sequence;

5'-cap – 5'-UTR (element) – ORF – IRES – ORF – 3'-UTR (element) – poly(A)/(C) sequence – histone stem-loop;

5'-cap – 5'-UTR (element) – ORF – IRES – ORF – 3'-UTR (element) – poly(A)/(C) sequence – poly(A)/(C) sequence – histone stem-loop;

5'-cap – 5'-UTR (element) – ORF – 3'-UTR (element) – poly(A)/(C) sequence – poly(A)/(C) sequence;

5'-cap – 5'-UTR (element) – ORF – 3'-UTR (element) – poly(A)/(C) sequence – poly(A)/(C) sequence – histone stem loop; etc.

In some embodiments, the artificial nucleic acid molecule comprises further elements such as a 5'-cap, a poly(C) sequence and/or an IRES-motif. A 5'-cap may be added during transcription or post-transcriptionally to the 5'end of an RNA. Furthermore, the inventive artificial nucleic acid molecule, particularly if the nucleic acid is in the form of an mRNA or codes for an mRNA, may be modified by a sequence of at least 10 cytidines, preferably at least 20 cytidines, more preferably at least 30 cytidines (so-called "poly(C) sequence"). In particular, the inventive artificial nucleic acid molecule may contain, especially if the nucleic acid is in the form of an (m)RNA or codes for an mRNA, a poly(C) sequence of typically about 10 to 200 cytidine nucleotides, preferably about 10 to 100 cytidine nucleotides, more preferably about 10 to 70 cytidine nucleotides or even more preferably about 20 to 50 or even 20 to 30 cytidine nucleotides. Most preferably, the inventive nucleic acid comprises a poly(C) sequence of 30 cytidine residues. Thus, preferably the artificial nucleic acid molecule according to the present invention comprises, preferably in 5'-to-3' direction, at least one 5'-UTR element as described above, an ORF, at least one 3'-UTR element as described above, a poly(A) sequence or a polyadenylation signal, and a poly(C) sequence or, in 5'-to-3' direction, optionally a further 5'-UTR, an ORF, at least one 3'-UTR element as described above, a poly(A) sequence or a polyadenylation signal, and a poly(C) sequence, or, in 5'-to-3' direction, at least one 5'-UTR element as described above, an ORF, optionally a further 3'-UTR, a poly(A) sequence or a polyadenylation signal, and a poly(C) sequence .

An internal ribosome entry site (IRES) sequence or IRES-motif may separate several open reading frames, for example if the artificial nucleic acid molecule encodes for two or more peptides or proteins. An IRES-sequence may be particularly helpful if the artificial nucleic acid molecule is a bi- or multicistronic nucleic acid molecule.

Furthermore, the artificial nucleic acid molecule may comprise additional 5'-elements, preferably a promoter or a promoter containing-sequence. The promoter may drive and or regulate transcription of the artificial nucleic acid molecule according to the present invention, for example of an artificial DNA-molecule according to the present invention.

Preferably, the artificial nucleic acid molecule according to the present invention, preferably the open reading frame, is at least partially G/C modified. Thus, the inventive artificial nucleic acid molecule may be thermodynamically stabilized by modifying the G (guanosine)/C (cytidine) content of the molecule. The G/C content of the open reading frame of an artificial nucleic acid molecule according to the present invention may be increased compared to the G/C content of the open reading frame of a corresponding wild type sequence, preferably by using the degeneration of the genetic code. Thus, the encoded amino acid sequence of the artificial nucleic acid molecule is preferably not modified by the G/C modification compared to the coded amino acid sequence of the particular wild type sequence. The codons of the coding sequence or the whole artificial nucleic acid molecule, e.g. an mRNA, may therefore be varied compared to the wild type coding sequence, such that they include an increased amount of G/C nucleotides while the translated amino acid sequence is maintained. Due to the fact that several codons code for one and the same amino acid (so-called degeneration of the genetic code), it is feasible to alter codons while not altering the encoded peptide/protein sequence (so-called alternative codon usage). Hence, it is possible to specifically introduce certain codons (in exchange for the respective wild-type codons encoding the same amino acid), which are more favourable with respect to stability of RNA and/or with respect to codon usage in a subject (so-called codon optimization).

Depending on the amino acid to be encoded by the coding region of the inventive artificial nucleic acid molecule as defined herein, there are various possibilities for modification of the nucleic acid sequence, e.g. the open reading frame, compared to its wild type coding region. In the case of amino acids, which are encoded by codons which contain exclusively G or C nucleotides, no modification of the codon is necessary. Thus, the codons for Pro (CCC or CCG), Arg (CGC or CGG), Ala (GCC or GCG) and Gly (GGC or GGG) require no modification, since no A or U/T is present.

In contrast, codons which contain A and/or U/T nucleotides may be modified by substitution

of other codons which code for the same amino acids but contain no A and/or U/T. For example

the codons for Pro can be modified from CC(U/T) or CCA to CCC or CCG;
the codons for Arg can be modified from CG(U/T) or CGA or AGA or AGG to CGC or CGG;
the codons for Ala can be modified from GC(U/T) or GCA to GCC or GCG;
the codons for Gly can be modified from GG(U/T) or GGA to GGC or GGG.

In other cases, although A or (U/T) nucleotides cannot be eliminated from the codons, it is however possible to decrease the A and (U/T) content by using codons which contain a lower content of A and/or (U/T) nucleotides. Examples of these are:

The codons for Phe can be modified from (U/T)(U/T)(U/T) to (U/T) (U/T)C;
the codons for Leu can be modified from (U/T) (U/T)A, (U/T) (U/T)G, C(U/T) (U/T) or C(U/T)A to C(U/T)C or C(U/T)G;
the codons for Ser can be modified from (U/T)C(U/T) or (U/T)CA or AG(U/T) to (U/T)CC, (U/T)CG or AGC;
the codon for Tyr can be modified from (U/T)A(U/T) to (U/T)AC;
the codon for Cys can be modified from (U/T)G(U/T) to (U/T)GC;
the codon for His can be modified from CA(U/T) to CAC;
the codon for Gln can be modified from CAA to CAG;
the codons for Ile can be modified from A(U/T)(U/T) or A(U/T)A to A(U/T)C;
the codons for Thr can be modified from AC(U/T) or ACA to ACC or ACG;
the codon for Asn can be modified from AA(U/T) to AAC;
the codon for Lys can be modified from AAA to AAG;
the codons for Val can be modified from G(U/T)(U/T) or G(U/T)A to G(U/T)C or G(U/T)G;
the codon for Asp can be modified from GA(U/T) to GAC;
the codon for Glu can be modified from GAA to GAG;
the stop codon (U/T)AA can be modified to (U/T)AG or (U/T)GA.

In the case of the codons for Met (A(U/T)G) and Trp ((U/T)GG), on the other hand, there is no possibility of sequence modification without altering the encoded amino acid sequence.

The substitutions listed above can be used either individually or in all possible combinations to increase the G/C content of the open reading frame of the inventive artificial nucleic acid molecule as defined herein, compared to its particular wild type open reading frame (i.e. the original sequence). Thus, for example, all codons for Thr occurring in the wild type sequence can be modified to ACC (or ACG).

Preferably, the G/C content of the open reading frame of the inventive artificial nucleic acid molecule as defined herein is increased by at least 7%, more preferably by at least 15%, particularly preferably by at least 20%, compared to the G/C content of the wild type coding region without altering the encoded amino acid sequence, i.e. using the degeneracy of the genetic code. According to a specific embodiment at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, more preferably at least 70 %, even more preferably at least 80% and most preferably at least 90%, 95% or even 100% of the substitutable codons in the open reading frame of the inventive artificial nucleic acid molecule or a fragment, variant or derivative thereof are substituted, thereby increasing the G/C content of said open reading frame.

In this context, it is particularly preferable to increase the G/C content of the open reading frame of the inventive artificial nucleic acid molecule as defined herein, to the maximum (i.e. 100% of the substitutable codons), compared to the wild type open reading frame, without altering the encoded amino acid sequence.

Furthermore, the open reading frame is preferably at least partially codon-optimized. Codon-optimization is based on the finding that the translation efficiency may be determined by a different frequency in the occurrence of transfer RNAs (tRNAs) in cells. Thus, if so-called "rare codons" are present in the coding region of the inventive artificial nucleic acid molecule as defined herein, to an increased extent, the translation of the corresponding modified nucleic acid sequence is less efficient than in the case where codons coding for relatively "frequent" tRNAs are present.

Thus, the open reading frame of the inventive artificial nucleic acid molecule is preferably modified compared to the corresponding wild type coding region such that at least one codon of the wild type sequence which codes for a tRNA which is relatively rare in the cell is exchanged for a codon which codes for a tRNA which is comparably frequent in the cell and carries the same amino acid as the relatively rare tRNA. By this modification, the open reading

frame of the inventive artificial nucleic acid molecule as defined herein, is modified such that codons for which frequently occurring tRNAs are available may replace codons which correspond to rare tRNAs. In other words, according to the invention, by such a modification all codons of the wild type open reading frame which code for a rare tRNA may be exchanged for a codon which codes for a tRNA which is more frequent in the cell and which carries the same amino acid as the rare tRNA. Which tRNAs occur relatively frequently in the cell and which, in contrast, occur relatively rarely is known to a person skilled in the art; cf. e.g. Akashi, Curr. Opin. Genet. Dev. 2001, 11(6): 660-666. Accordingly, preferably, the open reading frame is codon-optimized, preferably with respect to the system in which the artificial nucleic acid molecule according to the present invention is to be expressed, preferably with respect to the system in which the artificial nucleic acid molecule according to the present invention is to be translated. Preferably, the codon usage of the open reading frame is codon-optimized according to mammalian codon usage, more preferably according to human codon usage. Preferably, the open reading frame is codon-optimized and G/C-content modified.

For further improving degradation resistance, e.g. resistance to *in vivo* (or *in vitro* as defined above) degradation by an exo- or endonuclease, and/or for further improving stability of protein expression from the artificial nucleic acid molecule according to the present invention, the artificial nucleic acid molecule may further comprise modifications, such as backbone modifications, sugar modifications and/or base modifications, e.g., lipid-modifications or the like. Preferably, the transcription and/or the translation of the artificial nucleic acid molecule according to the present invention is not significantly impaired by said modifications.

Generally, the artificial nucleic acid molecule of the present invention may comprise any native (= naturally occurring) nucleotide, e.g. guanosine, uracil, adenosine, and/or cytosine or an analogue thereof. In this respect, nucleotide analogues are defined as natively and non-natively occurring variants of the naturally occurring nucleotides adenosine, cytosine, thymidine, guanosine and uridine. Accordingly, analogues are e.g. chemically derivatized nucleotides with non-natively occurring functional groups, which are preferably added to or deleted from the naturally occurring nucleotide or which substitute the naturally occurring functional groups of a nucleotide. Accordingly, each component of the naturally occurring nucleotide may be modified, namely the base component, the sugar (ribose) component

and/or the phosphate component forming the backbone (see above) of the RNA sequence. Analogues of guanosine, uridine, adenosine, thymidine and cytosine include, without implying any limitation, any natively occurring or non-natively occurring guanosine, uridine, adenosine, thymidine or cytosine that has been altered e.g. chemically, for example by acetylation, methylation, hydroxylation, etc., including 1-methyl-adenosine, 1-methyl-guanosine, 1-methyl-inosine, 2,2-dimethyl-guanosine, 2,6-diaminopurine, 2'-Amino-2'-deoxyadenosine, 2'-Amino-2'-deoxycytidine, 2'-Amino-2'-deoxyguanosine, 2'-Amino-2'-deoxyuridine, 2-Amino-6-chloropurineriboside, 2-Aminopurine-riboside, 2'-Araadenosine, 2'-Aracytidine, 2'-Arauridine, 2'-Azido-2'-deoxyadenosine, 2'-Azido-2'-deoxycytidine, 2'-Azido-2'-deoxyguanosine, 2'-Azido-2'-deoxyuridine, 2-Chloroadenosine, 2'-Fluoro-2'-deoxyadenosine, 2'-Fluoro-2'-deoxycytidine, 2'-Fluoro-2'-deoxyguanosine, 2'-Fluoro-2'-deoxyuridine, 2'-Fluorothymidine, 2-methyl-adenosine, 2-methyl-guanosine, 2-methyl-thio-N6-isopenenyl-adenosine, 2'-O-Methyl-2-aminoadenosine, 2'-O-Methyl-2'-deoxyadenosine, 2'-O-Methyl-2'-deoxycytidine, 2'-O-Methyl-2'-deoxyguanosine, 2'-O-Methyl-2'-deoxyuridine, 2'-O-Methyl-5-methyluridine, 2'-O-Methylinosine, 2'-O-Methylpseudouridine, 2-Thiocytidine, 2-thio-cytosine, 3-methyl-cytosine, 4-acetyl-cytosine, 4-Thiouridine, 5-(carboxyhydroxymethyl)-uracil, 5,6-Dihydrouridine, 5-Aminoallylcytidine, 5-Aminoallyl-deoxy-uridine, 5-Bromouridine, 5-carboxymehtylaminomethyl-2-thio-uracil, 5-carboxymethylamonomethyl-uracil, 5-Chloro-Ara-cytosine, 5-Fluoro-uridine, 5-Iodouridine, 5-methoxycarbonylmethyl-uridine, 5-methoxy-uridine, 5-methyl-2-thio-uridine, 6-Azacytidine, 6-Azauridine, 6-Chloro-7-deaza-guanosine, 6-Chloropurineriboside, 6-Mercapto-guanosine, 6-Methyl-mercaptopurine-riboside, 7-Deaza-2'-deoxy-guanosine, 7-Deazaadenosine, 7-methyl-guanosine, 8-Azaadenosine, 8-Bromo-adenosine, 8-Bromo-guanosine, 8-Mercapto-guanosine, 8-Oxoguanosine, Benzimidazole-riboside, Beta-D-mannosyl-queosine, Dihydro-uracil, Inosine, N1-Methyladenosine, N6-([6-Aminohexyl]carbamoylmethyl)-adenosine, N6-isopentenyl-adenosine, N6-methyl-adenosine, N7-Methyl-xanthosine, N-uracil-5-oxyacetic acid methyl ester, Puromycin, Queosine, Uracil-5-oxyacetic acid, Uracil-5-oxyacetic acid methyl ester, Wybutoxosine, Xanthosine, and Xylo-adenosine. The preparation of such analogues is known to a person skilled in the art, for example from US Patents 4,373,071, US 4,401,796, US 4,415,732, US 4,458,066, US 4,500,707, US 4,668,777, US 4,973,679, US 5,047,524, US 5,132,418, US 5,153,319, US 5,262,530 and 5,700,642. In the case of an analogue as described above, particular preference may be given according to certain embodiments of the invention to

those analogues that increase the protein expression of the encoded peptide or protein or that increase the immunogenicity of the artificial nucleic acid molecule of the invention and/or do not interfere with a further modification of the artificial nucleic acid molecule that has been introduced.

According to a particular embodiment, the artificial nucleic acid molecule of the present invention can contain a lipid modification.

In a preferred embodiment, the artificial nucleic acid molecule comprises, preferably from 5' to 3' direction, the following elements:

a 5'-UTR element which prolongs and/or increases protein production from said artificial nucleic acid molecule, preferably from a nucleic acid sequence according to any of SEQ ID NO: 25 to 30 and SEQ ID NOs: 319 to 382, more preferably of the 5'-UTR of MP68 or NDUFA4; or a further 5'-UTR, preferably a 5'-TOP UTR;

at least one open reading frame (ORF), wherein the ORF preferably comprises at least one modification with respect to the wild type sequence;

a 3'-UTR element which prolongs and/or increases protein production from said artificial nucleic acid molecule, preferably from a nucleic acid sequence according to any of SEQ ID NO: 1 to 24 and SEQ ID NOs: 49 to 318, more preferably of the 3'-UTR of GNAS, MORN2, GSTM1, NDUFA1, CBR2, YBX1, NDUFB8, or CNTN1; or a further 3'-UTR, preferably an albumin7 3'-UTR;

a poly(A) sequence, preferably comprising 64 adenylates;

a poly(C) sequence, preferably comprising 30 cytidylates;

a histone stem-loop sequence.

In another preferred embodiment, the artificial nucleic acid molecule comprises or consists of a nucleotide sequence selected from the group consisting of nucleic acid sequences according to SEQ ID NOs: 36 to 40, SEQ ID NOs: 42 and 43, SEQ ID NOs: 45 to 48, and SEQ ID NOs: 384 to 388 (see Fig. 2 to 6, Fig. 8, 9, 11, Fig. 19 to 21 and Fig. 26 to 30) or the complementary DNA sequence.

In a particularly preferred embodiment, the artificial nucleic acid molecule according to the invention may further comprise one or more of the modifications described in the following:

Chemical modifications:

The term "modification" as used herein with regard to the artificial nucleic acid molecule may refer to chemical modifications comprising backbone modifications as well as sugar modifications or base modifications.

In this context, the artificial nucleic acid molecule, preferably an RNA molecule, as defined herein may contain nucleotide analogues/modifications, e.g. backbone modifications, sugar modifications or base modifications. A backbone modification in connection with the present invention is a modification, in which phosphates of the backbone of the nucleotides contained in a nucleic acid molecule as defined herein are chemically modified. A sugar modification in connection with the present invention is a chemical modification of the sugar of the nucleotides of the nucleic acid molecule as defined herein. Furthermore, a base modification in connection with the present invention is a chemical modification of the base moiety of the nucleotides of the nucleic acid molecule of the nucleic acid molecule. In this context, nucleotide analogues or modifications are preferably selected from nucleotide analogues which are applicable for transcription and/or translation.

Sugar Modifications:

The modified nucleosides and nucleotides, which may be incorporated into the artificial nucleic acid molecule, preferably an RNA, as described herein, can be modified in the sugar moiety. For example, the 2' hydroxyl group (OH) of an RNA molecule can be modified or replaced with a number of different "oxy" or "deoxy" substituents. Examples of "oxy" -2' hydroxyl group modifications include, but are not limited to, alkoxy or aryloxy (-OR, e.g., R = H, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or sugar); polyethyleneglycols (PEG), -0(CH2CH2o)nCH2CH2OR; "locked" nucleic acids (LNA) in which the 2' hydroxyl is connected, e.g., by a methylene bridge, to the 4' carbon of the same ribose sugar; and amino groups (-O-amino, wherein the amino group, e.g., NRR, can be alkylamino, dialkylamino, heterocyclyl, arylamino, diarylamino, heteroarylamino, or diheteroaryl amino, ethylene diamine, polyamino) or aminoalkoxy.

"Deoxy" modifications include hydrogen, amino (e.g. NH2; alkylamino, dialkylamino, heterocyclyl, arylamino, diaryl amino, heteroaryl amino, diheteroaryl amino, or amino acid);

or the amino group can be attached to the sugar through a linker, wherein the linker comprises one or more of the atoms C, N, and O.

The sugar group can also contain one or more carbons that possess the opposite stereochemical configuration than that of the corresponding carbon in ribose. Thus, a modified nucleic acid molecule can include nucleotides containing, for instance, arabinose as the sugar.

Backbone Modifications:

The phosphate backbone may further be modified in the modified nucleosides and nucleotides, which may be incorporated into the artificial nucleic acid molecule, preferably an RNA, as described herein. The phosphate groups of the backbone can be modified by replacing one or more of the oxygen atoms with a different substituent. Further, the modified nucleosides and nucleotides can include the full replacement of an unmodified phosphate moiety with a modified phosphate as described herein. Examples of modified phosphate groups include, but are not limited to, phosphorothioate, phosphoroselenates, borano phosphates, borano phosphate esters, hydrogen phosphonates, phosphoroamidates, alkyl or aryl phosphonates and phosphotriesters. Phosphorodithioates have both non-linking oxygens replaced by sulfur. The phosphate linker can also be modified by the replacement of a linking oxygen with nitrogen (bridged phosphoroamidates), sulfur (bridged phosphorothioates) and carbon (bridged methylene-phosphonates).

Base Modifications:

The modified nucleosides and nucleotides, which may be incorporated into the artificial nucleic acid molecule, preferably an RNA molecule, as described herein, can further be modified in the nucleobase moiety. Examples of nucleobases found in RNA include, but are not limited to, adenine, guanine, cytosine and uracil. For example, the nucleosides and nucleotides described herein can be chemically modified on the major groove face. In some embodiments, the major groove chemical modifications can include an amino group, a thiol group, an alkyl group, or a halo group.

In particularly preferred embodiments of the present invention, the nucleotide analogues/modifications are selected from base modifications, which are preferably selected

from 2-amino-6-chloropurineriboside-5'-triphosphate, 2-Aminopurine-riboside-5'-triphosphate; 2-aminoadenosine-5'-triphosphate, 2'-Amino-2'-deoxycytidine-triphosphate, 2-thiocytidine-5'-triphosphate, 2-thiouridine-5'-triphosphate, 2'-Fluorothymidine-5'-triphosphate, 2'-O-Methyl inosine-5'-triphosphate 4-thiouridine-5'-triphosphate, 5-aminoallylcytidine-5'-triphosphate, 5-aminoallyluridine-5'-triphosphate, 5-bromocytidine-5'-triphosphate, 5-bromouridine-5'-triphosphate, 5-Bromo-2'-deoxycytidine-5'-triphosphate, 5-Bromo-2'-deoxyuridine-5'-triphosphate, 5-iodocytidine-5'-triphosphate, 5-Iodo-2'-deoxycytidine-5'-triphosphate, 5-iodouridine-5'-triphosphate, 5-Iodo-2'-deoxyuridine-5'-triphosphate, 5-methylcytidine-5'-triphosphate, 5-methyluridine-5'-triphosphate, 5-Propynyl-2'-deoxycytidine-5'-triphosphate, 5-Propynyl-2'-deoxyuridine-5'-triphosphate, 6-azacytidine-5'-triphosphate, 6-azauridine-5'-triphosphate, 6-chloropurineriboside-5'-triphosphate, 7-deazaadenosine-5'-triphosphate, 7-deazaguanosine-5'-triphosphate, 8-azaadenosine-5'-triphosphate, 8-azidoadenosine-5'-triphosphate, benzimidazole-riboside-5'-triphosphate, N1-methyladenosine-5'-triphosphate, N1-methylguanosine-5'-triphosphate, N6-methyladenosine-5'-triphosphate, O6-methylguanosine-5'-triphosphate, pseudouridine-5'-triphosphate, or puromycin-5'-triphosphate, xanthosine-5'-triphosphate. Particular preference is given to nucleotides for base modifications selected from the group of base-modified nucleotides consisting of 5-methylcytidine-5'-triphosphate, 7-deazaguanosine-5'-triphosphate, 5-bromocytidine-5'-triphosphate, and pseudouridine-5'-triphosphate.

In some embodiments, modified nucleosides include pyridin-4-one ribonucleoside, 5-aza-uridine, 2-thio-5-aza-uridine, 2-thiouridine, 4-thio-pseudouridine, 2-thio-pseudouridine, 5-hydroxyuridine, 3-methyluridine, 5-carboxymethyl-uridine, 1-carboxymethyl-pseudouridine, 5-propynyl-uridine, 1-propynyl-pseudouridine, 5-taurinomethyluridine, 1-taurinomethyl-pseudouridine, 5-taurinomethyl-2-thio-uridine, l-taurinomethyl-4-thio-uridine, 5-methyl-uridine, 1-methyl-pseudouridine, 4-thio- 1-methyl-pseudouridine, 2-thio-l-methyl-pseudouridine, 1 -methyl- 1-deaza-pseudouridine, 2-thio- 1 -methyl- 1 -deaza-pseudouridine, dihydrouridine, dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-dihydropseudouridine, 2-methoxyuridine, 2-methoxy-4-thio-uridine, 4-methoxy-pseudouridine, and 4-methoxy-2-thio-pseudouridine.

In some embodiments, modified nucleosides include 5-aza-cytidine, pseudoisocytidine, 3-methyl-cytidine, N4-acetylcytidine, 5-formylcytidine, N4-methylcytidine, 5-

hydroxymethylcytidine, 1-methyl-pseudoisocytidine, pyrrolo-cytidine, pyrrolo-pseudoisocytidine, 2-thio-cytidine, 2-thio-5-methyl-cytidine, 4-thio-pseudoisocytidine, 4-thio- 1-methyl-pseudoisocytidine, 4-thio- 1 -methyl- 1 -deaza-pseudoisocytidine, 1 -methyl-1 -deaza-pseudoisocytidine, zebularine, 5-aza-zebularine, 5-methyl-zebularine, 5-aza-2-thio-zebularine, 2-thio-zebularine, 2-methoxy-cytidine, 2-methoxy-5-methyl-cytidine, 4-methoxy-pseudoisocytidine, and 4-methoxy-l-methyl-pseudoisocytidine .

In other embodiments, modified nucleosides include 2-aminopurine, 2, 6-diaminopurine, 7-deaza-adenine, 7-deaza-8-aza-adenine, 7-deaza-2-aminopurine, 7-deaza-8-aza-2-aminopurine, 7-deaza-2,6-diaminopurine, 7-deaza-8-aza-2,6-diaminopurine, 1-methyladenosine, N6-methyladenosine, N6-isopentenyladenosine, N6-(cis-hydroxyisopentenyl)adenosine, 2-methylthio-N6-(cis-hydroxyisopentenyl) adenosine, N6-glycinylcarbamoyladenosine, N6-threonylcarbamoyladenosine, 2-methylthio-N6-threonyl carbamoyladenosine, N6,N6-dimethyladenosine, 7-methyladenine, 2-methylthio-adenine, and 2-methoxy-adenine.

In other embodiments, modified nucleosides include inosine, 1-methyl-inosine, wyosine, wybutosine, 7-deaza-guanosine, 7-deaza-8-aza-guanosine, 6-thio-guanosine, 6-thio-7-deaza-guanosine, 6-thio-7-deaza-8-aza-guanosine, 7-methyl-guanosine, 6-thio-7-methyl-guanosine, 7-methylinosine, 6-methoxy-guanosine, 1-methylguanosine, N2-methylguanosine, N2,N2-dimethylguanosine, 8-oxo-guanosine, 7-methyl-8-oxo-guanosine, l-methyl-6-thio-guanosine, N2-methyl-6-thio-guanosine, and N2,N2-dimethyl-6-thio-guanosine.

In some embodiments, the nucleotide can be modified on the major groove face and can include replacing hydrogen on C-5 of uracil with a methyl group or a halo group.

In specific embodiments, a modified nucleoside is 5'-0-(l-Thiophosphate)-Adenosine, 5 ' -0-(1 -Thiophosphate)-Cytidine, 5 ' -0-(1 -Thiophosphate)-Guanosine, 5 ' -0-(1 -Thiophosphate)-Uridine or 5 '-0-(l-Thiophosphate)-Pseudouridine.

In further specific embodiments the artificial nucleic acid molecule, preferably an RNA molecule, may comprise nucleoside modifications selected from 6-aza-cytidine, 2-thio-

cytidine, alpha-thio-cytidine, Pseudo-iso-cytidine, 5-aminoallyl-uridine, 5-iodo-uridine, N1-methyl-pseudouridine, 5,6-dihydrouridine, alpha-thio-uridine, 4-thio-uridine, 6-aza-uridine, 5-hydroxy-uridine, deoxy-thymidine, 5-methyl-uridine, Pyrrolo-cytidine, inosine, alpha-thio-guanosine, 6-methyl-guanosine, 5-methyl-cytdine, 8-oxo-guanosine, 7-deaza-guanosine, N1-methyl-adenosine, 2-amino-6-Chloro-purine, N6-methyl-2-amino-purine, Pseudo-iso-cytidine, 6-Chloro-purine, N6-methyl-adenosine, alpha-thio-adenosine, 8-azido-adenosine, 7-deaza-adenosine.

Lipid modification:

According to a further embodiment, the artificial nucleic acid molecule, preferably an RNA, as defined herein can contain a lipid modification. Such a lipid-modified RNA typically comprises an RNA as defined herein. Such a lipid-modified RNA molecule as defined herein typically further comprises at least one linker covalently linked with that RNA molecule, and at least one lipid covalently linked with the respective linker. Alternatively, the lipid-modified RNA molecule comprises at least one RNAmolecule as defined herein and at least one (bifunctional) lipid covalently linked (without a linker) with that RNA molecule. According to a third alternative, the lipid-modified RNA molecule comprises an artificial nucleic acid molecule, preferably an RNA molecule, as defined herein, at least one linker covalently linked with that RNA molecule, and at least one lipid covalently linked with the respective linker, and also at least one (bifunctional) lipid covalently linked (without a linker) with that RNA molecule. In this context, it is particularly preferred that the lipid modification is present at the terminal ends of a linear RNA sequence.

Modification of the 5'-end of the modified RNA:

According to another preferred embodiment of the invention, the artificial nucleic acid molecule, preferably an RNA molecule, as defined herein, can be modified by the addition of a so-called "5' CAP" structure.

A 5'-cap is an entity, typically a modified nucleotide entity, which generally "caps" the 5'-end of a mature mRNA. A 5'-cap may typically be formed by a modified nucleotide, particularly by a derivative of a guanine nucleotide. Preferably, the 5'-cap is linked to the 5'-terminus via a 5'-5'-triphosphate linkage. A 5'-cap may be methylated, e.g. m7GpppN, wherein N is the terminal 5' nucleotide of the nucleic acid carrying the 5'-cap, typically the 5'-end of an RNA. m7GpppN is the 5'-CAP structure which naturally occurs in mRNA

transcribed by polymerase II and is therefore not considered as modification comprised in the modified RNA according to the invention. This means the artificial nucleic acid molecule, preferably an RNA molecule, according to the present invention may comprise a m7GpppN as 5'-CAP, but additionally the artificial nucleic acid molecule, preferably an RNA molecule, comprises at least one further modification as defined herein.

Further examples of 5'cap structures include glyceryl, inverted deoxy abasic residue (moiety), 4',5' methylene nucleotide, 1-(beta-D-erythrofuranosyl) nucleotide, 4'-thio nucleotide, carbocyclic nucleotide, 1,5-anhydrohexitol nucleotide, L-nucleotides, alpha-nucleotide, modified base nucleotide, threo-pentofuranosyl nucleotide, acyclic 3',4'-seco nucleotide, acyclic 3,4-dihydroxybutyl nucleotide, acyclic 3,5 dihydroxypentyl nucleotide, 3'-3'-inverted nucleotide moiety, 3'-3'-inverted abasic moiety, 3'-2'-inverted nucleotide moiety, 3'-2'-inverted abasic moiety, 1,4-butanediol phosphate, 3'-phosphoramidate, hexylphosphate, aminohexyl phosphate, 3'-phosphate, 3'phosphorothioate, phosphorodithioate, or bridging or non-bridging methylphosphonate moiety. These modified 5'-CAP structures are regarded as at least one modification comprised in the artificial nucleic acid molecule, preferably in an RNA molecule, according to the present invention.

Particularly preferred modified 5'-CAP structures are CAP1 (methylation of the ribose of the adjacent nucleotide of m7G), CAP2 (methylation of the ribose of the 2nd nucleotide downstream of the m7G), CAP3 (methylation of the ribose of the 3rd nucleotide downstream of the m7G), CAP4 (methylation of the ribose of the 4th nucleotide downstream of the m7G), ARCA (anti-reverse CAP analogue, modified ARCA (e.g. phosphothioate modified ARCA), inosine, N1-methyl-guanosine, 2'-fluoro-guanosine, 7-deaza-guanosine, 8-oxo-guanosine, 2-amino-guanosine, LNA-guanosine, and 2-azido-guanosine.

In a preferred embodiment, the at least one open reading frame encodes a therapeutic protein or peptide. In another embodiment, an antigen is encoded by the at least one open reading frame, such as a pathogenic antigen, a tumour antigen, an allergenic antigen or an autoimmune antigen. Therein, the administration of the artificial nucleic acid molecule encoding the antigen is used in a genetic vaccination approach against a disease involving said antigen.

In an alternative embodiment, an antibody or an antigen-specific T cell receptor or a fragment thereof is encoded by the at least one open reading frame of the artificial nucleic acid molecule according to the invention.

Antigens:

Pathogenic antigens:

The artificial nucleic acid molecule according to the present invention may encode a protein or a peptide, which comprises a pathogenic antigen or a fragment, variant or derivative thereof. Such pathogenic antigens are derived from pathogenic organisms, in particular bacterial, viral or protozoological (multicellular) pathogenic organisms, which evoke an immunological reaction in a subject, in particular a mammalian subject, more particularly a human. More specifically, pathogenic antigens are preferably surface antigens, e.g. proteins (or fragments of proteins, e.g. the exterior portion of a surface antigen) located at the surface of the virus or the bacterial or protozoological organism.

Pathogenic antigens are peptide or protein antigens preferably derived from a pathogen associated with infectious disease which are preferably selected from antigens derived from the pathogens Acinetobacter baumannii, Anaplasma genus, Anaplasma phagocytophilum, Ancylostoma braziliense, Ancylostoma duodenale, Arcanobacterium haemolyticum, Ascaris lumbricoides, Aspergillus genus, Astroviridae, Babesia genus, Bacillus anthracis, Bacillus cereus, Bartonella henselae, BK virus, Blastocystis hominis, Blastomyces dermatitidis, Bordetella pertussis, Borrelia burgdorferi, Borrelia genus, Borrelia spp, Brucella genus, Brugia malayi, Bunyaviridae family, Burkholderia cepacia and other Burkholderia species, Burkholderia mallei, Burkholderia pseudomallei, Caliciviridae family, Campylobacter genus, Candida albicans, Candida spp, Chlamydia trachomatis, Chlamydophila pneumoniae, Chlamydophila psittaci, CJD prion, Clonorchis sinensis, Clostridium botulinum, Clostridium difficile, Clostridium perfringens, Clostridium perfringens, Clostridium spp, Clostridium tetani, Coccidioides spp, coronaviruses, Corynebacterium diphtheriae, Coxiella burnetii, Crimean-Congo hemorrhagic fever virus, Cryptococcus neoformans, Cryptosporidium genus, Cytomegalovirus (CMV), Dengue viruses (DEN-1, DEN-2, DEN-3 and DEN-4), Dientamoeba fragilis, Ebolavirus (EBOV), Echinococcus genus, Ehrlichia chaffeensis, Ehrlichia ewingii, Ehrlichia genus, Entamoeba histolytica, Enterococcus genus, Enterovirus genus, Enteroviruses, mainly Coxsackie A virus and Enterovirus 71 (EV71), Epidermophyton spp, Epstein-Barr Virus

(EBV), Escherichia coli O157:H7, O111 and O104:H4, Fasciola hepatica and Fasciola gigantica, FFI prion, Filarioidea superfamily, Flaviviruses, Francisella tularensis, Fusobacterium genus, Geotrichum candidum, Giardia intestinalis, Gnathostoma spp, GSS prion, Guanarito virus, Haemophilus ducreyi, Haemophilus influenzae, Helicobacter pylori, Henipavirus (Hendra virus Nipah virus), Hepatitis A Virus, Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Hepatitis D Virus, Hepatitis E Virus, Herpes simplex virus 1 and 2 (HSV-1 and HSV-2), Histoplasma capsulatum, HIV (Human immunodeficiency virus), Hortaea werneckii, Human bocavirus (HBoV), Human herpesvirus 6 (HHV-6) and Human herpesvirus 7 (HHV-7), Human metapneumovirus (hMPV), Human papillomavirus (HPV), Human parainfluenza viruses (HPIV), Japanese encephalitis virus, JC virus, Junin virus, Kingella kingae, Klebsiella granulomatis, Kuru prion, Lassa virus, Legionella pneumophila, Leishmania genus, Leptospira genus, Listeria monocytogenes, Lymphocytic choriomeningitis virus (LCMV), Machupo virus, Malassezia spp, Marburg virus, Measles virus, Metagonimus yokagawai, Microsporidia phylum, Molluscum contagiosum virus (MCV), Mumps virus, Mycobacterium leprae and Mycobacterium lepromatosis, Mycobacterium tuberculosis, Mycobacterium ulcerans, Mycoplasma pneumoniae, Naegleria fowleri, Necator americanus, Neisseria gonorrhoeae, Neisseria meningitidis, Nocardia asteroides, Nocardia spp, Onchocerca volvulus, Orientia tsutsugamushi, Orthomyxoviridae family (Influenza), Paracoccidioides brasiliensis, Paragonimus spp, Paragonimus westermani, Parvovirus B19, Pasteurella genus, Plasmodium genus, Pneumocystis jirovecii, Poliovirus, Rabies virus, Respiratory syncytial virus (RSV), Rhinovirus, rhinoviruses, Rickettsia akari, Rickettsia genus, Rickettsia prowazekii, Rickettsia rickettsii, Rickettsia typhi, Rift Valley fever virus, Rotavirus, Rubella virus, Sabia virus, Salmonella genus, Sarcoptes scabiei, SARS coronavirus, Schistosoma genus, Shigella genus, Sin Nombre virus, Hantavirus, Sporothrix schenckii, Staphylococcus genus, Staphylococcus genus, Streptococcus agalactiae, Streptococcus pneumoniae, Streptococcus pyogenes, Strongyloides stercoralis, Taenia genus, Taenia solium, Tick-borne encephalitis virus (TBEV), Toxocara canis or Toxocara cati, Toxoplasma gondii, Treponema pallidum, Trichinella spiralis, Trichomonas vaginalis, Trichophyton spp, Trichuris trichiura, Trypanosoma brucei, Trypanosoma cruzi, Ureaplasma urealyticum, Varicella zoster virus (VZV), Varicella zoster virus (VZV), Variola major or Variola minor, vCJD prion, Venezuelan equine encephalitis virus, Vibrio cholerae, West Nile virus, Western equine encephalitis virus, Wuchereria bancrofti, Yellow fever virus, Yersinia enterocolitica, Yersinia pestis, and Yersinia pseudotuberculosis.

In this context particularly preferred are antigens from the pathogens selected from Influenza virus, respiratory syncytial virus (RSV), Herpes simplex virus (HSV), human Papilloma virus (HPV), Human immunodeficiency virus (HIV), Plasmodium, Staphylococcus aureus, Dengue virus, Chlamydia trachomatis, Cytomegalovirus (CMV), Hepatitis B virus (HBV), Mycobacterium tuberculosis, Rabies virus, and Yellow Fever Virus.

Tumour antigens:

In a further embodiment the artificial nucleic acid molecule according to the present invention may encode a protein or a peptide, which comprises a peptide or protein comprising a tumour antigen, a fragment, variant or derivative of said tumour antigen, preferably, 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; and wherein each of the nucleic acid sequences encodes a different peptide or protein; and wherein at least one of the nucleic acid sequences encodes for 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-1, 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. Particularly preferred in this context are the tumour antigens NY-ESO-1, 5T4, MAGE-C1, MAGE-C2, Survivin, Muc-1, PSA, PSMA, PSCA, STEAP and PAP.

In a preferred embodiment, the artificial nucleic acid molecule encodes a protein or a peptide, which comprises a therapeutic protein or a fragment, variant or derivative thereof.

Therapeutic proteins as defined herein are peptides or proteins, which are beneficial for the treatment of any inherited or acquired disease or which improves the condition of an individual. Particularly, therapeutic proteins play an important role in the creation of therapeutic agents that could modify and repair genetic errors, destroy cancer cells or pathogen infected cells, treat immune system disorders, treat metabolic or endocrine disorders, among other functions. For instance, Erythropoietin (EPO), a protein hormone can be utilized in treating patients with erythrocyte deficiency, which is a common cause of kidney complications. Furthermore adjuvant proteins, therapeutic antibodies are encompassed by therapeutic proteins and also hormone replacement therapy which is e.g. used in the therapy of women in menopause. In more recent approaches, somatic cells of a

patient are used to reprogram them into pluripotent stem cells, which replace the disputed stem cell therapy. Also these proteins used for reprogramming of somatic cells or used for differentiating of stem cells are defined herein as therapeutic proteins. Furthermore, therapeutic proteins may be used for other purposes, e.g. wound healing, tissue regeneration, angiogenesis, etc. Furthermore, antigen-specific B cell receptors and fragments and variants thereof are defined herein as therapeutic proteins.

Therefore therapeutic proteins can be used for various purposes including treatment of various diseases like e.g. infectious diseases, neoplasms (e.g. cancer or tumour diseases), diseases of the blood and blood-forming organs, endocrine, nutritional and metabolic diseases, diseases of the nervous system, diseases of the circulatory system, diseases of the respiratory system, diseases of the digestive system, diseases of the skin and subcutaneous tissue, diseases of the musculoskeletal system and connective tissue, and diseases of the genitourinary system, independently if they are inherited or acquired.

In this context, particularly preferred therapeutic proteins which can be used inter alia in the treatment of metabolic or endocrine disorders are selected from (in brackets the particular disease for which the therapeutic protein is used in the treatment): Acid sphingomyelinase (Niemann-Pick disease), Adipotide (obesity), Agalsidase-beta (human galactosidase A) (Fabry disease; prevents accumulation of lipids that could lead to renal and cardiovascular complications), Alglucosidase (Pompe disease (glycogen storage disease type II)), alpha-galactosidase A (alpha-GAL A, Agalsidase alpha) (Fabry disease), alpha-glucosidase (Glycogen storage disease (GSD), Morbus Pompe), alpha-L-iduronidase (mucopolysaccharidoses (MPS), Hurler syndrome, Scheie syndrome), alpha-N-acetylglucosaminidase (Sanfilippo syndrome), Amphiregulin (cancer, metabolic disorder), Angiopoietin ((Ang1, Ang2, Ang3, Ang4, ANGPTL2, ANGPTL3, ANGPTL4, ANGPTL5, ANGPTL6, ANGPTL7) (angiogenesis, stabilize vessels), Betacellulin (metabolic disorder), Beta-glucuronidase (Sly syndrome), Bone morphogenetic protein BMPs (BMP1, BMP2, BMP3, BMP4, BMP5, BMP6, BMP7, BMP8a, BMP8b, BMP10, BMP15) (regenerative effect, bone-related conditions, chronic kidney disease (CKD)), CLN6 protein (CLN6 disease - Atypical Late Infantile, Late Onset variant, Early Juvenile, Neuronal Ceroid Lipofuscinoses (NCL)), Epidermal growth factor (EGF) (wound healing, regulation of cell growth, proliferation, and differentiation), Epigen (metabolic disorder), Epiregulin (metabolic disorder), Fibroblast

Growth Factor (FGF, FGF-1, FGF-2, FGF-3, FGF-4, FGF-5, FGF-6, FGF-7, FGF-8, FGF-9, FGF-10, FGF-11, FGF-12, FGF-13, FGF-14, FGF-16, FGF-17, FGF-17, FGF-18, FGF-19, FGF-20, FGF-21, FGF-22, FGF-23) (wound healing, angiogenesis, endocrine disorders, tissue regeneration), Galsulphase (Mucopolysaccharidosis VI), Ghrelin (irritable bowel syndrome (IBS), obesity, Prader-Willi syndrome, type II diabetes mellitus), Glucocerebrosidase (Gaucher's disease), GM-CSF (regenerative effect, production of white blood cells, cancer), Heparin-binding EGF-like growth factor (HB-EGF) (wound healing, cardiac hypertrophy and heart development and function), Hepatocyte growth factor HGF (regenerative effect, wound healing), Hepcidin (iron metabolism disorders, Beta-thalassemia), Human albumin (Decreased production of albumin (hypoproteinaemia), increased loss of albumin (nephrotic syndrome), hypovolaemia, hyperbilirubinaemia), Idursulphase (Iduronate-2-sulphatase) (Mucopolysaccharidosis II (Hunter syndrome)), Integrins αVβ3, αVβ5 and α5β1 (Bind matrix macromolecules and proteinases, angiogenesis), Iuduronate sulfatase (Hunter syndrome), Laronidase (Hurler and Hurler-Scheie forms of mucopolysaccharidosis I), N-acetylgalactosamine-4-sulfatase (rhASB; galsulfase, Arylsulfatase A (ARSA), Arylsulfatase B (ARSB)) (arylsulfatase B deficiency, Maroteaux–Lamy syndrome, mucopolysaccharidosis VI), N-acetylglucosamine-6-sulfatase (Sanfilippo syndrome), Nerve growth factor (NGF, Brain-Derived Neurotrophic Factor (BDNF), Neurotrophin-3 (NT-3), and Neurotrophin 4/5 (NT-4/5) (regenerative effect, cardiovascular diseases, coronary atherosclerosis, obesity, type 2 diabetes, metabolic syndrome, acute coronary syndromes, dementia, depression, schizophrenia, autism, Rett syndrome, anorexia nervosa, bulimia nervosa, wound healing, skin ulcers, corneal ulcers, Alzheimer's disease), Neuregulin (NRG1, NRG2, NRG3, NRG4) (metabolic disorder, schizophrenia), Neuropilin (NRP-1, NRP-2) (angiogenesis, axon guidance, cell survival, migration), Obestatin (irritable bowel syndrome (IBS), obesity, Prader-Willi syndrome, type II diabetes mellitus), Platelet Derived Growth factor (PDGF (PDFF-A, PDGF-B, PDGF-C, PDGF-D) (regenerative effect, wound healing, disorder in angiogenesis, Arteriosclerosis, Fibrosis, cancer), TGF beta receptors (endoglin, TGF-beta 1 receptor, TGF-beta 2 receptor, TGF-beta 3 receptor) (renal fibrosis, kidney disease, diabetes, ultimately end-stage renal disease (ESRD), angiogenesis), Thrombopoietin (THPO) (Megakaryocyte growth and development factor (MGDF)) (platelets disorders, platelets for donation, recovery of platelet counts after myelosuppressive chemotherapy), Transforming Growth factor (TGF (TGF-alpha, TGF-beta (TGFbeta1, TGFbeta2, and TGFbeta3))) (regenerative effect, wound healing, immunity, cancer, heart disease, diabetes, Marfan syndrome, Loeys–Dietz

syndrome), VEGF (VEGF-A, VEGF-B, VEGF-C, VEGF-D, VEGF-E, VEGF-F und PlGF) (regenerative effect, angiogenesis, wound healing, cancer, permeability), Nesiritide (Acute decompensated congestive heart failure), Trypsin (Decubitus ulcer, varicose ulcer, debridement of eschar, dehiscent wound, sunburn, meconium ileus), adrenocorticotrophic hormone (ACTH) ("Addison's disease, Small cell carcinoma, Adrenoleukodystrophy, Congenital adrenal hyperplasia, Cushing's syndrome, Nelson's syndrome, Infantile spasms), Atrial-natriuretic peptide (ANP) (endocrine disorders), Cholecystokinin (diverse), Gastrin (hypogastrinemia), Leptin (Diabetes, hypertriglyceridemia, obesity), Oxytocin (stimulate breastfeeding, non-progression of parturition), Somatostatin (symptomatic treatment of carcinoid syndrome, acute variceal bleeding, and acromegaly, polycystic diseases of the liver and kidney, acromegaly and symptoms caused by neuroendocrine tumors), Vasopressin (antidiuretic hormone) (diabetes insipidus), Calcitonin (Postmenopausal osteoporosis, Hypercalcaemia, Paget's disease, Bone metastases, Phantom limb pain, Spinal Stenosis), Exenatide (Type 2 diabetes resistant to treatment with metformin and a sulphonylurea), Growth hormone (GH), somatotropin (Growth failure due to GH deficiency or chronic renal insufficiency, Prader-Willi syndrome, Turner syndrome, AIDS wasting or cachexia with antiviral therapy), Insulin (Diabetes mellitus, diabetic ketoacidosis, hyperkalaemia), Insulin-like growth factor 1 IGF-1 (Growth failure in children with GH gene deletion or severe primary IGF1 deficiency, neurodegenerative disease, cardiovascular diseases, heart failure), Mecasermin rinfabate, IGF-1 analog (Growth failure in children with GH gene deletion or severe primary IGF1 deficiency, neurodegenerative disease, cardiovascular diseases, heart failure), Mecasermin, IGF-1 analog (Growth failure in children with GH gene deletion or severe primary IGF1 deficiency, neurodegenerative disease, cardiovascular diseases, heart failure), Pegvisomant (Acromegaly), Pramlintide (Diabetes mellitus, in combination with insulin), Teriparatide (human parathyroid hormone residues 1–34) (Severe osteoporosis), Becaplermin (Debridement adjunct for diabetic ulcers), Dibotermin-alpha (Bone morphogenetic protein 2) (Spinal fusion surgery, bone injury repair), Histrelin acetate (gonadotropin releasing hormone; GnRH) (Precocious puberty), Octreotide (Acromegaly, symptomatic relief of VIP-secreting adenoma and metastatic carcinoid tumours), and Palifermin (keratinocyte growth factor; KGF) (Severe oral mucositis in patients undergoing chemotherapy, wound healing).

These and other proteins are understood to be therapeutic, as they are meant to treat the subject by replacing its defective endogenous production of a functional protein in sufficient amounts. Accordingly, such therapeutic proteins are typically mammalian, in particular human proteins.

For the treatment of blood disorders, diseases of the circulatory system, diseases of the respiratory system, cancer or tumour diseases, infectious diseases or immunedeficiencies following therapeutic proteins may be used: Alteplase (tissue plasminogen activator; tPA) (Pulmonary embolism, myocardial infarction, acute ischaemic stroke, occlusion of central venous access devices), Anistreplase (Thrombolysis), Antithrombin III (AT-III) (Hereditary AT-III deficiency, Thromboembolism), Bivalirudin (Reduce blood-clotting risk in coronary angioplasty and heparin-induced thrombocytopaenia), Darbepoetin-alpha (Treatment of anaemia in patients with chronic renal insufficiency and chronic renal failure (+/- dialysis)), Drotrecogin-alpha (activated protein C) (Severe sepsis with a high risk of death), Erythropoietin, Epoetin-alpha, erythropoetin, erthropoyetin (Anaemia of chronic disease, myleodysplasia, anaemia due to renal failure or chemotherapy, preoperative preparation), Factor IX (Haemophilia B), Factor VIIa (Haemorrhage in patients with haemophilia A or B and inhibitors to factor VIII or factor IX), Factor VIII (Haemophilia A), Lepirudin (Heparin-induced thrombocytopaenia), Protein C concentrate (Venous thrombosis, Purpura fulminans), Reteplase (deletion mutein of tPA) (Management of acute myocardial infarction, improvement of ventricular function), Streptokinase (Acute evolving transmural myocardial infarction, pulmonary embolism, deep vein thrombosis, arterial thrombosis or embolism, occlusion of arteriovenous cannula), Tenecteplase (Acute myocardial infarction), Urokinase (Pulmonary embolism), Angiostatin (Cancer), Anti-CD22 immunotoxin (Relapsed CD33+ acute myeloid leukaemia), Denileukin diftitox (Cutaneous T-cell lymphoma (CTCL)), Immunocyanin (bladder and prostate cancer), MPS (Metallopanstimulin) (Cancer), Aflibercept (Non-small cell lung cancer (NSCLC), metastatic colorectal cancer (mCRC), hormone-refractory metastatic prostate cancer, wet macular degeneration), Endostatin (Cancer, inflammatory diseases like rheumatoid arthritis as well as Crohn's disease, diabetic retinopathy, psoriasis, and endometriosis), Collagenase (Debridement of chronic dermal ulcers and severely burned areas, Dupuytren's contracture, Peyronie's disease), Human deoxy-ribonuclease I, dornase (Cystic fibrosis; decreases respiratory tract infections in selected patients with FVC greater than 40% of predicted), Hyaluronidase (Used as an adjuvant to increase the absorption and

dispersion of injected drugs, particularly anaesthetics in ophthalmic surgery and certain imaging agents), Papain (Debridement of necrotic tissue or liquefication of slough in acute and chronic lesions, such as pressure ulcers, varicose and diabetic ulcers, burns, postoperative wounds, pilonidal cyst wounds, carbuncles, and other wounds), L-Asparaginase (Acute lymphocytic leukaemia, which requires exogenous asparagine for proliferation), Peg-asparaginase (Acute lymphocytic leukaemia, which requires exogenous asparagine for proliferation), Rasburicase (Paediatric patients with leukaemia, lymphoma, and solid tumours who are undergoing anticancer therapy that may cause tumour lysis syndrome), Human chorionic gonadotropin (HCG) (Assisted reproduction), Human follicle-stimulating hormone (FSH) (Assisted reproduction), Lutropin-alpha (Infertility with luteinizing hormone deficiency), Prolactin (Hypoprolactinemia, serum prolactin deficiency, ovarian dysfunction in women, anxiety, arteriogenic erectile dysfunction, premature ejaculation, oligozoospermia, asthenospermia, hypofunction of seminal vesicles, hypoandrogenism in men), alpha-1-Proteinase inhibitor (Congenital antitrypsin deficiency), Lactase (Gas, bloating, cramps and diarrhoea due to inability to digest lactose), Pancreatic enzymes (lipase, amylase, protease) (Cystic fibrosis, chronic pancreatitis, pancreatic insufficiency, post-Billroth II gastric bypass surgery, pancreatic duct obstruction, steatorrhoea, poor digestion, gas, bloating), Adenosine deaminase (pegademase bovine, PEG-ADA) (Severe combined immunodeficiency disease due to adenosine deaminase deficiency), Abatacept (Rheumatoid arthritis (especially when refractory to TNFalpha inhibition)), Alefacept (Plaque Psoriasis), Anakinra (Rheumatoid arthritis), Etanercept (Rheumatoid arthritis, polyarticular-course juvenile rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, plaque psoriasis, ankylosing spondylitis), Interleukin-1 (IL-1) receptor antagonist, Anakinra (inflammation and cartilage degradation associated with rheumatoid arthritis), Thymulin (neurodegenerative diseases, rheumatism, anorexia nervosa), TNF-alpha antagonist (autoimmune disorders such as rheumatoid arthritis, ankylosing spondylitis, Crohn's disease, psoriasis, hidradenitis suppurativa, refractory asthma), Enfuvirtide (HIV-1 infection), and Thymosin α1 (Hepatitis B and C).
(in brackets is the particular disease for which the therapeutic protein is used in the treatment)

In a further aspect, the present invention provides a vector comprising

a. an open reading frame (ORF) and/or a cloning site, e.g. for insertion of an open reading frame or a sequence comprising an open reading frame; and

b. at least one 3'-untranslated region element (3'-UTR element) and/or at least one 5'-untranslated region element (5'-UTR element), wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element prolongs and/or increases protein production from said artificial nucleic acid molecule and wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element is derived from a stable mRNA.

In general, the vector according to the present invention may comprise an artificial nucleic acid molecule according to the present invention as described above. In particular, the preferred embodiments described above for an artificial nucleic acid molecule according to the present invention also apply for an artificial nucleic acid molecule according to the present invention, which is comprised by a vector according to the present invention. For example, in the inventive vector the at least one 3'-UTR element and/or the at least one 5'-UTR element and the ORF are as described above for the artificial nucleic acid molecule according to the present invention, including the preferred embodiments. For example, in the vector according to the present invention, the stable mRNA from which the at least one 3'-UTR element and/or the at least one 5'-UTR element is derived may be preferably characterized by an mRNA decay wherein the ratio of the amount of said mRNA at a second point in time to the amount of said mRNA at a first point in time is at least 0.5 (50%), at least 0.6 (60%), at least 0.7 (70%), at least 0.75 (75%), at least 0.8 (80%), at least 0.85 (85%), at least 0.9 (90%), or at least 0.95 (95%).

The cloning site may be any sequence that is suitable for introducing an open reading frame or a sequence comprising an open reading frame, such as one or more restriction sites. Thus, the vector comprising a cloning site is preferably suitable for inserting an open reading frame into the vector, preferably for inserting an open reading frame 3' to the 5'-UTR element and/or 5' to the 3'-UTR element. Preferably the cloning site or the ORF is located 3' to the 5'-UTR element and/or 5' to the 3'-UTR element, preferably in close proximity to the 3'-end of the 5'-UTR element and/or to the 5'-end of the 3'-UTR element. For example, the cloning site or the ORF may be directly connected to the 3'-end of the 5'-UTR element and/or to the 5'-end of the 3'-UTR element or they may be connected via a stretch of nucleotides, such as by a stretch of 2, 4, 6, 8, 10, 20 etc. nucleotides as described above for the artificial nucleic acid molecule according to the present invention.

Preferably, the vector according to the present invention is suitable for producing the artificial nucleic acid molecule according to the present invention, preferably for producing an artificial mRNA according to the present invention, for example, by optionally inserting an open reading frame or a sequence comprising an open reading frame into the vector and transcribing the vector. Thus, preferably, the vector comprises elements needed for transcription, such as a promoter, e.g. an RNA polymerase promoter. Preferably, the vector is suitable for transcription using eukaryotic, prokaryotic, viral or phage transcription systems, such as eukaryotic cells, prokaryotic cells, or eukaryotic, prokaryotic, viral or phage *in vitro* transcription systems. Thus, for example, the vector may comprise a promoter sequence, which is recognized by a polymerase, such as by an RNA polymerase, e.g. by a eukaryotic, prokaryotic, viral, or phage RNA polymerase. In a preferred embodiment, the vector comprises a phage RNA polymerase promoter such as an SP6, T3 or T7, preferably a T7 promoter. Preferably, the vector is suitable for *in vitro* transcription using a phage based *in vitro* transcription system, such as a T7 RNA polymerase based *in vitro* transcription system. In another preferred embodiment, the vector may be used directly for expression of the encoded peptide or protein in cells or tissue. For this purpose, the vector comprises particular elements, which are necessary for expression in those cells/tissue e.g. particular promoter sequences, such as a CMV promoter.

The vector may further comprise a poly(A) sequence and/or a polyadenylation signal as described above for the artificial nucleic acid molecule according to the present invention.

The vector may be an RNA vector or a DNA vector. Preferably, the vector is a DNA vector. The vector may be any vector known to the skilled person, such as a viral vector or a plasmid vector. Preferably, the vector is a plasmid vector, preferably a DNA plasmid vector.

In a preferred embodiment, the vector according to the present invention comprises the artificial nucleic acid molecule according to the present invention.

Preferably, a DNA vector according to the invention comprises a nucleic acid sequence which has an identity of at least about 1, 2, 3, 4, 5, 10, 15, 20, 30 or 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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%, most preferably of 100% to the nucleic acid sequence of a 3'-UTR of a transcript of a gene, such as to the nucleic acid sequences according to SEQ ID NOs: 1 to 24 and SEQ ID NOs: 49 to 318.

Preferably, a DNA vector according to the invention comprises a nucleic acid sequence which has an identity of at least about 1, 2, 3, 4, 5, 10, 15, 20, 30 or 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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%, most preferably of 100% to the nucleic acid sequence of a 5'-UTR of a transcript of a gene, such as to the nucleic acid sequences according to SEQ ID NOs: 25 to 30 and SEQ ID NOs: 319 to 382.

Preferably, a DNA vector according to the present invention comprises a sequence selected from the group consisting of DNA sequences according to SEQ ID NOs. 1 to 30 or a sequence having an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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% sequence identity to the DNA sequences according to SEQ ID NOs. 1 to 30 or a fragment thereof as described above, preferably a functional fragment thereof.

Preferably, an RNA vector according to the present invention comprises a sequence selected from the group consisting of the sequences according to RNA sequences corresponding to DNA sequences according to SEQ ID NOs: 1 to 30 or a sequence having an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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% sequence identity to the RNA sequences corresponding to the DNA sequences according to SEQ ID NOs: 1 to 30 or to a fragment thereof, preferably a functional fragment thereof.

Preferably, the vector is a circular molecule. Preferably, the vector is a double-stranded molecule, such as a double-stranded DNA molecule. Such circular, preferably double stranded DNA molecule may be used conveniently as a storage form for the inventive artificial

nucleic acid molecule. Furthermore, it may be used for transfection of cells, for example, cultured cells. Also it may be used for *in vitro* transcription for obtaining an artificial RNA molecule according to the invention.

Preferably, the vector, preferably the circular vector, is linearizable, for example, by restriction enzyme digestion. In a preferred embodiment, the vector comprises a cleavage site, such as a restriction site, preferably a unique cleavage site, located immediately 3' to the ORF, or - if present - located immediately 3' to the 3'-UTR element, or - if present - located 3' to the poly(A) sequence or polyadenylation signal, or - if present - located 3' to the poly(C) sequence, or - if present - located 3' to the histone stem-loop. Thus, preferably, the product obtained by linearizing the vector terminates at the 3'end with the 3'-end of the ORF, or - if present - with the 3'-end of the 3'-UTR element, or - if present - with the 3'-end of the poly(A) sequence or polyadenylation signal, or - if present - with the 3'-end of the poly(C) sequence. In the embodiment, wherein the vector according to the present invention comprises the artificial nucleic acid molecule according to the present invention, a restriction site, preferably a unique restriction site, is preferably located immediately 3' to the 3'-end of the artificial nucleic acid molecule.

In a further aspect, the present invention relates to a cell comprising the artificial nucleic acid molecule according to the present invention or the vector according to present invention. The cell may be any cell, such as a bacterial cell, insect cell, plant cell, vertebrate cell, e.g. a mammalian cell. Such cell may be, e.g., used for replication of the vector of the present invention, for example, in a bacterial cell. Furthermore, the cell may be used for transcribing the artificial nucleic acid molecule or the vector according to the present invention and/or translating the open reading frame of the artificial nucleic acid molecule or the vector according to the present invention. For example, the cell may be used for recombinant protein production.

The cells according to the present invention are, for example, obtainable by standard nucleic acid transfer methods, such as standard transfection, transduction or transformation methods. For example, the artificial nucleic acid molecule or the vector according to the present invention may be transferred into the cell by electroporation, lipofection, e.g. based on cationic lipids and/or liposomes, calcium phosphate precipitation, nanoparticle based

transfection, virus based transfection, or based on cationic polymers, such as DEAE-dextran or polyethylenimine etc.

Preferably, the cell is a mammalian cell, such as a cell of human subject, a domestic animal, a laboratory animal, such as a mouse or rat cell. Preferably the cell is a human cell. The cell may be a cell of an established cell line, such as a CHO, BHK, 293T, COS-7, HELA, HEK, etc. or the cell may be a primary cell, such as a human dermal fibroblast (HDF) cell etc., preferably a cell isolated from an organism. In a preferred embodiment, the cell is an isolated cell of a mammalian subject, preferably of a human subject. For example, the cell may be an immune cell, such as a dendritic cell, a cancer or tumor cell, or any somatic cell etc., preferably of a mammalian subject, preferably of a human subject.

In a further aspect, the present invention provides a pharmaceutical composition comprising the artificial nucleic acid molecule according to the present invention, the vector according the present invention, or the cell according to the present invention. The pharmaceutical composition according to the invention may be used, e.g., as a vaccine, for example, for genetic vaccination. Thus, the ORF may, e.g., encode an antigen to be administered to a patient for vaccination. Thus, in a preferred embodiment, the pharmaceutical composition according to the present invention is a vaccine. Furthermore, the pharmaceutical composition according to the present invention may be used, e.g., for gene therapy.

Preferably, the pharmaceutical composition further comprises one or more pharmaceutically acceptable vehicles, diluents and/or excipients and/or one or more adjuvants. In the context of the present invention, a pharmaceutically acceptable vehicle typically includes a liquid or non-liquid basis for the inventive pharmaceutical composition. In one embodiment, the pharmaceutical composition is provided in liquid form. In this context, preferably, the vehicle is based on water, such as pyrogen-free water, isotonic saline or buffered (aqueous) solutions, e.g phosphate, citrate etc. buffered solutions. The buffer may be hypertonic, isotonic or hypotonic with reference to the specific reference medium, i.e. the buffer may have a higher, identical or lower salt content with reference to the specific reference medium, wherein preferably such concentrations of the afore mentioned salts may be used, which do not lead to damage of mammalian cells due to osmosis or other concentration effects. Reference media are e.g. liquids occurring in "*in vivo*" methods, such as blood, lymph, cytosolic liquids, or

other body liquids, or e.g. liquids, which may be used as reference media in "*in vitro*" methods, such as common buffers or liquids. Such common buffers or liquids are known to a skilled person. Ringer-Lactate solution is particularly preferred as a liquid basis.

One or more compatible solid or liquid fillers or diluents or encapsulating compounds suitable for administration to a patient may be used as well for the inventive pharmaceutical composition. The term "compatible" as used herein preferably means that these components of the inventive pharmaceutical composition are capable of being mixed with the inventive artificial nucleic acid, vector or cells as defined herein in such a manner that no interaction occurs which would substantially reduce the pharmaceutical effectiveness of the inventive pharmaceutical composition under typical use conditions.

The pharmaceutical composition according to the present invention may optionally further comprise one or more additional pharmaceutically active components. A pharmaceutically active component in this context is a compound that exhibits a therapeutic effect to heal, ameliorate or prevent a particular indication or disease. Such compounds include, without implying any limitation, peptides or proteins, nucleic acids, (therapeutically active) low molecular weight organic or inorganic compounds (molecular weight less than 5000, preferably less than 1000), sugars, antigens or antibodies, therapeutic agents already known in the prior art, antigenic cells, antigenic cellular fragments, cellular fractions, cell wall components (e.g. polysaccharides), modified, attenuated or de-activated (e.g. chemically or by irradiation) pathogens (virus, bacteria etc.).

Furthermore, the inventive pharmaceutical composition may comprise a carrier for the artificial nucleic acid molecule or the vector. Such a carrier may be suitable for mediating dissolution in physiological acceptable liquids, transport and cellular uptake of the pharmaceutical active artificial nucleic acid molecule or the vector. Accordingly, such a carrier may be a component which may be suitable for depot and delivery of an artificial nucleic acid molecule or vector according to the invention. Such components may be, for example, cationic or polycationic carriers or compounds which may serve as transfection or complexation agent.

Particularly preferred transfection or complexation agents in this context are cationic or polycationic compounds, including protamine, nucleoline, spermine or spermidine, or other

cationic peptides or proteins, such as poly-L-lysine (PLL), poly-arginine, basic polypeptides, cell penetrating peptides (CPPs), including HIV-binding peptides, HIV-1 Tat (HIV), Tat-derived peptides, Penetratin, VP22 derived or analog peptides, HSV VP22 (Herpes simplex), MAP, KALA or protein transduction domains (PTDs), PpT620, proline-rich peptides, arginine-rich peptides, lysine-rich peptides, MPG-peptide(s), Pep-1, L-oligomers, Calcitonin peptide(s), Antennapedia-derived peptides (particularly from *Drosophila antennapedia*), pAntp, pIsl, FGF, Lactoferrin, Transportan, Buforin-2, Bac715-24, SynB, SynB(1), pVEC, hCT-derived peptides, SAP, or histones.

Furthermore, such cationic or polycationic compounds or carriers may be cationic or polycationic peptides or proteins, which preferably comprise or are additionally modified to comprise at least one –SH moiety. Preferably, a cationic or polycationic carrier is selected from cationic peptides having the following sum formula (I):

$$\{(Arg)_l;(Lys)_m;(His)_n;(Orn)_o;(Xaa)_x\}; \quad \text{formula (I)}$$

wherein l + m + n + o + x = 3-100, and l, m, n or o independently of each other is any number selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90 and 91-100 provided that the overall content of Arg (Arginine), Lys (Lysine), His (Histidine) and Orn (Ornithine) represents at least 10% of all amino acids of the oligopeptide; and Xaa is any amino acid selected from native (= naturally occurring) or non-native amino acids except of Arg, Lys, His or Orn; and x is any number selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90, provided, that the overall content of Xaa does not exceed 90 % of all amino acids of the oligopeptide. Any of amino acids Arg, Lys, His, Orn and Xaa may be positioned at any place of the peptide. In this context cationic peptides or proteins in the range of 7-30 amino acids are particular preferred.

Further, the cationic or polycationic peptide or protein, when defined according to formula $\{(Arg)_l;(Lys)_m;(His)_n;(Orn)_o;(Xaa)_x\}$ (formula (I)) as shown above and which comprise or are additionally modified to comprise at least one –SH moeity, may be, without being restricted thereto, selected from subformula (Ia):

$\{(Arg)_l;(Lys)_m;(His)_n;(Orn)_o;(Xaa')_x (Cys)_y\}$ subformula (Ia)

wherein $(Arg)_l;(Lys)_m;(His)_n;(Orn)_o;$ and x are as defined herein, Xaa' is any amino acid selected from native (= naturally occurring) or non-native amino acids except of Arg, Lys, His, Orn or Cys and y is any number selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80 and 81-90, provided that the overall content of Arg (Arginine), Lys (Lysine), His (Histidine) and Orn (Ornithine) represents at least 10% of all amino acids of the oligopeptide. Further, the cationic or polycationic peptide may be selected from subformula (Ib):

$Cys_1 \{(Arg)_l;(Lys)_m;(His)_n;(Orn)_o;(Xaa)_x\} Cys_2$ subformula (Ib)

wherein empirical formula $\{(Arg)_l;(Lys)_m;(His)_n;(Orn)_o;(Xaa)_x\}$ (formula (III)) is as defined herein and forms a core of an amino acid sequence according to (semiempirical) formula (III) and wherein Cys_1 and Cys_2 are Cysteines proximal to, or terminal to $(Arg)_l;(Lys)_m;(His)_n;(Orn)_o;(Xaa)_x$.

Further preferred cationic or polycationic compounds, which can be used as transfection or complexation agent may include cationic polysaccharides, for example chitosan, polybrene, cationic polymers, e.g. polyethyleneimine (PEI), cationic lipids, e.g. DOTMA: [1-(2,3-sioleyloxy)propyl)]-N,N,N-trimethylammonium chloride, DMRIE, di-C14-amidine, DOTIM, SAINT, DC-Chol, BGTC, CTAP, DOPC, DODAP, DOPE: Dioleyl phosphatidylethanol-amine, DOSPA, DODAB, DOIC, DMEPC, DOGS: Dioctadecylamidoglicylspermin, DIMRI: Dimyristo-oxypropyl dimethyl hydroxyethyl ammonium bromide, DOTAP: dioleoyloxy-3-(trimethylammonio)propane, DC-6-14: O,O-ditetradecanoyl-N-(α-trimethylammonioacetyl)diethanolamine chloride, CLIP1: rac-[(2,3-dioctadecyloxypropyl)(2-hydroxyethyl)]-dimethylammonium chloride, CLIP6: rac-[2(2,3-dihexadecyloxypropyl-oxymethyloxy)ethyl]-trimethylammonium, CLIP9: rac-[2(2,3-dihexadecyloxypropyl-oxysuccinyloxy)ethyl]-trimethylammonium, oligofectamine, or cationic or polycationic polymers, e.g. modified polyaminoacids, such as β-aminoacid-polymers or reversed polyamides, etc., modified polyethylenes, such as PVP (poly(N-ethyl-4-vinylpyridinium bromide)), etc., modified acrylates, such as pDMAEMA (poly(dimethylaminoethyl methylacrylate)), etc., modified Amidoamines such as pAMAM (poly(amidoamine)), etc.,

modified polybetaaminoester (PBAE), such as diamine end modified 1,4 butanediol diacrylate-co-5-amino-1-pentanol polymers, etc., dendrimers, such as polypropylamine dendrimers or pAMAM based dendrimers, etc., polyimine(s), such as PEI: poly(ethyleneimine), poly(propyleneimine), etc., polyallylamine, sugar backbone based polymers, such as cyclodextrin based polymers, dextran based polymers, chitosan, etc., silan backbone based polymers, such as PMOXA-PDMS copolymers, etc., blockpolymers consisting of a combination of one or more cationic blocks (e.g. selected from a cationic polymer as mentioned above) and of one or more hydrophilic or hydrophobic blocks (e.g polyethyleneglycole); etc.

According to another embodiment, the pharmaceutical composition according to the invention may comprise an adjuvant in order to enhance the immunostimulatory properties of the pharmaceutical composition. In this context, an adjuvant may be understood as any compound, which is suitable to support administration and delivery of the components such as the artificial nucleic acid molecule or vector comprised in the pharmaceutical composition according to the invention. Furthermore, such an adjuvant may, without being bound thereto, initiate or increase an immune response of the innate immune system, i.e. a non-specific immune response. With other words, when administered, the pharmaceutical composition according to the invention typically initiates an adaptive immune response directed to the antigen encoded by the artificial nucleic acid molecule. Additionally, the pharmaceutical composition according to the invention may generate an (supportive) innate immune response due to addition of an adjuvant as defined herein to the pharmaceutical composition according to the invention.

Such an adjuvant may be selected from any adjuvant known to a skilled person and suitable for the present case, i.e. supporting the induction of an immune response in a mammal. Preferably, the adjuvant may be selected from the group consisting of, without being limited thereto, TDM, MDP, muramyl dipeptide, pluronics, alum solution, aluminium hydroxide, ADJUMERTM (polyphosphazene); aluminium phosphate gel; glucans from algae; algammulin; aluminium hydroxide gel (alum); highly protein-adsorbing aluminium hydroxide gel; low viscosity aluminium hydroxide gel; AF or SPT (emulsion of squalane (5%), Tween 80 (0.2%), Pluronic L121 (1.25%), phosphate-buffered saline, pH 7.4); AVRIDINETM (propanediamine); BAY R1005TM ((N-(2-deoxy-2-L-leucylamino-b-D-glucopyranosyl)-N-

octadecyl-dodecanoyl-amide hydroacetate); CALCITRIOLTM (1-alpha,25-dihydroxy-vitamin D3); calcium phosphate gel; CAPTM (calcium phosphate nanoparticles); cholera holotoxin, cholera-toxin-A1-protein-A-D-fragment fusion protein, sub-unit B of the cholera toxin; CRL 1005 (block copolymer P1205); cytokine-containing liposomes; DDA (dimethyldioctadecylammonium bromide); DHEA (dehydroepiandrosterone); DMPC (dimyristoylphosphatidylcholine); DMPG (dimyristoylphosphatidylglycerol); DOC/alum complex (deoxycholic acid sodium salt); Freund's complete adjuvant; Freund's incomplete adjuvant; gamma inulin; Gerbu adjuvant (mixture of: i) N-acetylglucosaminyl-(P1-4)-N-acetylmuramyl-L-alanyl-D-glutamine (GMDP), ii) dimethyldioctadecylammonium chloride (DDA), iii) zinc-L-proline salt complex (ZnPro-8); GM-CSF); GMDP (N-acetylglucosaminyl-(b1-4)-N-acetylmuramyl-L-alanyl-D-isoglutamine); imiquimod (1-(2-methypropyl)-1H-imidazo[4,5-c]quinoline-4-amine); ImmTherTM (N-acetylglucosaminyl-N-acetylmuramyl-L-Ala-D-isoGlu-L-Ala-glycerol dipalmitate); DRVs (immunoliposomes prepared from dehydration-rehydration vesicles); interferon-gamma; interleukin-1beta; interleukin-2; interleukin-7; interleukin-12; ISCOMSTM; ISCOPREP 7.0.3. TM; liposomes; LOXORIBINETM (7-allyl-8-oxoguanosine); LT oral adjuvant (E.coli labile enterotoxin-protoxin); microspheres and microparticles of any composition; MF59TM; (squalene-water emulsion); MONTANIDE ISA 51TM (purified incomplete Freund's adjuvant); MONTANIDE ISA 720TM (metabolisable oil adjuvant); MPLTM (3-Q-desacyl-4'-monophosphoryl lipid A); MTP-PE and MTP-PE liposomes ((N-acetyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1,2-dipalmitoyl-sn-glycero-3-(hydroxyphosphoryloxy))-ethylamide, monosodium salt); MURAMETIDETM (Nac-Mur-L-Ala-D-Gln-OCH3); MURAPALMITINETM and D-MURAPALMITINETM (Nac-Mur-L-Thr-D-isoGln-sn-glyceroldipalmitoyl); NAGO (neuraminidase-galactose oxidase); nanospheres or nanoparticles of any composition; NISVs (non-ionic surfactant vesicles); PLEURANTM (-glucan); PLGA, PGA and PLA (homo- and co-polymers of lactic acid and glycolic acid; microspheres/nanospheres); PLURONIC L121TM; PMMA (polymethyl methacrylate); PODDSTM (proteinoid microspheres); polyethylene carbamate derivatives; poly-rA: poly-rU (polyadenylic acid-polyuridylic acid complex); polysorbate 80 (Tween 80); protein cochleates (Avanti Polar Lipids, Inc., Alabaster, AL); STIMULONTM (QS-21); Quil-A (Quil-A saponin); S-28463 (4-amino-otec-dimethyl-2-ethoxymethyl-1H-imidazo[4,5 c]quinoline-1-ethanol); SAF-1TM ("Syntex adjuvant formulation"); Sendai proteoliposomes and Sendai-containing lipid matrices; Span-85 (sorbitan trioleate); Specol (emulsion of Marcol 52, Span 85 and Tween 85); squalene or Robane® (2,6,10,15,19,23-hexamethyltetracosan and

2,6,10,15,19,23-hexamethyl-2,6,10,14,18,22-tetracosahexane); stearyltyrosine (octadecyltyrosine hydrochloride); Theramid® (N-acetylglucosaminyl-N-acetylmuramyl-L-Ala-D-isoGlu-L-Ala-dipalmitoxypropylamide); Theronyl-MDP (TermurtideTM or [thr 1]-MDP; N-acetylmuramyl-L-threonyl-D-isoglutamine); Ty particles (Ty-VLPs or virus-like particles); Walter-Reed liposomes (liposomes containing lipid A adsorbed on aluminium hydroxide), and lipopeptides, including Pam3Cys, in particular aluminium salts, such as Adju-phos, Alhydrogel, Rehydragel; emulsions, including CFA, SAF, IFA, MF59, Provax, TiterMax, Montanide, Vaxfectin; copolymers, including Optivax (CRL1005), L121, Poloaxmer4010), etc.; liposomes, including Stealth, cochleates, including BIORAL; plant derived adjuvants, including QS21, Quil A, Iscomatrix, ISCOM; adjuvants suitable for costimulation including Tomatine, biopolymers, including PLG, PMM, Inulin,; microbe derived adjuvants, including Romurtide, DETOX, MPL, CWS, Mannose, CpG nucleic acid sequences, CpG7909, ligands of human TLR 1-10, ligands of murine TLR 1-13, ISS-1018, IC31, Imidazoquinolines, Ampligen, Ribi529, IMOxine, IRIVs, VLPs, cholera toxin, heat-labile toxin, Pam3Cys, Flagellin, GPI anchor, LNFPIII/Lewis X, antimicrobial peptides, UC-1V150, RSV fusion protein, cdiGMP; and adjuvants suitable as antagonists including CGRP neuropeptide.

Suitable adjuvants may also be selected from cationic or polycationic compounds wherein the adjuvant is preferably prepared upon complexing the artificial nucleic acid molecule or the vector of the pharmaceutical composition with the cationic or polycationic compound. Association or complexing the artificial nucleic acid molecule or the vector of the pharmaceutical composition with cationic or polycationic compounds as defined herein preferably provides adjuvant properties and confers a stabilizing effect to the artificial nucleic acid molecule or the vector of the pharmaceutical composition. Particularly such preferred, such cationic or polycationic compounds are selected from cationic or polycationic peptides or proteins, including protamine, nucleoline, spermin or spermidine, or other cationic peptides or proteins, such as poly-L-lysine (PLL), poly-arginine, basic polypeptides, cell penetrating peptides (CPPs), including HIV-binding peptides, Tat, HIV-1 Tat (HIV), Tat-derived peptides, Penetratin, VP22 derived or analog peptides, HSV VP22 (Herpes simplex), MAP, KALA or protein transduction domains (PTDs, PpT620, prolin-rich peptides, arginine-rich peptides, lysine-rich peptides, MPG-peptide(s), Pep-1, L-oligomers, Calcitonin peptide(s), Antennapedia-derived peptides (particularly from Drosophila antennapedia), pAntp, pIsl,

FGF, Lactoferrin, Transportan, Buforin-2, Bac715-24, SynB, SynB(1), pVEC, hCT-derived peptides, SAP, protamine, spermine, spermidine, or histones. Further preferred cationic or polycationic compounds may include cationic polysaccharides, for example chitosan, polybrene, cationic polymers, e.g. polyethyleneimine (PEI), cationic lipids, e.g. DOTMA: 1-(2,3-sioleyloxy)propyl) -N,N,N-trimethylammonium chloride, DMRIE, di-C14-amidine, DOTIM, SAINT, DC-Chol, BGTC, CTAP, DOPC, DODAP, DOPE: Dioleyl phosphatidylethanol-amine, DOSPA, DODAB, DOIC, DMEPC, DOGS: Dioctadecylamidoglicylspermin, DIMRI: Dimyristo-oxypropyl dimethyl hydroxyethyl ammonium bromide, DOTAP: dioleoyloxy-3-(trimethylammonio)propane, DC-6-14: O,O-ditetradecanoyl-N-(-trimethylammonioacetyl)diethanolamine chloride, CLIP1: rac-[(2,3-dioctadecyloxypropyl)(2-hydroxyethyl)]-dimethylammonium chloride, CLIP6: rac-[2(2,3-dihexadecyloxypropyl-oxymethyloxy)ethyl]-trimethylammonium, CLIP9: rac-[2(2,3-dihexadecyloxypropyl-oxysuccinyloxy)ethyl]-trimethylammonium, oligofectamine, or cationic or polycationic polymers, e.g. modified polyaminoacids, such as -aminoacid-polymers or reversed polyamides, etc., modified polyethylenes, such as PVP (poly(N-ethyl-4-vinylpyridinium bromide)), etc., modified acrylates, such as pDMAEMA (poly(dimethylaminoethyl methylacrylate)), etc., modified Amidoamines such as pAMAM (poly(amidoamine)), etc., modified polybetaaminoester (PBAE), such as diamine end modified 1,4 butanediol diacrylate-co-5-amino-1-pentanol polymers, etc., dendrimers, such as polypropylamine dendrimers or pAMAM based dendrimers, etc., polyimine(s), such as PEI: poly(ethyleneimine), poly(propyleneimine), etc., polyallylamine, sugar backbone based polymers, such as cyclodextrin based polymers, dextran based polymers, Chitosan, etc., silan backbone based polymers , such as PMOXA-PDMS copolymers, etc., Blockpolymers consisting of a combination of one or more cationic blocks (e.g. selected of a cationic polymer as mentioned above) and of one or more hydrophilic- or hydrophobic blocks (e.g polyethyleneglycole); etc.

Additionally, preferred cationic or polycationic proteins or peptides, which can be used as an adjuvant by complexing the artificial nucleic acid molecule or the vector, preferably an RNA, of the composition, may be selected from following proteins or peptides having the following total formula (I): (Arg)l;(Lys)m;(His)n;(Orn)o;(Xaa)x, wherein l + m + n +o + x = 8-15, and l, m, n or o independently of each other may be any number selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15, provided that the overall content of Arg, Lys, His

and Orn represents at least 50% of all amino acids of the oligopeptide; and Xaa may be any amino acid selected from native (= naturally occurring) or non-native amino acids except of Arg, Lys, His or Orn; and x may be any number selected from 0, 1, 2, 3 or 4, provided, that the overall content of Xaa does not exceed 50 % of all amino acids of the oligopeptide. Particularly preferred oligoarginines in this context are e.g. Arg7, Arg8, Arg9, Arg7, H3R9, R9H3, H3R9H3, YSSR9SSY, (RKH)4, Y(RKH)2R, etc.

The ratio of the artificial nucleic acid or the vector to the cationic or polycationic compound may be calculated on the basis of the nitrogen/phosphate ratio (N/P-ratio) of the entire nucleic acid complex. For example, 1 µg RNA typically contains about 3 nmol phosphate residues, provided the RNA exhibits a statistical distribution of bases. Additionally, 1 µg peptide typically contains about x nmol nitrogen residues, dependent on the molecular weight and the number of basic amino acids. When exemplarily calculated for (Arg)9 (molecular weight 1424 g/mol, 9 nitrogen atoms), 1 µg (Arg)9 contains about 700 pmol (Arg)9 and thus 700 x 9=6300 pmol basic amino acids = 6.3 nmol nitrogen atoms. For a mass ratio of about 1:1 RNA/(Arg)9 an N/P ratio of about 2 can be calculated. When exemplarily calculated for protamine (molecular weight about 4250 g/mol, 21 nitrogen atoms, when protamine from salmon is used) with a mass ratio of about 2:1 with 2 µg RNA, 6 nmol phosphate are to be calulated for the RNA; 1 µg protamine contains about 235 pmol protamine molecues and thus 235 x 21 = 4935 pmol basic nitrogen atoms = 4.9 nmol nitrogen atoms. For a mass ratio of about 2:1 RNA/protamine an N/P ratio of about 0.81 can be calculated. For a mass ratio of about 8:1 RNA/protamine an N/P ratio of about 0.2 can be calculated. In the context of the present invention, an N/P-ratio is preferably in the range of about 0.1-10, preferably in a range of about 0.3-4 and most preferably in a range of about 0.5-2 or 0.7-2 regarding the ratio of nucleic acid:peptide in the complex, and most preferably in the range of about 0.7-1.5.

Patent application WO2010/037539, the disclosure of which is incorporated herein by reference, describes an immunostimulatory composition and methods for the preparation of an immunostimulatory composition. Accordingly, in a preferred embodiment of the invention, the composition is obtained in two separate steps in order to obtain both, an efficient immunostimulatory effect and efficient translation of the artificial nucleic acid molecule according to the invention. Therein, a so called "adjuvant component" is prepared

by complexing – in a first step - the artificial nucleic acid molecule or vector, preferably an RNA, of the adjuvant component with a cationic or polycationic compound in a specific ratio to form a stable complex. In this context, it is important, that no free cationic or polycationic compound or only a neglibly small amount remains in the adjuvant component after complexing the nucleic acid. Accordingly, the ratio of the nucleic acid and the cationic or polycationic compound in the adjuvant component is typically selected in a range that the nucleic acid is entirely complexed and no free cationic or polycationic compound or only a neclectably small amount remains in the composition. Preferably the ratio of the adjuvant component, i.e. the ratio of the nucleic acid to the cationic or polycationic compound is selected from a range of about 6:1 (w/w) to about 0,25:1 (w/w), more preferably from about 5:1 (w/w) to about 0,5:1 (w/w), even more preferably of about 4:1 (w/w) to about 1:1 (w/w) or of about 3:1 (w/w) to about 1:1 (w/w), and most preferably a ratio of about 3:1 (w/w) to about 2:1 (w/w).

According to a preferred embodiment, the artificial nucleic acid molecule or vector, preferably an RNA molecule, according to the invention is added in a second step to the complexed nucleic acid molecule, preferably an RNA, of the adjuvant component in order to form the (immunostimulatory) composition of the invention. Therein, the artificial acid molecule or vector, preferably an RNA, of the invention is added as free nucleic acid, i.e. nucleic acid, which is not complexed by other compounds. Prior to addition, the free artificial nucleic acid molecule or vector is not complexed and will preferably not undergo any detectable or significant complexation reaction upon the addition of the adjuvant component.

Suitable adjuvants may furthermore be selected from nucleic acids having the formula (II): GlXmGn, wherein: G is guanosine, uracil or an analogue of guanosine or uracil; X is guanosine, uracil, adenosine, thymidine, cytosine or an analogue of the above-mentioned nucleotides; l is an integer from 1 to 40, wherein when l = 1 G is guanosine or an analogue thereof, when l > 1 at least 50% of the nucleotides are guanosine or an analogue thereof; m is an integer and is at least 3; wherein when m = 3 X is uracil or an analogue thereof, when m > 3 at least 3 successive uracils or analogues of uracil occur; n is an integer from 1 to 40, wherein when n = 1 G is guanosine or an analogue thereof, when n > 1 at least 50% of the nucleotides are guanosine or an analogue thereof.

Other suitable adjuvants may furthermore be selected from nucleic acids having the formula (III): ClXmCn, wherein: C is cytosine, uracil or an analogue of cytosine or uracil; X is guanosine, uracil, adenosine, thymidine, cytosine or an analogue of the above-mentioned nucleotides; l is an integer from 1 to 40, wherein when l = 1 C is cytosine or an analogue thereof, when l > 1 at least 50% of the nucleotides are cytosine or an analogue thereof; m is an integer and is at least 3; wherein when m = 3 X is uracil or an analogue thereof, when m > 3 at least 3 successive uracils or analogues of uracil occur; n is an integer from 1 to 40, wherein when n = 1 C is cytosine or an analogue thereof, when n > 1 at least 50% of the nucleotides are cytosine or an analogue thereof.

The pharmaceutical composition according to the present invention preferably comprises a "safe and effective amount" of the components of the pharmaceutical composition, particularly of the inventive artificial nucleic acid molecule, the vector and/or the cells as defined herein. As used herein, a "safe and effective amount" means an amount sufficient to significantly induce a positive modification of a disease or disorder as defined herein. At the same time, however, a "safe and effective amount" preferably avoids serious side-effects and permits a sensible relationship between advantage and risk. The determination of these limits typically lies within the scope of sensible medical judgment.

In a further aspect, the present invention provides the artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention for use as a medicament, for example, as vaccine (in genetic vaccination) or in gene therapy.

The artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention are particularly suitable for any medical application which makes use of the therapeutic action or effect of peptides, polypeptides or proteins, or where supplementation of a particular peptide or protein is needed. Thus, the present invention provides the artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention for use in

the treatment or prevention of diseases or disorders amenable to treatment by the therapeutic action or effect of peptides, polypeptides or proteins or amenable to treatment by supplementation of a particular peptide, polypeptide or protein. For example, the artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention may be used for the treatment or prevention of genetic diseases, autoimmune diseases, cancerous or tumour-related diseases, infectious diseases, chronic diseases or the like, e.g., by genetic vaccination or gene therapy.

In particular, such therapeutic treatments which benefit from an increased and prolonged presence of therapeutic peptides, polypeptides or proteins in a subject to be treated are especially suitable as medical application in the context of the present invention, since the inventive 3'-UTR element provides for a stable and prolonged expression of the encoded peptide or protein of the inventive artificial nucleic acid molecule or vector and/or the inventive 5'-UTR element provides for an increased expression of the encoded peptide or protein of the inventive artificial nucleic acid molecule or vector. Thus, a particularly suitable medical application for the artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention is vaccination. Thus, the present invention provides the artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention for vaccination of a subject, preferably a mammalian subject, more preferably a human subject. Preferred vaccination treatments are vaccination against infectious diseases, such as bacterial, protozoal or viral infections, and anti-tumour-vaccination. Such vaccination treatments may be prophylactic or therapeutic.

Depending on the disease to be treated or prevented, the ORF may be selected. For example, the open reading frame may code for a protein that has to be supplied to a patient suffering from total lack or at least partial loss of function of a protein, such as a patient suffering from a genetic disease. Additionally the open reading frame may be chosen from an ORF coding for a peptide or protein which beneficially influences a disease or the condition of a subject. Furthermore, the open reading frame may code for a peptide or protein which effects down-

regulation of a pathological overproduction of a natural peptide or protein or elimination of cells expressing pathologically a protein or peptide. Such lack, loss of function or overproduction may, e.g., occur in the context of tumour and neoplasia, autoimmune diseases, allergies, infections, chronic diseases or the like. Furthermore, the open reading frame may code for an antigen or immunogen, e.g. for an epitope of a pathogen or for a tumour antigen. Thus, in preferred embodiments, the artificial nucleic acid molecule or the vector according to the present invention comprises an ORF encoding an amino acid sequence comprising or consisting of an antigen or immunogen, e.g. an epitope of a pathogen or a tumour-associated antigen, a 3'-UTR element as described above and/or a 5'-UTR element as described above, and optional further components, such as a poly(A) sequence etc.

In the context of medical application, in particular, in the context of vaccination, it is preferred that the artificial nucleic acid molecule according to the present invention is RNA, preferably mRNA, since DNA harbours the risk of eliciting an anti-DNA immune response and tends to insert into genomic DNA. However, in some embodiments, for example, if a viral delivery vehicle, such as an adenoviral delivery vehicle is used for delivery of the artificial nucleic acid molecule or the vector according to the present invention, e.g., in the context of gene therapeutic treatments, it may be desirable that the artificial nucleic acid molecule or the vector is a DNA molecule.

The artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention may be administered orally, parenterally, by inhalation spray, topically, rectally, nasally, buccally, vaginally, via an implanted reservoir or via jet injection. The term parenteral as used herein includes subcutaneous, intravenous, intramuscular, intra-articular, intra-synovial, intrasternal, intrathecal, intrahepatic, intralesional, intracranial, transdermal, intradermal, intrapulmonal, intraperitoneal, intracardial, intraarterial, and sublingual injection or infusion techniques. In a preferred embodiment, the artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention is administered via needle-free injection (e.g. jet injection).

Preferably, the artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention is administered parenterally, e.g. by parenteral injection, more preferably by subcutaneous, intravenous, intramuscular, intra-articular, intra-synovial, intrasternal, intrathecal, intrahepatic, intralesional, intracranial, transdermal, intradermal, intrapulmonal, intraperitoneal, intracardial, intraarterial, sublingual injection or via infusion techniques. Particularly preferred is intradermal and intramuscular injection. Sterile injectable forms of the inventive pharmaceutical composition may be aqueous or oleaginous suspension. These suspensions may be formulated according to techniques known in the art using suitable dispersing or wetting agents and suspending agents. Preferably, the solutions or suspensions are administered via needle-free injection (e.g. jet injection).

The artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention may also be administered orally in any orally acceptable dosage form including, but not limited to, capsules, tablets, aqueous suspensions or solutions.

The artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention may also be administered topically, especially when the target of treatment includes areas or organs readily accessible by topical application, e.g. including diseases of the skin or of any other accessible epithelial tissue. Suitable topical formulations are readily prepared for each of these areas or organs. For topical applications, the artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention may be formulated in a suitable ointment suspended or dissolved in one or more carriers.

In one embodiment, the use as a medicament comprises the step of transfection of mammalian cells, preferably *in vitro* or *ex vivo* transfection of mammalian cells, more

preferably *in vitro* transfection of isolated cells of a subject to be treated by the medicament. If the use comprises the *in vitro* transfection of isolated cells, the use as a medicament may further comprise the readministration of the transfected cells to the patient. The use of the inventive artificial nucleic acid molecules or the vector as a medicament may further comprise the step of selection of successfully transfected isolated cells. Thus, it may be beneficial if the vector further comprises a selection marker. Also, the use as a medicament may comprise *in vitro* transfection of isolated cells and purification of an expression-product, i.e. the encoded peptide or protein from these cells. This purified peptide or protein may subsequently be administered to a subject in need thereof.

The present invention also provides a method for treating or preventing a disease or disorder as described above comprising administering the artificial nucleic acid molecule according to the present invention, the vector according to the present invention, the cell according to the present invention, or the pharmaceutical composition according to the present invention to a subject in need thereof.

Furthermore, the present invention provides a method for treating or preventing a disease or disorder comprising transfection of a cell with an artificial nucleic acid molecule according to the present invention or with the vector according to the present invention. Said transfection may be performed *in vitro*, *ex vivo* or *in vivo*. In a preferred embodiment, transfection of a cell is performed *in vitro* and the transfected cell is administered to a subject in need thereof, preferably to a human patient. Preferably, the cell which is to be transfected *in vitro* is an isolated cell of the subject, preferably of the human patient. Thus, the present invention provides a method of treatment comprising the steps of isolating a cell from a subject, preferably from a human patient, transfecting the isolated cell with the artificial nucleic acid according to the present invention or the vector according to the present invention, and administering the transfected cell to the subject, preferably the human patient.

The method of treating or preventing a disorder according to the present invention is preferably a vaccination method or a gene therapy method as described above.

As described above, the inventive 3'-UTR element and/or the inventive 5'-UTR element are capable of prolonging and/or increasing the protein production from an mRNA. Thus, in a

further aspect, the present invention relates to a method for increasing and/or prolonging protein production from an artificial nucleic acid molecule, preferably from an mRNA molecule or a vector, the method comprising the step of associating an open reading frame with a 3'-UTR element and/or a 5'-UTR element, wherein the 3'-UTR element and/or the 5'-UTR element prolongs and/or increases protein production from a resulting artificial nucleic acid molecule and wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element is derived from a stable mRNA, to obtain an artificial nucleic acid molecule, preferably an mRNA molecule, according to the present invention as described above or a vector according to the present invention as described above.

Preferably, in the method for increasing and/or prolonging protein production from an artificial nucleic acid molecule, preferably from an mRNA molecule or a vector, according to the present invention the 3'-UTR element and/or the 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a transcript of a gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, SUPT3H, TMEM14A, GRAMD1C, C11orf80, C9orf46, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5,NT5DC1, RAB7A, AGA, TPK1, MBNL3, HADHB, MCCC2, CAT, ANAPC4, PCCB, PHKB, ABCB7, PGCP, GPD2, TMEM38B, NFU1, OMA1, LOC128322/NUTF2, NUBPL, LANCL1, HHLA3, PIR, ACAA2, CTBS, GSTM4, ALG8, Atp5e, Gstm5, Uqcr11, Ifi27l2a, Anapc13, Atp5l, Tmsb10, Nenf, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufs5, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Hexa, Ndufb11, Map1lc3a, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8,

Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Ybx1, Sepp1, Gaa, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1; preferably from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

The term "associating the artificial nucleic acid molecule or the vector with a 3'-UTR element and/or a 5'-UTR element" in the context of the present invention preferably means functionally associating or functionally combining the artificial nucleic acid molecule or the vector with the 3'-UTR element and/or with the 5'-UTR element. This means that the artificial nucleic acid molecule or the vector and the 3'-UTR element and/or the 5'-UTR element, preferably the 3'-UTR element and/or the 5'-UTR element as described above, are associated or coupled such that the function of the 3'-UTR element and/or of the 5'-UTR element, e.g., the RNA and/or protein production prolonging and/or increasing function, is exerted. Typically, this means that the 3'-UTR element and/or the 5'-UTR element is integrated into the artificial nucleic acid molecule or the vector, preferably the mRNA molecule, 3' and/or 5', respectively, to an open reading frame, preferably immediately 3' to an open reading frame and/or immediately 5' to an open reading frame, the 3'-UTR element preferably between the open reading frame and a poly(A) sequence or a polyadenylation signal. Preferably, the 3'-UTR element and/or the 5'-UTR element is integrated into the artificial nucleic acid molecule or the vector, preferably the mRNA, as 3'-UTR and/or as 5'-UTR respectively, i.e. such that

the 3'-UTR element and/or the 5'-UTR element is the 3'-UTR and/or the 5'-UTR, respectively, of the artificial nucleic acid molecule or the vector, preferably the mRNA, i.e., such that the 5'-UTR ends immediately before the 5'-end of the ORF and the 3'-UTR extends from the 3'-side of the open reading frame to the 5'-side of a poly(A) sequence or a polyadenylation signal, optionally connected via a short linker, such as a sequence comprising or consisting of one or more restriction sites. Thus, preferably, the term "associating the artificial nucleic acid molecule or the vector with a 3'-UTR element and/or a 5'-UTR element" means functionally associating the 3'-UTR element and/or the 5'-UTR element with an open reading frame located within the artificial nucleic acid molecule or the vector, preferably within the mRNA molecule. The 3'-UTR and/or the 5'-UTR and the ORF are as described above for the artificial nucleic acid molecule according to the present invention, for example, preferably the ORF and the 3'-UTR are heterologous and/or the ORF and the 5'-UTR are heterologous,respectively, e.g. derived from different genes, as described above.

In a further aspect, the present invention provides the use of a 3'-UTR element and/or of a 5'-UTR element, preferably the 3'-UTR element as described above and/or the 5'-UTR element as described above, for increasing and/or prolonging protein production from an artificial nucleic acid molecule, preferably from an mRNA molecule or a vector, wherein the 3'-UTR element and/or the 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a transcript of a gene selected from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, SUPT3H, TMEM14A, GRAMD1C, C11orf80, C9orf46, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, NT5DC1, RAB7A, AGA, TPK1, MBNL3, HADHB, MCCC2, CAT, ANAPC4, PCCB, PHKB, ABCB7, PGCP, GPD2, TMEM38B, NFU1, OMA1, LOC128322/NUTF2, NUBPL, LANCL1, HHLA3, PIR, ACAA2, CTBS, GSTM4, ALG8, Atp5e, Gstm5, Uqcr11, Ifi27l2a, Anapc13, Atp5l, Tmsb10, Nenf, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13,

Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufs5, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Hexa, Ndufb11, Map1lc3a, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Ybx1, Sepp1, Gaa, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1; preferably from the group consisting of GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

The uses according to the present invention preferably comprise associating the artificial nucleic acid molecule, the vector, or the RNA with the 3'-UTR element as described above and/or with the 5'-UTR element as described above.

The compounds and ingredients of the inventive pharmaceutical composition may also be manufactured and traded separately of each other. Thus, the invention relates further to a kit or kit of parts comprising an artificial nucleic acid molecule according to the invention, a vector according to the invention, a cell according to the invention, and/or a pharmaceutical composition according to the invention. Preferably, such kit or kits of parts may, additionally, comprise instructions for use, cells for transfection, an adjuvant, a means for administration

of the pharmaceutical composition, a pharmaceutically acceptable carrier and/or a pharmaceutically acceptable solution for dissolution or dilution of the artificial nucleic acid molecule, the vector, the cells or the pharmaceutical composition.

In a further aspect the present invention provides a method for identifying a 3'-untranslated region element (3'-UTR element) and/or a 5'-untranslated region element (5'-UTR element), which is derived from a stable mRNA, comprising the following steps:

a) Analyzing the stability of an mRNA comprising the following sub-steps:
   i. Determining the amount of said mRNA at a first point in time during a decay process of said mRNA,
   ii. Determining the amount of said mRNA at a second point in time during a decay process of said mRNA, and
   iii. Calculating the ratio of the amount of said mRNA determined in step (i) to the the amount of said mRNA determined in step (ii);
b) Selecting a stable mRNA having a ratio calculated in sub-step (iii) of at least 0.5 (50%), at least 0.6 (60%), at least 0.7 (70%), at least 0.75 (75%), at least 0.8 (80%), at least 0.85 (85%), at least 0.9 (90%), or at least 0.95 (95%); and
c) Determining the nucleotide sequence of a 3'- and/or 5'-UTR element of said stable mRNA.

Thereby, the stability of the mRNA is preferably assessed under standard conditions, for example standard conditions (standard medium, incubation, etc.) for a certain cell line or cell type used.

In order to analyze the stability of an mRNA, the decay process of this mRNA is assessed by determining the amount or concentration of said mRNA at a first and at a second point in time during the decay process of said mRNA (cf. steps a) i. and a) ii.).

To determine the amount or concentration of mRNA during the RNA decay process *in vivo* or *in vitro* as defined above (i.e. *in vitro* referring in particular to ("living") cells and/or tissue, including tissue of a living subject; cells include in particular cell lines, primary cells, cells in tissue or subjects, preferred are mammalian cells, e.g. human cells and mouse cells and particularly preferred are the human cell lines HeLa, and U-937 and the mouse cell lines

NIH3T3, JAWSII and L929 are used; furthermore primary cells are particularly preferred, in particular preferred embodiments human dermal fibroblasts (HDF)), various methods may be used, which are known to the skilled person. Non-limiting examples of such methods include general inhibition of transcription, e.g. with a transcription inhibitor such as Actinomycin D, use of inducible promotors to specifically promote transient transcription, e.g. c-fos serum-inducible promotor system and Tet-off regulatory promotor system, and kinetic labelling techniques, e.g. pulse labelling.

For example, if transcriptional inhibitor-mediated transcriptional arrest is used in step a) to determine the amount or concentration of mRNA during the RNA decay process *in vivo* or *in vitro* as defined above, transcriptional inhibitors such as Actinomycin D (ActD), 5,6-dichloro-1–D-ribofuranosyl-benzimidazole (DRB) or -amanitin (α-Am) may be used. Hereby, to assess mRNA decay, the transcriptional inhibitors are usually added to the cells and, thereby the transcription is generally inhibited and RNA decay can be observed without interferences of ongoing transcription.

Alternatively, inducible promotors to specifically promote transient transcription may be used in step a), whereby the rationale is to provide a stimulus that activates transcription and leads to a burst of mRNA synthesis, then remove the stimulus to shut off transcription and monitor the decay of mRNA. Thereby, the inducible promoter enables a stringent control, so that induction and silencing of transcription is accomplished within a narrow window of time. In mammalian cells, the *cfos* promoter is known to be valuable for this purpose, because it can be induced in response to serum addition quickly and transiently, thereby providing a reliable and simple way of achieving a transient burst in transcription. The Tet-off promotor system offers another option that further broadens the application of a transcriptional pulsing approach to study mRNA turnover in mammalian cells.

However, in the present invention kinetic labelling techniques are preferred in step a) for determining the amount of mRNA during the RNA decay process *in vivo* or *in vitro* as defined above. In kinetic labelling RNA is usually labelled, whereby labels include in particular labelled nucleotides and labelled nucleosides and labelled uridine and labelled uracil are particularly preferred. Examples of preferred labels include 4-thiouridine (4sU), 2-thiouridine, 6-thioguanosine, 5-ethynyluridine (EU), 5-bromo-uridine (BrU), Biotin-16-Aminoallyluridine,

5-Aminoallyluridine, 5-Aminoallylcytidine, etc., whereby 4-Thiouridine (4sU), 5-Ethynyluridine (EU) or 5'-Bromo-Uridine (BrU) are more preferred. Particularly preferred is 4-thiouridine (4sU). 4-Thiouridine (4sU) is preferably used in a concentration of 100-500 µM. Moreover, also radioactively labelled nucleotides may be used, e.g. with Uridine-^{3}H. Also combinations of the above mentioned labelled nucleotides may be used, whereby a combination of 4-thiouridine and 6-thioguanosine is particularly preferred.

In kinetic labelling, usually the emerging RNA is labelled, e.g. by incorporation of labelled uridine or uracil during transcription. After a while, the provision of label is stopped and RNA decay may then be observed by assessing specifically labelled RNA without generally inhibiting transcription.

For determining the amount of mRNA during the RNA decay process in step a), pulse labelling is preferred, and a pulse-chase methodology is particularly preferred. As used herein, the term "pulse labelling refers to a technique in which a label, e.g. the labels described above, is used for the measurement of the rates of synthesis and/or decay of compounds within living cells. Typically, cells are exposed to a small quantity of a label for a brief period, hence the term 'pulse'. In the pulse-chase methodology, after pulse-labelling usually a much larger quantity of an unlabeled compound corresponding to the "pulse" (e.g. unlabelled uridine, if labelled uridine is used as pulse) is added following the required period of exposure to the label. The effect of competition between the labelled and the unlabeled compound is to reduce to a negligible level the further uptake of the labelled compound, hence the term "chase".

To determine the amount or concentration of mRNA usually the mRNA has to be isolated. Different techniques for RNA isolation are known to the skilled person, e.g. by Guanidinium thiocyanate-phenol-chloroform extraction or by silica-column based extraction. Also commercially available kits may be used, e.g. RNeasy Kit from Qiagen.

Furthermore, an extraction step may be required, in particular if kinetic labelling is used (in contrast to a transcription inhibitor, wherein the total RNA represents "decaying" RNA since transcription is generally inhibited). In the extraction step, labelled RNA (i.e. representing "decaying" RNA) is extracted from total isolated RNA. Thus, the means of extraction may be

selected depending on the label used. For example, immunopurification with antibodies to the label may be used.

Furthermore, for example, for extraction of thio-labelled, e.g. 4-thiouridine (4sU)-labelled, RNA, HPDP-Biotin (pyridyldithiol-activated, sulfhydryl-reactive biotinylation reagent that conjugates via a cleavable (reversible) disulfide bond) may be incubated with the isolated "total RNA". This reagent specifically reacts with the reduced thiols (-SH) in the 4-thiouridine (4sU)-labelled RNA to form reversible disulfide bonds. The biotinylation allows for binding of the thio-labelled e.g. 4-thiouridine (4sU)-labelled RNA to streptavidin and therefore can be extracted from the total RNA by reduction of the disulfide bond with dithiothreitol or beta-mercaptoethanol (or any other reduction agent).

In case biotin-labelled nucleotides, e.g. Biotin-16-Aminoallyluridine, streptavidin can directly be used to extract the labelled RNA from total RNA.

For example, for extraction of newly transcribed 5-ethynyluridine (EU)-labelled cellular RNAs from total RNA, biotinylation of EU in a copper-catalyzed cycloaddition reaction (often referred to as click chemistry) may be used, which is followed by purification by streptavidin affinity. This method is commercially available as the Click-iT Nascent RNA Capture Kit (Catalog no. C10365, Invitrogen). The manufacturer's instruction of this kit recommends that the pulse labeling time is 30 to 60 min for a 0.5 mM EU dose, or 1 to 24 h for a 0.1 or 0.2 mM EU dose.

For example, BrU-labeled RNA molecules may be extracted by immunopurification with an anti-Bromodeoxyuridine antibody (e.g. Clone. 2B1,Catalog no. MI-11–3, MBL), and Protein G Sepharose.

The amount or concentration of mRNA, i.e. the transcript level, may then be measured by various methods known to the person skilled in the art. Non-limiting examples for such methods include micro array analysis, Northern Blot analysis, quantitative PCR or by next generation sequencing (high throughput sequencing). Particularly preferred are micro array analysis and next generation sequencing. Moreover, whole-genome approaches/whole transcriptome approaches are particularly preferred, e.g. in micro array analysis whole

genome micro array analysis, e.g. Affymetrix Human Gene 1.0 ST or 2.0 ST or Affymetrix Mouse Gene 1.0 ST or 2.0 ST or whole transcriptome analysis by next generation sequencing.

In substeps i. and ii. of step a), the amount of mRNA is determined at a first and at a second point in time during a decay process of the mRNA. Typically, this means that mRNA is in particular isolated at a first and at a second point in time during a decay process of the mRNA to determine the respective amounts. Therefore, "the first point in time" and "the second point in time" are in particular points in time during the RNA decay process, at which RNA is isolated to determine the RNA amount. In general, "the second point in time" is later in the RNA decay process than the "the first point in time".

Preferably, the first point in time is selected such, that only mRNA undergoing a decay process is considered, i.e. emerging mRNA – e.g. in ongoing transcription – is avoided. For example, if kinetic labelling techniques, e.g. pulse labelling, are used, the first point in time is preferably selected such that the incorporation of the label into mRNA is completed, i.e. no ongoing incorporation of the label into mRNA occurs. Thus, if kinetic labelling is used, the first point in time may be at least 10 min, at least 20 min, at least 30 min, at least 40 min, at least 50 min, at least 60 min, at least 70 min, at least 80 min, or at least 90 min after the end of the experimental labelling procedure, e.g. after the end of the incubation of cells with the label.

For example, the first point in time may be preferably from 0 to 6 h after the stop of transcription (e.g. by a transcriptional inhibitor), stop of promotor induction in case of inducible promotors or after stop of pulse or label supply, e.g. after end of labelling. More preferably, the first point in time may be from 30 min to 5 h, even more preferably from 1 h to 4 h and particularly preferably about 3 h after the stop of transcription (e.g. by a transcriptional inhibitor), stop of promotor induction in case of inducible promotors or after stop of pulse or label supply, e.g. after end of labelling.

Preferably, the second point in time is selected as late as possible during the mRNA decay process. However, if a plurality of mRNA species is considered, the second point in time is preferably selected such that still a considerable amount of the plurality of mRNA species, preferably at least 10% of the mRNA species, is present in a detectable amount, i.e. in an amount higher than 0. Preferably, the second point in time is at least 5 h, at least 6 h, at least

7 h, at least 8 h, at least 9 h, at least 10 h, at least 11 h, at least 12 h, at least 13 h, at least 14 h, or at least 15 h after the stop of transcription (e.g. by a transcriptional inhibitor), stop of promotor induction in case of inducible promotors or after stop of pulse or label supply, e.g. after end of labelling.

For example, the second point in time may be preferably from 3 to 48 h after the stop of transcription (e.g. by a transcriptional inhibitor), stop of promotor induction in case of inducible promotors or after stop of pulse or label supply, e.g. after end of labelling. More preferably, the second point in time may be from 6 min to 36 h, even more preferably from 10 h to 24 h and particularly preferably about 15 h after the stop of transcription (e.g. by a transcriptional inhibitor), stop of promotor induction in case of inducible promotors or after stop of pulse or label supply, e.g. after end of labelling.

Thus, the time span between the first point in time and the second point in time is preferably as large as possible within the above described limits. Therefore, the time span between the first point in time and the second point in time is preferably at least 4 h, at least 5 h, at least 6 h, at least 7 h, at least 8 h, at least 9 h, at least 10 h, at least 11 h, or at least 12 h, whereby a time span of about 12 h is particularly preferred. In general, the second later point in time is at least 10 minutes later than the first point in time.

In sub-step iii. of step a) the ratio of the amount of the mRNA determined in step (i) to the the amount of the mRNA determined in step (ii) is calculated. To this end, the amount of the mRNA (transcript level) determined as described above at the second point in time is divided by the amount of the mRNA (transcript level) determined as described above at the first point in time. This ratio prevents that stable mRNAs, which are already at the first point in time present only in very low amounts, are disregarded in respect to mRNAs, which are present in high amounts.

In step b), such an mRNA is selected, which has a ratio calculated in sub-step (iii) of step a) of at least 0.5 (50%), at least 0.6 (60%), at least 0.7 (70%), at least 0.75 (75%), at least 0.8 (80%), at least 0.85 (85%), at least 0.9 (90%), or at least 0.95 (95%). Such mRNA is in the present invention considered as a particular stable mRNA.

In step c), the nucleotide sequence of a 3'- and/or 5'-UTR element of said mRNA, i.e. the mRNA selected in step b), is determined. To this end, different methods known to the skilled person may be applied, e.g. sequencing or selection from a publicly available database, such as e.g. NCBI (National Center for Biotechnology Information). For example, the mRNA sequence of the mRNA selected in step b) may be searched in a database and the 3'- and/or 5'-UTR may then be extracted from the mRNA sequence present in the database.

In particular, in the above described method for identifying a 3'-untranslated region element (3'-UTR element) and/or a 5'-untranslated region element (5'-UTR element), which is derived from a stable mRNA, the term "mRNA" and/or "stable mRNA", respectively, may also refer to an mRNA species as defined herein and/or to a stable mRNA species, respectively.

Furthermore, it is preferred in the present invention that a "stable mRNA" may have a slower mRNA decay compared to average mRNA decay, preferably assessed *in vivo* or *in vitro* as defined above. Thereby, "average mRNA decay" may be assessed by investigating mRNA decay of a plurality of mRNA species.

Accordingly, the present invention provides in a further aspect a method for identifying a 3'-untranslated region element (3'-UTR element) and/or a 5'-untranslated region element (5'-UTR element), which is derived from a stable mRNA, comprising the following steps:

a) Analyzing the stability of a plurality of mRNA species comprising the following sub-steps:
    i. Determining the amount of each mRNA species of said plurality of mRNA species at a first point in time during a decay process of said mRNA species,
    ii. Determining the amount of each mRNA species of said plurality of mRNA species at a second point in time during a decay process of said mRNA species, and
    iii. Calculating for each mRNA species of said plurality of mRNA species the ratio of the amount of said mRNA species determined in step (i) to the the amount of said mRNA species determined in step (ii);
b) Ranking of the mRNA species of the plurality of mRNA species according to the ratio calculated in sub-step (iii) for each mRNA species;

c) Selecting one or more mRNA species having the highest ratio or the highest ratios calculated in sub-step (iii); and

d) Determining the nucleotide sequence of a 3'- and/or 5'-UTR element of said mRNA.

An "mRNA species", as used herein, corresponds to a genomic transcription unit, i.e. usually to a gene. Thus, within one "mRNA species" different transcripts may occur, for example, due to mRNA processing. For example, an mRNA species may be represented by a spot on a microarray. Accordingly, a microarray provides an advantageous tool to determine the amount of a plurality of mRNA species, e.g. at a certain point in time during mRNA decay. However, also other techniques known to the skilled person, e.g. RNA-seq (also called Whole Transcriptome Shotgun Sequencing which is a technology that uses the capabilities of next-generation sequencing to reveal a snapshot of RNA presence and quantity from a genome at a given moment in time), quantitative PCR etc. may be used.

Preferably, "a plurality of mRNA species", refers to at least 100, at least 300, at least 500, at least 1000, at least 2000, at least 3000, at least 4000, at least 5000, at least 6000, at least 7000, at least 8000, at least 9000, at least 10000, at least 11000, at least 12000, at least 13000, at least 14000, at least 15000, at least 16000, at least 17000, at least 18000, at least 19000, at least 20000, at least 21000, at least 22000, at least 23000, at least 24000, at least 25000, at least 26000, at least 27000, at least 28000, at least 29000, or at least 30000 mRNA species. It is particularly preferred that the whole transcriptome is assessed, or as many mRNA species of the transcriptome as possible. This may be achieved, for example, by using a micro array providing whole transcript coverage.

Step a) of this method with its sub-steps i. to iii. corresponds essentially to step a) with its sub-steps i. to iii. of the previously described inventive method, but differs only in that the amount of each mRNA species of a plurality of mRNA species is determined at a first and at a second point in time and in that the ratio is calculated for each mRNA species. Accordingly, the detailed methods and preferred embodiments outlined above apply here as well and the ratio for a single mRNA species (and each single mRNA species, respectively) may be determined as outlined above for "an mRNA".

However, in contrast to the above method, the stability of the mRNA is not assessed by the absolute value of the ratio, but by a ranking of the mRNA species of the plurality of mRNA species according to the ratio calculated in sub-step (iii) of step a) for each mRNA species. In sub-step c) one or more mRNA species having the highest ratio or the highest ratios calculated in sub-step (iii) of step a) are then selected.

In this context it is particularly preferred to select the 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 2%, 3%, 4%, 5%, 10%, 15%, 20% most stable mRNA species in step c). Alternatively or additionally, in step c) such mRNA species may be selected which show a ratio calculated in sub-step iii. of step a) corresponding to a least 100% of the average ratio calculated from all mRNA species analyzed. More preferably such mRNA species are selected showing a ratio of at least 150%, even more preferably of at least 200% and most preferably of at least 300% of the average ratio calculated from all mRNA species analyzed.

In step d) the nucleotide sequence of a 3'- and/or 5'-UTR element of the mRNA selected in step c) is determined as described above, for step c) of the previously described inventive method.

Preferably, in both of the above described methods for identifying a 3'-UTR element and/or a 5'-UTR element according to the present invention, the time period between the first point in time and the second point in time is at least 5h, preferably at least 6h, preferably at least 7h, more preferably at least 8h, more preferably at least 9h, even more preferably at least 10h, even more preferably at least 11h, and particularly preferably at least 12h.

Preferably, in both of the above described methods for identifying a 3'-UTR element and/or a 5'-UTR element according to the present invention, the stability of an mRNA is analysed by pulse labelling, preferably using a pulse-chase methodology.

In a further aspect, the present invention also provides a method for identifying a 3'-untranslated region element (3'-UTR element) and/or a 5'-untranslated region element (5'-UTR element), which prolongs and/or increases protein production from an artificial nucleic acid molecule and which is derived from a stable mRNA comprising the following steps:

a) identifying a 3'-UTR element and/or a 5'-UTR element which is derived from a stable mRNA by a method for identifying a 3'-UTR element and/or a 5'-UTR element according to any of the methods described above;

b) synthesizing an artificial nucleic acid molecule comprising at least one open reading frame and at least one 3'-UTR element and/or at least one 5'-UTR element which corresponds to or is comprised by the 3'-UTR element and/or the 5'-UTR element identified in step a);

c) analyzing the expression of the protein encoded by the at least one open reading frame (ORF) of the artificial nucleic acid molecule synthesized in step b);

d) analyzing the expression of a protein encoded by at least one open reading frame of a reference artificial nucleic acid molecule lacking a 3'-UTR element and/or a 5'-UTR element;

e) comparing the protein expression from the artificial nucleic acid molecule analysed in step c) to the protein expression from the reference artificial nucleic acid molecule analysed in step d); and

f) selecting the 3'-UTR element and/or the 5'-UTR element if the protein expression from the artificial nucleic acid molecule analysed in step c) is prolonged and/or increased in comparison to the protein expression from the reference artificial nucleic acid molecule analysed in step d).

In this method, at first a 3'-UTR element and/or a 5'-UTR element are identified by a method according to the present invention as described above. This enables synthesis of the 3'- and/or the 5'-UTR element by methods known to the skilled person, e.g. by PCR amplification. The primers used for such a PCR may preferably comprise restriction sites for cloning. Alternatively, the 3'- and/or 5'-UTR element may be synthesized e.g. by chemical synthesis or oligo annealing. Accordingly, in step b), an artificial nucleic acid molecule is synthesized comprising at least one open reading frame and at least one 3'-UTR element and/or at least one 5'-UTR element which corresponds to or is comprised by the 3'-UTR element and/or the 5'-UTR element identified in step a). In particular, the at least one 3'-UTR element and/or at least one 5'-UTR element is usually combined with an open reading frame, which results in an artificial nucleic acid comprising a 3'- and/or 5'-UTR element according to the present invention, if the 3'- and/or 5'-UTR element fulfil the respective requirements, i.e. if they

prolong and/or increase protein expression. To test this, the 3'- and/or the 5'-UTR element identified in step a), or a PCR fragment or synthesized sequence thereof respectively, may be cloned into a particular vector, preferably in an expression vector, in order to assess protein expression from the respective ORF.

The protein expression from the artificial nucleic acid molecule comprising the at least one 3'-UTR element and/or the at least one 5'-UTR element is then assessed in step c) as described herein and compared to the protein expression assessed in step d) from a respective reference artificial nucleic acid molecule lacking a 3'-UTR element and/or a 5'-UTR element as described herein in step e).

Thereafter, in step f), such a 3'-UTR element and/or 5'-UTR element is selected, which prolongs and/or increases the protein expression from the artificial nucleic acid molecule analysed in step c) in comparison to the protein expression from the reference artificial nucleic acid molecule analysed in step d). The comparison of the protein expression of the inventive nucleic acid molecule to the reference nucleic acid molecule is carried out as described herein, in particular in the context of the inventive artificial nucleic acid molecule.

Furthermore, the present invention provides a particularly preferred method for identifying a 3'-untranslated region element (3'-UTR element) and/or a 5'-untranslated region element (5'-UTR element), which prolongs and/or increases protein production from an artificial nucleic acid molecule and which is derived from a stable mRNA comprising the following steps:

a) feeding/incubating cells with a labelled nucleotide for incorporation in newly transcribed RNA molecules (pulse-chase labelling);
b) isolating total RNA of the cells at a first point in time and at at least one second later point in time;
c) extracting of the labelled RNA molecules from the total RNA isolated in step b);
d) measuring of the amount/transcript level of the different mRNA species comprised in the labelled RNA;
e) calculating the ratio of the amount/transcript level of an mRNA species present at the at least one second later point in time to the amount/transcript level of the mRNA species present at the first point in time;
f) ranking of the mRNA species according to the ratio determined in step e);

g) selecting the most stable mRNA species;

h) determinating the nucleotide sequence of the 3'- and/or 5'-UTR of the most stable mRNA species selected in step g);

i) synthesizing a 3'- and/or a 5'-UTR element comprised in the 3'- and/or 5'-UTR determined in step h);

j) combination of the 3'- and/or 5'-UTR element synthesized in step i) with an open reading frame to get a nucleic acid according to the invention as described herein; and

k) optionally comparing the expression of the open reading frame present in the inventive nucleic acid compared to the expression of the open reading frame present in a reference nucleic acid without a 3'- and/or 5'-UTR element as described herein.

Thereby, the details and preferred embodiments described for the inventive methods above also apply herein, within the respective limitation outlined in steps a) to k).

In particular, the following labelled nucleotides are preferred for feeding the cells in step a) of the inventive method: 4-thiouridine (4sU), 2-thiouridine, 6-thioguanosine, 5-ethynyluridine (EU), 5-bromo-uridine (BrU), Biotin-16-Aminoallyluridine, 5-Aminoallyluridine, 5-Aminoallylcytidine, etc. Particularly preferred is 4-thiouridine (4sU). 4-thiouridine is preferably used in a concentration of 100-500 µM. Alternatively radioactively labelled nucleotides may be used, e.g. Uridine-^{3}H. Combinations of the above mentioned labelled nucleotides may be used. Particularly preferred is the combination of 4-thiouridine and 6-thioguanosine

The incubation of the cells with the labelled nucleotide in step a) can be varied. Particularly preferred is an incubation (feeding time) from 10 minutes to 24 hours. Particularly preferred are 2 to 6 hours, more preferably 2 to 3 hours.

Cells, which can be used for the inventive method, include in particular cell lines, primary cells, cells in tissue or subjects. In specific embodiments cell types allowing cell culture may be suitable for the inventive method. Particularly preferred are mammalian cells, e.g. human cells and mouse cells. In particularly preferred embodiments the human cell lines HeLa, and U-937 and the mouse cell lines NIH3T3, JAWSII and L929 are used. Furthermore primary

cells are particularly preferred; in particular preferred embodiments particularly human dermal fibroblasts (HDF) can be used. Alternatively the labelled nucleotide may also be applied to a tissue of a subject and after the incubation time the RNA of the tissue is isolated according to step c).

For determination of the most stable mRNAs of a cell (type), total RNA is extracted at a first point in time as described above, e.g. 0 to 6 h after labelling, preferably 3 h after labelling and at a second later point in time as described above, e.g. 3 to 48 h after labelling, preferably 10 to 24 h, most preferably 15 h after labelling. The second later point in timeis at least 10 minutes later than the first time.

In step f) the mRNA species are ranked according to the ratio calculated in step e). In this context it is particularly preferred to select the 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 2%, 3%, 4%, 5%, 10%, 15%, 20% most stable mRNA species.

In this context it is further preferred to select these mRNA species showing at least 50% (0,5 fold), at least 60% (0,6 fold), at least 70% (0,7 fold), at least 90% (0,9 fold) or at least 95% (0,95 fold) transcript level/amount of the mRNA species at the second later time compared to the first time. This embodiment is particularly preferred if the RNA is isolated at 3 hours (first point in time) and at 15 hours (second point in time) after labelling.

Alternatively or additionally, these mRNA species are selected showing a ratio calculated in step e) corresponding to a least 100% of the average ratio calculated from all mRNA species analyzed. More preferably these mRNA species are selected showing a ratio of at least 150% and more preferably of at least 200% and most preferably of at least 300% of the average ratio calculated from all mRNA species analyzed.

In a further step of the inventive method the nucleotide sequence of the 3'- and/or 5'-UTR of the most stable mRNA species selected in step g) is determined and in step i) the 3'- and/or 5'-UTR element is synthesized e.g. by PCR amplification. The primers used for the PCR may preferably comprise restriction sites for cloning.Alternatively the 3'- and/or 5'-UTR element may be synthesized (e.g. by chemical synthesis or oligo annealing).

In step j) of the inventive method the resulting PCR fragment or synthesized sequence is combined with an open reading frame resulting in an artificial nucleic acid comprising a 3'- and/or 5'-UTR element according to the invention. Preferably, the PCR fragment or sequence may be cloned into a vector.

In a particularly preferred embodiment the invention provides a method comprising the steps a) to k) for identifying 3'-untranslated region elements (3'-UTR elements) and/or 5'-untranslated region elements (5'-UTR elements), wherein the 3'-UTR elements and/or the 5'-UTR elements prolong protein production from an artificial nucleic acid molecule comprising at least one of the 3'-UTR elements and/or at least one of the 5'-UTR elements.

In a further aspect, the present invention also provides a method for generating an artificial nucleic acid molecule, wherein an artificial nucleic acid molecule comprising at least one open reading frame and at least one 3'-UTR element and/or at least one 5'-UTR element identified by a method for identifying a 3'-UTR element and/or a 5'-UTR element according to the present invention as described above is synthesized. Synthesizing of such an artificial nucleic acid molecule is typically carried out by methods known to the skilled person, e.g. cloning methods for example as generally known or described herein.

Preferably, a vector according to the present invention as described herein is used in such an inventive method for generating an artificial nucleic acid molecule.

Preferably, the artificial nucleic acid molecule generated by such a method for generating an artificial nucleic acid molecule is a nucleic acid molecule according to the present invention as described herein.

In addition, the present invention also provides an artificial nucleic acid molecule obtainable by a method for generating an artificial nucleic acid molecule according to the present invention as described herein.

The following Figures, Sequences and Examples are intended to illustrate the invention further. They are not intended to limit the subject matter of the invention thereto.

Figures 1 to 11, 19 to 21 and 25 to 30 show sequences encoding mRNAs that can be obtained by in vitro transcription. The following abbreviations are used:

- PpLuc (GC): GC-enriched mRNA sequence coding for *Photinus pyralis* luciferase
- A64: poly(A)-sequence with 64 adenylates
- C30: poly(C)-sequence with 30 cytidylates
- hSL: a histone stem-loop sequence taken from (Cakmakci, Lerner, Wagner, Zheng, & William F Marzluff, 2008. Mol. Cell. Biol. 28(3):1182-94)
- 32L4: 5′-UTR of human ribosomal protein Large 32 lacking the 5′ terminal oligopyrimidine tract
- albumin7: 3′-UTR of human albumin with three single point mutations introduced to remove a T7 termination signal as well as a HindIII and XbaI restriction site
- gnas: 3′-UTR element derived from the 3′-UTR of murine gnas; Mus musculus GNAS (guanine nucleotide binding protein, alpha stimulating) complex locus (Gnas), mRNA
- morn2: 3′-UTR element derived from the 3′-UTR of murine morn2; Mus musculus MORN repeat containing 2 (Morn2), mRNA
- gstm1: 3′-UTR element derived from the 3′-UTR of murine gstm1; Mus musculus glutathione S-transferase, mu 1 (Gstm1), mRNA
- ndufa1: 3′-UTR element derived from the 3′-UTR of murine ndufa1; Mus musculus NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, (Ndufa1), mRNA
- cbr2: 3′-UTR element derived from the 3′-UTR of murine cbr2; Mus musculus carbonyl reductase 2 (Cbr2), mRNA
- mp68: 5′-UTR element derived from the 5′-UTR of murine mp68; Mus musculus RIKEN cDNA 2010107E04 gene (2010107E04Rik), mRNA
- ndufa4: 5′-UTR element derived from the 5′-UTR of murine nudfa4; Mus musculus NADH dehydrogenase (ubiquinone) 1 alpha subcomplex,4, (Ndufa4), mRNA
- Ybx1: 3′-UTR element derived from the 3′-UTR of murine Ybx1 (Y-Box binding protein 1)
- Ndufb8: 3′-UTR element derived from the 3′-UTR of murine Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8)
- CNTN1: 3′-UTR element derived from the 3′-UTR of human CNTN1 (contactin 1)

Fig. 1: shows SEQ ID NO. 35, i.e. the mRNA sequence of 32L4 – PpLuc(GC) – A64 - C30 - hSL. (R2464). The 5'-UTR is derived of human ribosomal protein Large 32 mRNA lacking the 5' terminal oligopyrimidine tract. The PpLuc(GC) ORF is highlighted in italics.

Fig. 2: shows SEQ ID NO. 36, i.e. the mRNA sequence of 32L4 – PpLuc(GC) – gnas-A64-C30-hSL. (R3089). The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from mouse Gnas transcript, is underlined.

Fig. 3: shows SEQ ID NO. 37, i.e. the mRNA sequence of 32L4 - PpLuc(GC) – morn2–A64 - C30 - hSL. (R3106). The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from mouse morn2, is underlined.

Fig. 4: shows SEQ ID NO. 38, i.e. the mRNA sequence of 32L4 - PpLuc(GC) – gstm1–A64 - C30 - hSL. (R3107). The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from mouse gstm1, is underlined.

Fig. 5: shows SEQ ID NO. 39, i.e. the mRNA sequence of 32L4 - PpLuc(GC) – ndufa1 – A64 - C30 - hSL. (R3108). The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from mouse ndufa1, is underlined.

Fig. 6: shows SEQ ID NO. 40, i.e. the mRNA sequence of 32L4 - PpLuc(GC) – cbr2 – A64 - C30 - hSL. (R3109). The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from mouse cbr2, is underlined.

Fig. 7: shows SEQ ID NO. 41, i.e. the mRNA sequence of PpLuc(GC) - albumin7– A64 - C30 - hSL. (R2463). The 3'-UTR is derived from human albumin with three single point mutations introduced to remove a T7 termination signal as well as a HindIII and XbaI restriction site (albumin7). The PpLuc(GC) ORF is highlighted in italics.

Fig. 8: shows SEQ ID NO. 42, i.e. the mRNA sequence of Mp68 - PpLuc(GC) - albumin7–A64 - C30 - hSL. (R3111). The PpLuc(GC) ORF is highlighted in italics. The 5'-UTR element, which is derived from mouse mp68, is underlined.

Fig. 9: shows SEQ ID NO. 43, i.e. the mRNA sequence of Ndufa4 - PpLuc(GC) - albumin7– A64 - C30 - hSL. (R3112). The PpLuc(GC) ORF is highlighted in italics. The 5'-UTR element, which is derived from mouse Ndufa4, is underlined.

Fig. 10: shows SEQ ID NO. 44, i.e. the mRNA sequence of PpLuc(GC) – A64 - C30 - hSL (R2462) The PpLuc(GC) ORF is highlighted in italics.

Fig. 11: shows SEQ ID NO. 45, i.e. the mRNA sequence of PpLuc(GC) – gnas- A64 - C30 – hSL (R3116). The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from mouse Gnas, is underlined.

Fig. 12: shows that different 3'-UTR elements, namely 3'-UTR elements derived from gnas, morn2, gstm1, ndufa1 and cbr2 markedly prolong protein expression from mRNA. The effect of the inventive 3'-UTR elements derived from gnas, morn2, gstm1, ndufa1 and cbr2 3'-UTRs on luciferase expression from mRNA was examined, compared to luciferase expression from mRNA lacking a 3'-UTR. To this end, human HeLa were transfected with different mRNAs by lipofection. Luciferase levels were measured at different times after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Normalized PpLuc levels at 24h were set to 100% and relative expression to 24h was calculated. The 3'-UTRs prolong luciferase expression. Mean values from three independent experiments are shown. Values are summarized in Example 7.a.

Fig. 13: shows that different 3'-UTR elements, namely 3'-UTR elements derived from gnas, morn2, gstm1, ndufa1 and cbr2 markedly prolong protein expression from mRNA. The effect of the inventive 3'-UTR elements derived from gnas, morn2, gstm1, ndufa1 and cbr2 3'-UTRs on luciferase expression from mRNA was examined, compared to luciferase expression from mRNA lacking a 3'-UTR. To this end, HDF (human dermal fibroblasts) cells were transfected with different mRNAs by lipofection. Luciferase levels were measured at different times after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of

cotransfected RrLuc. Normalized PpLuc levels at 24h were set to 100% and relative expression to 24h was calculated. The 3'-UTRs prolong luciferase expression. Mean values from three independent experiments are shown. Values are summarized in Example 7.a.

Fig. 14: shows that different 5'-UTR elements, namely 5'-UTR elements derived from Mp68 and ndufa4 markedly increase total protein expression from mRNA.
The effect of the inventive 5'-UTR elements derived from Mp68 and ndufa4 on luciferase expression from mRNA was examined. To this end, human HeLa cells were transfected with different mRNAs by lipofection. Luciferase levels were measured 6, 24, 48, and 72 hours after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Total protein expression (area under the curve) was calculated. To compare the expression levels of the mRNAs containing the inventive 5'-UTR elements to an mRNA lacking a 5'-UTR, expression levels of the control construct without 5' UTR was set to 1. Mean values from three independent experiments are shown. Values are summarized in Example 7.b.

Fig. 15: shows that different 5'-UTR elements, namely 5'-UTR elements derived from Mp68 and ndufa4 markedly increase total protein expression from mRNA.
The effect of the inventive 5'-UTR elements derived from Mp68 and ndufa4 on luciferase expression from mRNA was examined. To this end, HDF cells were transfected with different mRNAs by lipofection. Luciferase levels were measured 6, 24, 48, and 72 hours after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Total protein expression (area under the curve) was calculated. To compare the expression levels of the mRNAs containing the inventive 5'-UTR elements to an mRNA lacking a 5'-UTR, expression levels of the control construct without 5' UTR was set to 1. Mean values from three independent experiments are shown. Values are summarized in Example 7.b.

Fig. 16: shows that the 3'-UTR element derived from gnas markedly prolongs protein expression from mRNA.

The effect of the inventive 3'-UTR element derived from gnas 3'-UTR on luciferase expression from mRNA was examined, compared to luciferase expression from mRNA lacking a 3'-UTR. To this end, HDF cells were transfected with respective mRNAs by lipofection. Luciferase levels were measured at 24, 48, and 72 hours after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Normalized PpLuc levels at 24h were set to 100% and relative expression to 24h was calculated. The gnas 3'-UTR prolongs luciferase expression. Values are summarized in Example 7.c.

Fig. 17: shows that the 3'-UTR element derived from gnas markedly prolongs protein expression from mRNA.

The effect of the inventive 3'-UTR element derived from gnas 3'-UTR on luciferase expression from mRNA was examined, compared to luciferase expression from mRNA lacking a 3'-UTR. To this end, HeLa cells were transfected with respective mRNAs by lipofection. Luciferase levels were measured at d2 and d3 after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Normalized PpLuc levels at 24h were set to 100% and relative expression to 24h was calculated. The gnas 3'-UTR prolongs luciferase expression. Values are summarized in Example 7.c.

Fig. 18: shows that different 3'-UTR elements, namely 3'-UTR elements derived from ybx1(V2), ndufb8, and cntn1-004(V2) markedly prolong protein expression from mRNA.

The effect of the inventive 3'-UTR elements derived from ybx1(V2), ndufb8, and cntn1-004(V2) 3'-UTRs on luciferase expression from mRNA was examined, compared to luciferase expression from mRNA lacking a 3'-UTR. To this end, HDF cells were transfected with the different mRNAs by lipofection. Luciferase levels were measured at different times after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Normalized PpLuc levels at 24h were set to 100% and relative expression to 24h was calculated. The 3'-UTRs prolong luciferase expression. Values are summarized in Example 7.d.

Fig. 19: shows SEQ ID NO. 46 , i.e. the mRNA sequence of 32L4 – PpLuc(GC) – Ybx1-001(V2)-A64-C30-hSL (R3623) mus musculus 3´UTR with mutation T128bpG and deletion del236-237bp. The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from mouse Ybx1 transcript, is underlined.

Fig. 20: shows SEQ ID NO. 47, i.e. the mRNA sequence of 32L4 – PpLuc(GC) – Ndufb8-A64-C30-hSL (R3624) The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from mouse Ndufb8 transcript, is underlined.

Fig. 21: shows SEQ ID NO. 48, i.e. the mRNA sequence of 32L4 – PpLuc(GC) – Cntn1-004(V2)-A64-C30-hSL (R3625) +T at pos. 30bp, mutations G727bpT, A840bpG. The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from human Cntn1 transcript, is underlined.

Fig. 22: shows that different 3'-UTR elements, namely 3'-UTR elements derived from gnas, morn2, ndufa1 (Mm; mus musculus), and NDUFA1 (Hs; homo sapiens) markedly prolong protein expression from mRNA. The effect of the inventive 3'-UTR elements derived from gnas, morn2, ndufa1 (Mm; mus musculus), and NDUFA1 (Hs; homo sapiens) on luciferase expression from mRNA was examined, compared to luciferase expression from mRNA lacking a 3'-UTR. To this end, human Hela cells were transfected with respective mRNAs by lipofection. Luciferase levels were measured at different times after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Normalized PpLuc levels at 24h were set to 100% and relative expression to 24h is calculated. The 3'UTRs prolong luciferase expression. Mean values from 3 independent experiments are shown. Values are summarized in Table 8.

Fig. 23: shows that different 5'-UTR elements, namely 5'-UTR elements derived from Mp68 and ndufa4, markedly increase total protein expression from mRNA. The effect of the inventive 5'-UTR elements derived from Mp68 and ndufa4 on luciferase expression from mRNA was examined. To this end, human HeLa cells were transfected with different mRNAs by lipofection. Luciferase levels were measured 6, 24, 48, and 72 hours after transfection. The PpLuc signal was

corrected for transfection efficiency by the signal of cotransfected RrLuc. Total protein expression (area under the curve) was calculated. To compare the expression levels of the mRNAs containing the inventive 5'-UTR elements to an mRNA lacking a 5'-UTR, expression levels of the control construct without 5' UTR was set to 1. Mean values are shown. Values are summarized in Table 9.

Fig. 24: shows that different 5'-UTR elements, namely 5'-UTR elements derived from Mp68 and ndufa4, markedly increase total protein expression from mRNA. The effect of the inventive 5'-UTR elements derived from Mp68 and ndufa4 on luciferase expression from mRNA was examined. To this end, human Hela cells were transfected with different mRNAs by lipofection. Luciferase levels were measured 24, 48, and 72 hours after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Total protein expression (area under the curve) was calculated. To compare the expression levels of the mRNAs containing the inventive 5'-UTR elements to an mRNA lacking a 5'-UTR, expression levels of the control construct without 5' UTR was set to 1. Mean values are shown. Values are summarized in Table 9.

Fig. 25: shows SEQ ID NO. 383, i.e. the mRNA sequence of 32L4 – PpLuc(GC) – A64-C30-hSL (R2462). The PpLuc(GC) ORF is highlighted in italics.

Fig. 26: shows SEQ ID NO. 384, i.e. the mRNA sequence of PpLuc(GC) – morn2– A64 - C30 - hSL. (R3948). The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from murine morn2 is underlined.

Fig. 27: shows SEQ ID NO. 385, i.e. the mRNA sequence of PpLuc(GC) – ndufa1– A64 - C30 - hSL. (R4043). The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from murine ndufa1 is underlined.

Fig. 28: shows SEQ ID NO. 386, i.e. the mRNA sequence of PpLuc(GC) – NDFUA1– A64 - C30 - hSL. (R3948). The PpLuc(GC) ORF is highlighted in italics. The 3'-UTR element, which is derived from human NDUFA1 is underlined.

Fig. 29: shows SEQ ID NO. 387, i.e. the mRNA sequence of Mp68 - PpLuc(GC) – A64 - C30 - hSL. (R3954). The PpLuc(GC) ORF is highlighted in italics. The 5'-UTR element, which is derived from murine mp68 is underlined.

Fig. 30: shows SEQ ID NO. 388, i.e. the mRNA sequence of Ndufa4 - PpLuc(GC) – A64 - C30 - hSL. (R3951). The PpLuc(GC) ORF is highlighted in italics. The 5'-UTR element, which is derived from murine ndufa4 is underlined.

Examples

1. Identification of 3'-untranslated region elements (3'-UTR elements) and/or 5'-untranslated region elements (5'-UTR elements) prolonging and/or increasing protein production:

mRNA decay in different human and murine cell types was assessed by pulse-chase methodology. To this end, three different human cell types (HeLa, HDF and U-937) and three different mouse cell types (NIH3T3, JAWSII and L929) were plated over night in their respective medium: HeLa, U-937, L929 in RPMI medium, JAWSII und NIH3T3 in DMEM and HDF in Fibroblast Growth Medium 2. The cells were incubated for 3 h with the respective medium containing 200 µM 4-thiouridine (4sU) for labelling of newly synthesized RNA ("pulse"). After incubation (labelling), cells are washed once and the medium was replaced by fresh medium supplemented with 2mM Uridine ("chase"). Cells were incubated further for 3 h (1st point in time) or 15 h (2nd point in time) before harvesting.

Accordingly, cells were harvested 3 h (1st point in time) and 15 h (2nd point in time) after end of labelling. The total RNA was isolated from these cells using RNeasy Mini Kit (Qiagen).

HPDP-Biotin (EZ-Link Biotin-HPDP, Thermo Scientific; pyridyldithiol-activated, sulfhydryl-reactive biotinylation reagent that conjugates via a cleavable (reversible) disulfide bond) was then incubated with the total RNA in order to extract the 4-thiouridine (4sU)-labelled RNA. HPDP-Biotin specifically reacts with the reduced thiols (-SH) in the 4-thiouridine (4sU)-labelled RNA to form reversible disulfide bonds. The biotinylated RNA was ultrafiltrated using

an Amicon-30 device, incubated with streptavidin-coupled dynabeads (Life Technologies) and recovered from streptavidin by DTT. Subsequently, the RNA was purified using RNeasy Mini Kit. For each cell line 3 independent experiments were performed.

The extracted 4sU-labelled RNA was used in a micro array analysis in order to determine the transcript levels of a large variety of mRNA species (i.e. the amounts of the mRNA species) present at a first point in time (3 h after labelling) and the transcript levels of a large variety of mRNA species (i.e. the amounts of the mRNA species) present at a second point in time (15 h after labelling). Affymetrix Human Gene 1.0 ST and Affymetrix Mouse Gene 1.0 ST micro arrays were used. Affymetrix Human Gene 1.0 ST comprises 36079 mRNA species. Affymetrix Mouse Gene 1.0 ST comprises 26166 mRNA species.

Since these micro arrays provide a whole transcript coverage, i.e. they provide a complete expression profile of mRNA, the ratio of the transcript level of a certain mRNA species at the second point in time to the transcript level of the same mRNA species at the first point in time was accordingly determined for a large number of mRNA species. The ratios thus reflect the x-fold transcript level of the mRNA species (shown as Gene Symbol) at the second point in time as compared to the first point in time.

The results from these experiments are shown in Tables 1 – 3 below. Each of the Tables 1 – 3 shows a ranking of the most stable mRNA species, i.e. according to the ratio of the transcript level of this mRNA species at the second point in time to the transcript level of this mRNA species at the first point in time (Table 1: combined analysis of human cell types (HeLa, HDF and U-937); Table 2: combined analysis of mouse cell lines (NIH3T3, JAWSII and L929); Table 3: human cell line HDF (human dermal fibroblasts)). Such mRNA species were considered as "most stable mRNA species", which show a value for the ratio of the transcript level at the first point in time/ the transcript level at the second point in time of at least 0,549943138 (approximately 55%; Table 1), 0,676314425 (approximately 68%, Table 2) or 0,8033973 (approximately 80%, Table 3).

Furthermore, the relationship of the ratio of a certain mRNA species to the average ratio (i.e. the average of the ratios of all mRNA species determined, which is shown in the Tables as "Average of the ratio") was calculated and given as % of average.

Table 1: stable mRNAs resulting from the combined analysis of human cell types (HeLa, HDF and U-937) with the Affymetrix Human Gene 1.0 ST micro array. 113 mRNA species of the 36079 mRNA species on the micro array were selected as "most stable" mRNA species. This corresponds to 0,31% of the mRNA species present on the micro array.

Gene symbol	Ratio of the transcript level at the 2nd time to the transcript level at the 1st time	Average of the ratio	% of average
LTA4H	0,982490359	0,258826017	379,5948991
SLC38A6	0,953694877		368,4694789
DECR1	0,927429689		358,3216631
PIGK	0,875178367		338,1338462
FAM175A	0,849392515		328,1712266
PHYH	0,827905031		319,8693239
NT5DC1	0,815986179		315,2643572
TBC1D19	0,805960687		311,3909086
PIGB	0,805108608		311,0616997
ALG6	0,804875859		310,9717748
CRYZ	0,797694475		308,1971756
BRP44L	0,796150905		307,6008021
ACADSB	0,792385554		306,1460216
SUPT3H	0,792305264		306,1150005
TMEM14A	0,792128439		306,0466827
GRAMD1C	0,78766459		304,3220303
C11orf80	0,778391775		300,739386
C9orf46	0,776061355		299,8390053
ANXA4	0,765663559		295,8217134
RAB7A	0,757621668		292,7146492
TBCK	0,753324047		291,0542204
AGA	0,751782245		290,4585303
IFI6	0,742389518		286,829557
C2orf34	0,737633511		284,9920263
TPK1	0,731359535		282,5680135
ALDH6A1	0,731062569		282,4532776
AGTPBP1	0,725606511		280,3452757
CCDC53	0,725535697		280,3179158
LRRC28	0,722761729		279,2461657
MBNL3	0,716905277		276,9834674
CCDC109B	0,713320794		275,5985668

Gene symbol	Ratio of the transcript level at the 2nd time to the transcript level at the 1st time	Average of the ratio	% of average
PUS10	0,70905743		273,9513739
CCDC104	0,706185858		272,8419137
CASP1	0,699081435		270,0970494
SNX14	0,689529842		266,4066965
SKAP2	0,686417578		265,2042424
NDUFB6	0,683568924		264,1036366
EFHA1	0,680321463		262,8489478
BCKDHB	0,679714289		262,6143601
BBS2	0,677825758		261,8847077
LMBRD1	0,676629332		261,4224565
ITGA6	0,660264393		255,0996998
HERC5	0,654495807		252,8709496
HADHB	0,651220796		251,6056164
MCCC2	0,650460461		251,3118537
CAT	0,647218183		250,0591672
ANAPC4	0,646761056		249,8825517
PCCB	0,641145931		247,7130926
PHKB	0,639806797		247,1957046
ABCB7	0,639415266		247,0444329
PGCP	0,636830107		246,0456309
GPD2	0,63484437		245,2784217
TMEM38B	0,634688463		245,2181856
NFU1	0,63202654		244,1897253
OMA1	0,631592924		244,0221934
LOC128322	0,630915328		243,7603974
NUBPL	0,627949735		242,6146113
LANCL1	0,627743069		242,5347636
HHLA3	0,62723119		242,3369941
PIR	0,625871255		241,8115696
ACAA2	0,624054189		241,1095284
CTBS	0,621758355		240,22251
GSTM4	0,618559637		238,9866536
ALG8	0,617468882		238,5652294
ACTR10	0,614629804		237,4683237
PIGF	0,612863425		236,7858655
MGST3	0,607459796		234,6981198
SCP2	0,604745109		233,6492735
HPRT1	0,604586436		233,5879689

Gene symbol	Ratio of the transcript level at the 2nd time to the transcript level at the 1st time	Average of the ratio	% of average
ACSF2	0,603568827		233,1948052
VPS13A	0,60079506		232,1231332
CTH	0,598492068		231,2333494
NXT2	0,597938464		231,0194589
MGST2	0,596121512		230,3174615
C11orf67	0,59596274		230,2561181
PCCA	0,595915054		230,2376943
GLMN	0,594596168		229,7281295
DHRS1	0,594391166		229,6489249
PON2	0,594025719		229,5077308
NME7	0,593140523		229,1657265
ETFDH	0,59290737		229,0756456
ALG13	0,591519568		228,5394547
DDX60	0,590567649		228,1716714
DYNC2LI1	0,590400874		228,1072359
VPS8	0,586233686		226,4972016
ITFG1	0,585791975		226,3265424
CDK5	0,584517109		225,8339853
C1orf112	0,58415003		225,6921603
IFT52	0,579757269		223,9949738
CLYBL	0,577777391		223,230028
FAM114A2	0,575975081		222,533688
NUDT7	0,575398988		222,3111085
AKD1	0,57519887		222,233791
MAGED2	0,575157132		222,217665
HRSP12	0,574805797		222,0819235
STX8	0,573508131		221,5805571
ACAT1	0,569067306		219,8648003
IFT74	0,568627867		219,695019
KIFAP3	0,567709483		219,3401921
CAPN1	0,567537877		219,2738902
COX11	0,566354405		218,8166442
GLT8D4	0,566035014		218,6932442
HACL1	0,56371793		217,7980159
IFT88	0,562663344		217,3905661
NDUFB3	0,561240987		216,8410243
ANO10	0,561096127		216,7850564
ARL6	0,560155258		216,4215424

Gene symbol	Ratio of the transcript level at the 2nd time to the transcript level at the 1st time	Average of the ratio	% of average
LPCAT3	0,559730076		216,2572689
ABCD3	0,55747212		215,3848853
COPG2	0,557180095		215,2720583
MIPEP	0,554396343		214,1965281
LEPR	0,551799358		213,1931572
C2orf76	0,549943138		212,4759882

Table 2: stable mRNAs resulting from the combined analysis of mouse cell lines (NIH3T3, JAWSII and L929) with the Affymetrix Mouse Gene 1.0 ST micro array: 99 mRNA species of the 26166 mRNA species on the micro array were selected as the "most stable" mRNA species. This corresponds to 0,38% of the mRNA species present on the micro array.

ene symbol	Ratio of the transcript level at the 2nd time to the transcript level at the 1st time	Average of the ratio	% of average
Ndufa1	1,571557917	0,209425963	750,4121719
Atp5e	1,444730129		689,8524465
Gstm5	1,436992822		686,1579154
Uqcr11	1,221605816		583,3115431
Ifi27l2a	1,203811772		574,8149632
Cbr2	1,162403907		555,0428852
Anapc13	1,153679871		550,8771953
Atp5l	1,126858713		538,0702074
Tmsb10	1,048459674		500,6350022
Nenf	1,045891853		499,4088786
Ndufa7	1,03898238		496,1096349
Atp5k	1,03623698		494,7987179
1110008P14Rik	1,029513775		491,5884162
Cox4i1	0,991815573		473,5876865
Cox6a1	0,991620272		473,4944312
Ndufs6	0,989419978		472,4438002
Sec61b	0,984420709		470,0566705
Romo1	0,981642576		468,7301241
Gnas	0,969128675		462,7547898
Snrpd2	0,962862199		459,7625743
Mgst3	0,96060161		458,6831531
Aldh2	0,949761281		453,5069425
2010107E04Rik	0,933570825		445,776069
Ssr4	0,930263069		444,1966294
Myl6	0,920572238		439,5692993
Prdx4	0,914830854		436,8278128
Ubl5	0,902505176		430,9423544
1110001J03Rik	0,888041155		424,0358468
Ndufa13	0,881735594		421,0249684
Ndufa3	0,880861551		420,6076163
Gstp2	0,87970004		420,0529997
Tmem160	0,878001416		419,2419142
Ergic3	0,87481135		417,7186716
Pgcp	0,870441149		415,6319192
Slpi	0,868909664		414,9006418
Myeov2	0,868175997		414,5503186
Ndufa4	0,862009116		411,6056594
Ndufs5	0,857586364		409,4938143

Gstm1	0,856672742		409,0575637
1810027O10Rik	0,855929863		408,7028424
Atp5o	0,848957424		405,3735324
Shfm1	0,841951399		402,0281856
Tspo	0,840567742		401,3674952
S100a6	0,840163495		401,1744691
Taldo1	0,8400757		401,1325475
Bloc1s1	0,838838894		400,541978
Hexa	0,826597959		394,6969835
Ndufb11	0,821601877		392,311376
Map1lc3a	0,816696063		389,968871
Morn2	0,810862522		387,18338
Gpx4	0,808459051		386,0357329
Mif	0,804105552		383,9569558
Cox6b1	0,803409855		383,6247633
2900010J23Rik	0,802900813		383,3816981
Sec61g	0,797138268		380,6301077
2900010M23Rik	0,793618387		378,9493795
Anapc5	0,793224505		378,7613023
Mars2	0,787395376		375,9779182
Phpt1	0,785668786		375,153479
Ndufb8	0,784300334		374,5000492
Pfdn5	0,779021933		371,9796349
Arpc3	0,77876305		371,8560197
Ndufb7	0,774103875		369,6312833
Atp5h	0,772255845		368,7488573
Mrpl23	0,77034041		367,834245
Tomm6	0,75481818		360,4224467
Mtch1	0,752594518		359,3606576
Pcbd2	0,752256847		359,199421
Ecm1	0,752254099		359,1981094
Hrsp12	0,749135357		357,708923
Mecr	0,746269148		356,3403207
Uqcrq	0,734462177		350,7025426
Gstm3	0,733839044		350,4049993
Lsm4	0,732100345		349,5747779
Park7	0,7307842		348,9463242
Usmg5	0,724562823		345,9756436
Cox8a	0,720194618		343,8898445
Ly6c1	0,716087602		341,9287619
Cox7b	0,713519017		340,7022736
Ppib	0,706106711		337,1629288

Bag1	0,70488561		336,5798584
S100a4	0,701675201		335,046902
Bcap31	0,700846929		334,6514056
Tecr	0,699592215		334,0522852
Rabac1	0,699161282		333,8465165
Robld3	0,694068018		331,4145049
Sod1	0,691852987		330,356837
Nedd8	0,691415017		330,1477083
Higd2a	0,689498548		329,2326025
Trappc6a	0,688046277		328,5391491
Ldhb	0,686084572		327,6024437
Nme2	0,685974394		327,5498339
Snrpg	0,684247073		326,7250454
Ndufa2	0,683350661		326,2970129
Serf1	0,681148053		325,2452768
Oaz1	0,681139695		325,2412861
Ybx1	0,678927132		324,1847964
Sepp1	0,677551422		323,5279009
Gaa	0,676314425		322,9372402

Table 3: stable mRNAs resulting from the analysis of the human cell line HDF (human dermal fibroblasts) with the Affymetrix Human Gene 1.0 ST micro array: 46 mRNA species of the 36079 mRNA species on the micro array were selected as the "most stable" mRNA species. This corresponds to 0,13% of the mRNA species present on the micro array.

Gene symbol	Ratio of the transcript level at the 2nd time to thetranscript level at the 1st time	Average of the ratio	% of average
ABCA6	2,062835692	0,278262352	741,3276273
LY96	1,719983635		618,1158256
CROT	1,422424006		511,1809038
ENPP5	1,315849211		472,880791
SERPINB7	1,12288882		403,5360196
TCP11L2	1,103519648		396,5752607
IRAK1BP1	1,05490107		379,1030521
CDKL2	1,042002646		374,4677057
GHR	1,039327135		373,5061992
KIAA1107	1,020519239		366,7471477
RPS6KA6	1,017695602		365,7324085
CLGN	1,007943464		362,2277524
TMEM45A	1,006063873		361,5522781
TBC1D8B	0,979626826		352,0515148
ACP6	0,964241225		346,5223439
RP6-213H19.1	0,960702414		345,2505905
C11orf74	0,960086216		345,0291458
SNRPN	0,939315038		337,5645433
GLRB	0,923441342		331,8599644
HERC6	0,919865006		330,5747254
CFH	0,908835974		326,6111879
GALC	0,90862766		326,5363257
PDE1A	0,908445187		326,4707497
GSTM5	0,902862912		324,4646303
CADPS2	0,89753131		322,5485959
AASS	0,894768872		321,5558503
TRIM6-TRIM34	0,892150571		320,6149031
SEPP1	0,891344657		320,3252795
PDE5A	0,890221551		319,9216656
SATB1	0,885139895		318,0954552
CCPG1	0,88148167		316,7807873
CNTN1	0,87246423		313,5401621
LMBRD2	0,871500964		313,1939903
TLR3	0,86777981		311,8567077
BCAT1	0,864255836		310,5902863
TOM1L1	0,86240499		309,925142
SLC35A1	0,857201353		308,055095
GLYATL2	0,85132258		305,9424223

STAT4	0,840572034		302,0789653
GULP1	0,839518351		301,7003001
EHHADH	0,82971807		298,1783427
NBEAL1	0,82554089		296,6771768
KIAA1598	0,820341324		294,8085928
HFE	0,815037603		292,9025779
KIAA1324L	0,808279102		290,4737547
MANSC1	0,8033973		288,7193664

2. Cloning of 5'- and 3'-UTR elements of stably expressed mRNAs:

The nucleotide sequence of the 5'- and/or 3'-UTRs of the mRNA species shown in Table 1 – 3 were determined by data base search and amplified by PCR or synthesized by oligo annealing. The resulting PCR fragments were cloned into a vector as described in detail in Example 3 below. 5'-UTR elements were cloned into the vector PpLuc(GC) – albumin7 – A64 – C30 – hSL (SEQ ID NO. 41, Fig. 7); and 3'-UTR elements were cloned into the vector 32L4 – PpLuc(GC) – A64 – C30 – hSL (SEQ ID NO. 35, Fig. 1) or into the vector PpLuc(GC) – A64 – C30 – hSL (SEQ ID NO. 44, Fig. 10).

3. Preparation of DNA-templates

A vector for *in vitro* transcription was constructed containing a T7 promoter and a GC-enriched sequence coding for *Photinus pyralis* luciferase (PpLuc(GC)). An A64 poly(A) sequence, followed by C30 and a histone stem-loop sequence, was inserted 3' of PpLuc(GC). The histone stem-loop sequence was followed by a restriction site used for linearization of the vector before in vitro transcription.

To investigate the effect of different 3'-UTR elements on protein expression, a vector as described above was used (control) and this vector was modified to include a 3'-UTR element of interest. Alternatively, a vector was constructed as described above, whereby the 5' untranslated region (5'-UTR) of 32L4 (ribosomal protein Large 32) was inserted 5' of PpLuc(GC). This vector was then modified to include either different 3'-UTR elements or no 3'-UTR (control).

Particularly, the following mRNAs were obtained from these vectors accordingly by *in vitro* transcription (the mRNA sequences are depicted in Figures 1 to 6, Figures 10, 11 and Figures 19 to 21):

32L4 – PpLuc(GC) – A64 – C30 – hSL (SEQ ID NO. 35, Fig. 1);
32L4 – PpLuc(GC) – gnas – A64 – C30 – hSL (SEQ ID NO. 36, Fig. 2);
32L4 – PpLuc(GC) – morn2 – A64 – C30 – hSL (SEQ ID NO. 37, Fig. 3);
32L4 – PpLuc(GC) – gstm1 – A64 – C30 – hSL (SEQ ID NO. 38, Fig. 4);
32L4 – PpLuc(GC) – ndufa1 – A64 – C30 – hSL (SEQ ID NO. 39, Fig. 5);
32L4 – PpLuc(GC) – cbr2 – A64 – C30 – hSL (SEQ ID NO. 40, Fig. 6);
PpLuc(GC) – A64 – C30 – hSL (SEQ ID NO. 44, Fig. 10);
PpLuc(GC) – gnas – A64 – C30 – hSL (SEQ ID NO. 45, Fig. 11);
32L4 – PpLuc(GC) – Ybx1(V2)-A64-C30-hSL (SEQ ID NO. 46, Fig. 19);
32L4 – PpLuc(GC) – Ndufb8-A64-C30-hSL (SEQ ID NO. 47, Fig. 20); and
32L4 – PpLuc(GC) – Cntn1-004(V2)-A64-C30-hSL (SEQ ID NO. 48, Fig. 21).

An alternative sequence for the construct 32L4 – PpLuc(GC) – A64 – C30 – hSL is shown in Fig. 25 (SEQ ID NO. 383). However, SEQ ID NO. 35, Fig. 1 was used in the Examples as described herein and is, thus, preferred for the construct 32L4 – PpLuc(GC) – A64 – C30 – hSL.

To investigate the effect of different 5'-UTR elements on protein expression, a vector was constructed as described above, whereby the 3' untranslated region (3'-UTR) of albumin7 (3'-UTR of human albumin with three single point mutations introduced to remove a T7 termination signal as well as a HindIII and XbaI restriction site) was inserted 3' of PpLuc(GC). This vector was modified to include either different 5'-UTR elements or no 5'-UTR (control).

Particularly, the following mRNAs were obtained from these vectors accordingly by *in vitro* transcription (the mRNA sequences are depicted in Figures 7 to 9):

PpLuc(GC) – albumin7 – A64 – C30 – hSL (SEQ ID NO. 41, Fig. 7);
Mp68 – PpLuc(GC) – albumin7 – A64 – C30 – hSL (SEQ ID NO. 42, Fig. 8); and
Ndufa4 – PpLuc(GC) – albumin7 – A64 – C30 – hSL (SEQ ID NO. 43, Fig. 9);

4. *In vitro* transcription

The DNA templates according to Example 2 and 3 were linearized and transcribed *in vitro* using T7-RNA polymerase. The DNA templates were then digested by DNase-treatment. mRNA transcripts contained a 5'-CAP structure obtained by adding an excess of N7-Methyl-Guanosine-5'-Triphosphate-5'-Guanosine to the transcription reaction. mRNA thus obtained was purified and resuspended in water.

5. Luciferase expression by mRNA lipofection

Human dermal fibroblasts (HDF) and HeLa cells were seeded in 96 well plates at a density of $1x10^4$ cells per well. The following day, cells were washed in Opti-MEM and then transfected with 12.5 ng per well of Lipofectamine2000-complexed PpLuc-encoding mRNA in Opti-MEM. Untransfected cells served as control. mRNA coding for *Renilla reniformis* luciferase (RrLuc) was transfected together with PpLuc mRNA to control for transfection efficiency (1 ng of RrLuc mRNA per well). 90 minutes after start of transfection, Opti-MEM was exchanged for medium. 6, 24, 48, 72 hours after transfection, medium was aspirated and cells were lysed in 100 µl of Passive Lysis buffer (Promega). Lysates were stored at -80°C until luciferase activity was measured.

6. Luciferase measurement

Luciferase activity was measured as relative light units (RLU) in a Hidex Chameleon plate reader. The activities of Ppluc and Rrluc are measured sequentially from a single sample in a dual luciferase assay. The PpLuc activity was measured first at 2 seconds measuring time using 20 µl of lysate and 50 µl of Beetle juice (pjk GmbH). After 1500ms delay RrLuc activity is measured with 50 µl Renilla juice (pjk GmbH).

7. Results

a. Protein expression from mRNA containing 3'-UTR elements according to the invention is increased and/or prolonged.

To investigate the effect of various 3'-UTR elements on protein expression from mRNA, mRNAs containing different 3'-UTR elements were compared to an mRNA lacking a 3'-UTR.

Human HeLa and HDF cells were transfected with Luciferase encoding mRNAs and Luciferase levels (in RLU) were measured 6, 24, 48, and 72 hours after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Normalized PpLuc levels at 24h were set to 100% and relative expression to 24h is calculated (see following Table 4 and Figures 12 (HeLa cells) and 13 (HDF cells)).

Table 4:

mRNA	HeLa			HDF		
	24h	48h	72h	24h	48h	72h
32L4-PpLuc(GC)-A64-C30-hSL	100	12,3	2,7	100	34,8	10,9
32L4-PpLuc(GC)-gnas-A64-C30-hSL	100	50,5	30,9	100	79,8	27,8
32L4-PpLuc(GC)-morn2-A64-C30-hSL	100	32,9	10,5	100	44,5	14,6
32L4-PpLuc(GC)-gstm1-A64-C30-hSL	100	24,8	7,6	100	46,5	21,4
32L4-PpLuc(GC)-ndufa1-A64-C30-hSL	100	29,4	10,6	100	41,9	13,9
32L4-PpLuc(GC)-cbr2-A64-C30-hSL	100	21,9	4,9	100	60,0	23,2

Table 4 shows relative PpLuc expression normalized to RrLuc (mean values of three independent experiments are given).

Luciferase was expressed from mRNA lacking a 3'-UTR. However, the inventive 3'-UTR elements gnas, morn2, gstm1, ndufa and cbr2 significantly prolonged luciferase expression.

b. Protein expression from mRNA containing 5'-UTR elements according to the invention is increased and/or prolonged.

To investigate the effect of various 5'-UTR elements on protein expression from mRNA, mRNAs containing different 5'-UTRs were compared to an mRNA lacking a 5'-UTR.

Human HeLa and HDF cells were transfected with Luciferase encoding mRNAs and Luciferase levels were measured 6, 24, 48, and 72 hours after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Total protein expression from 0 to 72 hours was calculated as the area under the curve (AUC). The levels of the control construct without 5' UTR was set to 1 (see following Table 5 and Figure 14 (HeLa cells) and 15 (HDF cells)).

Table 5:

mRNA	AUC HeLa	AUC HDF
PpLuc(GC)-albumin7-A64-C30-hSL	1,00	1,07
Mp68-PpLuc(GC)-albumin7-A64-C30-hSL	1,79	3,03
Ndufa4-PpLuc(GC)-albumin7-A64-C30-hSL	1,92	2,83

Table 5 shows the total PpLuc expression normalized to RrLuc (mean values of three independent experiments are given).

Luciferase was expressed from mRNA lacking a 5'-UTR. However, the inventive 5'-UTR elements mp68 and ndufa4 significantly increased luciferase expression.

c. Protein expression from mRNA containing 3'-UTR elements according to the invention is prolonged.

To investigate the effect of various 3'UTRs on protein expression from mRNA, mRNAs containing different 3'UTRs were compared to an mRNA lacking a 3'UTR.

Human HeLa and HDF cells were transfected with Luciferase encoding mRNAs and Luciferase levels (in RLU) were measured 24, 48, and 72 hours after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Normalized PpLuc levels at 24h were set to 100% and relative expression to 24h is calculated (see following Table 6 and Figures 16 (HeLa cells) and 17 (HDF cells)).

Table 6:

mRNA	HeLa			HDF		
	24h	48h	72h	24h	48h	72h
PpLuc(GC)-gnas-A64-C30-hSL	100	61,1	30,3	100	53,6	34,2
PpLuc(GC)-A64-C30-hSL	100	17,1	2,7	100	29,0	12,4

Table 6 shows relative PpLuc expression normalized to RrLuc (mean values of three independent experiments are given).

d. Protein expression from mRNA containing 3'-UTR elements according to the invention is prolonged.

To investigate the effect of various 3'UTRs on protein expression from mRNA, mRNAs containing different 3'UTRs were compared to an mRNA lacking a 3'UTR.

Human HeLa and HDF cells were transfected with Luciferase encoding mRNAs and Luciferase levels were measured 6, 24, 48, and 72 hours after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Total protein expression from 0 to 72 hours was calculated as the area under the curve (AUC). The levels of the control construct without 5' UTR was set to 1 (see following Table 7 and Figure 18 (HDF cells) and 17 (HeLa cells)).

Human HeLa and HDF cells were transfected with Luciferase encoding mRNAs and Luciferase levels (in RLU) were measured 24, 48, and 72 hours after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Normalized PpLuc levels at 24h were set to 100% and relative expression to 24h is calculated (see following Table 7 and Figure 18 (HDF cells)).

Table 7:

mRNA	HDF		
	24h	48h	72h
32L4-PpLuc(GC)-Ybx1-001(V2)-A64-C30-hSL	100	57,0	28,5
32L4-PpLuc(GC)-Ndufb8-A64-C30-hSL	100	65,4	37,6

32L4-PpLuc(GC)-Cntn1004(V2)-A64-C30-hSL	100	71,0	47,7
32L4-PpLuc(GC)-A64-C30-hSL	100	45,2	21,87

Table 7 shows relative PpLuc expression normalized to RrLuc (mean values of three independent experiments are given).

8. Effect of further 3'UTRs on protein expression

To further investigate the effect of various 3'UTRs on protein expression from mRNA, new mRNA constructs were prepared and those mRNAs containing different 3'UTRs were compared to an mRNA lacking a 3'UTR.

To this end, selected 3'-UTR elements (gnas, morn2, ndufa1 and NDUFA1) were cloned into the vector PpLuc(GC) – A64 – C30 – hSL (SEQ ID NO. 44, Fig. 10), which was constructed containing a T7 promoter and a GC-enriched sequence coding for *Photinus pyralis* luciferase (PpLuc(GC)). An A64 poly(A) sequence, followed by C30 and a histone stem-loop sequence, was inserted 3' of PpLuc(GC). The histone stem-loop sequence was followed by a restriction site used for linearization of the vector before in vitro transcription.

In particular, the following mRNAs were obtained from such vectors by *in vitro* transcription (the mRNA sequences are depicted in Figures 11 and 26 to 28:
PpLuc(GC) – gnas – A64 – C30 – hSL (SEQ ID NO. 45, Fig. 11);
PpLuc(GC) – morn2 – A64 – C30 – hSL (SEQ ID NO. 384, Fig. 26);
PpLuc(GC) – ndufa1 – A64 – C30 – hSL (SEQ ID NO. 385, Fig. 27); and
PpLuc(GC) – NDUFA1 – A64 – C30 – hSL (SEQ ID NO. 386, Fig. 28).

Human HeLa cells were transfected with Luciferase encoding mRNAs and Luciferase levels were measured 24, 48, and 72 hours after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc (see following Table 8 and Fig. 22).

mRNA	HeLa (expression in %)		
	24h	48h	72h
PpLuc(GC)-gnas-A64-C30-hSL	100	77,9	36,7
PpLuc(GC)-morn2-A64-C30-hSL	100	53,8	17,2
PpLuc(GC)-ndufa1-A64-C30-hSL	100	55,2	17,9
PpLuc(GC)-NDUFA1-A64-C30-hSL	100	66,9	29,4
PpLuc(GC)-A64-C30-hSL	100	41,5	9,6

Table 8: relative PpLuc expression normalized to RrLuc (mean values of 3 independent experiments are given).

These data and the data shown in Fig. 22 show that protein expression from mRNA containing 3'-UTR elements according to the invention is prolonged.

9. Effect of further 5'UTRs on protein expression

To further investigate the effect of various 5'UTRs on protein expression from mRNA, new mRNA constructs were prepared and those mRNAs containing different 5'UTRs were compared to an mRNA lacking a 5'UTR.

To this end, selected 5'-UTR elements (mp68 and ndufa4) were cloned into the vector PpLuc(GC) – A64 – C30 – hSL (SEQ ID NO. 44, Fig. 10), which was constructed containing a T7 promoter and a GC-enriched sequence coding for *Photinus pyralis* luciferase (PpLuc(GC)). An A64 poly(A) sequence, followed by C30 and a histone stem-loop sequence, was inserted 3' of PpLuc(GC). The histone stem-loop sequence was followed by a restriction site used for linearization of the vector before in vitro transcription.

In particular, the following mRNAs were obtained from such vectors by *in vitro* transcription (the mRNA sequences are depicted in Figures 29 and 30:

Mp68 – PpLuc(GC) – A64 – C30 – hSL (SEQ ID NO. 387, Fig. 29); and

Ndufa4 – PpLuc(GC) –A64 – C30 – hSL (SEQ ID NO. 388, Fig. 30).

Human HDF and HeLa cells were transfected with Luciferase encoding mRNAs and Luciferase levels were measured 24, 48, and 72 hours after transfection. The PpLuc signal was corrected for transfection efficiency by the signal of cotransfected RrLuc. Total protein expression (area under the curve) was calculated. The levels of the control construct without 5′ UTR was set to 1 (see following Table 9 and Figures 23 and 24).

mRNA	AUC HDF	AUC HeLa
PpLuc(GC) -A64-C30-hSL	1,0	1,0
Mp68-PpLuc(GC)- A64-C30-hSL	3,9	2,3
Ndufa4-PpLuc(GC)- A64-C30-hSL	4,0	2,0

Table 9: total PpLuc expression normalized to RrLuc (mean RLU values are given).

These data and the data shown in Figures 23 and 24 show that protein expression from mRNA containing 5′-UTR elements according to the invention is increased.

Claims

1. An artificial nucleic acid molecule comprising

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

   b. at least one 3'-untranslated region element (3'-UTR element) and/or at least one 5'-untranslated region element (5'-UTR element), wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element prolongs and/or increases protein production from said artificial nucleic acid molecule and wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element is derived from a stable mRNA.

2. The artificial nucleic acid molecule according to claim 1, wherein the open reading frame is derived from a gene, which is distinct from a gene from which the at least one 3'-UTR element and/or the at least one 5'-UTR element is derived.

3. The artificial nucleic acid molecule according to claim 1 or 2 comprising at least one 3'-UTR element and at least one 5'-UTR element.

4. The artificial nucleic acid molecule according to claim 3, wherein each of the at least one open reading frame, the at least one 3'-UTR element and the at least one 5'-UTR element are heterologous to each other.

5. The artificial nucleic acid molecule according to any of claims 1 to 4, wherein the stable mRNA from which the at least one 3'-UTR element and/or the at least one 5'-UTR element is derived is characterized by an mRNA decay wherein the ratio of the amount of said mRNA at a second point in time to the amount of said mRNA at a first point in time is at least 0.5 (50%), at least 0.6 (60%), at least 0.7 (70%), at least 0.75 (75%), at least 0.8 (80%), at least 0.85 (85%), at least 0.9 (90%), or at least 0.95 (95%).

6. The artificial nucleic acid molecule according to any of claims 1 to 5, wherein the artificial nucleic acid molecule does not comprise a 3'-UTR and/or a 5'-UTR of ribosomal protein S6, of RPL36AL, of rps16 or of ribosomal protein L9 and wherein

the open reading frame of the artificial nucleic acid molecule does not code for a GFP protein.

7. The artificial nucleic acid molecule according to claim 6, wherein the open reading frame of the artificial nucleic acid molecule does not code for a reporter protein.

8. The artificial nucleic acid molecule according to any one of claims 1 to 7, wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a eukaryotic protein coding gene, preferably from the 3'-UTR and/or the 5'-UTR of a vertebrate protein coding gene, more preferably from the 3'-UTR and/or the 5'-UTR of a mammalian protein coding gene, even more preferably from the 3'-UTR and/or the 5'-UTR of a primate protein coding gene.

9. The artificial nucleic acid molecule according to claim 8, wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a human or murine protein coding gene.

10. The artificial nucleic acid molecule according to claim 8 or 9, wherein:
(i) the nucleic acid molecule comprises at least one 3'-UTR element and at least one 5'-UTR element;
(ii) the at least one 3'-UTR element, the at least one 5'-UTR element and the at least one open reading frame are all heterologous to each other;
(iii) the at least one 3' UTR element is derived from a gene selected from the group consisting of: housekeeping genes, genes coding for a membrane protein, genes involved in cellular metabolism, genes involved in transcription, translation and replication processes, genes involved in protein modification and genes involved in cell division; and
(iv) the 3'UTR is not derived from a gene coding for a ribosomal protein or from the Fig4 gene.

11. The artificial nucleic acid molecule according to any of claims 8 to 10, wherein:
(i) the nucleic acid molecule comprises at least one 3'-UTR element and at least one 5'-UTR element;

(ii) the at least one 3'-UTR element, the at least one 5'-UTR element and the at least one open reading frame are all heterologous to each other;

(iii) the at least one 5'-UTR element is derived from a gene selected from the group consisting of: housekeeping genes, genes coding for a membrane protein, genes involved in cellular metabolism, genes involved in transcription, translation and replication processes, genes involved in protein modification and genes involved in cell division;

(iv) the 5'-UTR is preferably not a 5' TOP UTR; and

(v) the 3'-UTR is preferably not derived from a gene coding for a ribosomal protein or for albumin or from the Fig4 gene.

12. The artificial nucleic acid molecule according to claim 10 or 11, wherein:

(i) the nucleic acid molecule comprises at least one 3'-UTR element and at least one 5'-UTR element;

(ii) the at least one 3'-UTR element, the at least one 5'-UTR element and the at least one open reading frame are all heterologous to each other;

(iii) the at least one 3' UTR element is derived from a human or a murine gene selected from the group consisting of: housekeeping genes, genes coding for a membrane protein, genes involved in cellular metabolism, genes involved in transcription, translation and replication processes, genes involved in protein modification and genes involved in cell division;

(iv) the 3'UTR is not derived from a gene coding for a ribosomal protein or for albumin or from the Fig4 gene;

(v) the at least one 5'-UTR element is derived from a human or a murine gene selected from the group consisting of: housekeeping genes, genes coding for a membrane protein, genes involved in cellular metabolism, genes involved in transcription, translation and replication processes, genes involved in protein modification and genes involved in cell division; and

(vi) the 5'-UTR is not a 5' TOP UTR.

13. The artificial nucleic acid molecule according to any of claims 10 to 12, wherein the 3'-UTR and the 5'-UTR are derived from a human or a murine housekeeping gene.

14. The artificial nucleic acid molecule according to claim 12, wherein the 3'-UTR and the 5'-UTR are derived from a human or a murine gene selected from the group consisting of: genes coding for a membrane protein, genes involved in cellular metabolism, genes involved in transcription, translation and replication processes, genes involved in protein modification and genes involved in cell division and wherein the 3'-UTR and the 5'-UTR are selected from distinct gene classes.

15. The artificial nucleic acid molecule according to any of claims 1 to 14, wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element prolongs protein production from said artificial nucleic acid molecule at least 1.2 fold, preferably at least 1.5 fold, more preferably at least 2 fold, even more preferably at least 2.5 fold, compared to the protein production from a reference nucleic acid molecule lacking a 3'-UTR and/or the at least one 5'-UTR, respectively, and/or wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element increases protein production from said artificial nucleic acid molecule at least 1.5 fold, preferably at least 2 fold, more preferably at least 2.5 fold, compared to the protein production from a reference nucleic acid molecule lacking a 3'-UTR and/or the at least one 5'-UTR, respectively.

16. The artificial nucleic acid molecule according to any one of claims 1 to 15, wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a transcript of a gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, SUPT3H, TMEM14A, GRAMD1C, C11orf80, C9orf46, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, NT5DC1, RAB7A, AGA, TPK1, MBNL3, HADHB, MCCC2, CAT, ANAPC4, PCCB, PHKB, ABCB7, PGCP, GPD2, TMEM38B, NFU1, OMA1, LOC128322/NUTF2, NUBPL, LANCL1, HHLA3, PIR, ACAA2, CTBS, GSTM4, ALG8, Ndufa1, Atp5e, Gstm5, Uqcr11, Ifi27I2a, Cbr2, Anapc13, Atp5I, Tmsb10, Nenf, Ndufa7, Atp5k,

1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Gnas, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufa4, Ndufs5, Gstm1, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Hexa, Ndufb11, Map1lc3a, Morn2, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Ybx1, Sepp1, Gaa, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1; preferably from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

17. The artificial nucleic acid molecule according to claim 16, wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a transcript of a human gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), MP68 (RIKEN

cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), CNTN1 (contactin 1), LTA4H, SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, SUPT3H, TMEM14A, GRAMD1C, C11orf80, C9orf46, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, NT5DC1, RAB7A, AGA, TPK1, MBNL3, HADHB, MCCC2, CAT, ANAPC4, PCCB, PHKB, ABCB7, PGCP, GPD2, TMEM38B, NFU1, OMA1, LOC128322/NUTF2, NUBPL, LANCL1, HHLA3, , PIR, ACAA2, CTBS, GSTM4, ALG8, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1.

18. The artificial nucleic acid molecule according to claim 16, wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a transcript of a murine gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), CNTN1 (contactin 1), Atp5e, Gstm5, Uqcr11, Ifi27I2a, Anapc13, Atp5I, Tmsb10, Nenf, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5,

1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufs5, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Hexa, Ndufb11, Map1lc3a, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Sepp1, and Gaa.

19. The artificial nucleic acid molecule according to any one of claims 16 to 18, wherein the at least one 3'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, TMEM14A, GRAMD1C, C11orf80, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, HADHB, ANAPC4, PCCB, ABCB7, PGCP, NFU1, OMA1, HHLA3, ACAA2, GSTM4, ALG8, Ndufa1, Atp5e, Gstm5, Uqcr11, Ifi27l2a, Cbr2, Atp5I, Tmsb10, Nenf, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Gnas, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufa4, Ndufs5, Gstm1, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Ndufb11, Map1lc3a, Morn2, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Ybx1, Sepp1, Gaa, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3,

ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1; preferably, the at least one 3'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

20. The artificial nucleic acid molecule according to claim 19, wherein the at least one 3'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a human gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, TMEM14A, GRAMD1C, C11orf80, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, HADHB, ANAPC4, PCCB, ABCB7, PGCP, NFU1, OMA1, HHLA3, ACAA2, GSTM4, ALG8, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough

transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1; preferably, the at least one 3'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a human gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

21. The artificial nucleic acid molecule according to claim 19, wherein the at least one 3'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a murine gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1), Ndufa1, Atp5e, Gstm5, Uqcr11, Ifi27I2a, Cbr2, Atp5I, Tmsb10, Nenf, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Gnas, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufa4, Ndufs5, Gstm1, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Ndufb11, Map1lc3a, Morn2, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Ybx1, Sepp1, and Gaa; preferably, the at least one 3'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a murine gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase

2), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

22. The artificial nucleic acid molecule according to any one of claims 16 to 18, wherein the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 5'-UTR of a transcript of a gene selected from the group consisting of MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, DECR1, PIGK, TBC1D19, BRP44L, ACADSB, SUPT3H, TMEM14A, C9orf46, ANXA4, IFI6, C2orf34, ALDH6A1, CCDC53, CCDC104, CASP1, NDUFB6, BCKDHB, BBS2, HERC5, FAM175A, NT5DC1, RAB7A, AGA, TPK1, MBNL3, MCCC2, CAT, ANAPC4, PHKB, ABCB7, GPD2, TMEM38B, NFU1, LOC128322/NUTF2, NUBPL, LANCL1, PIR, CTBS, GSTM4, Ndufa1, Atp5e, Gstm5, Cbr2, Anapc13, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Ndufs6, Sec61b, Snrpd2, Mgst3, Prdx4; Pgcp; Myeov2; Ndufa4; Ndufs5; Gstm1; Atp5o; Tspo; Taldo1; Bloc1s1; and Hexa; preferably, the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 5'-UTR of a transcript of MP68 (RIKEN cDNA 2010107E04 gene) or NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4).

23. The artificial nucleic acid molecule according to claim 22, wherein the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 5'-UTR of a transcript of a human gene selected from the group consisting of MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, DECR1, PIGK, TBC1D19, BRP44L, ACADSB, SUPT3H, TMEM14A, C9orf46, ANXA4, IFI6, C2orf34, ALDH6A1, CCDC53, CCDC104, CASP1, NDUFB6, BCKDHB, BBS2, HERC5, FAM175A, NT5DC1, RAB7A, AGA, TPK1, MBNL3, MCCC2, CAT, ANAPC4, PHKB, ABCB7, GPD2, TMEM38B, NFU1, LOC128322/NUTF2, NUBPL, LANCL1, PIR, CTBS, and GSTM4; preferably, the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 5'-UTR of a human transcript of MP68 (RIKEN cDNA 2010107E04 gene) or NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4).

24. The artificial nucleic acid molecule according to claim 22, wherein the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 5'-UTR of

a transcript of a murine gene selected from the group consisting of MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ndufa1, Atp5e, Gstm5, Cbr2, Anapc13, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Ndufs6, Sec61b, Snrpd2, Mgst3, Prdx4; Pgcp; Myeov2; Ndufa4; Ndufs5; Gstm1; Atp5o; Tspo; Taldo1; Bloc1s1; and Hexa; preferably, the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 5'-UTR of a murine transcript of MP68 (RIKEN cDNA 2010107E04 gene) or NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4).

25. The artificial nucleic acid molecule according to any one of claims 1 – 21, wherein the at least one 3'-UTR element comprises or consists of a nucleic acid sequence which has an identity of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 the group consisting of SEQ ID NOs: 1 to 24 and SEQ ID NOs: 49 to 318 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 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 fragment of a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1 to 24 and SEQ ID NOs: 49 to 318.

26. The artificial nucleic acid molecule according to any one of claims 1 – 18 and 22 to 24, wherein the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which has an identity of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 the group consisting of SEQ ID NOs: 25 to 30 and SEQ ID NOs: 319 to 382 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 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 the group consisting of SEQ ID NOs: 25 to 30 and SEQ ID NOs: 319 to 382.

27. The artificial nucleic acid molecule according to claim 25 or 26, wherein the fragment exhibits a length of between 3 and about 500 nucleotides, preferably of between 5 and about 150 nucleotides, more preferably of between 10 and 100 nucleotides, even more preferably of between 15 and 90, most preferably of between 20 and 70.

28. The artificial nucleic acid molecule according to any one of claims 1 – 27, wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element exhibits a length of between 3 and about 500 nucleotides, preferably of between 5 and about 150 nucleotides, more preferably of between 10 and 100 nucleotides, even more preferably of between 15 and 90, most preferably of between 20 and 70.

29. The artificial nucleic acid molecule according to any one of claims 1 – 28 further comprising

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

30. The artificial nucleic acid molecule according to claim 29, wherein the poly(A) sequence or the polyadenylation signal is located 3' of the 3'-UTR element.

31. The artificial nucleic acid molecule according to claim 29 or 30, 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.

32. The artificial nucleic acid molecule according to any one of claims 29 – 31, wherein the polyadenylation signal, preferably the consensus sequence NNUANA, is located less than about 50 nucleotides downstream of the 3'-end of the 3'-UTR element.

33. The artificial nucleic acid molecule according to any one of claims 29 – 32, 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, even more preferably of about 60 to about 70 adenine nucleotides.

34. The artificial nucleic acid molecule according to any one of claims 1 – 33, further comprising a 5'-cap structure, a poly(C) sequence, a histone stem-loop, and/or an IRES-motif.

35. The artificial nucleic acid molecule according to any one of claims 1 – 34, wherein the histone stem-loop comprises a sequence according to SEQ ID NO: 34.

36. The artificial nucleic acid molecule according to any one of claims 1 – 35, wherein the nucleic acid comprises a promoter.

37. The artificial nucleic acid molecule according to any one of claims 1 – 36, wherein the nucleic acid comprises a 5'-TOP UTR.

38. The artificial nucleic acid molecule according to any one of claims 1 – 37, wherein the nucleic acid comprises a 3'-UTR, which comprises or consists of a nucleic acid sequence which is derived from a 3'-UTR of an albumin gene.

39. The artificial nucleic acid molecule according to any one of claims 1 – 38, 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.

40. The artificial nucleic acid molecule according to any one of claims 1 – 39, wherein the open reading frame comprises a codon-optimized region, preferably, wherein the open reading frame is codon-optimized.

41. The artificial nucleic acid molecule according to any one of claims 1 – 40, which is an RNA, preferably an mRNA molecule.

42. A vector comprising an artificial nucleic acid molecule according to any one of claims 1 – 41.

43. The vector according to claim 42, which is a DNA vector.

44. The vector according to claim 42 or 43, which is a plasmid vector or a viral vector, preferably a plasmid vector.

45. The vector according to any one of claims 42 – 44, which is a circular molecule.

46. The vector according to claim 42, wherein the poly(A) sequence, the poly(C) sequence, the histone stem loop 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.

47. A cell comprising the artificial nucleic acid molecule according to any one of claims 1 – 39 or the vector according to any one of claims 42 – 46.

48. The cell according to claim 47, which is a mammalian cell.

49. The cell according to claim 47 or 48, which is a cell of a mammalian subject, preferably an isolated cell of a mammalian subject, preferably of a human subject.

50. A pharmaceutical composition comprising the artificial nucleic acid molecule according to any one of claims 1 – 41, the vector according to any one of claims 42 – 46, or the cell according to any one of claims 47 – 49.

51. The pharmaceutical composition according to claim 50, further comprising one or more pharmaceutically acceptable vehicles, diluents and/or excipients and/or one or more adjuvants.

52. The artificial nucleic acid molecule according to any one of claims 1 – 41, the vector according to any one of claims 42 – 46, the cell according to any one of claims 47 – 49, or the pharmaceutical composition according to claim 50 or 51 for use as a medicament.

53. The artificial nucleic acid molecule according to any one of claims 1 – 41, the vector according to any one of claims 42 - 46, the cell according to any one of claims 47 - 49, or the pharmaceutical composition according to claim 50 or 51 for use as a vaccine or for use in gene therapy.

54. A method for treating or preventing a disorder comprising administering the artificial nucleic acid molecule according to any one of claims 1 – 41, the vector according to any one of claims 42 – 46, the cell according to any one of claims 47 – 49, or the pharmaceutical composition according to claim 50 or 51 to a subject in need thereof.

55. A method of treating or preventing a disorder comprising transfection of a cell with an artificial nucleic acid molecule according to any one of claims 1 – 41 or the vector according to any one of claims 42 – 46.

56. The method according to claim 55, wherein transfection of a cell is performed *in vitro/ex vivo* and the transfected cell is administered to a subject in need thereof, preferably to a human patient.

57. The method according to claim 56, wherein the cell which is to be transfected *in vitro* is an isolated cell of the subject, preferably of the human patient.

58. The method according to any one of claims 54 – 57, which is a vaccination method or a gene therapy method.

59. A method for increasing and/or prolonging protein production from an artificial nucleic acid molecule, preferably from an mRNA molecule or a vector, the method comprising the step of associating an open reading frame with a 3'-UTR element and/or a 5'-UTR element, wherein the 3'-UTR element and/or the 5'-UTR element prolongs and/or increases protein production from a resulting artificial nucleic acid molecule and wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element is derived from a stable mRNA, to obtain an artificial nucleic acid molecule, preferably an mRNA molecule, according to any of claims 1 – 41 or a vector according to any of claims 42 – 46.

60. A method for increasing and/or prolonging protein production from an artificial nucleic acid molecule, preferably from an mRNA molecule or a vector, according to claim 59, wherein the 3'-UTR element and/or the 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a transcript of a gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, SUPT3H, TMEM14A, GRAMD1C, C11orf80, C9orf46, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1,

AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, NT5DC1, RAB7A, AGA, TPK1, MBNL3, HADHB, MCCC2, CAT, ANAPC4, PCCB, PHKB, ABCB7, PGCP, GPD2, TMEM38B, NFU1, OMA1, LOC128322/NUTF2, NUBPL, LANCL1, HHLA3, PIR, ACAA2, CTBS, GSTM4, ALG8, Atp5e, Gstm5, Uqcrl1, Ifi27I2a, Anapc13, Atp5I, Tmsb10, Nenf, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Snrpd2, Mgst3, Aldh2, , Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufs5, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Hexa, Ndufb11, Map1lc3a, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Ybx1, Sepp1, Gaa, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1; preferably from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

61. Use of a 3'-UTR element and/or a 5'-UTR element for increasing and/or prolonging protein production from an artificial nucleic acid molecule, preferably from an mRNA molecule or a vector, wherein the 3'-UTR element and/or the 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a transcript of a gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, SUPT3H, TMEM14A, GRAMD1C, C11orf80, C9orf46, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, NT5DC1, RAB7A, AGA, TPK1, MBNL3, HADHB, MCCC2, CAT, ANAPC4, PCCB, PHKB, ABCB7, PGCP, GPD2, TMEM38B, NFU1, OMA1, LOC128322/NUTF2, NUBPL, LANCL1, HHLA3, PIR, ACAA2, CTBS, GSTM4, ALG8, Atp5e, Gstm5, Uqcr11, Ifi27I2a, Anapc13, Atp5I, Tmsb10, Nenf, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufs5, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Hexa, Ndufb11, Map1lc3a, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Ybx1, Sepp1, Gaa, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6,

CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1; preferably from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

62. The method according to claim 60 or the use according to claim 61, wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a transcript of a human gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), CNTN1 (contactin 1), LTA4H, SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L, ACADSB, SUPT3H, TMEM14A, GRAMD1C, C11orf80, C9orf46, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, NT5DC1, RAB7A, AGA, TPK1, MBNL3, HADHB, MCCC2, CAT, ANAPC4, PCCB, PHKB, ABCB7, PGCP, GPD2, TMEM38B, NFU1, OMA1, LOC128322/NUTF2, NUBPL, LANCL1, HHLA3, PIR, ACAA2, CTBS, GSTM4, ALG8, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7,

TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1.

63. The method according to claim 60 or the use according to claim 61, wherein the at least one 3'-UTR element and/or the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR and/or the 5'-UTR of a transcript of a murine gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), CNTN1 (contactin 1), Atp5e, Gstm5, Uqcr11, Ifi27I2a, Anapc13, Atp5I, Tmsb10, Nenf, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufs5, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Hexa, Ndufb11, Map1lc3a, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Sepp1, and Gaa.

64. The method or the use according to any one of the claims 60 – 63, wherein the at least one 3'-UTR element comprises a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), SLC38A6, DECR1, PIGK, FAM175A, PHYH, TBC1D19, PIGB, ALG6, CRYZ, BRP44L,

ACADSB, TMEM14A, GRAMD1C, C11orf80, ANXA4, TBCK, IFI6, C2orf34, ALDH6A1, AGTPBP1, CCDC53, LRRC28, CCDC109B, PUS10, CCDC104, CASP1, SNX14, SKAP2, NDUFB6, EFHA1, BCKDHB, BBS2, LMBRD1, ITGA6, HERC5, HADHB, ANAPC4, PCCB, ABCB7, PGCP, NFU1, OMA1, HHLA3, ACAA2, GSTM4, ALG8, Ndufa1, Atp5e, Gstm5, Uqcr11, Ifi27l2a, Cbr2, Atp5I, Tmsb10, Nenf, Atp5k, 1110008P14Rik, Cox4i1, Cox6a1, Ndufs6, Sec61b, Romo1, Gnas, Snrpd2, Mgst3, Aldh2, Ssr4, Myl6, Prdx4, Ubl5, 1110001J03Rik, Ndufa13, Ndufa3, Gstp2, Tmem160, Ergic3, Pgcp, Slpi, Myeov2, Ndufa4, Ndufs5, Gstm1, 1810027O10Rik, Atp5o, Shfm1, Tspo, S100a6, Taldo1, Bloc1s1, Ndufb11, Map1lc3a, Morn2, Gpx4, Mif, Cox6b1, RIKEN cDNA2900010J23 (Swi5), Sec61g, 2900010M23Rik, Anapc5, Mars2, Phpt1, Ndufb8, Pfdn5, Arpc3, Ndufb7, Atp5h, Mrpl23, Uba52, Tomm6, Mtch1, Pcbd2, Ecm1, Hrsp12, Mecr, Uqcrq, Gstm3, Lsm4, Park7, Usmg5, Cox8a, Ly6c1, Cox7b, Ppib, Bag1, S100a4, Bcap31, Tecr, Rabac1, Robld3, Sod1, Nedd8, Higd2a, Trappc6a, Ldhb, Nme2, Snrpg, Ndufa2, Serf1, Oaz1, Rps4x, Rps13, Ybx1, Sepp1, Gaa, ACTR10, PIGF, MGST3, SCP2, HPRT1, ACSF2, VPS13A, CTH, NXT2, MGST2, C11orf67, PCCA, GLMN, DHRS1, PON2, NME7, ETFDH, ALG13, DDX60, DYNC2LI1, VPS8, ITFG1, CDK5, C1orf112, IFT52, CLYBL, FAM114A2, NUDT7, AKD1, MAGED2, HRSP12, STX8, ACAT1, IFT74, KIFAP3, CAPN1, COX11, GLT8D4, HACL1, IFT88, NDUFB3, ANO10, ARL6, LPCAT3, ABCD3, COPG2, MIPEP, LEPR, C2orf76, ABCA6, LY96, CROT, ENPP5, SERPINB7, TCP11L2, IRAK1BP1, CDKL2, GHR, KIAA1107, RPS6KA6, CLGN, TMEM45A, TBC1D8B, ACP6, RP6-213H19.1, SNRPN, GLRB, HERC6, CFH, GALC, PDE1A, GSTM5, CADPS2, AASS, TRIM6-TRIM34 (readthrough transcript), SEPP1, PDE5A, SATB1, CCPG1, CNTN1, LMBRD2, TLR3, BCAT1, TOM1L1, SLC35A1, GLYATL2, STAT4, GULP1, EHHADH, NBEAL1, KIAA1598, HFE, KIAA1324L, and MANSC1; preferably, the at least one 3'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 3'-UTR of a transcript of a gene selected from the group consisting of NDUFA1 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex), GNAS (guanine nucleotide binding protein, alpha stimulating complex locus), MORN2 (MORN repeat containing 2), GSTM1 (glutathione S-transferase, mu 1), CBR2 (carbonyl reductase 2), Ybx1 (Y-Box binding protein 1), Ndufb8 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex 8), and CNTN1 (contactin 1).

65. The method or the use according to any one of the claims 60 – 63, wherein the at least one 5'-UTR element comprises a nucleic acid sequence which is derived from the 5'-UTR of a transcript of a gene selected from the group consisting of MP68 (RIKEN cDNA 2010107E04 gene), NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4), LTA4H, DECR1, PIGK, TBC1D19, BRP44L, ACADSB, SUPT3H, TMEM14A, C9orf46, ANXA4, IFI6, C2orf34, ALDH6A1, CCDC53, CCDC104, CASP1, NDUFB6, BCKDHB, BBS2, HERC5, FAM175A, NT5DC1, RAB7A, AGA, TPK1, MBNL3, MCCC2, CAT, ANAPC4, PHKB, ABCB7, GPD2, TMEM38B, NFU1, LOC128322/NUTF2, NUBPL, LANCL1, PIR, CTBS, GSTM4, Ndufa1, Atp5e, Gstm5, Cbr2, Anapc13, Ndufa7, Atp5k, 1110008P14Rik, Cox4i1, Ndufs6, Sec61b, Snrpd2, Mgst3, , Prdx4; Pgcp; Myeov2; Ndufa4; Ndufs5; Gstm1; Atp5o; Tspo; Taldo1; Bloc1s1; and Hexa; preferably, the at least one 5'-UTR element comprises or consists of a nucleic acid sequence which is derived from the 5'-UTR of a transcript of MP68 (RIKEN cDNA 2010107E04 gene) or NDUFA4 (NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4).

66. The method or the use according to any one of the claims 60 – 64, wherein the 3'-UTR element comprises or consists of a nucleic acid sequence which has an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 sequence selected from the group consisting of SEQ ID NOs: 1 to 24 and SEQ ID NOs: 49 to 318 or wherein the 3'-UTR element comprises or consists of a fragment of a nucleic acid sequence that has an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 sequence selected from the group consisting of SEQ ID NOs: 1 to 24 and SEQ ID NOs: 49 to 318.

67. The method or the use according to any one of the claims 60 – 63 and 65, wherein the 5'-UTR element comprises or consists of a nucleic acid sequence which has an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 sequence selected from the group consisting of SEQ ID NOs: 25 to 30 and SEQ ID NOs: 319 to 382 or wherein the 5'-UTR element comprises or consists of a fragment of a nucleic acid sequence that has an identity of at least about 40%, preferably of at least about 50%, preferably of at least about 60%, preferably of at least about 70%, more preferably 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 sequence selected from the group consisting of SEQ ID NOs: 25 to 30 and SEQ ID NOs: 319 to 382.

68. The method or the use according to claim 66 or 67, wherein the fragment exhibits a length of between 3 and about 500 nucleotides, preferably of between 5 and about 150 nucleotides, more preferably of between 10 and 100 nucleotides, even more preferably of between 15 and 90, most preferably of between 20 and 70.

69. The method or the use according to any one of claims 60 – 68, wherein the 3'-UTR element and/or the 5'-UTR element exhibits a length of between 3 and about 500 nucleotides, preferably of between 5 and about 150 nucleotides, more preferably of between 10 and 100 nucleotides, even more preferably of between 15 and 90, most preferably of between 20 and 70.

70. A kit or kit of parts comprising an artificial nucleic acid molecule according to any one of claims 1 – 41, a vector according to any one of claims 42 – 46, a cell according to any one of claims 47 – 49, and/or a pharmaceutical composition according to claim 50 or 51.

71. The kit according to claim 70 further comprising instructions for use, cells for transfection, an adjuvant, a means for administration of the pharmaceutical composition, a pharmaceutically acceptable carrier and/or a pharmaceutically acceptable solution for dissolution or dilution of the artificial nucleic acid molecule, the vector, the cells or the pharmaceutical composition.

72. A method for identifying a 3'-untranslated region element (3'-UTR element) and/or a 5'-untranslated region element (5'-UTR element), which is derived from a stable mRNA comprising the following steps:

a) Analyzing the stability of a plurality of mRNA species comprising the following sub-steps:

i. Determining the amount of each mRNA species of said plurality of mRNA species at a first point in time during a decay process of said mRNA species,

ii. Determining the amount of each mRNA species of said plurality of mRNA species at a second point in time during a decay process of said mRNA species, and

iii. Calculating for each mRNA species of said plurality of mRNA species the ratio of the amount of said mRNA species determined in step (i) to the the amount of said mRNA species determined in step (ii);

b) Ranking of the mRNA species of the plurality of mRNA species according to the ratio calculated in sub-step (iii) for each mRNA species;

c) Selecting one or more mRNA species having the highest ratio or the highest ratios calculated in sub-step (iii); and

d) Determining the nucleotide sequence of a 3'- and/or 5'-UTR element of said mRNA.

73. The method for identifying a 3'-UTR element and/or a 5'-UTR element according to claim 72, wherein the time period between the first point in time and the second point in time is at least 5h, preferably at least 6h, preferably at least 7h, more preferably at least 8h, more preferably at least 9h, even more preferably at least 10h, even more preferably at least 11h, and particularly preferably at least 12h.

74. The method for identifying a 3'-UTR element and/or a 5'-UTR element according to any of claims 72 – 73, wherein the stability of an mRNA is analysed by pulse labelling, preferably using a pulse-chase methodology.

75. A method for identifying a 3'-untranslated region element (3'-UTR element) and/or a 5'-untranslated region element (5'-UTR element), which prolongs and/or increases protein production from an artificial nucleic acid molecule and which is derived from a stable mRNA comprising the following steps:

a) identifying a 3'-UTR element and/or a 5'-UTR element which is derived from a stable mRNA by a method for identifying a 3'-UTR element and/or a 5'-UTR element according to any of claims 72 – 74;

b) synthesizing an artificial nucleic acid molecule comprising at least one open reading frame and at least one 3'-UTR element and/or at least one 5'-UTR

element which corresponds to or is comprised by the 3'-UTR element and/or the 5'-UTR element identified in step a);

c) analyzing the expression of the protein encoded by the at least one open reading frame of the artificial nucleic acid molecule synthesized in step b);

d) analyzing the expression of a protein encoded by at least one open reading frame (ORF) of a reference artificial nucleic acid molecule lacking a 3'-UTR element and/or a 5'-UTR element;

e) comparing the protein expression from the artificial nucleic acid molecule analysed in step c) to the protein expression from the reference artificial nucleic acid molecule analysed in step d); and

f) selecting the 3'-UTR element and/or the 5'-UTR element if the protein expression from the artificial nucleic acid molecule analysed in step c) is prolonged and/or increased in comparison to the protein expression from the reference artificial nucleic acid molecule analysed in step d).

76. A method for generating an artificial nucleic acid molecule, wherein an artificial nucleic acid molecule comprising at least one open reading frame and at least one 3'-UTR element and/or at least one 5'-UTR element identified by a method for identifying a 3'-UTR element and/or a 5'-UTR element according to any of claims 72 – 75 is synthesized.

77. The method for generating an artificial nucleic acid molecule according to claim 76, wherein a vector according to any of claims 42 – 46 is used for synthesizing the artificial nucleic acid molecule.

78. The method for generating an artificial nucleic acid molecule according to claim 76 or 77, wherein the artificial nucleic acid molecule is an artificial nucleic acid molecule according to any of claims 1 to 41.

79. An artificial nucleic acid molecule obtainable by a method for generating an artificial nucleic acid molecule according to any of claims 76 – 78.