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(54) Title: ISOLATION OF ACTIVELY TRANSLATED MRNAS FROM A SMALL NUMBER OF CELLS

(57) Abstract: The present invention provides a method of separating an actively translated RNA from a biological sample comprising the step of contacting a biological sample with a chaperone -binding molecule. The present invention allows for isolating, detecting, determining expression of, and profiling actively translated RNA. The invention provides a kit for working the invention.

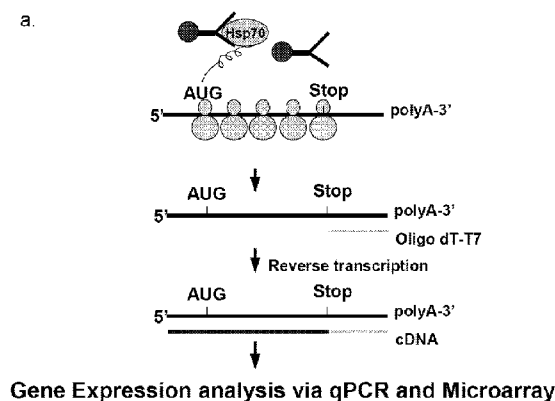


Fig. 1



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ISOLATION OF ACTIVELY TRANSLATED mRNAs FROM A SMALL NUMBER OF CELLS

FIELD OF THE INVENTION

[0001] The invention relates to methods for the isolation of actively translated mRNAs from a small number of cells and kits for performing the methods.

BACKGROUND OF THE INVENTION

[0002] Transcriptional regulation has been the main focus for the study of gene regulation. However, evidence from recent studies indicates that translational regulation plays a key role in a number of physiological processes including during development, in cell cycle control, and in mechanisms related to acute drug resistance. In addition, with the recent discovery that non-coding microRNAs are important regulators of translation, it is important to develop a simple and accurate approach to investigate genes regulated at the post-transcriptional and translational levels. However, previous studies have relied on methods, such as traditional sucrose gradient ultracentrifugation to isolate polysome complexes, which require a large amount of cells (up to 500 million cells). As a result, isolation of polysomes remains a major bottleneck for the investigation of post transcriptional regulation particularly where large numbers of cells are not available (*e.g.*, cell cultures, serum, plasma, lavage, saliva, urine, amniotic fluid, microaspirates, microbiopsies, laser-captured cells, formalin fixed paraffin embedded tissue, CSF, lymphatic fluid, rodent tissues, primate tissues, cultured stem cells, oocytes, sperm, etc.).

[0003] Actively translated mRNAs are associated with multi-subunit ribosomes (polyribosomes or polysomes). MicroRNAs and other non-coding RNAs have also been isolated from polysomes (Brandhorst, B., Isolating DNA, RNA, polysomes and protein. *Methods Cell Biol.* 2004;74:579-99; Arava, Y., Isolation of polysomal RNA for microarray analysis. *Methods Mol Biol.* 2003;224:79-87).

[0004] Chaperones are proteins that assist in the folding and assembly of macromolecular structures, but are not themselves part of the final structure. Chaperones are an essential component of and always found in polysomes (Chen, M.S., Characterization of an hsp70 related clone encoding a 33kDa protein with homology to a protein which associates with polysomes. *Biochim. Biophys. Acta.* 1996 Oct 17; 1297:124-6; Ohashi, S. et

al., HSP60 interacts with YB-1 and affects its polysome association and subcellular localization. *Biochem. Biophys. Res. Commun.* 2009 Aug 7;385:545-50). Many chaperones are heat shock proteins (HSPs), which are a class of proteins whose expression is increased when the cell is exposed to elevated temperatures or other stress, though other chaperones are constitutively expressed. In general, heat shock proteins are named according to their weight. For example, HSP60, HSP70 and HSP90 are about 60, 70, and 90 kiloDaltons, respectively. In addition, these designations generally represent a family of HSPs. For example, the majority of genomes code for multiple members of the Hsp70 molecular chaperone family, with higher organisms possessing more Hsp70s. In humans, there are 13 known HSP70 proteins, plus four related HSP110 proteins.

[0005] Previous methods can not distinguish monosome bound vs. polysome bound mRNA transcripts (Sanz, E. et al., Cell-type-specific isolation of ribosome-associated mRNA from complex tissues. *Proc. Natl. Acad. Sci. U S A.* 2009 Aug 18;106(33):13939-44; Mustroph, A. et al., Isolation of plant polysomal mRNA by differential centrifugation and ribosome immunopurification methods. *Methods Mol Biol.* 2009;553:109-26). In one embodiment, the present invention provides the capability to isolate mRNAs (and other RNAs), that are associated specifically with polysomes, from limited amounts of biological tissues and fluids. Thus, the present method allows the specific isolation from limited source material of polysomal complexes containing actively translated RNA.

SUMMARY OF THE INVENTION

[0006] In general, in a first aspect, the invention features a method of isolating an actively translated RNA from a biological sample having the step of contacting a biological sample with a chaperone binding molecule. Actively translated RNAs include, but are not limited to, mRNA, microRNAs, siRNAs. In one embodiment, the chaperone binding molecule is an antibody. In a further embodiment, the chaperone-binding molecule selectively binds a chaperone protein selected from the group consisting of a HSP40 family chaperone protein, a HSP70 family chaperone protein, a HSP90 family chaperone protein, and combinations thereof. In another embodiment the chaperone-binding molecule selectively binds a HSP70 family chaperone protein. In another embodiment the chaperone-binding molecule selectively binds HSC70 or HSP73.

[0007] In one embodiment, the invention features a method of isolating actively translated RNA from a biological sample comprising contacting the biological sample with a chaperone binding molecule to form a chaperone binding molecule – chaperone complex, separating the chaperone binding molecule – chaperone complex from the sample, and isolating the actively translated mRNA from the chaperone binding molecule – chaperone complex. In an embodiment, the chaperone binding molecule – chaperone complex is separated from the sample by binding chaperone-binding molecule to a solid support.

[0008] In another embodiment, the invention includes methods for isolating microRNA and/or other non-coding RNAs associated with actively-transcribed mRNAs in a biological sample. In this embodiment, a chaperone binding molecule is mixed with a biological sample, a chaperone binding molecule – chaperone complex is formed, the chaperone binding molecule – chaperone complex is separated from the sample, then microRNA and other non-coding RNAs are purified from the complexes.

[0009] In one embodiment the antibody selectively binds a chaperone protein selected from the group consisting of a HSP40 family chaperone protein, a HSP70 family chaperone protein, a HSP90 family chaperone protein, a HSP110 family chaperone protein, and combinations thereof. In another embodiment the chaperone-binding molecule selectively binds a HSP70 family chaperone protein. In another embodiment the chaperone-binding molecule selectively binds HSC70/HSP73.

[0010] The method is used to isolate actively translated RNA from samples containing any number of cells, and is particularly advantageous where the number of cells is small (*e.g.*, 5000 cells or fewer. Thus, in one embodiment, the biological sample contains less than about 5000 cells. In another embodiment, the biological sample contains less than 500 cells. In still other embodiments, the biological sample contains less than 50, or less than 20, or less than 5 cells. In one embodiment, the sample contains one cell. In one embodiment of the invention, the biological sample contains from 500 cells to 5000 cells. In another embodiment, the biological sample contains from 50 to 500 cells. In another embodiment, the biological sample contains from 20 cells to 50 cells. In yet another embodiment, the biological sample contains from 5 cells to 20 cells. In still another embodiment, the biological sample contains from 1 cell to 5 cells.

[0011] In another embodiment, the invention features a method for analysis of actively translated mRNA from a biological sample comprising contacting the biological

sample with an chaperone binding molecule that binds to a chaperone protein to form a chaperone binding molecule – chaperone complex, isolating the antibody – chaperone complex, and analyzing the actively translated mRNA from the antibody – chaperone complex.

[0012] In a further embodiment analyzing the actively translated mRNA includes amplification of the isolated actively translated mRNA. In another embodiment, analyzing the actively translated mRNA includes microarray analysis of the isolated actively translated mRNA. In another embodiment, analyzing the actively translated mRNA includes quantitative RT-PCR of the isolated actively translated mRNA. In yet another embodiment, analyzing the actively translated mRNA includes sequencing the RNA. In one such embodiment, deep sequencing is employed to identify somatic mutations in a population of cells or tissue. In one embodiment, the antibody selectively binds a chaperone protein selected from the group consisting of a HSP40 family chaperone protein, a HSP70 family chaperone protein, a HSP90 family chaperone protein, a HSP110 family chaperone protein, and combinations thereof. In another embodiment the antibody selectively binds a HSP70 family chaperone protein. In another embodiment the antibody selectively binds HSC70/HSP73.

[0013] In the analysis method, any number of cells can be used. For example, in an embodiment, the biological sample contains less than about 5000 cells. In certain embodiments, the biological sample contains less than 500 cells, or less than 50, or less than 20, or less than 5 cells. In one embodiment, the sample contains one cell. In other embodiments, the biological sample contains from 500 cells to 5000 cells, or from 50 to 500 cells, or from 20 cells to 50 cells, or from 5 cells to 20 cells, or from 1 cell to 5 cells.

[0014] In another embodiment, the invention features a kit for isolating actively translated mRNA from a biological sample comprising: (a) one or more chaperone-binding molecules, and (b) instructions for use. In one embodiment, the kit further contains a solid support for immobilizing the one or more chaperone-binding molecules. In one embodiment, the one or more chaperone-binding molecules are one or more antibodies. In an embodiment of the invention, the kit comprises one or more reagents suitable for separating a complex comprising an actively translated mRNA and a chaperone protein from a biological sample. As discussed below, suitable lysis solutions and buffers are those that minimize disruption of protein:protein interactions, particularly disruption of cellular complexes comprising RNA

and one or more chaperone proteins. In an embodiment of the invention, the kit includes reagents for working the invention, such as, *e.g.*, PBS and wash buffer.

[0015] In one embodiment, the one or more antibodies selectively bind a chaperone protein selected from the group consisting of a HSP40 family chaperone protein, a HSP70 family chaperone protein, a HSP90 family chaperone protein, a HSP110 family chaperone protein, and combinations thereof. In one embodiment, the antibody selectively binds to a HSP70 family chaperone protein. In one embodiment, the antibody selectively binds to HSC70/HSP73.

BRIEF DESCRIPTION OF THE FIGURES

[0016] Figure 1. Schematic diagram of TrIP-Chip approach. Affinity beads with covalently attached anti-Hsp70 antibodies are used to immunoprecipitate a cross-linked complex composed of Hsp70, nascent peptides, polysomes and an actively translating mRNA. The mRNA is used to conduct qPCR or converted to a labeled cRNA in a two step reaction, and hybridized to whole genome microarrays. If translation is not taking place, there are no nascent peptides with which Hsp70 can be associated (A); Schematic diagram of antibody affinity bead preparation and polysome isolation procedure (B).

[0017] Figure 2. Western immunoblot analysis of *in vitro* translated TS protein expression isolated using hsp70/hsc70 antibody affinity capture beads (lane 2); unrelated α -tubulin antibody beads were used as negative control (lane 1) (A). Real time qRT-PCR analysis of *in vitro* transcribed TS mRNA expression (B).

[0018] Figure 3. HCT-116 colon cancer cells were treated with 400 μ M puromycin for 1 hour, and total RNA was isolated with hsp70 antibody affinity capture beads isolated RNP complex. The amount of total RNA was quantified by O.D. measurement at 260 nm using Nanodrop Spectrophotometer. Concentration of control RNA sample was set at 100% compared to puromycin treated sample (A). Real time qRT-PCR analysis of translational initiation factor eIF-4E expression level in both control cells and cells treated with 400 μ M puromycin (B).

[0019] Figure 4. Real time qRT-PCR analysis of TS and p53 mRNA expression from total RNA isolated from control and 5-FU treated HCT116 cells (lane 1, control; lane 2, 5-FU-treated) (n=3, P < 0.05). (A); Real time qRT-PCR analysis of TS and p53 mRNA

expression from hsp70/hsc70 antibody affinity capture bead isolated RNAs from control and 5-FU treated HCT116 cells (n=3, $P < 0.05$) (B); Western immunoblot analysis of TS and p53 protein expression isolated using hsp70/hsc70s antibody affinity capture beads (C).

[0020] Figure 5. Gene Ontology (GO) analysis was performed using the DAVID bioinformatics suite. DAVID Gene Functional Classification algorithm allows a gene list to be condensed into organized classes based on cellular functions. The genes are grouped and clustered based on their cellular and molecular functions which helps to identify functional related genes presented as a fuzzy heat map graphic view. The annotation terms are ordered based on their enrichment scores associated with the group. A bright areas represents a positive association between the gene-term: conversely, black represents an unknown relationship. The scattered pattern shows the functional difference. More than 20 clusters were represented with unique functions such as protein synthesis, cell cycle control, and RNA binding (A). A zoomed in view of cluster one was represented as genes involved in translational initiation (B). The distribution of each set of classified genes is presented in Table 3.

[0021] Figure 6. Western immunoblot analysis of PP2A protein expression isolated using hsp70/hsc70 antibody affinity capture beads from control and 5-FU treated HCT116 colon cancer cells (lane 1, control; lane 2, plus 5-FU) (A). Real time qRT-PCR analysis of total PP2A mRNA and polysome associated mRNA levels in control and 5-FU treated HCT-116 colon cancer cells (B).

DETAILED DESCRIPTION OF THE INVENTION

[0022] Chaperones are proteins that assist in the folding and assembly of macromolecular structures, but are not themselves part of the final structure. One of the major functions of chaperone proteins is to prevent newly synthesized polypeptide chains from misfolding or mis-associating with other cellular molecules. Proteins may not be able to fold fully until their polypeptide chain and/or other subunits are fully synthesized.

[0023] The Hsp70 family of heat shock proteins contains multiple homologs ranging in size from 66-78 kDa, and are the eukaryotic equivalents of the bacterial DnaK. The most studied Hsp70 members include the cytosolic stress-induced Hsp70 (Hsp72), the constitutive cytosolic Hsc70 (Hsp73), and the ER-localized BiP (Grp78). Hsp70 family members contain

highly conserved N-terminal ATP-ase and C-terminal protein binding domains. In one embodiment, the chaperone protein is Hsc70 (Hsp73).

[0024] Chaperone proteins of the present invention include any chaperone that associates directly or indirectly with a newly translated polypeptide chain including, but not limited to, members of the HSP70, HSP40, HSP90, and HSP110 families. For example, the Hsp40 family of heat-shock proteins contain a domain by which they interact with Hsp70s.

[0025] One embodiment of the actively translated RNA isolation process is illustrated in Fig. 1A. Translationally active mRNAs are associated with multiple units of ribosomes and the newly synthesized polypeptides are closely associated with molecular chaperones, such as hsp70s. These molecular chaperones, which assist in the proper folding of nascent polypeptides into higher ordered structures, provide an anchor for separating translationally active mRNAs associated with polysomes from free mRNAs. Affinity antibody capture beads will capture hsp70s chaperones associated with the polysome complexes so that polysomes can be separated from monosomes and free mRNAs. The isolated translationally active mRNAs can then be used for array based or real time qRT-PCR gene expression analysis.

[0026] Biological samples may be from any source of cells including samples from a patient and cultured cells, such as fibroblasts, white blood cells, sperm, oocytes, and stem cells. Examples of sources of cells include, but are not limited to an aspirate, a microaspirate, a biopsy including an aspiration biopsy or a microbiopsy, a frozen biopsy sample, a lavage, and circulating cancer cells in body fluid or bone marrow. Other sources of cells include a body tissue such as skin, bone marrow, liver, lung, brain, or other body tissue, and body fluids including plasma, serum, blood, amniotic fluid, lymphatic fluid, cerebrospinal fluid, saliva, or urine. The cells can be from any organism, such as a mammal, including but not limited to a human, a primate, a rat, a mouse, or other rodent. In an embodiment of the invention, the cells are dissected from tissue, such as by microdissection, including laser-capture microdissection. The cells can be fixed cells, including, but not limited to formalin fixed paraffin embedded tissue.

[0027] In some embodiments, the method of the invention may include contacting the biological sample with a crosslinking agent. Crosslinking includes covalently linking macromolecules in a complex and may be accomplished by exposure to agents such as UV, heat, formaldehyde, glutaraldehyde, paraformaldehyde, bissulfosuccinimidyl suberate,

disuccinimidyl suberate, and dithiobissuccinimidyl propionate (DSP). The condition of the cell lysis, buffer compositions, incubation time, and washing conditions are chosen to maintain or promote protein-mRNA complex stability and minimize mRNA degradation.

[0028] In order to contact a chaperone-binding molecule to chaperones bound to newly translated polypeptides, the cells may be permeablized and/or lysed by methods known in the art. For example, the cells may be contacted with one or more detergents suitable for immunoprecipitation such as, but not limited to, Triton X-100, Triton X-102, and/or Tween-20. Preferred buffers are those that minimize disruption of protein:protein interactions.

[0029] Chaperone-binding molecules include any molecule that can selectively bind chaperone proteins. In one embodiment, the chaperone binding molecule is an antibody that selectively binds one or more chaperone proteins. In another embodiment, the chaperone binding molecule is an aptamer.

[0030] Chaperone binding molecules used in the present invention may be linked directly or indirectly to a solid support. Alternatively, the solid support may be linked to a secondary antibody, which binds to the chaperone binding molecule. A variety of secondary antibodies are known in the art. Solid supports useful for isolation of the chaperone binding molecule - chaperone protein complex include, but are not limited to, multi-well plates, membranes, affinity columns, agarose beads, sepharose beads, and magnetic beads.

[0031] Thus, a chaperone protein (and any associated molecules) may be immobilized by being bound to a chaperone binding molecule, which is directly or indirectly linked to a solid support. Such immobilizing of a chaperone binding molecule – chaperone complex to a solid support does not require permanent attachment, but means that the binding is sufficient to allow separation and/or detection of the bound complex.

[0032] In one embodiment, the present invention provides antibodies, fragments, or variants of antibodies that recognize an epitope in a chaperone protein.

[0033] The term "epitope" refers to an antigenic determinant on an antigen to which an antibody binds. Epitopes usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains, and typically have specific three-dimensional structural characteristics, as well as specific charge characteristics. Epitopes generally have at least five contiguous amino acids.

[0034] The terms "antibody" and "antibodies" include polyclonal antibodies, monoclonal antibodies, humanized or chimeric antibodies, and antigen binding fragments of

antibodies, including, but not limited to, single chain Fv antibody fragments, Fab fragments, and F(ab')₂ fragments. Polyclonal antibodies are heterogeneous populations of antibody molecules that are specific for a particular antigen, while monoclonal antibodies are homogeneous populations of antibodies to a particular epitope contained within an antigen.

[0035] Chaperone-binding molecules include any synthetic and naturally occurring molecules that bind specifically to a chaperone protein. Examples include proteins, fragments thereof, polypeptides, polynucleotides, and synthetic analogs. Because the binding substances are simply a source of "binding sites," there is no requirement that the sequences be derived from a natural source, or that the structures resemble any naturally occurring protein. Synthetic analogs include, for instance, polypeptide- and polynucleotide-like polymers having modified backbones, side chains, or bases.

[0036] Antibodies can be obtained by any technique, for example, from naturally occurring antibodies, or Fab or scFv phage display libraries. Antibodies of the invention can be obtained by standard hybridoma technology (Harlow & Lane, ed., *Antibodies: A Laboratory Manual*, Cold Spring Harbor, 211-213 (1988), which is incorporated by reference herein).

[0037] Antibody fragments that have specific binding affinity for the polypeptide of interest can be generated by known techniques. Such antibody fragments include, but are not limited to, F(ab')₂ fragments that can be produced by pepsin digestion of an antibody molecule, and Fab fragments that can be generated by reducing the disulfide bridges of F(ab')₂ fragments. Alternatively, Fab expression libraries can be constructed. See, for example, Huse et al. (1989) *Science* 246:1275-1281. Single chain Fv antibody fragments are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge (e.g., 15 to 18 amino acids), resulting in a single chain polypeptide. Single chain Fv antibody fragments can be produced through standard techniques, such as those disclosed in U.S. Pat. No. 4,946,778. Antibody fragments further include single domain antibodies, also known as nanobodies. These fragments were developed when it was discovered that camels and llamas possess fully functional antibodies that lack light chains, and thus comprise only one binding domain. It is understood that, to make a single domain antibody from an antibody comprising a VH and a VL domain, certain amino acid substitutions outside the CDRs can be desired to enhance binding, expression or solubility. For example, it can be desirable to modify amino acid residues that would otherwise be buried in the VH-VL interface.

[0038] Once produced, antibodies or fragments thereof can be tested for recognition of the target polypeptide by standard immunoassay methods including, for example, enzyme-linked immunosorbent assay (ELISA) or radioimmunoassay assay (RIA). See, Short Protocols in Molecular Biology eds. Ausubel et al., Green Publishing Associates and John Wiley & Sons (1992).

[0039] Useful aptamers include nucleic acid aptamers that have been engineered through repeated rounds of selection *in vitro* to bind to a molecular target. Aptamers provide binding characteristics similar to antibodies, can be engineered completely in a test tube, and are readily produced by chemical synthesis. Peptide aptamers are also useful as chaperone-binding molecules. Peptide aptamers typically comprise a variable peptide loop of about 10 to 20 amino acids attached at both ends to a protein scaffold. A commonly used scaffold is the bacterial protein Thioredoxin-A.

[0040] It has been demonstrated that peptides can be generated in numbers several orders of magnitude greater than by conventional one-at-a-time methods by synthesis on polyethylene rods or pins, arranged, for example, in a microtiter plate format. The pin technology is representative of techniques that generate libraries of single compounds in a spatially-differentiated manner. An alternative approach, to rapidly prepare large mixtures of compounds, is the split-pool approach (e.g., Houghten, R.A., 1985, *Proc. Natl. Acad. Sci. U.S.A.* 82:5131-5135) where a solid support material (e.g., beads) is physically segregated into equal portions for coupling to each of the individual initial reactants. This affords uniform coupling since competition between reactants is eliminated. The individual polymers are combined in a single vessel for washing and deprotection and then divided again into individual portions for the next coupling. Using this approach, a complete set of possible molecular combinations is rapidly prepared in approximately equimolar amounts.

[0041] Alternatives to peptide libraries include production of polymers of peptide-like and small organic molecules. For example, peptide libraries are a collection of N-substituted glycines as peptide monomers which are assembled in a modular fashion. (Zuckermann, R.N. et al, 1994, *J. Med. Chem.* 37:2678-2685.) The structures of the resulting compounds are unique, display unique binding properties, and incorporate the important functionalities of peptides in a novel backbone.

[0042] Specificity of the chaperone-binding molecules, including antibodies, or fragments thereof, can be determined based on affinity and/or avidity. Affinity, represented

by the equilibrium constant for the dissociation of an antigen with an antibody (K_d), measures the binding strength between an antigenic determinant and an antibody-binding site. Avidity is a measure of the strength of binding between an antibody with its antigen, which is related to both the affinity between an epitope with its antigen-binding site on the antibody and the valence of the antibody. Valence refers to the number of antigen binding sites of a particular epitope. Antibodies typically bind with a dissociation constant (K_d) of 10^{-5} to 10^{-11} liters/mol. Any K_d less than 10^{-4} liters/mol is generally considered to indicate nonspecific binding. The lesser the value of the K_d , the stronger the binding strength between an antigenic determinant and the antibody-binding site.

[0043] Higher affinity antibodies may be preferred in order to ensure effective binding to HSPs associated with actively translated mRNA. This is because the chaperone-associated epitopes to which an antibody can bind may be spatially separated to an extent that limits avidity. In an embodiment of the invention, the K_d of the chaperone-binding molecule is less than about 10^{-8} . In another embodiment, the K_d is less than about 10^{-9} . In yet another embodiment, the K_d is less than about 10^{-10} . In still another embodiment, K_d is less than about 10^{-11} .

[0044] As used herein, “antibodies” and “antibody fragments” includes modifications that retain specificity for a specific antigen. Proteins and non-protein agents may be conjugated to the antibodies by methods that are known in the art. Conjugation methods include direct linkage, linkage via covalently attached linkers, and specific binding pair members (*e.g.*, avidin-biotin). Such methods include, for example, that described by Greenfield *et al.*, Cancer Research **50**:6600-6607 (1990) for the conjugation of doxorubicin and those described by Arnon *et al.*, Adv. Exp. Med. Biol. **303**, 79-90 (1991) and by Kiseleva *et al.*, Mol. Biol. (USSR) **25**:508-514 (1991) for the conjugation of platinum compounds.

[0045] Antibodies and antibody fragments of the present invention further include those for which binding characteristics have been improved by direct mutation, methods of affinity maturation, phage display, or chain shuffling. Affinity and specificity can be modified or improved by mutating CDRs and screening for antigen binding sites having the desired characteristics (see, *e.g.*, Yang *et al.*, J. Mol. Biol., **254**: 392-403 (1995)). CDRs are mutated in a variety of ways. One way is to randomize individual residues or combinations of residues so that in a population of otherwise identical antigen binding sites, all twenty amino acids are found at particular positions. Alternatively, mutations are induced over a range of CDR residues by error prone PCR methods (*see, e.g.*, Hawkins *et al.*, J. Mol. Biol.,

226: 889-896 (1992)). For example, phage display vectors containing heavy and light chain variable region genes can be propagated in mutator strains of *E. coli* (see, e.g., Low *et al.*, *J. Mol. Biol.*, **250**: 359-368 (1996)). These methods of mutagenesis are illustrative of the many methods known to one of skill in the art.

[0046] Isolated mRNA may be used as a template for amplification using methods known in the art. For example, methods for linear or exponential amplification of the isolated mRNA sequences. Some suitable techniques are described in: Van Gelder *et al.*, (1990) *Proc. Natl. Acad. Sci. USA* 87, 1663-67; Belyavsky *et al.*, (1989) *Nucleic Acids Res.* 17, 2919-2932; Tam *et al.*, (1989) *Nucleic Acids Res.* 17, 1269; Brady *et al.*, (1989) *Meth. Mol. Cell. Biol.* 21, 17-2; U.S. Patent Application 6,706,476; U.S. Patent Application 20030104432; Chenchik, *et al.*, (1998) In Siebert, P., and Larrick, J. (eds), *Gene Cloning and Analysis by RT-PCR*, Biotechnology Books, Natick, MA, pp. 305-319; U.S. Patent 5,104,792; Klein *et al.*, (2002) *Nature Biotech.* 20, 387-392; Castle *et al.*, (2003) *Genome Biol.* 4, R66. Isolated mRNA may be analyzed by a variety of methods including, but not limited to, quantitative real-time PCR, microarray analysis, and deep sequencing. Suitable techniques are described in: Lipshutz, R.J., Fodor, S.P., Gingeras, T.R. & Lockhart, D.J. High density synthetic oligonucleotide arrays. *Nature Genet.* 21, 20-24 (1999); Singh-Gasson, S. *et al.* Maskless fabrication of light-directed oligonucleotide microarrays using a digital micromirror array. *Nature Biotechnol.* 17, 974-978 (1999); Hughes, T.R. *et al.* Expression profiling using microarrays fabricated by an ink-jet oligonucleotide synthesizer. *Nature Biotechnol.* 19, 342-347 (2001); Margulies *et al.*, (2005) *Genome sequencing in microfabricated high-density picolitre wells. Nature* 437, 376-80; 't Hoen, P. A. C. *et al.* Deep sequencing-based expression analysis shows major advances in robustness, resolution and inter-lab partability over five microarray platforms. *Nucl. Acids Res.* 36, No. 21, e141 (2008); Cloonan, N., Stem cell transcriptome profiling via massive-scale mRNA sequencing. *Nature Methods* 5, 613-619 (2008). The method of the invention is not limited to the methods of RNA isolation described here. Any suitable RNA isolation procedure known in the art is included herein.

[0047] In one embodiment, the invention features a kit for isolating actively translated mRNA from a biological sample. The kit is used to perform isolation and purification of actively translated mRNA according to the invention. Accordingly, the kit contains a chaperone-binding molecule, which can be supplied conjugated to a solid support such as a bead or microtiter plate. In another embodiment, the chaperone-binding molecule is conjugated to a secondary reagent that can be immobilized and/or detected. The kit also

includes instructions for use. The kit may contain one or more additional reagents, including a cross-linking agent, lysis buffer, RNase inhibitor, wash buffer, and a solid support.

[0048] In one embodiment, the methods and kits of the present invention are useful in the identification of genes that are differentially translated in diseased cells or cells of different developmental stages. In another embodiment, the methods and kits are useful in detection or identification of genes that are differentially translated in response to external factors such as infectious agents and chemical agents. Thus, the methods and kits are useful for prediction, detection and diagnosis of disease.

[0049] All references referred to herein are incorporated in their entirety.

EXAMPLES

[0050] **Example 1. Preparation of antibody affinity capture beads.**

[0051] To prepare and characterize the affinity capture beads (chaperone binding molecule linked to a solid support), a number of different hsp70/hsc70 antibodies were evaluated to optimize the conditions for binding to the actively translated mRNA.

[0052] In addition, three different types of magnetic beads were systematically evaluated, Dynabeads®M-280 Sheep anti-Mouse IgG, Dynabeads®M-280 Sheep anti-Rabbit IgG and Dynabeads®Sheep anti-Rat IgG (Invitrogen, Inc). The required amount of thoroughly suspended beads was transferred into an Eppendorf tube. Beads were washed two times with washing buffer (PBS with 0.1% BSA, pH 7.4 for Dynabeads®M-280 Sheep anti-Mouse IgG and Dynabeads®M-280 Sheep anti-Rabbit IgG, and PBS with 0.1% BSA and 2 mM EDTA, pH 7.4 for Dynabeads®Sheep anti-Rat IgG). Then 1 µg/µl target immunoglobulin was added (a ratio of 1 µg/10⁷ beads was found to produce sufficient binding). Three antibodies were used: HSP70 mouse monoclonal antibody; HSC70 (HSP73) rabbit polyclonal antibody (Millipore Inc.); and HSC70 (HSP73) rat monoclonal antibody (BioVision Inc.). Beads with antibody were incubated with slow tilt rotation for 24 hours at 2-8°C. The tube was then placed on a magnet for 2 minutes and supernatant was removed with a pipette. Antibody-coated beads were washed three times with washing buffer and used for immunoprecipitation.

[0053] **Example 2. Translationally regulated genes can be captured by affinity capture beads.**

[0054] To determine the feasibility of isolating the hsp70 associated translational complex, an *in vitro* rabbit reticulocyte lysate coupled transcription/translation system was utilized. Promega's TnT Quick Coupled rabbit reticulocyte lysate Transcription/Translation System was utilized to transcribe thymidylate synthase (TS) mRNA and subsequently synthesize TS protein. A plasmid, pGEMpcHTS- 1, containing the full length human TS cDNA (1 µg), was used as the template for the *in vitro* transcription/translation reaction. TS mRNA expression was determined by real time qRT-PCR analysis and the TS protein was analyzed using Western immunoblot analysis.

[0055] Real-time quantitative reverse transcription-PCR (qRT-PCR) analysis was performed on the control mRNAs. PCR primers and probes were purchased from Applied Biosystems (Foster City, CA). qRT-PCR was performed on an ABI 7500HT instrument under the following conditions: 25°C, 10 min and 37°C, 30 min of reverse transcription; up to 45 cycles of PCR at 95°C, 10 min; 95°C, 15 s; 60°C, 1 min per cycle.

[0056] Western blot analysis was performed as follows. Equal amounts of protein (25 µg) from the transcription/translation lysate were separated on 10% sodium dodecyl sulfate-polyacrylamide gels by the method of Laemmli. Proteins were probed with mouse anti-TS monoclonal antibody (1:5000 dilution) (Zymed Laboratories, CA) and anti- α -tubulin (1:1000) (Santa Cruz Biotech Inc., CA). Horseradish peroxidase-conjugated antibodies against mouse or rabbit (1:1000, Santa Cruz Biotechnology) were used as the secondary antibodies. Protein bands were visualized with a chemiluminescence detection system using the Super Signal substrate.

[0057] The results clearly show immunoprecipitation the TS translation complex with hsp70 antibody affinity capture beads as showed in Fig.2. The absence of TS protein with control beads coupled to an anti-tubulin antibody (Lane 1) indicates the specificity of the hsp70 antibody affinity capture beads (Fig. 2A). One-tenth (70 µl) of the above lysate was transferred to the Ig-coated beads, and incubation was carried out for 1-2 hours at 2-8°C. After incubation with the hsp70/hsp73 antibody conjugated magnetic beads, the chaperone complexes containing polysomes and translationally active mRNA transcripts were isolated, and the mRNAs eluted from beads conjugated with HSP70/HSP73 using the Array Pure Nanoscale RNA Purification Kit (Epicenter, WI).

[0058] Detection of the presence of newly synthesized TS protein in the isolated complex was accomplished by Western immunoblot analysis (Lane 2) (Fig.2A). The associated TS mRNA template was also detected using real time qRT-PCR analysis (Fig. 2B).

[0059] **Example 3. Translationally regulated genes can be captured by affinity capture beads from HCT-116 colon cancer cells.**

[0060] To directly demonstrate the capture of polysomes with affinity capture beads, HCT-116 human colon cancer cells were incubated with 400 μ M puromycin, a drug that triggers premature polypeptide termination and polysome disassembly. The HCT-116 cell line was obtained from ATCC and maintained at 37°C and 5% CO₂ in 75-cm² plastic tissue culture flasks with McCoy's 5A medium containing 10% fetal bovine serum.

[0061] To prepare cytoplasmic extracts, cells from 6-well tissue culture plates were harvested with 0.05% Trypsin-EDTA (Invitrogen, CA) and washed with ice-cold PBS containing 100 μ g/ml cycloheximide (Sigma, MO). Cells were counted and 10,000 cells were incubated with 800 μ l of McCoy's 5A medium containing 10% fetal bovine serum and 100 μ g/ml cycloheximide (Sigma, MO) for 5 min at 37°C. After incubation, 200 μ l of DSP (PIERCE, IL) was introduced as a cross-linking reagent and incubation was carried out for 5 min at 37°C. The cells were washed twice by centrifugation at 1,000 rpm for 3 min, discarding the supernatant, and rinsing the cell pellets with ice-cold PBS containing 100 μ g/ml cycloheximide (Sigma, MO). The final pellets were swollen for 20 min in 500 μ l of low salt buffer (LSB) (20 mM HEPES, pH 7.4, 100mM KCl, 2 mM MgCl₂) containing 1 mM dithiothreitol and lysed by the addition of 200 μ l lysis buffer (1 $\times$ LSB containing 1.2% Triton X- 100) (Sigma) followed by brief vortexing. One-tenth (70 μ l) of the above lysate was transferred to the Ig-coated beads, and incubation was carried out for 1-2 hours at 2-8°C. After incubation with the hsp70/hsp73 antibody conjugated magnetic beads, the chaperone complexes containing polysomes and translationally active mRNA transcripts were isolated, and the mRNAs eluted from beads conjugated with HSP70/HSP73 using the Array Pure Nanoscale RNA Purification Kit (EPICENTRE, WI).

[0062] Treating HCT-116 colon cancer cells with 400 μ M puromycin reduced the total RNA levels associated with the hsp70 RNP complex compared to control cells (Fig.

3A). Real time qRT-PCR (performed as described above) analysis further revealed decreased level of translational initiation factor eIF4E with puromycin treatment (Fig. 3B).

[0063] Example 4. Isolation of translationally active mRNA from cells treated with 5-fluorouracil

[0064] Translational control plays an important role in chemoresistance, such as acute resistance to 5-fluorouracil (5-FU) treatment. Previous studies have identified that the target enzyme of 5-FU, thymidylate synthase (TS), is regulated at the translational level. In addition, as an RNA binding protein, TS not only negatively regulates its own synthesis at the translational level, but also interacts directly with p53 mRNA to down-regulate p53 protein expression.

[0065] Isolation of translationally active mRNA complexes associated with hsp70 proteins was further demonstrated directly *in vivo* by exposing the HCT-116 human colon cancer cell line model to 5-FU. Two genes were monitored, p53 and TS, which were previously shown to be translationally regulated to monitor the isolation and quantification process.

[0066] HCT-116 cells at 2×10^5 density were plated in 6-well tissue culture plates for 24 hrs. Cells were then treated with 5 μ M 5-FU for 24 hours; untreated cells were used as controls. Actively translating mRNA was isolated as described in Example 3.

[0067] Isolation of actively translating mRNAs was successful with this affinity capture approach as determined by both the presence of p53 and TS mRNAs. As shown in Fig. 4A, the steady state total cellular mRNA levels of TS and p53 was unchanged after 5-FU exposure ($n=3$, $P < 0.05$) (15, 18). By contrast, both TS and p53 mRNA transcripts isolated from the polysome complex were elevated by 5-FU treatment ($n=3$, $P < 0.01$, $CV < 5\%$) (Fig. 4B.). These results were supported by the corresponding increases of TS and p53 proteins determined by Western blot analysis (Fig. 4C.). Western blot on Equal amounts of protein (25 μ g) extracted from lysed cell lines was performed as described above. Anti-p53 mouse monoclonal antibody was used at a 1:1000 dilution and were obtained from Santa Cruz Biotech Inc., CA.

[0068] **Example 5. Gene expression analysis of 5-FU responsive translationally active genes isolated from polysome complexes in HCT-116 cells.**

[0069] After confirmation and optimization of the isolation process, analysis to determine novel post-transcriptionally regulated genes affected by 5-FU treatment was performed. To do so, the mRNAs isolated with the antibody affinity capture beads were used to quantify mRNA expression using human Codelink™ whole genome microarray analysis.

[0070] To systematically discover post transcriptionally and translationally regulated genes affected by 5- FU treatment, isolated translationally active mRNAs were used to profile gene expression using human whole genome array analysis. Due to the limited quantities of cellular RNA isolated from 500 control HCT116 cells and cells treated with 5-FU, two rounds of RNA amplification were employed using the Agilent Low RNA Input Linear Amplification Kit (Agilent, CA), which was also used to amplify mRNAs isolated from polysomes. The T7 promoter primer (1.2 µl) was added and the total reaction volume was adjusted to 11.5 µl with nuclease free water. The primer and template were incubated at 65°C for 10 min and then placed on ice for 5 min. cDNA Master Mix (8.5 µl) was added to each sample and incubation carried out at 40°C for 2 hours, 65°C for 15 min, and on ice for 5 min. Then 60 µl of amplification reaction buffer was added to 20 µl of cDNA product and incubation proceeded at 40°C for 4 hours. After purification, cRNA products were dried in a Speed Vacuum apparatus and the total volume adjusted to 10.5 µl. Random Hexamers (1.0 µl) were added to the cRNA products, incubation performed at 65°C for 10 min and the tube chilled to 4°C for 5min. 59 µl of amplification reaction buffer was added to 21 µl of cDNA product and incubation proceeded at 40°C for 4 hours. 9.5 µl of cDNA Master Mix supplemented with Cy3 labeled NTPs, which was added to each sample and incubation run at 40°C for 2 hours, 65°C for 15 min and on ice for 5 min. Mini elute clean up kits (Qiagen, CA) were used to purify the amplified samples after the 1st round amplification, and RNeasy mini kits to purify labeled RNA (Qiagen, CA) after the 2nd round in preparation for expression analysis.

[0071] For array hybridization, all reagents were provided in the Gene expression Hybridization Kit (Agilent, CA). Eleven µl of 10 x Blocking Agent and nuclease-free water was added to 1.65 µg of Cy3-labeled linearly amplified cRNA to bring the volume to 52.8 µl. Then 2.2 µl of 25x Fragmentation buffer was added. After vortexing 4 times at 44,000 rpm, this was incubated at 60°C for 30 min to fragment RNA. To prepare hybridization mix, 55 µl of fragmented cRNA and 55 µl of 2 x GE Hybridization Buffer HI-RPM were mixed and

carefully loaded onto the array gasket well to avoid bubbles. Hybridization was carried out at 10 rpm at 65°C for 17 hours in a hybridization oven. After hybridization, the arrays were washed with Gene Expression Wash Buffer 1 (Agilent, CA). The slides were then dried and kept in the dark until scanning. Images were captured on an Axon GenePix 4200A scanner.

[0072] The resulting image was quantified and the intensity of each spot divided by the median spot intensity to provide a scaled and comparable number across multiple arrays. After dot grid and quality control analysis, gene expression analysis was conducted using GeneSpring software 7.2 (Agilent, CA), which allows multifilter comparisons using data from different experiments to perform the normalization, generation of restriction lists and functional classification of differentially expressed genes. Under the Cross-Gene Error Model, normalization was applied in two steps: (a) “per chip normalization” in which each measurement was divided by the 50th percentile of all measurements in its array; and (b) “per gene normalization” in which all the samples were normalized against specific control samples. Then data were filtered for ≥ 4 -fold changes. The expression profiles of the different groups were compared using One-way ANOVA with cut-off $p < 0.05$. Comparisons of gene lists across different groups were performed using Venn diagrams and clustering was performed with the Condition Tree algorithm. The Gene Ontology groupings and Gen Maps 2.0 program were used in conjunction with GeneSpring to identify pathways and functional groups of genes.

[0073] Over 500 genes were identified that were differentially regulated by 5-FU treatment, including the positive control genes p53 and TS. A selected gene list is shown in Table 1.

Table 1. Genes differentially regulated by 5-FU treatment			
Genbank	Common	Fold Change	Description
NM_006640	SEPT-nine	44.28	Homo sapiens septin 9 (SEPT9), mRNA [NM_006640]
NM_004261	SEP-fifteen	5.285	Homo sapiens 15 kDa selenoprotein (SEP15), transcript variant 1, mRNA [NM_004261]
NM_001003408	ABLIM1	27.52	Homo sapiens actin binding LIM protein 1 (ABLIM1), transcript variant 3, mRNA [NM_001003408]
AF119889	AF119889	0.166	Homo sapiens PRO2667 mRNA, complete cds. [AF119889]
AK128222	AK128222	9.223	Homo sapiens cDNA FLJ46355 fis, clone TESTI4049110. [AK128222]
NM_016201	AMOTL2	10.46	Homo sapiens angiotensin like 2 (AMOTL2), mRNA [NM_016201]

NM_004037	AMPD2	4.639	Homo sapiens adenosine monophosphate deaminase 2 (isoform L) (AMPD2), transcript variant 1, mRNA [NM_004037]
NM_001002244	ANAPC11	25.86	Homo sapiens APC11 anaphase promoting complex subunit 11 homolog (yeast) (ANAPC11), transcript variant 1, mRNA [NM_001002244]
NM_138797	ANKRD54	5.442	Homo sapiens ankyrin repeat domain 54 (ANKRD54), mRNA [NM_138797]
ENST00000267918	ANP32A	6.35	Acidic leucine-rich nuclear phosphoprotein 32 family member A (Potent heat-stable protein phosphatase 2A inhibitor I1PP2A) (Acidic nuclear phosphoprotein pp32) (Leucine-rich acidic nuclear protein) (Lanp) (Putative HLA-DR-associated protein I) (PHAPI) (Ma [Source:Uniprot/SWISSPROT;Acc:P39687] [ENST00000267918])
NM_001284	AP3S1	32.24	Homo sapiens adaptor-related protein complex 3, sigma 1 subunit (AP3S1), mRNA [NM_001284]
NM_001657	AREG	14.87	Homo sapiens amphiregulin (schwannoma-derived growth factor) (AREG), mRNA [NM_001657]
NM_001658	ARF1	14.83	Homo sapiens ADP-ribosylation factor 1 (ARF1), transcript variant 4, mRNA [NM_001658]
NM_012106	ARL2BP	4.482	Homo sapiens ADP-ribosylation factor-like 2 binding protein (ARL2BP), mRNA [NM_012106]
NM_015161	ARL6IP1	4.814	Homo sapiens ADP-ribosylation factor-like 6 interacting protein 1 (ARL6IP1), mRNA [NM_015161]
NM_018184	ARL8B	6.34	Homo sapiens ADP-ribosylation factor-like 8B (ARL8B), mRNA [NM_018184]
NM_018120	ARMC1	0.17	Homo sapiens armadillo repeat containing 1 (ARMC1), mRNA [NM_018120]
NM_004849	ATG5	0.01	Homo sapiens ATG5 autophagy related 5 homolog (S. cerevisiae) (ATG5), mRNA [NM_004849]
NM_000701	ATP1A1	34.38	Homo sapiens ATPase, Na+/K+ transporting, alpha 1 polypeptide (ATP1A1), transcript variant 1, mRNA [NM_000701]
NM_001677	ATP1B1	8.034	Homo sapiens ATPase, Na+/K+ transporting, beta 1 polypeptide (ATP1B1), transcript variant 1, mRNA [NM_001677]
NM_006886	ATP5E	6.422	Homo sapiens ATP synthase, H+ transporting, mitochondrial F1 complex, epsilon subunit (ATP5E), nuclear gene encoding mitochondrial protein, mRNA [NM_006886]
NM_001002031	ATP5G2	6.354	Homo sapiens ATP synthase, H+ transporting, mitochondrial F0 complex, subunit C2 (subunit 9) (ATP5G2), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA [NM_001002031]
NM_001002258	ATP5G3	12.48	Homo sapiens ATP synthase, H+ transporting, mitochondrial F0 complex, subunit C3 (subunit 9) (ATP5G3), nuclear gene encoding mitochondrial protein, transcript variant 3, mRNA [NM_001002258]
NM_006356	ATP5H	31.53	Homo sapiens ATP synthase, H+ transporting, mitochondrial F0 complex, subunit d (ATP5H), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA [NM_006356]

NM_006476	ATP5L	8.456	Homo sapiens ATP synthase, H ⁺ transporting, mitochondrial F0 complex, subunit G (ATP5L), nuclear gene encoding mitochondrial protein, mRNA [NM_006476]
NM_001697	ATP5O	5.68	Homo sapiens ATP synthase, H ⁺ transporting, mitochondrial F1 complex, O subunit (oligomycin sensitivity conferring protein) (ATP5O), nuclear gene encoding mitochondrial protein, mRNA [NM_001697]
NM_001694	ATP6V0C	18.3	Homo sapiens ATPase, H ⁺ transporting, lysosomal 16kDa, V0 subunit c (ATP6V0C), mRNA [NM_001694]
NM_004231	ATP6V1F	5.796	Homo sapiens ATPase, H ⁺ transporting, lysosomal 14kDa, V1 subunit F (ATP6V1F), mRNA [NM_004231]
NM_178191	ATPIF1	7.619	Homo sapiens ATPase inhibitory factor 1 (ATPIF1), nuclear gene encoding mitochondrial protein, transcript variant 3, mRNA [NM_178191]
NM_003779	B4GALT3	6.752	Homo sapiens UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 3 (B4GALT3), mRNA [NM_003779]
NM_014417	BBC3	16.84	Homo sapiens BCL2 binding component 3 (BBC3), mRNA [NM_014417]
BC032472	BC032472	400.8	Homo sapiens cDNA clone IMAGE:5216666, partial cds. [BC032472]
NM_005581	BCAM	10.34	Homo sapiens basal cell adhesion molecule (Lutheran blood group) (BCAM), transcript variant 1, mRNA [NM_005581]
NM_015379	BRI3	11.84	Homo sapiens brain protein I3 (BRI3), mRNA [NM_015379]
NM_001207	BTF3	53.41	Homo sapiens basic transcription factor 3 (BTF3), transcript variant 2, mRNA [NM_001207]
NM_006806	BTG3	5.67	Homo sapiens BTG family, member 3 (BTG3), mRNA [NM_006806]
NM_017589	BTG4	7.105	Homo sapiens B-cell translocation gene 4 (BTG4), mRNA [NM_017589]
NM_003910	BUD31	20.96	Homo sapiens BUD31 homolog (S. cerevisiae) (BUD31), mRNA [NM_003910]
NM_014038	BZW2	5.958	Homo sapiens basic leucine zipper and W2 domains 2 (BZW2), mRNA [NM_014038]
NM_024099	C11orf48	4.985	Homo sapiens chromosome 11 open reading frame 48 (C11orf48), mRNA [NM_024099]
NM_031210	C14orf156	7.407	Homo sapiens chromosome 14 open reading frame 156 (C14orf156), mRNA [NM_031210]
NM_016039	C14orf166	9.597	Homo sapiens chromosome 14 open reading frame 166 (C14orf166), mRNA [NM_016039]
NM_001005266	C15orf21	14.56	Homo sapiens chromosome 15 open reading frame 21 (C15orf21), transcript variant 1, mRNA [NM_001005266]
NM_020154	C15orf24	5.751	Homo sapiens chromosome 15 open reading frame 24 (C15orf24), mRNA [NM_020154]
NM_144600	C16orf63	6.026	Homo sapiens chromosome 16 open reading frame 63 (C16orf63), mRNA [NM_144600]
NM_152350	C17orf45	6.981	Homo sapiens chromosome 17 open reading frame 45 (C17orf45), mRNA [NM_152350]

NM_021731	C19orf28	4.558	Homo sapiens chromosome 19 open reading frame 28 (C19orf28), transcript variant 1, mRNA [NM_021731]
NM_024709	C1orf115	4.608	Homo sapiens chromosome 1 open reading frame 115 (C1orf115), mRNA [NM_024709]
NR_003242	C1orf152	5.659	Homo sapiens chromosome 1 open reading frame 152 (C1orf152) on chromosome 1 [NR_003242]
NM_001212	C1QBP	13.47	Homo sapiens complement component 1, q subcomponent binding protein (C1QBP), nuclear gene encoding mitochondrial protein, mRNA [NM_001212]
NM_020531	C20orf3	8.986	Homo sapiens chromosome 20 open reading frame 3 (C20orf3), mRNA [NM_020531]
NM_001009924	C20orf30	13.48	Homo sapiens chromosome 20 open reading frame 30 (C20orf30), transcript variant 2, mRNA [NM_001009924]
NM_012264	C22orf5	17.11	Homo sapiens chromosome 22 open reading frame 5 (C22orf5), mRNA [NM_012264]
NM_020194	C2orf33	5.058	Homo sapiens chromosome 2 open reading frame 33 (C2orf33), mRNA [NM_020194]
NM_152539	C3orf30	4.661	Homo sapiens chromosome 3 open reading frame 30 (C3orf30), mRNA [NM_152539]
NM_199417	C3orf60	5.886	Homo sapiens chromosome 3 open reading frame 60 (C3orf60), transcript variant 5, mRNA [NM_199417]
NM_032313	C4orf14	0.186	Homo sapiens chromosome 4 open reading frame 14 (C4orf14), mRNA [NM_032313]
NM_199184	C6orf108	4.992	Homo sapiens chromosome 6 open reading frame 108 (C6orf108), transcript variant 2, mRNA [NM_199184]
ENST00000378119	C6orf62	4.917	Uncharacterized protein C6orf62 (HBV X-transactivated gene 12 protein). [Source:Uniprot/SWISSPROT;Acc:Q9GZU0] [ENST00000378119]
NM_018398	CACNA2D3	0.153	Homo sapiens calcium channel, voltage-dependent, alpha 2/delta 3 subunit (CACNA2D3), mRNA [NM_018398]
NM_031897	CACNG6	5.65	Homo sapiens calcium channel, voltage-dependent, gamma subunit 6 (CACNG6), transcript variant 3, mRNA [NM_031897]
NM_005831	CALCOCO2	7.976	Homo sapiens calcium binding and coiled-coil domain 2 (CALCOCO2), mRNA [NM_005831]
NM_001743	CALM2	16.85	Homo sapiens calmodulin 2 (phosphorylase kinase, delta) (CALM2), mRNA [NM_001743]
NM_033259	CAMK2N2	10.08	Homo sapiens calcium/calmodulin-dependent protein kinase II inhibitor 2 (CAMK2N2), mRNA [NM_033259]
NM_006549	CAMKK2	0.206	Homo sapiens calcium/calmodulin-dependent protein kinase kinase 2, beta (CAMKK2), transcript variant 1, mRNA [NM_006549]
NM_001748	CAPN2	6.305	Homo sapiens calpain 2, (m/II) large subunit (CAPN2), mRNA [NM_001748]
NM_006135	CAPZA1	12.54	Homo sapiens capping protein (actin filament) muscle Z-line, alpha 1 (CAPZA1), mRNA [NM_006135]
NM_024537	CARS2	7.534	Homo sapiens cysteinyl-tRNA synthetase 2, mitochondrial (putative) (CARS2), mRNA [NM_024537]

NM_016587	CBX3	13.39	Homo sapiens chromobox homolog 3 (HP1 gamma homolog, Drosophila) (CBX3), transcript variant 2, mRNA [NM_016587]
AK023399	CC2D1A	23.85	Homo sapiens cDNA FLJ13337 fis, clone OVARC1001880. [AK023399]
NM_015933	CCDC72	37.09	Homo sapiens coiled-coil domain containing 72 (CCDC72), mRNA [NM_015933]
NM_024098	CCDC86	5.348	Homo sapiens coiled-coil domain containing 86 (CCDC86), mRNA [NM_024098]
NM_006431	CCT2	13.71	Homo sapiens chaperonin containing TCP1, subunit 2 (beta) (CCT2), mRNA [NM_006431]
NM_006430	CCT4	39.21	Homo sapiens chaperonin containing TCP1, subunit 4 (delta) (CCT4), mRNA [NM_006430]
NM_012073	CCT5	9.103	Homo sapiens chaperonin containing TCP1, subunit 5 (epsilon) (CCT5), mRNA [NM_012073]
NM_006429	CCT7	23.67	Homo sapiens chaperonin containing TCP1, subunit 7 (eta) (CCT7), transcript variant 1, mRNA [NM_006429]
NM_006585	CCT8	31.65	Homo sapiens chaperonin containing TCP1, subunit 8 (theta) (CCT8), mRNA [NM_006585]
NM_000610	CD44	8.152	Homo sapiens CD44 molecule (Indian blood group) (CD44), transcript variant 1, mRNA [NM_000610]
NM_001780	CD63	28.53	Homo sapiens CD63 molecule (CD63), transcript variant 1, mRNA [NM_001780]
NM_004356	CD81	7.793	Homo sapiens CD81 molecule (CD81), mRNA [NM_004356]
NM_001255	CDC20	5.068	Homo sapiens cell division cycle 20 homolog (S. cerevisiae) (CDC20), mRNA [NM_001255]
NM_001793	CDH3	7.588	Homo sapiens cadherin 3, type 1, P-cadherin (placental) (CDH3), mRNA [NM_001793]
NM_001798	CDK2	17.38	Homo sapiens cyclin-dependent kinase 2 (CDK2), transcript variant 1, mRNA [NM_001798]
NM_001800	CDKN2D	4.826	Homo sapiens cyclin-dependent kinase inhibitor 2D (p1,9 inhibits CDK4) (CDKN2D), transcript variant 1, mRNA [NM_001800]
NM_001806	CEBPG	6.633	Homo sapiens CCAAT/enhancer binding protein (C/EBP), gamma (CEBPG), mRNA [NM_001806]
NM_014246	CELSR1	0.207	Homo sapiens cadherin, EGF LAG seven-pass G-type receptor 1 (flamingo homolog, Drosophila) (CELSR1), mRNA [NM_014246]
NM_016139	CHCHD2	55.82	Homo sapiens coiled-coil-helix-coiled-coil-helix domain containing 2 (CHCHD2), mRNA [NM_016139]
NM_016565	CHCHD8	5.027	Homo sapiens coiled-coil-helix-coiled-coil-helix domain containing 8 (CHCHD8), mRNA [NM_016565]
NM_007236	CHP	7.844	Homo sapiens calcium binding protein P22 (CHP), mRNA [NM_007236]
NM_014918	CHSY1	7.857	Homo sapiens carbohydrate (chondroitin) synthase 1 (CHSY1), mRNA [NM_014918]
NM_006825	CKAP4	5.756	Homo sapiens cytoskeleton-associated protein 4 (CKAP4), mRNA [NM_006825]
NM_001827	CKS2	4.646	Homo sapiens CDC28 protein kinase regulatory subunit 2 (CKS2), mRNA [NM_001827]

NM_016369	CLDN18	0.0211	Homo sapiens claudin 18 (CLDN18), transcript variant 1, mRNA [NM_016369]
NM_001305	CLDN4	5.861	Homo sapiens claudin 4 (CLDN4), mRNA [NM_001305]
NM_006012	CLPP	5.885	Homo sapiens ClpP caseinolytic peptidase, ATP-dependent, proteolytic subunit homolog (E. coli) (CLPP), nuclear gene encoding mitochondrial protein, mRNA [NM_006012]
NM_004859	CLTC	11.95	Homo sapiens clathrin, heavy chain (Hc) (CLTC), mRNA [NM_004859]
NM_016057	COPZ1	5.801	Homo sapiens coatomer protein complex, subunit zeta 1 (COPZ1), mRNA [NM_016057]
ENST00000361624	COX1	4.693	Cytochrome c oxidase subunit 1 (EC 1.9.3.1) (Cytochrome c oxidase polypeptide I). [Source:Uniprot/SWISSPROT;Acc:P00395] [ENST00000361624]
NM_001861	COX4I1	5.392	Homo sapiens cytochrome c oxidase subunit IV isoform 1 (COX4I1), mRNA [NM_001861]
NM_006067	COX4NB	17.11	Homo sapiens COX4 neighbor (COX4NB), mRNA [NM_006067]
NM_004373	COX6A1	20.31	Homo sapiens cytochrome c oxidase subunit VIa polypeptide 1 (COX6A1), nuclear gene encoding mitochondrial protein, mRNA [NM_004373]
NM_144613	COX6B2	5.292	Homo sapiens cytochrome c oxidase subunit VIb polypeptide 2 (testis) (COX6B2), mRNA [NM_144613]
NM_001865	COX7A2	9.331	Homo sapiens cytochrome c oxidase subunit VIIa polypeptide 2 (liver) (COX7A2), mRNA [NM_001865]
NM_001867	COX7C	9.3	Homo sapiens cytochrome c oxidase subunit VIIc (COX7C), nuclear gene encoding mitochondrial protein, mRNA [NM_001867]
NM_016190	CRNN	0.14	Homo sapiens cornulin (CRNN), mRNA [NM_016190]
NM_001316	CSE1L	5.82	Homo sapiens CSE1 chromosome segregation 1-like (yeast) (CSE1L), mRNA [NM_001316]
NM_003798	CTNNAL1	5.217	Homo sapiens catenin (cadherin-associated protein), alpha-like 1 (CTNNAL1), mRNA [NM_003798]
NM_015921	CUTA	4.874	Homo sapiens cutA divalent cation tolerance homolog (E. coli) (CUTA), transcript variant 2, mRNA [NM_015921]
NM_005088	CXYorf3	12.09	Homo sapiens chromosome X and Y open reading frame 3 (CXYorf3), mRNA [NM_005088]
NM_000398	CYB5R3	15.35	Homo sapiens cytochrome b5 reductase 3 (CYB5R3), transcript variant M, mRNA [NM_000398]
NM_000398	CYB5R3	11.23	Homo sapiens cytochrome b5 reductase 3 (CYB5R3), transcript variant M, mRNA [NM_000398]
D00022	D00022	22.07	Homo sapiens mRNA for F1 beta subunit, complete cds. [D00022]
NM_004394	DAP	4.549	Homo sapiens death-associated protein (DAP), mRNA [NM_004394]
NM_033657	DAP3	8.364	Homo sapiens death associated protein 3 (DAP3), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA [NM_033657]
DarkCorner	DarkCorner	7.15	

NM_170711	DAZAP1	8.405	Homo sapiens DAZ associated protein 1 (DAZAP1), transcript variant 1, mRNA [NM_170711]
NM_014764	DAZAP2	9.077	Homo sapiens DAZ associated protein 2 (DAZAP2), mRNA [NM_014764]
NM_001919	DCI	5.413	Homo sapiens dodecenoyl-Coenzyme A delta isomerase (3,2 trans-enoyl-Coenzyme A isomerase) (DCI), nuclear gene encoding mitochondrial protein, mRNA [NM_001919]
NM_018403	DCP1A	7.257	Homo sapiens DCP1 decapping enzyme homolog A (S. cerevisiae) (DCP1A), mRNA [NM_018403]
NM_032299	DCUN1D5	8.175	Homo sapiens DCN1, defective in cullin neddylation 1, domain containing 5 (S. cerevisiae) (DCUN1D5), mRNA [NM_032299]
NM_001355	DDT	6.842	Homo sapiens D-dopachrome tautomerase (DDT), mRNA [NM_001355]
NM_014829	DDX46	5.538	Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 46 (DDX46), mRNA [NM_014829]
NM_017996	DET1	0.0262	Homo sapiens de-etiolated homolog 1 (Arabidopsis) (DET1), mRNA [NM_017996]
NM_001357	DHX9	4.996	Homo sapiens DEAH (Asp-Glu-Ala-His) box polypeptide 9 (DHX9), mRNA [NM_001357]
NM_005147	DNAJA3	14.55	Homo sapiens DnaJ (Hsp40) homolog, subfamily A, member 3 (DNAJA3), mRNA [NM_005147]
NM_015190	DNAJC9	5.269	Homo sapiens DnaJ (Hsp40) homolog, subfamily C, member 9 (DNAJC9), mRNA [NM_015190]
NM_001379	DNMT1	4.616	Homo sapiens DNA (cytosine-5-)-methyltransferase 1 (DNMT1), mRNA [NM_001379]
NM_001011546	DSTN	6.822	Homo sapiens destrin (actin depolymerizing factor) (DSTN), transcript variant 2, mRNA [NM_001011546]
NM_012145	DTYMK	6.216	Homo sapiens deoxythymidylate kinase (thymidylate kinase) (DTYMK), mRNA [NM_012145]
NM_004417	DUSP1	0.119	Homo sapiens dual specificity phosphatase 1 (DUSP1), mRNA [NM_004417]
NM_004419	DUSP5	9.712	Homo sapiens dual specificity phosphatase 5 (DUSP5), mRNA [NM_004419]
NM_181870	DVL1	4.894	Homo sapiens dishevelled, dsh homolog 1 (Drosophila) (DVL1), transcript variant 2, mRNA [NM_181870]
NM_006824	EBNA1BP2	31.19	Homo sapiens EBNA1 binding protein 2 (EBNA1BP2), mRNA [NM_006824]
NM_014329	EDC4	9.509	Homo sapiens enhancer of mRNA decapping 4 (EDC4), mRNA [NM_014329]
NM_152991	EED	4.466	Homo sapiens embryonic ectoderm development (EED), transcript variant 2, mRNA [NM_152991]
NM_001959	EEF1B2	117.4	Homo sapiens eukaryotic translation elongation factor 1 beta 2 (EEF1B2), transcript variant 1, mRNA [NM_001959]
NM_032378	EEF1D	5.24	Homo sapiens eukaryotic translation elongation factor 1 delta (guanine nucleotide exchange protein) (EEF1D), transcript variant 1, mRNA [NM_032378]
NM_001961	EEF2	5.996	Homo sapiens eukaryotic translation elongation factor 2 (EEF2), mRNA [NM_001961]

NM_139265	EHD4	0.0334	Homo sapiens EH-domain containing 4 (EHD4), mRNA [NM_139265]
NM_005801	EIF1	39.98	Homo sapiens eukaryotic translation initiation factor 1 (EIF1), mRNA [NM_005801]
NM_003908	EIF2S2	5.995	Homo sapiens eukaryotic translation initiation factor 2, subunit 2 beta, 38kDa (EIF2S2), mRNA [NM_003908]
NM_003758	EIF3S1	4.192	Homo sapiens eukaryotic translation initiation factor 3, subunit 1 alpha, 35kDa (EIF3S1), mRNA [NM_003758]
NM_003750	EIF3S10	5.434	Homo sapiens eukaryotic translation initiation factor 3, subunit 10 theta, 150/170kDa (EIF3S10), mRNA [NM_003750]
NM_013234	EIF3S12	7.172	Homo sapiens eukaryotic translation initiation factor 3, subunit 12 (EIF3S12), mRNA [NM_013234]
NM_003756	EIF3S3	61.64	Homo sapiens eukaryotic translation initiation factor 3, subunit 3 gamma, 40kDa (EIF3S3), mRNA [NM_003756]
NM_003751	EIF3S9	24.08	Homo sapiens eukaryotic translation initiation factor 3, subunit 9 eta, 116kDa (EIF3S9), transcript variant 1, mRNA [NM_003751]
NM_001416	EIF4A1	4.515	Homo sapiens eukaryotic translation initiation factor 4A, isoform 1 (EIF4A1), mRNA [NM_001416]
NM_022170	EIF4H	9.517	Homo sapiens eukaryotic translation initiation factor 4H (EIF4H), transcript variant 1, mRNA [NM_022170]
NM_001419	ELAVL1	12.02	Homo sapiens ELAV (embryonic lethal, abnormal vision, Drosophila)-like 1 (Hu antigen R) (ELAVL1), mRNA [NM_001419]
NM_006331	EMG1	14.34	Homo sapiens EMG1 nucleolar protein homolog (S. cerevisiae) (EMG1), mRNA [NM_006331]
NM_001424	EMP2	6.226	Homo sapiens epithelial membrane protein 2 (EMP2), mRNA [NM_001424]
NM_001427	EN2	9.828	Homo sapiens engrailed homeobox 2 (EN2), mRNA [NM_001427]
ENST00000285605	ENST00000285605	6.228	MARVEL domain-containing protein 1. [Source:Uniprot/SWISSPROT;Acc:Q9BSK0] [ENST00000285605]
ENST00000342773	ENST00000342773	4.803	Homo sapiens mRNA for FLJ00248 protein. [AK074175]
NM_001429	EP300	8.615	Homo sapiens E1A binding protein p300 (EP300), mRNA [NM_001429]
NM_022772	EPS8L2	0.01	Homo sapiens EPS8-like 2 (EPS8L2), mRNA [NM_022772]
NM_006459	ERLIN1	7.225	Homo sapiens ER lipid raft associated 1 (ERLIN1), mRNA [NM_006459]
NM_018948	ERRFI1	17.05	Homo sapiens ERBB receptor feedback inhibitor 1 (ERRFI1), mRNA [NM_018948]
NM_004730	ETF1	6.176	Homo sapiens eukaryotic translation termination factor 1 (ETF1), mRNA [NM_004730]
NM_000126	ETFA	11.25	Homo sapiens electron-transfer-flavoprotein, alpha polypeptide (glutaric aciduria II) (ETFA), nuclear gene encoding mitochondrial protein, mRNA [NM_000126]
NM_004456	EZH2	6.766	Homo sapiens enhancer of zeste homolog 2 (Drosophila) (EZH2), transcript variant 1, mRNA [NM_004456]

NM_144503	F11R	6.451	Homo sapiens F11 receptor (F11R), transcript variant 4, mRNA [NM_144503]
NM_152424	FAM123B	19.34	Homo sapiens family with sequence similarity 123B (FAM123B), mRNA [NM_152424]
BC064950	FAM134A	5.442	Homo sapiens chromosome 2 open reading frame 17, mRNA (cDNA clone IMAGE:6048607), partial cds. [BC064950]
BC106020	FAM39B	5.128	Homo sapiens family with sequence similarity 3,9 member B, mRNA (cDNA clone MGC:111476 IMAGE:4991752), complete cds. [BC106020]
NM_005687	FARSB	5.791	Homo sapiens phenylalanyl-tRNA synthetase, beta subunit (FARSB), mRNA [NM_005687]
NM_001997	FAU	10.03	Homo sapiens Finkel-Biskis-Reilly murine sarcoma virus (FBR-MuSV) ubiquitously expressed (fox derived); ribosomal protein S30 (FAU), mRNA [NM_001997]
NM_001436	FBL	40.36	Homo sapiens fibrillarin (FBL), mRNA [NM_001436]
NM_022452	FBRS	7.315	Homo sapiens fibrosin 1 (FBS1), mRNA [NM_022452]
NM_213647	FGFR4	0.213	Homo sapiens fibroblast growth factor receptor 4 (FGFR4), transcript variant 3, mRNA [NM_213647]
NM_201555	FHL2	50.35	Homo sapiens four and a half LIM domains 2 (FHL2), transcript variant 2, mRNA [NM_201555]
NM_032822	FLJ14668	5.612	Homo sapiens hypothetical protein FLJ14668 (FLJ14668), mRNA [NM_032822]
NM_024829	FLJ22662	8.429	Homo sapiens hypothetical protein FLJ22662 (FLJ22662), mRNA [NM_024829]
NM_173627	FLJ35220	0.108	Homo sapiens hypothetical protein FLJ35220 (FLJ35220), mRNA [NM_173627]
NM_001456	FLNA	5.249	Homo sapiens filamin A, alpha (actin binding protein 280) (FLNA), mRNA [NM_001456]
NM_001462	FPRL1	0.222	Homo sapiens formyl peptide receptor-like 1 (FPRL1), transcript variant 1, mRNA [NM_001462]
NM_004477	FRG1	6.076	Homo sapiens FSHD region gene 1 (FRG1), mRNA [NM_004477]
NM_002032	FTH1	47.78	Homo sapiens ferritin, heavy polypeptide 1 (FTH1), mRNA [NM_002032]
NM_007285	GABARAPL2	4.457	Homo sapiens GABA(A) receptor-associated protein-like 2 (GABARAPL2), mRNA [NM_007285]
NM_152237	GAS2L1	5.204	Homo sapiens growth arrest-specific 2 like 1 (GAS2L1), transcript variant 3, mRNA [NM_152237]
NM_198460	GBP6	16.33	Homo sapiens guanylate binding protein family, member 6 (GBP6), mRNA [NM_198460]
NM_006302	GCS1	6.643	Homo sapiens glucosidase I (GCS1), mRNA [NM_006302]
NM_004483	GCSH	13.17	Homo sapiens glycine cleavage system protein H (aminomethyl carrier) (GCSH), mRNA [NM_004483]
NM_004864	GDF15	54.41	Homo sapiens growth differentiation factor 15 (GDF15), mRNA [NM_004864]
NM_001001560	GGA1	5.958	Homo sapiens golgi associated, gamma adaptin ear containing, ARF binding protein 1 (GGA1), transcript variant 2, mRNA [NM_001001560]

NM_014394	GHITM	5.222	Homo sapiens growth hormone inducible transmembrane protein (GHITM), mRNA [NM_014394]
NM_016080	GLOD4	8.961	Homo sapiens glyoxalase domain containing 4 (GLOD4), mRNA [NM_016080]
NM_015710	GLTSCR2	10.87	Homo sapiens glioma tumor suppressor candidate region gene 2 (GLTSCR2), mRNA [NM_015710]
NM_016548	GOLPH2	8.253	Homo sapiens golgi phosphoprotein 2 (GOLPH2), transcript variant 1, mRNA [NM_016548]
NM_022913	GPBP1	7.644	Homo sapiens GC-rich promoter binding protein 1 (GPBP1), mRNA [NM_022913]
NM_019858	GPR162	0.131	Homo sapiens G protein-coupled receptor 162 (GPR162), transcript variant A-2, mRNA [NM_019858]
NM_201397	GPX1	8.859	Homo sapiens glutathione peroxidase 1 (GPX1), transcript variant 2, mRNA [NM_201397]
NM_000852	GSTP1	31.13	Homo sapiens glutathione S-transferase pi (GSTP1), mRNA [NM_000852]
NM_012412	H2AFV	6.627	Homo sapiens H2A histone family, member V (H2AFV), transcript variant 1, mRNA [NM_012412]
NM_002106	H2AFZ	10.55	Homo sapiens H2A histone family, member Z (H2AFZ), mRNA [NM_002106]
NM_001194	HCN2	6.184	Homo sapiens hyperpolarization activated cyclic nucleotide-gated potassium channel 2 (HCN2), mRNA [NM_001194]
NM_015987	HEBP1	6.634	Homo sapiens heme binding protein 1 (HEBP1), mRNA [NM_015987]
NM_015382	HECTD1	7.417	Homo sapiens HECT domain containing 1 (HECTD1), mRNA [NM_015382]
NM_014685	HERPUD1	5.11	Homo sapiens homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1 (HERPUD1), transcript variant 1, mRNA [NM_014685]
NM_004712	HGS	19.99	Homo sapiens hepatocyte growth factor-regulated tyrosine kinase substrate (HGS), mRNA [NM_004712]
NM_014362	HIBCH	6.026	Homo sapiens 3-hydroxyisobutyryl-Coenzyme A hydrolase (HIBCH), transcript variant 1, mRNA [NM_014362]
NM_005340	HINT1	14.93	Homo sapiens histidine triad nucleotide binding protein 1 (HINT1), mRNA [NM_005340]
NM_033500	HK1	8.496	Homo sapiens hexokinase 1 (HK1), nuclear gene encoding mitochondrial protein, transcript variant 5, mRNA [NM_033500]
BC002463	HLA-C	4.472	Homo sapiens major histocompatibility complex, class I, C, mRNA (cDNA clone MGC:2285 IMAGE:3345005), complete cds. [BC002463]
NM_178580	HM13	5.386	Homo sapiens histocompatibility (minor) 13 (HM13), transcript variant 2, mRNA [NM_178580]
NM_003483	HMGA2	5.302	Homo sapiens high mobility group AT-hook 2 (HMGA2), transcript variant 1, mRNA [NM_003483]
NM_002129	HMGB2	4.671	Homo sapiens high-mobility group box 2 (HMGB2), mRNA [NM_002129]
NM_012292	HMHA1	6.656	Homo sapiens histocompatibility (minor) HA-1 (HMHA1), mRNA [NM_012292]

NM_001002033	HN1	61.87	Homo sapiens hematological and neurological expressed 1 (HN1), transcript variant 3, mRNA [NM_001002033]
NM_194247	HNRPA3	10.75	Homo sapiens heterogeneous nuclear ribonucleoprotein A3 (HNRPA3), mRNA [NM_194247]
NM_004966	HNRPF	0.0187	Homo sapiens heterogeneous nuclear ribonucleoprotein F (HNRPF), mRNA [NM_004966]
NM_005968	HNRPM	14.41	Homo sapiens heterogeneous nuclear ribonucleoprotein M (HNRPM), transcript variant 1, mRNA [NM_005968]
NM_004501	HNRPU	9.142	Homo sapiens heterogeneous nuclear ribonucleoprotein U (scaffold attachment factor A) (HNRPU), transcript variant 2, mRNA [NM_004501]
NM_153631	HOXA3	4.663	Homo sapiens homeobox A3 (HOXA3), transcript variant 2, mRNA [NM_153631]
NM_018952	HOXB6	5.68	Homo sapiens homeobox B6 (HOXB6), mRNA [NM_018952]
NM_003299	HSP90B1	17.54	Homo sapiens heat shock protein 90kDa beta (Grp94), member 1 (HSP90B1), mRNA [NM_003299]
NM_005347	HSPA5	7.297	Homo sapiens heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa) (HSPA5), mRNA [NM_005347]
NM_006597	HSPA8	11.35	Homo sapiens heat shock 70kDa protein 8 (HSPA8), transcript variant 1, mRNA [NM_006597]
NM_004134	HSPA9	6.291	Homo sapiens heat shock 70kDa protein 9 (mortalin) (HSPA9), nuclear gene encoding mitochondrial protein, mRNA [NM_004134]
NM_016391	HSPC111	6.091	Homo sapiens hypothetical protein HSPC111 (HSPC111), mRNA [NM_016391]
NM_002156	HSPD1	49.44	Homo sapiens heat shock 60kDa protein 1 (chaperonin) (HSPD1), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA [NM_002156]
NM_002157	HSPE1	18.92	Homo sapiens heat shock 10kDa protein 1 (chaperonin 10) (HSPE1), mRNA [NM_002157]
NM_006644	HSPH1	8.282	Homo sapiens heat shock 105kDa/110kDa protein 1 (HSPH1), mRNA [NM_006644]
NM_000871	HTR6	10.07	Homo sapiens 5-hydroxytryptamine (serotonin) receptor 6 (HTR6), mRNA [NM_000871]
NM_016400	HYPK	11.26	Homo sapiens Huntingtin interacting protein K (HYPK), mRNA [NM_016400]
NM_002165	ID1	18.43	Homo sapiens inhibitor of DNA binding 1, dominant negative helix-loop-helix protein (ID1), transcript variant 1, mRNA [NM_002165]
NM_004907	IER2	9.82	Homo sapiens immediate early response 2 (IER2), mRNA [NM_004907]
NM_016545	IER5	9.981	Homo sapiens immediate early response 5 (IER5), mRNA [NM_016545]
NM_000597	IGFBP2	4.951	Homo sapiens insulin-like growth factor binding protein 2, 36kDa (IGFBP2), mRNA [NM_000597]
NM_006839	IMMT	12.89	Homo sapiens inner membrane protein, mitochondrial (mitofilin) (IMMT), mRNA [NM_006839]
NM_018285	IMP3	12.55	Homo sapiens IMP3, U3 small nucleolar ribonucleoprotein, homolog (yeast) (IMP3), mRNA [NM_018285]

J04208	IMPDH2	24.33	Human inosine-5'-monophosphate dehydrogenase (IMP) mRNA, complete cds. [J04208]
NM_003870	IQGAP1	5.497	Homo sapiens IQ motif containing GTPase activating protein 1 (IQGAP1), mRNA [NM_003870]
NM_194279	ISCA2	10.76	Homo sapiens iron-sulfur cluster assembly 2 homolog (S. cerevisiae) (ISCA2), mRNA [NM_194279]
ENST00000379389	ISG15	4.828	Interferon-induced 17 kDa protein precursor [Contains: Ubiquitin cross-reactive protein (hUCRP) (Interferon-induced 15 kDa protein)]. [Source:Uniprot/SWISSPROT;Acc:P05161] [ENST00000379389]
NM_002229	JUNB	6.04	Homo sapiens jun B proto-oncogene (JUNB), mRNA [NM_002229]
X56681	JUND	4.399	Human junD mRNA. [X56681]
NM_014736	KIAA0101	9.537	Homo sapiens KIAA0101 (KIAA0101), transcript variant 1, mRNA [NM_014736]
NM_014949	KIAA0907	4.995	Homo sapiens KIAA0907 (KIAA0907), mRNA [NM_014949]
NM_017641	KIF21A	0.144	Homo sapiens kinesin family member 21A (KIF21A), mRNA [NM_017641]
NM_016270	KLF2	4.456	Homo sapiens Kruppel-like factor 2 (lung) (KLF2), mRNA [NM_016270]
NM_000421	KRT10	7.118	Homo sapiens keratin 10 (epidermolytic hyperkeratosis; keratosis palmaris et plantaris) (KRT10), mRNA [NM_000421]
NM_000224	KRT18	8.532	Homo sapiens keratin 18 (KRT18), transcript variant 1, mRNA [NM_000224]
NM_002276	KRT19	34.27	Homo sapiens keratin 19 (KRT19), mRNA [NM_002276]
NM_175068	KRT73	0.0519	Homo sapiens keratin 73 (KRT73), mRNA [NM_175068]
NM_002273	KRT8	4.932	Homo sapiens keratin 8 (KRT8), mRNA [NM_002273]
NM_005561	LAMP1	9.2	Homo sapiens lysosomal-associated membrane protein 1 (LAMP1), mRNA [NM_005561]
NM_018407	LAPTM4B	13.7	Homo sapiens lysosomal associated protein transmembrane 4 beta (LAPTM4B), mRNA [NM_018407]
NM_033551	LARP1	23.8	Homo sapiens La ribonucleoprotein domain family, member 1 (LARP1), transcript variant 2, mRNA [NM_033551]
NM_002296	LBR	22.12	Homo sapiens lamin B receptor (LBR), transcript variant 1, mRNA [NM_002296]
NM_002300	LDHB	9.918	Homo sapiens lactate dehydrogenase B (LDHB), mRNA [NM_002300]
NM_032737	LMNB2	8.076	Homo sapiens lamin B2 (LMNB2), mRNA [NM_032737]
AK002085	LOC144438	8.716	Homo sapiens cDNA FLJ11223 fis, clone PLACE1008209. [AK002085]
BC062368	LOC152217	7.949	Homo sapiens hypothetical protein BC007882, mRNA (cDNA clone MGC:71256 IMAGE:6730791), complete cds. [BC062368]
NM_004125	LOC552891	5.92	Homo sapiens hypothetical protein LOC552891 (LOC552891), mRNA [NM_004125]

NM_016199	LSM7	10.32	Homo sapiens LSM7 homolog, U6 small nuclear RNA associated (S. cerevisiae) (LSM7), mRNA [NM_016199]
NM_001003690	MAD2L1BP	6.979	Homo sapiens MAD2L1 binding protein (MAD2L1BP), transcript variant 1, mRNA [NM_001003690]
NM_001017405	MAEA	19.06	Homo sapiens macrophage erythroblast attacher (MAEA), transcript variant 1, mRNA [NM_001017405]
NM_002372	MAN2A1	0.212	Homo sapiens mannosidase, alpha, class 2A, member 1 (MAN2A1), mRNA [NM_002372]
NM_152496	MANEAL	5.623	Homo sapiens mannosidase, endo-alpha-like (MANEAL), transcript variant 2, mRNA [NM_152496]
NM_002446	MAP3K10	7.627	Homo sapiens mitogen-activated protein kinase kinase kinase 10 (MAP3K10), mRNA [NM_002446]
NM_004526	MCM2	4.565	Homo sapiens MCM2 minichromosome maintenance deficient 2, mitotin (S. cerevisiae) (MCM2), mRNA [NM_004526]
NM_002388	MCM3	4.871	Homo sapiens MCM3 minichromosome maintenance deficient 3 (S. cerevisiae) (MCM3), mRNA [NM_002388]
NM_182776	MCM7	9.245	Homo sapiens MCM7 minichromosome maintenance deficient 7 (S. cerevisiae) (MCM7), transcript variant 2, mRNA [NM_182776]
NM_005917	MDH1	15.06	Homo sapiens malate dehydrogenase 1, NAD (soluble) (MDH1), mRNA [NM_005917]
NM_005918	MDH2	9.425	Homo sapiens malate dehydrogenase 2, NAD (mitochondrial) (MDH2), mRNA [NM_005918]
NM_014166	MED4	22.22	Homo sapiens mediator of RNA polymerase II transcription, subunit 4 homolog (S. cerevisiae) (MED4), mRNA [NM_014166]
NM_006838	METAP2	20.24	Homo sapiens methionyl aminopeptidase 2 (METAP2), mRNA [NM_006838]
BC004943	MGC10814	5.282	Homo sapiens hypothetical protein MGC10814, mRNA (cDNA clone MGC:10814 IMAGE:3613095), complete cds. [BC004943]
NM_001037984	MGC15523	4.897	Homo sapiens hypothetical protein MGC15523 (MGC15523), transcript variant 1, mRNA [NM_001037984]
BC026177	MGC27348	13.47	Homo sapiens ribosomal protein S2 pseudogene, mRNA (cDNA clone MGC:27348 IMAGE:4671259), complete cds. [BC026177]
NM_203477	MGC70863	5.188	Homo sapiens similar to RPL23AP7 protein (MGC70863), transcript variant 1, mRNA [NM_203477]
NM_012215	MGEA5	6.061	Homo sapiens meningioma expressed antigen 5 (hyaluronidase) (MGEA5), mRNA [NM_012215]
NM_002415	MIF	21.21	Homo sapiens macrophage migration inhibitory factor (glycosylation-inhibiting factor) (MIF), mRNA [NM_002415]
NM_014048	MKL2	5.137	Homo sapiens MKL/myocardin-like 2 (MKL2), mRNA [NM_014048]
NM_006818	MLLT11	0.141	Homo sapiens myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 11 (MLLT11), mRNA [NM_006818]
NM_019556	MOSPD1	7.908	Homo sapiens motile sperm domain containing 1 (MOSPD1), mRNA [NM_019556]

NM_005792	MPHOSPH6	4.65	Homo sapiens M-phase phosphoprotein 6 (MPHOSPH6), mRNA [NM_005792]
NM_006471	MRCL3	4.765	Homo sapiens myosin regulatory light chain MRCL3 (MRCL3), mRNA [NM_006471]
NM_033296	MRFAP1	8.762	Homo sapiens Mof4 family associated protein 1 (MRFAP1), mRNA [NM_033296]
NM_015134	M-RIP	5.273	Homo sapiens myosin phosphatase-Rho interacting protein (M-RIP), transcript variant 1, mRNA [NM_015134]
NM_017840	MRPL16	6.905	Homo sapiens mitochondrial ribosomal protein L16 (MRPL16), nuclear gene encoding mitochondrial protein, mRNA [NM_017840]
NM_032112	MRPL43	6.91	Homo sapiens mitochondrial ribosomal protein L43 (MRPL43), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA [NM_032112]
NM_022163	MRPL46	4.521	Homo sapiens mitochondrial ribosomal protein L46 (MRPL46), nuclear gene encoding mitochondrial protein, mRNA [NM_022163]
NM_021107	MRPS12	6.026	Homo sapiens mitochondrial ribosomal protein S12 (MRPS12), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA [NM_021107]
NM_031280	MRPS15	7.642	Homo sapiens mitochondrial ribosomal protein S15 (MRPS15), nuclear gene encoding mitochondrial protein, mRNA [NM_031280]
NM_016065	MRPS16	6.26	Homo sapiens mitochondrial ribosomal protein S16 (MRPS16), nuclear gene encoding mitochondrial protein, mRNA [NM_016065]
NM_014046	MRPS18B	5.995	Homo sapiens mitochondrial ribosomal protein S18B (MRPS18B), nuclear gene encoding mitochondrial protein, mRNA [NM_014046]
NM_016067	MRPS18C	5.037	Homo sapiens mitochondrial ribosomal protein S18C (MRPS18C), nuclear gene encoding mitochondrial protein, mRNA [NM_016067]
NM_032014	MRPS24	10.9	Homo sapiens mitochondrial ribosomal protein S24 (MRPS24), nuclear gene encoding mitochondrial protein, mRNA [NM_032014]
NM_021821	MRPS35	8.853	Homo sapiens mitochondrial ribosomal protein S35 (MRPS35), nuclear gene encoding mitochondrial protein, mRNA [NM_021821]
NM_033281	MRPS36	5.685	Homo sapiens mitochondrial ribosomal protein S36 (MRPS36), nuclear gene encoding mitochondrial protein, mRNA [NM_033281]
NM_031902	MRPS5	4.92	Homo sapiens mitochondrial ribosomal protein S5 (MRPS5), nuclear gene encoding mitochondrial protein, mRNA [NM_031902]
NM_182640	MRPS9	4.873	Homo sapiens mitochondrial ribosomal protein S9 (MRPS9), nuclear gene encoding mitochondrial protein, mRNA [NM_182640]
NM_005946	MT1A	4.519	Homo sapiens metallothionein 1A (MT1A), mRNA [NM_005946]
NM_005947	MT1B	4.879	Homo sapiens metallothionein 1B (MT1B), mRNA [NM_005947]

NM_175617	MT1E	4.98	Homo sapiens metallothionein 1E (MT1E), mRNA [NM_175617]
NM_005950	MT1G	8.655	Homo sapiens metallothionein 1G (MT1G), mRNA [NM_005950]
NM_176870	MT1M	8.142	Homo sapiens metallothionein 1M (MT1M), mRNA [NM_176870]
ENST00000245185	MT2A	37.4	Metallothionein-2 (MT-2) (Metallothionein-II) (MT-II) (Metallothionein-2A). [Source:Uniprot/SWISSPROT;Acc:P02795] [ENST00000245185]
NM_005953	MT2A	26.93	Homo sapiens metallothionein 2A (MT2A), mRNA [NM_005953]
NM_006636	MTHFD2	6.788	Homo sapiens methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase (MTHFD2), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA [NM_006636]
NM_002457	MUC2	0.0989	Homo sapiens mucin 2, oligomeric mucus/gel-forming (MUC2), mRNA [NM_002457]
NM_002466	MYBL2	4.967	Homo sapiens v-myb myeloblastosis viral oncogene homolog (avian)-like 2 (MYBL2), mRNA [NM_002466]
NM_002467	MYC	8.723	Homo sapiens v-myc myelocytomatosis viral oncogene homolog (avian) (MYC), mRNA [NM_002467]
NM_016132	MYEF2	0.191	Homo sapiens myelin expression factor 2 (MYEF2), mRNA [NM_016132]
NM_139207	NAP1L1	6.297	Homo sapiens nucleosome assembly protein 1-like 1 (NAP1L1), transcript variant 1, mRNA [NM_139207]
NM_172164	NASP	18.68	Homo sapiens nuclear autoantigenic sperm protein (histone-binding) (NASP), transcript variant 1, mRNA [NM_172164]
NM_005381	NCL	19.24	Homo sapiens nucleolin (NCL), mRNA [NM_005381]
NM_015331	NCSTN	5.171	Homo sapiens nicastrin (NCSTN), mRNA [NM_015331]
ENST00000361227	ND3	12.07	NADH-ubiquinone oxidoreductase chain 3 (EC 1.6.5.3) (NADH dehydrogenase subunit 3). [Source:Uniprot/SWISSPROT;Acc:P03897] [ENST00000361227]
NM_002489	NDUFA4	4.877	Homo sapiens NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 4, 9kDa (NDUFA4), nuclear gene encoding mitochondrial protein, mRNA [NM_002489]
NM_002490	NDUFA6	6.95	Homo sapiens NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 6, 14kDa (NDUFA6), nuclear gene encoding mitochondrial protein, mRNA [NM_002490]
NM_004548	NDUFB10	16.77	Homo sapiens NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 10, 22kDa (NDUFB10), mRNA [NM_004548]
NM_004547	NDUFB4	6.467	Homo sapiens NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 4, 15kDa (NDUFB4), nuclear gene encoding mitochondrial protein, mRNA [NM_004547]
NM_005004	NDUFB8	23.13	Homo sapiens NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 8, 19kDa (NDUFB8), mRNA [NM_005004]
NM_005005	NDUFB9	35.24	Homo sapiens NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 9 22kDa (NDUFB9), mRNA [NM_005005]

NM_004551	NDUFS3	5.518	Homo sapiens NADH dehydrogenase (ubiquinone) Fe-S protein 3, 30kDa (NADH-coenzyme Q reductase) (NDUFS3), mRNA [NM_004551]
NM_004552	NDUFS5	24.67	Homo sapiens NADH dehydrogenase (ubiquinone) Fe-S protein 5, 15kDa (NADH-coenzyme Q reductase) (NDUFS5), mRNA [NM_004552]
NM_006156	NEDD8	4.721	Homo sapiens neural precursor cell expressed, developmentally down-regulated 8 (NEDD8), mRNA [NM_006156]
NM_181832	NF2	6.257	Homo sapiens neurofibromin 2 (bilateral acoustic neuroma) (NF2), transcript variant 8, mRNA [NM_181832]
NM_181832	NF2	5.332	Homo sapiens neurofibromin 2 (bilateral acoustic neuroma) (NF2), transcript variant 8, mRNA [NM_181832]
NM_020529	NFKBIA	5.211	Homo sapiens nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha (NFKBIA), mRNA [NM_020529]
NM_016645	NGRN	6.242	Homo sapiens neugrin, neurite outgrowth associated (NGRN), transcript variant 1, mRNA [NM_016645]
NM_030922	NIPA2	4.252	Homo sapiens non imprinted in Prader-Willi/Angelman syndrome 2 (NIPA2), transcript variant 1, mRNA [NM_030922]
NM_002512	NME2	7.492	Homo sapiens non-metastatic cells 2, protein (NM23B) expressed in (NME2), transcript variant 1, mRNA [NM_002512]
BC006769	NOLC1	5.51	Homo sapiens nucleolar and coiled-body phosphoprotein 1, mRNA (cDNA clone MGC:5049 IMAGE:2900024), complete cds. [BC006769]
NM_000903	NQO1	13.51	Homo sapiens NAD(P)H dehydrogenase, quinone 1 (NQO1), transcript variant 1, mRNA [NM_000903]
ENST00000380068	NR2F1	12.66	COUP transcription factor 1 (COUP-TF1) (COUP-TF I) (V-ERBA-related protein EAR-3). [Source:Uniprot/SWISSPROT;Acc:P10589] [ENST00000380068]
NM_021005	NR2F2	13.16	Homo sapiens nuclear receptor subfamily 2, group F, member 2 (NR2F2), mRNA [NM_021005]
NM_014142	NUDT5	6.392	Homo sapiens nudix (nucleoside diphosphate linked moiety X)-type motif 5 (NUDT5), mRNA [NM_014142]
NM_013248	NXT1	7.718	Homo sapiens NTF2-like export factor 1 (NXT1), mRNA [NM_013248]
NM_004152	OAZ1	26.8	Homo sapiens ornithine decarboxylase antizyme 1 (OAZ1), mRNA [NM_004152]
NM_001014446	OCIAD2	9.146	Homo sapiens OCIA domain containing 2 (OCIAD2), transcript variant 1, mRNA [NM_001014446]
NM_001005203	OR8S1	0.193	Homo sapiens olfactory receptor, family 8, subfamily S, member 1 (OR8S1), mRNA [NM_001005203]
NM_006452	PAICS	4.292	Homo sapiens phosphoribosylaminoimidazole carboxylase, phosphoribosylaminoimidazole succinocarboxamide synthetase (PAICS), transcript variant 2, mRNA [NM_006452]

NM_007262	PARK7	18.16	Homo sapiens Parkinson disease (autosomal recessive, early onset) 7 (PARK7), mRNA [NM_007262]
NM_006196	PCBP1	5.54	Homo sapiens poly(rC) binding protein 1 (PCBP1), mRNA [NM_006196]
NM_032088	PCDHGA8	0.217	Homo sapiens protocadherin gamma subfamily A, 8 (PCDHGA8), transcript variant 1, mRNA [NM_032088]
NM_005020	PDE1C	0.196	Homo sapiens phosphodiesterase 1C, calmodulin-dependent 70kDa (PDE1C), mRNA [NM_005020]
NM_004911	PDIA4	4.625	Homo sapiens protein disulfide isomerase family A, member 4 (PDIA4), mRNA [NM_004911]
NM_014887	PFAAP5	4.26	Homo sapiens phosphonoformate immuno-associated protein 5 (PFAAP5), mRNA [NM_014887]
NM_007273	PHB2	7.634	Homo sapiens prohibitin 2 (PHB2), mRNA [NM_007273]
NM_007350	PHLDA1	6.001	Homo sapiens pleckstrin homology-like domain, family A, member 1 (PHLDA1), mRNA [NM_007350]
NM_003311	PHLDA2	28.67	Homo sapiens pleckstrin homology-like domain, family A, member 2 (PHLDA2), mRNA [NM_003311]
AK026345	PIF1	9.649	Homo sapiens cDNA: FLJ22692 fis, clone HSI11184. [AK026345]
NM_017733	PIGG	0.01	Homo sapiens phosphatidylinositol glycan anchor biosynthesis, class G (PIGG), mRNA [NM_017733]
NM_012398	PIP5K1C	4.585	Homo sapiens phosphatidylinositol-4-phosphate 5-kinase, type I, gamma (PIP5K1C), mRNA [NM_012398]
NM_133373	PLCD3	5.194	Homo sapiens phospholipase C, delta 3 (PLCD3), mRNA [NM_133373]
NM_015549	PLEKHG3	4.693	Homo sapiens pleckstrin homology domain containing, family G (with RhoGef domain) member 3 (PLEKHG3), mRNA [NM_015549]
NM_018049	PLEKHJ1	280.2	Homo sapiens pleckstrin homology domain containing, family J member 1 (PLEKHJ1), mRNA [NM_018049]
NM_002668	PLP2	5.112	Homo sapiens proteolipid protein 2 (colonic epithelium-enriched) (PLP2), mRNA [NM_002668]
NM_002670	PLS1	4.873	Homo sapiens plastin 1 (I isoform) (PLS1), mRNA [NM_002670]
NM_020360	PLSCR3	5.118	Homo sapiens phospholipid scramblase 3 (PLSCR3), mRNA [NM_020360]
NM_017443	POLE3	6.232	Homo sapiens polymerase (DNA directed), epsilon 3 (p17 subunit) (POLE3), mRNA [NM_017443]
NM_000937	POLR2A	22.14	Homo sapiens polymerase (RNA) II (DNA directed) polypeptide A, 220kDa (POLR2A), mRNA [NM_000937]
NM_006232	POLR2H	6.268	Homo sapiens polymerase (RNA) II (DNA directed) polypeptide H (POLR2H), mRNA [NM_006232]
NM_032959	POLR2J2	5.668	Homo sapiens DNA directed RNA polymerase II polypeptide J-related gene (POLR2J2), transcript variant 3, mRNA [NM_032959]
NM_021128	POLR2L	6.834	Homo sapiens polymerase (RNA) II (DNA directed) polypeptide L, 7.6kDa (POLR2L), mRNA [NM_021128]
NM_005837	POP7	6.522	Homo sapiens processing of precursor 7, ribonuclease P subunit (S. cerevisiae) (POP7), mRNA [NM_005837]

NM_021129	PPA1	18.13	Homo sapiens pyrophosphatase (inorganic) 1 (PPA1), mRNA [NM_021129]
NM_000943	PPIC	0.0278	Homo sapiens peptidylprolyl isomerase C (cyclophilin C) (PPIC), mRNA [NM_000943]
NM_177983	PPM1G	4.641	Homo sapiens protein phosphatase 1G (formerly 2C), magnesium-dependent, gamma isoform (PPM1G), transcript variant 1, mRNA [NM_177983]
NM_138689	PPP1R14B	7.384	Homo sapiens protein phosphatase 1, regulatory (inhibitor) subunit 14B (PPP1R14B), mRNA [NM_138689]
NM_024607	PPP1R3B	11.47	Homo sapiens protein phosphatase 1, regulatory (inhibitor) subunit 3B (PPP1R3B), mRNA [NM_024607]
NM_138558	PPP1R8	8.723	Homo sapiens protein phosphatase 1, regulatory (inhibitor) subunit 8 (PPP1R8), transcript variant 2, mRNA [NM_138558]
NM_002715	PPP2CA	5.813	Homo sapiens protein phosphatase 2 (formerly 2A), catalytic subunit, alpha isoform (PPP2CA), mRNA [NM_002715]
NM_001009552	PPP2CB	10.09	Homo sapiens protein phosphatase 2 (formerly 2A), catalytic subunit, beta isoform (PPP2CB), transcript variant 2, mRNA [NM_001009552]
NM_006406	PRDX4	8.136	Homo sapiens peroxiredoxin 4 (PRDX4), mRNA [NM_006406]
NM_004905	PRDX6	5.192	Homo sapiens peroxiredoxin 6 (PRDX6), mRNA [NM_004905]
NM_001005354	PRR13	6.536	Homo sapiens proline rich 13 (PRR13), transcript variant 3, mRNA [NM_001005354]
NM_002773	PRSS8	5.035	Homo sapiens protease, serine, 8 (PRSS8), mRNA [NM_002773]
NM_020200	PRTFDC1	0.16	Homo sapiens phosphoribosyl transferase domain containing 1 (PRTFDC1), mRNA [NM_020200]
NM_002789	PSMA4	18.14	Homo sapiens proteasome (prosome, macropain) subunit, alpha type, 4 (PSMA4), mRNA [NM_002789]
NM_002791	PSMA6	9.663	Homo sapiens proteasome (prosome, macropain) subunit, alpha type, 6 (PSMA6), mRNA [NM_002791]
NM_002793	PSMB1	36.45	Homo sapiens proteasome (prosome, macropain) subunit, beta type, 1 (PSMB1), mRNA [NM_002793]
NM_002802	PSMC1	5.809	Homo sapiens proteasome (prosome, macropain) 26S subunit, ATPase, 1 (PSMC1), mRNA [NM_002802]
NM_005805	PSMD14	4.907	Homo sapiens proteasome (prosome, macropain) 26S subunit, non-ATPase, 14 (PSMD14), mRNA [NM_005805]
NM_002823	PTMA	23.85	Homo sapiens prothymosin, alpha (gene sequence 28) (PTMA), mRNA [NM_002823]
NM_001015509	PTRH2	4.636	Homo sapiens peptidyl-tRNA hydrolase 2 (PTRH2), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA [NM_001015509]
NM_004219	PTTG1	8.83	Homo sapiens pituitary tumor-transforming 1 (PTTG1), mRNA [NM_004219]
NM_004219	PTTG1	4.869	Homo sapiens pituitary tumor-transforming 1 (PTTG1), mRNA [NM_004219]

NM_015317	PUM2	7.61	Homo sapiens pumilio homolog 2 (Drosophila) (PUM2), mRNA [NM_015317]
NM_007062	PWP1	9.827	Homo sapiens PWP1 homolog (S. cerevisiae) (PWP1), mRNA [NM_007062]
ENST00000281243	QDPR	21.81	Dihydropteridine reductase (EC 1.5.1.34) (HDHPR) (Quinoid dihydropteridine reductase). [Source:Uniprot/SWISSPROT;Acc:P09417] [ENST00000281243]
NM_024638	QTRTD1	67.01	Homo sapiens queuine tRNA-ribosyltransferase domain containing 1 (QTRTD1), mRNA [NM_024638]
NM_004578	RAB4A	5.418	Homo sapiens RAB4A, member RAS oncogene family (RAB4A), mRNA [NM_004578]
AB007940	RABGAP1L	5.586	Homo sapiens mRNA for KIAA0471 protein, partial cds. [AB007940]
NM_004582	RABGGTB	5.997	Homo sapiens Rab geranylgeranyltransferase, beta subunit (RABGGTB), mRNA [NM_004582]
NM_002882	RANBP1	18.43	Homo sapiens RAN binding protein 1 (RANBP1), mRNA [NM_002882]
NM_002887	RARS	7.849	Homo sapiens arginyl-tRNA synthetase (RARS), mRNA [NM_002887]
NM_005105	RBM8A	15.63	Homo sapiens RNA binding motif protein 8A (RBM8A), mRNA [NM_005105]
NM_005669	REEP5	4.716	Homo sapiens receptor accessory protein 5 (REEP5), mRNA [NM_005669]
NM_031922	REPS1	5.774	Homo sapiens RALBP1 associated Eps domain containing 1 (REPS1), mRNA [NM_031922]
NM_015523	REXO2	10.14	Homo sapiens REX2, RNA exonuclease 2 homolog (S. cerevisiae) (REXO2), mRNA [NM_015523]
NM_017819	RG9MTD1	6.782	Homo sapiens RNA (guanine-9-) methyltransferase domain containing 1 (RG9MTD1), mRNA [NM_017819]
NM_003617	RGS5	78.66	Homo sapiens regulator of G-protein signalling 5 (RGS5), mRNA [NM_003617]
NM_005614	RHEB	4.841	Homo sapiens Ras homolog enriched in brain (RHEB), mRNA [NM_005614]
NM_001664	RHOA	4.654	Homo sapiens ras homolog gene family, member A (RHOA), mRNA [NM_001664]
NM_002939	RNH1	6.957	Homo sapiens ribonuclease/angiogenin inhibitor 1 (RNH1), transcript variant 1, mRNA [NM_002939]
NM_007104	RPL10A	121.4	Homo sapiens ribosomal protein L10a (RPL10A), mRNA [NM_007104]
NM_000975	RPL11	5.544	Homo sapiens ribosomal protein L11 (RPL11), mRNA [NM_000975]
NM_000976	RPL12	10.66	Homo sapiens ribosomal protein L12 (RPL12), mRNA [NM_000976]
NM_003973	RPL14	9.297	Homo sapiens ribosomal protein L14 (RPL14), transcript variant 2, mRNA [NM_003973]
NM_002948	RPL15	14.38	Homo sapiens ribosomal protein L15 (RPL15), mRNA [NM_002948]
NM_002948	RPL15	6.062	Homo sapiens ribosomal protein L15 (RPL15), mRNA [NM_002948]

NM_000985	RPL17	4.824	Homo sapiens ribosomal protein L17 (RPL17), transcript variant 1, mRNA [NM_000985]
NM_000979	RPL18	6.586	Homo sapiens ribosomal protein L18 (RPL18), mRNA [NM_000979]
NM_000981	RPL19	147.7	Homo sapiens ribosomal protein L19 (RPL19), mRNA [NM_000981]
NM_000983	RPL22	9.615	Homo sapiens ribosomal protein L22 (RPL22), mRNA [NM_000983]
NM_000983	RPL22	4.747	Homo sapiens ribosomal protein L22 (RPL22), mRNA [NM_000983]
NM_000984	RPL23A	26.27	Homo sapiens ribosomal protein L23a (RPL23A), mRNA [NM_000984]
NM_000984	RPL23A	11.89	Homo sapiens ribosomal protein L23a (RPL23A), mRNA [NM_000984]
NM_000986	RPL24	19.98	Homo sapiens ribosomal protein L24 (RPL24), mRNA [NM_000986]
NM_016093	RPL26L1	7.474	Homo sapiens ribosomal protein L26-like 1 (RPL26L1), mRNA [NM_016093]
NM_000988	RPL27	42.87	Homo sapiens ribosomal protein L27 (RPL27), mRNA [NM_000988]
NM_000989	RPL30	5.171	Homo sapiens ribosomal protein L30 (RPL30), mRNA [NM_000989]
NM_000993	RPL31	17.74	Homo sapiens ribosomal protein L31 (RPL31), mRNA [NM_000993]
NM_033625	RPL34	59.35	Homo sapiens ribosomal protein L34 (RPL34), transcript variant 2, mRNA [NM_033625]
NM_000996	RPL35A	21.23	Homo sapiens ribosomal protein L35a (RPL35A), mRNA [NM_000996]
NM_015414	RPL36	5.287	Homo sapiens ribosomal protein L36 (RPL36), transcript variant 2, mRNA [NM_015414]
NM_021029	RPL36A	17.53	Homo sapiens ribosomal protein L36a (RPL36A), mRNA [NM_021029]
NM_000998	RPL37A	8.972	Homo sapiens ribosomal protein L37a (RPL37A), mRNA [NM_000998]
NM_000999	RPL38	100.7	Homo sapiens ribosomal protein L38 (RPL38), transcript variant 1, mRNA [NM_000999]
NM_001000	RPL39	7.078	Homo sapiens ribosomal protein L39 (RPL39), mRNA [NM_001000]
NM_000972	RPL7A	10.35	Homo sapiens ribosomal protein L7a (RPL7A), mRNA [NM_000972]
NM_053275	RPLP0	7.848	Homo sapiens ribosomal protein, large, P0 (RPLP0), transcript variant 2, mRNA [NM_053275]
NM_001003	RPLP1	105	Homo sapiens ribosomal protein, large, P1 (RPLP1), transcript variant 1, mRNA [NM_001003]
NM_001014	RPS10	74.54	Homo sapiens ribosomal protein S10 (RPS10), mRNA [NM_001014]
NM_001015	RPS11	6.163	Homo sapiens ribosomal protein S11 (RPS11), mRNA [NM_001015]
NM_001016	RPS12	6.311	Homo sapiens ribosomal protein S12 (RPS12), mRNA [NM_001016]

NM_001017	RPS13	22.56	Homo sapiens ribosomal protein S13 (RPS13), mRNA [NM_001017]
NM_005617	RPS14	5.668	Homo sapiens ribosomal protein S14 (RPS14), transcript variant 3, mRNA [NM_005617]
NM_001019	RPS15A	17.61	Homo sapiens ribosomal protein S15a (RPS15A), transcript variant 2, mRNA [NM_001019]
NM_001020	RPS16	21.56	Homo sapiens ribosomal protein S16 (RPS16), mRNA [NM_001020]
NM_001021	RPS17	8.042	Homo sapiens ribosomal protein S17 (RPS17), mRNA [NM_001021]
NM_002952	RPS2	10.65	Homo sapiens ribosomal protein S2 (RPS2), mRNA [NM_002952]
NM_001023	RPS20	58.03	Homo sapiens ribosomal protein S20 (RPS20), mRNA [NM_001023]
NM_001024	RPS21	19.89	Homo sapiens ribosomal protein S21 (RPS21), mRNA [NM_001024]
NM_001025	RPS23	4.25	Homo sapiens ribosomal protein S23 (RPS23), mRNA [NM_001025]
NM_001028	RPS25	35.14	Homo sapiens ribosomal protein S25 (RPS25), mRNA [NM_001028]
NM_001030	RPS27	9.202	Homo sapiens ribosomal protein S27 (metallopanstimulin 1) (RPS27), mRNA [NM_001030]
NM_001032	RPS29	22.91	Homo sapiens ribosomal protein S29 (RPS29), transcript variant 1, mRNA [NM_001032]
NM_001005	RPS3	5.221	Homo sapiens ribosomal protein S3 (RPS3), mRNA [NM_001005]
NM_001010	RPS6	136.6	Homo sapiens ribosomal protein S6 (RPS6), mRNA [NM_001010]
NM_001011	RPS7	21.93	Homo sapiens ribosomal protein S7 (RPS7), mRNA [NM_001011]
NM_001033	RRM1	4.609	Homo sapiens ribonucleotide reductase M1 polypeptide (RRM1), mRNA [NM_001033]
NM_001034	RRM2	30.43	Homo sapiens ribonucleotide reductase M2 polypeptide (RRM2), mRNA [NM_001034]
NM_006917	RXRG	7.22	Homo sapiens retinoid X receptor, gamma (RXRG), transcript variant 1, mRNA [NM_006917]
NM_005500	SAE1	15.61	Homo sapiens SUMO1 activating enzyme subunit 1 (SAE1), mRNA [NM_005500]
NM_005499	SAE2	11.05	Homo sapiens SUMO1 activating enzyme subunit 2 (SAE2), mRNA [NM_005499]
NM_005505	SCARB1	5.28	Homo sapiens scavenger receptor class B, member 1 (SCARB1), transcript variant 1, mRNA [NM_005505]
NM_016479	SCOTIN	9.123	Homo sapiens scotin (SCOTIN), mRNA [NM_016479]
NM_182706	SCRIB	5.269	Homo sapiens scribbled homolog (Drosophila) (SCRIB), transcript variant 1, mRNA [NM_182706]
NM_182706	SCRIB	5.104	Homo sapiens scribbled homolog (Drosophila) (SCRIB), transcript variant 1, mRNA [NM_182706]
NM_022044	SDF2L1	38.01	Homo sapiens stromal cell-derived factor 2-like 1 (SDF2L1), mRNA [NM_022044]

NM_014300	SEC11A	10.58	Homo sapiens SEC11 homolog A (<i>S. cerevisiae</i>) (SEC11A), mRNA [NM_014300]
NM_021237	SELK	4.555	Homo sapiens selenoprotein K (SELK), mRNA [NM_021237]
NM_003009	SEPW1	5.002	Homo sapiens selenoprotein W, 1 (SEPW1), mRNA [NM_003009]
NM_004630	SF1	8.327	Homo sapiens splicing factor 1 (SF1), transcript variant 1, mRNA [NM_004630]
NM_005066	SFPQ	7.107	Homo sapiens splicing factor proline/glutamine-rich (polypyrimidine tract binding protein associated) (SFPQ), mRNA [NM_005066]
NM_003017	SFRS3	5.625	Homo sapiens splicing factor, arginine/serine-rich 3 (SFRS3), mRNA [NM_003017]
NM_003769	SFRS9	18.09	Homo sapiens splicing factor, arginine/serine-rich 9 (SFRS9), mRNA [NM_003769]
NM_003769	SFRS9	5.266	Homo sapiens splicing factor, arginine/serine-rich 9 (SFRS9), mRNA [NM_003769]
NM_152621	SGMS2	5.131	Homo sapiens sphingomyelin synthase 2 (SGMS2), mRNA [NM_152621]
NM_030791	SGPP1	7.055	Homo sapiens sphingosine-1-phosphate phosphatase 1 (SGPP1), mRNA [NM_030791]
NM_006427	SIVA1	17.05	Homo sapiens SIVA1, apoptosis-inducing factor (SIVA1), transcript variant 1, mRNA [NM_006427]
NM_006930	SKP1A	8.761	Homo sapiens S-phase kinase-associated protein 1A (p19A) (SKP1A), transcript variant 1, mRNA [NM_006930]
NM_006598	SLC12A7	6.025	Homo sapiens solute carrier family 12 (potassium/chloride transporters), member 7 (SLC12A7), mRNA [NM_006598]
NM_004207	SLC16A3	5.489	Homo sapiens solute carrier family 16, member 3 (monocarboxylic acid transporter 4) (SLC16A3), transcript variant 2, mRNA [NM_004207]
U81800	SLC16A3	5.346	Homo sapiens monocarboxylate transporter (MCT3) mRNA, complete cds. [U81800]
NM_004695	SLC16A5	5.882	Homo sapiens solute carrier family 16, member 5 (monocarboxylic acid transporter 6) (SLC16A5), mRNA [NM_004695]
NM_006996	SLC19A2	6.703	Homo sapiens solute carrier family 19 (thiamine transporter), member 2 (SLC19A2), mRNA [NM_006996]
NM_021734	SLC25A19	8.7	Homo sapiens solute carrier family 25 (mitochondrial thiamine pyrophosphate carrier), member 19 (SLC25A19), mRNA [NM_021734]
NM_213611	SLC25A3	5.807	Homo sapiens solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 3 (SLC25A3), nuclear gene encoding mitochondrial protein, transcript variant 3, mRNA [NM_213611]
NM_001152	SLC25A5	7.17	Homo sapiens solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 5 (SLC25A5), mRNA [NM_001152]
NM_198580	SLC27A1	4.457	Homo sapiens solute carrier family 27 (fatty acid transporter), member 1 (SLC27A1), mRNA [NM_198580]

NM_003041	SLC5A2	0.0193	Homo sapiens solute carrier family 5 (sodium/glucose cotransporter), member 2 (SLC5A2), mRNA [NM_003041]
NM_006938	SNRPD1	11.09	Homo sapiens small nuclear ribonucleoprotein D1 polypeptide 16kDa (SNRPD1), mRNA [NM_006938]
NM_003096	SNRPG	44.9	Homo sapiens small nuclear ribonucleoprotein polypeptide G (SNRPG), mRNA [NM_003096]
NM_000454	SOD1	12.57	Homo sapiens superoxide dismutase 1, soluble (amyotrophic lateral sclerosis 1 (adult)) (SOD1), mRNA [NM_000454]
NM_014978	SORCS3	0.164	Homo sapiens sortilin-related VPS10 domain containing receptor 3 (SORCS3), mRNA [NM_014978]
NM_003113	SP100	9.236	Homo sapiens SP100 nuclear antigen (SP100), transcript variant 2, mRNA [NM_003113]
AK055387	SPEG	6.818	Homo sapiens cDNA FLJ30825 fis, clone FEBRA2001706, highly similar to Human APEG-1 mRNA. [AK055387]
NR_003062	SPRR2C	0.127	Homo sapiens small proline-rich protein 2C (SPRR2C) on chromosome 1 [NR_003062]
NM_021199	SQRDL	8.771	Homo sapiens sulfide quinone reductase-like (yeast) (SQRDL), mRNA [NM_021199]
NM_001005291	SREBF1	9.678	Homo sapiens sterol regulatory element binding transcription factor 1 (SREBF1), transcript variant 1, mRNA [NM_001005291]
NM_003134	SRP14	5.374	Homo sapiens signal recognition particle 14kDa (homologous Alu RNA binding protein) (SRP14), mRNA [NM_003134]
NM_003142	SSB	7.796	Homo sapiens Sjogren syndrome antigen B (autoantigen La) (SSB), mRNA [NM_003142]
NM_003143	SSBP1	4.96	Homo sapiens single-stranded DNA binding protein 1 (SSBP1), mRNA [NM_003143]
NM_003144	SSR1	7.851	Homo sapiens signal sequence receptor, alpha (translocon-associated protein alpha) (SSR1), mRNA [NM_003144]
NM_003145	SSR2	11.51	Homo sapiens signal sequence receptor, beta (translocon-associated protein beta) (SSR2), mRNA [NM_003145]
NM_003153	STAT6	13.78	Homo sapiens signal transducer and activator of transcription 6, interleukin-4 induced (STAT6), mRNA [NM_003153]
NM_006819	STIP1	7.226	Homo sapiens stress-induced-phosphoprotein 1 (Hsp70/Hsp90-organizing protein) (STIP1), mRNA [NM_006819]
NM_203401	STMN1	24.76	Homo sapiens stathmin 1/oncoprotein 18 (STMN1), transcript variant 1, mRNA [NM_203401]
NM_015894	STMN3	6.697	Homo sapiens stathmin-like 3 (STMN3), mRNA [NM_015894]
NM_007178	STRAP	19.44	Homo sapiens serine/threonine kinase receptor associated protein (STRAP), mRNA [NM_007178]
NM_004177	STX3	7.214	Homo sapiens syntaxin 3 (STX3), mRNA [NM_004177]
NM_003352	SUMO1	16.12	Homo sapiens SMT3 suppressor of mif two 3 homolog 1 (S. cerevisiae) (SUMO1), transcript variant 1, mRNA [NM_003352]

NM_002354	TACSTD1	5.323	Homo sapiens tumor-associated calcium signal transducer 1 (TACSTD1), mRNA [NM_002354]
NM_007375	TARDBP	21.71	Homo sapiens TAR DNA binding protein (TARDBP), mRNA [NM_007375]
NM_004607	TBCA	13.62	Homo sapiens tubulin folding cofactor A (TBCA), mRNA [NM_004607]
NM_005648	TCEB1	7.365	Homo sapiens transcription elongation factor B (SIII), polypeptide 1 (15kDa, elongin C) (TCEB1), mRNA [NM_005648]
NM_003200	TCF3	7.147	Homo sapiens transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) (TCF3), mRNA [NM_003200]
NM_030752	TCP1	13.42	Homo sapiens t-complex 1 (TCP1), transcript variant 1, mRNA [NM_030752]
NM_001586	TEX28	319.6	Homo sapiens testis expressed 28 (TEX28), mRNA [NM_001586]
NM_016020	TFB1M	5.926	Homo sapiens transcription factor B1, mitochondrial (TFB1M), mRNA [NM_016020]
NM_003236	TGFA	7.588	Homo sapiens transforming growth factor, alpha (TGFA), mRNA [NM_003236]
THC2603796	THC2603796	5.22	RRAS2_HUMAN (P62070) Ras-related protein R-Ras2 (Ras-like protein TC21) (Teratocarcinoma oncogene), complete [THC2603796]
THC2650296	THC2650296	0.01	RL18A_MOUSE (P62717) 60S ribosomal protein L18a, complete [THC2650296]
NM_005782	THOC4	14.47	Homo sapiens THO complex 4 (THOC4), mRNA [NM_005782]
AK025280	THRAP2	5.301	Homo sapiens cDNA: FLJ21627 fis, clone COL08058. [AK025280]
NM_012458	TIMM13	4.639	Homo sapiens translocase of inner mitochondrial membrane 13 homolog (yeast) (TIMM13), nuclear gene encoding mitochondrial protein, mRNA [NM_012458]
NM_003254	TIMP1	4.622	Homo sapiens TIMP metalloproteinase inhibitor 1 (TIMP1), mRNA [NM_003254]
NM_003258	TK1	48.01	Homo sapiens thymidine kinase 1, soluble (TK1), mRNA [NM_003258]
NM_014255	TMEM4	13.7	Homo sapiens transmembrane protein 4 (TMEM4), mRNA [NM_014255]
NM_020644	TMEM9B	11.92	Homo sapiens TMEM9 domain family, member B (TMEM9B), mRNA [NM_020644]
NM_001065	TNFRSF1A	27.93	Homo sapiens tumor necrosis factor receptor superfamily, member 1A (TNFRSF1A), mRNA [NM_001065]
NM_003807	TNFSF14	24.95	Homo sapiens tumor necrosis factor (ligand) superfamily, member 14 (TNFSF14), transcript variant 1, mRNA [NM_003807]
NM_019059	TOMM7	7.526	Homo sapiens translocase of outer mitochondrial membrane 7 homolog (yeast) (TOMM7), mRNA [NM_019059]
NM_005079	TPD52	5.983	Homo sapiens tumor protein D52 (TPD52), transcript variant 3, mRNA [NM_005079]

NM_153649	TPM3	5.735	Homo sapiens tropomyosin 3 (TPM3), transcript variant 2, mRNA [NM_153649]
NM_016292	TRAP1	16.4	Homo sapiens TNF receptor-associated protein 1 (TRAP1), mRNA [NM_016292]
NM_001011658	TRAPPC2	0.176	Homo sapiens trafficking protein particle complex 2 (TRAPPC2), transcript variant 1, mRNA [NM_001011658]
NM_016399	TRIAP1	16.27	Homo sapiens TP53 regulated inhibitor of apoptosis 1 (TRIAP1), mRNA [NM_016399]
NM_021158	TRIB3	5.91	Homo sapiens tribbles homolog 3 (Drosophila) (TRIB3), mRNA [NM_021158]
NM_003302	TRIP6	7.623	Homo sapiens thyroid hormone receptor interactor 6 (TRIP6), mRNA [NM_003302]
NM_017646	TRIT1	0.0796	Homo sapiens tRNA isopentenyltransferase 1 (TRIT1), mRNA [NM_017646]
AK055659	TSPAN5	4.432	Homo sapiens cDNA FLJ31097 fis, clone IMR321000210. [AK055659]
NM_006082	TUBA1B	51.64	Homo sapiens tubulin, alpha 1b (TUBA1B), mRNA [NM_006082]
NM_006000	TUBA4A	5.129	Homo sapiens tubulin, alpha 4a (TUBA4A), mRNA [NM_006000]
NM_00546	TP53	5.75	Homo sapiens tumor protein p53 (TP53)
NM_032525	TUBB6	7.935	Homo sapiens tubulin, beta 6 (TUBB6), mRNA [NM_032525]
NM_003329	TXN	7.594	Homo sapiens thioredoxin (TXN), mRNA [NM_003329]
NM_030755	TXNDC1	17,111	Homo sapiens thioredoxin domain containing 1 (TXNDC1), mRNA [NM_030755]
NM_032731	TXNL5	5.082	Homo sapiens thioredoxin-like 5 (TXNL5), mRNA [NM_032731]
NM_001071	TYMS	4.999	Homo sapiens thymidylate synthetase (TYMS), mRNA [NM_001071]
NM_006758	U2AF1	4.789	Homo sapiens U2 small nuclear RNA auxiliary factor 1 (U2AF1), transcript variant a, mRNA [NM_006758]
NM_003333	UBA52	15.83	Homo sapiens ubiquitin A-52 residue ribosomal protein fusion product 1 (UBA52), transcript variant 2, mRNA [NM_003333]
NM_021009	UBC	67.28	Homo sapiens ubiquitin C (UBC), mRNA [NM_021009]
NM_006357	UBE2E3	5.679	Homo sapiens ubiquitin-conjugating enzyme E2E 3 (UBC4/5 homolog, yeast) (UBE2E3), transcript variant 1, mRNA [NM_006357]
NM_003350	UBE2V2	4.44	Homo sapiens ubiquitin-conjugating enzyme E2 variant 2 (UBE2V2), mRNA [NM_003350]
NM_001003684	UCRC	5.468	Homo sapiens ubiquinol-cytochrome c reductase complex (7.2 kD) (UCRC), transcript variant 2, mRNA [NM_001003684]
NM_013282	UHRF1	5.665	Homo sapiens ubiquitin-like, containing PHD and RING finger domains, 1 (UHRF1), transcript variant 2, mRNA [NM_013282]
NM_003362	UNG	5.482	Homo sapiens uracil-DNA glycosylase (UNG), transcript variant 1, mRNA [NM_003362]

NM_006830	UQCR	10.48	Homo sapiens ubiquinol-cytochrome c reductase, 6.4kDa subunit (UQCR), mRNA [NM_006830]
NM_006004	UQCRH	3-Feb	Homo sapiens ubiquinol-cytochrome c reductase hinge protein (UQCRH), mRNA [NM_006004]
NM_014402	UQCRQ	7.412	Homo sapiens ubiquinol-cytochrome c reductase, complex III subunit VII, 9.5kDa (UQCRQ), nuclear gene encoding mitochondrial protein, mRNA [NM_014402]
NM_032747	USMG5	9.398	Homo sapiens upregulated during skeletal muscle growth 5 homolog (mouse) (USMG5), mRNA [NM_032747]
NM_021645	UTP14C	4.899	Homo sapiens UTP14, U3 small nucleolar ribonucleoprotein, homolog C (yeast) (UTP14C), mRNA [NM_021645]
NM_003378	VGF	5.302	Homo sapiens VGF nerve growth factor inducible (VGF), mRNA [NM_003378]
NM_016079	VPS24	4.775	Homo sapiens vacuolar protein sorting 24 homolog (S. cerevisiae) (VPS24), transcript variant 1, mRNA [NM_016079]
NM_100264	WAC	4.309	Homo sapiens WW domain containing adaptor with coiled-coil (WAC), transcript variant 2, mRNA [NM_100264]
NM_016303	WBP5	11.53	Homo sapiens WW domain binding protein 5 (WBP5), transcript variant 1, mRNA [NM_016303]
NM_030798	WBSCR16	4.879	Homo sapiens Williams-Beuren syndrome chromosome region 16 (WBSCR16), mRNA [NM_030798]
NM_052950	WDFY2	0.192	Homo sapiens WD repeat and FYVE domain containing 2 (WDFY2), mRNA [NM_052950]
NM_032168	WDR75	17.99	Homo sapiens WD repeat domain 75 (WDR75), mRNA [NM_032168]
NM_145294	WDR90	0.0386	Homo sapiens WD repeat domain 90 (WDR90), mRNA [NM_145294]
NM_003400	XPO1	5.32	Homo sapiens exportin 1 (CRM1 homolog, yeast) (XPO1), mRNA [NM_003400]
NM_004559	YBX1	4.318	Homo sapiens Y box binding protein 1 (YBX1), mRNA [NM_004559]
NM_017798	YTHDF1	5.2	Homo sapiens YTH domain family, member 1 (YTHDF1), mRNA [NM_017798]
NM_139118	YY1AP1	5.12	Homo sapiens YY1 associated protein 1 (YY1AP1), transcript variant 2, mRNA [NM_139118]
AK098818	ZDHHC20	8.69	Homo sapiens cDNA FLJ25952 fis, clone SYN00911. [AK098818]
NM_178566	ZDHHC21	0.0838	Homo sapiens zinc finger, DHHC-type containing 21 (ZDHHC21), mRNA [NM_178566]
NM_004926	ZFP36L1	12.96	Homo sapiens zinc finger protein 36, C3H type-like 1 (ZFP36L1), mRNA [NM_004926]
NM_153813	ZFPM1	10.25	Homo sapiens zinc finger protein, multitype 1 (ZFPM1), mRNA [NM_153813]
NM_005857	ZMPSTE24	17.2	Homo sapiens zinc metalloproteinase (STE24 homolog, S. cerevisiae) (ZMPSTE24), mRNA [NM_005857]
NM_007149	ZNF184	5.475	Homo sapiens zinc finger protein 184 (ZNF184), mRNA [NM_007149]

ENST00000217537	ZNF516	27.35	Zinc finger protein 516. [Source:Uniprot/SWISSPROT;Acc:Q92618] [ENST00000217537]
NM_152600	ZNF579	11.09	Homo sapiens zinc finger protein 579 (ZNF579), mRNA [NM_152600]
AK024487	ZNF598	5.631	Homo sapiens mRNA for FLJ00086 protein, partial cds. [AK024487]
NM_001080417	ZNF629	4.674	Homo sapiens zinc finger protein 629 (ZNF629), mRNA [NM_001080417]
NM_152437	ZNF664	22.58	Homo sapiens zinc finger protein 664 (ZNF664), mRNA [NM_152437]
NM_016096	ZNF706	7.595	Homo sapiens zinc finger protein 706 (ZNF706), transcript variant 2, mRNA [NM_016096]
NM_153358	ZNF791	5.788	Homo sapiens zinc finger protein 791 (ZNF791), mRNA [NM_153358]

[0074] Many genes involved in translational control were up-regulated. This includes genes such as TS, p53, PP2A, hsp70, thymidine kinase, and ornithine decarboxylase, which have previously been shown to be regulated by 5-FU at the post-transcriptional or translational level. The microarray expression analysis data was also confirmed using real time qRT-PCR analysis with 10 random selected genes. The results showed that the expression levels of selected genes quantified by microarray analysis are in good correlation ($P < 0.02$) with real time qRT-PCR results (Table 2). It should be noted that although technically, changes in mRNA levels are being measured in these hybridization assays, increased mRNA abundance in this polysome fraction would be expected to indicate increased levels of translation. However, some of which will also reflect in the levels of increased transcription. Changes in transcription would only be revealed when total steady state mRNA abundance is measured if there is no translation control.

Table 2: Comparison of microarray and qRT-PCR results. (Two sided Pearson correlation analysis $P = 0.02$).		
Gene Name	Microarray (fold)	qRT-PCR (fold)
RRM1	4.60	5.80
OAZ1	26.1	11.5
TK1	48.2	8.90
EIF4A	4.50	5.50
PSMC1	5.80	7.50
RPS3	5.20	3.85
STIP1	7.22	5.60
HSPA5	7.29	6.14
STX3	7.21	5.78
NEDD8	4.72	6.30

[0075] Gene Ontology (GO) analysis was performed using the DAVID Bioinformatics Resource to discover important gene pathways involved in post-transcriptional regulation (<http://david.abcc.ncifcrf.gov/>) (Huang da, W. et al. (2007) The DAVID Gene Functional Classification Tool: a novel biological module-centric algorithm to functionally analyze large gene lists. *Genome Biol*, 8, R183)(Fig 5). DAVID Gene Functional Classification algorithm allows the gene list to be condensed into organized classes based on cellular functions. The genes are grouped and clustered based on their cellular and molecular functions, which helps to identify functional related genes presented as a fuzzy heat map graphic view (Fig. 5A). A zoomed in view of cluster one is shown in Fig. 5B. Most of the genes in cluster one are associated with protein translational initiation process. The fuzziness capability is a unique feature to maximally preserve biological patterns and to discover fine differences for a given gene. More than 20 clusters were represented with unique functions such as protein synthesis, cell cycle control, and RNA binding. The distribution of major classified genes clusters is presented in Table 3.

Table 3. Distribution of Major Classified Gene Clusters	
Gene clusters	Distribution
Ribosomal Protein	11 %
Ribonucleoprotein	13 %
Protein Biosynthesis	10 %
Chaperone	3 %
Phosphoprotein	40 %
RNA binding	1 %
Cell cycle	3 %
mRNA processing	5 %
Acetylation	14 %

[0076] **Example 6. Confirmation of post-transcriptionally regulated genes.**

[0077] To confirm directly that some of the newly identified genes were indeed regulated post-transcriptionally, protein expression was measured by Western blot analysis. Western blot analysis was performed as described above. Anti-PP2A/C antibodies were used at a 1:1000 dilution and were obtained from Santa Cruz Biotech Inc., CA. The results demonstrated that proteins such as PP2A were regulated most likely at the translational level

(Fig. 6A.) as the total mRNA level of PP2A was not changed but the polysome bound PP2A mRNA was increased as demonstrated by real time qRT-PCR analysis (Fig. 6B.).

[0078] These examples describe a novel approach to systematically study post transcriptionally regulated genes from as few as 500 cells with hsp70/hsc70 antibody affinity capture beads. The results obtained from puromycin treatment further confirmed that the RNAs captured by hsp70/hsc70 antibody affinity capture beads are indeed associated with active translation events (Fig. 3). In this study, a novel method was used to capture translationally actively mRNAs, and further used to identify a number of genes post-transcriptionally regulated by 5-FU treatment, some of which will be useful in understanding 5-FU related chemosensitivity. Many of these genes would have been missed if total RNAs were profiled, since translational control does not alter steady state mRNA levels but rather translational efficiency. A number of stress induced proteins were up-regulated by 5-FU exposure. Gene ontology analysis by DAVID provides an overview of genes associated with different biological processes (Fig. 5; Table 3). In this analysis over 40% of genes identified are related to protein biosynthesis (ribosomal proteins, translational initiation factors, RNA binding proteins). Other genes involved are protein chaperons, RNA processing proteins, cell cycle control genes, phosphoproteins. Known drug resistance related genes such as calmodulin, calpain, EIFs related to mTOR pathway, proteasome 26S subunit were all up-regulated. Our results clearly showed that translational control played a major role in response to 5-FU treatment.

[0079] The polysome isolation process was monitored using known translationally regulated genes such as TS and p53 to ensure that the isolation process is robust and reproducible (Fig. 4B-C). The band patterns of TS and p53 protein are mostly full length as analyzed by Western immunoblot. This phenomenon could be due to recognition by the antibodies of full length proteins rather than the shorter polypeptides. Ten genes were randomly selected from the gene expression array analysis and confirmed by real time qRT-PCR analysis (Table 2). The results showed that the two sets of data are in good correlation.

We claim:

1. A method of isolating an actively translated RNA from a biological sample comprising the step of contacting the biological sample with a chaperone-binding molecule.
2. The method of claim 1, wherein the RNA is an mRNA.
3. The method of claim 1, wherein the chaperone binding molecule is an antibody.
4. The method of claim 1, wherein the chaperone binding molecule selectively binds to a chaperone protein selected from the group consisting of a HSP40 family chaperone protein, a HSP70 family chaperone protein, a HSP90 family chaperone protein, a HSP110 family chaperone protein, and combinations thereof.
5. The method of claim 1, wherein the chaperone binding molecule selectively binds to a HSP70 family chaperone protein.
6. The method of claim 1, wherein the chaperone binding molecule selectively binds to HSC70/HSP73.
7. The method of claim 1, wherein the biological sample comprises less than about 5000 cells, or less than 500 cells, or less than 50 cells, or less than 20 cells, or less than 5 cells.
8. The method of claim 1, wherein the biological sample comprises from 500 cells to 5000 cells, or from 50 to 500 cells, or from 20 cells to 50 cells, or from 5 cells to 20 cells, or from 1 cell to 5 cells.
9. A method of separating an actively translated RNA from a biological sample comprising:
 - a. contacting the biological sample with a chaperone-binding molecule to form a chaperone-binding molecule – chaperone complex; and
 - b. separating the chaperone-binding molecule – chaperone complex from the sample.

10. A method of analyzing an actively translated RNA from a biological sample, comprising:
- a. separating the actively translated mRNA from the biological sample according to claim 9; and
 - b. analyzing the actively translated RNA from the chaperone-binding molecule – chaperone complex.
11. The method of claim 10, wherein analyzing the actively translated RNA from the chaperone-binding molecule – chaperone complex comprises sequence analysis.
12. The method of claim 10, wherein analyzing the actively translated RNA from the chaperone-binding molecule – chaperone complex comprises determining the amount of actively translated RNA.
13. The method of claim 10, wherein analyzing the actively translated RNA from the chaperone-binding molecule – chaperone complex comprises amplification of the actively translated RNA.
14. The method of claim 10, wherein analyzing the actively translated RNA from the chaperone-binding molecule – chaperone complex comprises hybridization of the actively translated RNA to a probe.
15. The method of claim 10, wherein analyzing the actively translated RNA from the chaperone-binding molecule – chaperone complex comprises microarray analysis.
16. A method of generating an expression profile of actively translated RNA from a biological sample, comprising
- a. separating a plurality of actively translated RNAs from the biological sample according to claim 10; and
 - b. determining the relative amounts of the actively translated RNAs.
17. The method of claim 16, wherein determining the relative amounts of actively translated RNAs comprises hybridization analysis of the actively translated RNA.
18. The method of claim 16, wherein determining the relative amounts of actively translated RNAs comprises amplification analysis of the actively translated RNA.

19. The method of claim 9, wherein the biological sample is a cell lysate.
20. The method of claim 9, wherein the RNA is mRNA.
21. The method of claim 9, wherein the chaperone binding molecule is an antibody.
22. The method of claim 9, wherein the chaperone binding molecule selectively binds to a chaperone protein selected from the group consisting of a HSP40 family chaperone protein, a HSP70 family chaperone protein, a HSP90 family chaperone protein, a HSP110 family chaperone protein, and combinations thereof.
23. The method of claim 9, wherein the chaperone binding molecule selectively binds to a HSP70 family chaperone protein.
24. The method of claim 9, wherein the chaperone binding molecule selectively binds to HSC70/HSP73.
25. The method of claim 9, wherein the chaperone binding molecule selectively binds to HSP70.
26. The method of claim 9, wherein the biological sample comprises less than about 5000 cells, or less than 500 cells, or less than 50 cells, or less than 20 cells, or less than 5 cells.
27. The method of claim 9, wherein the biological sample comprises from 500 cells to 5000 cells, or from 50 to 500 cells, or from 20 cells to 50 cells, or from 5 cells to 20 cells, or from 1 cell to 5 cells.
28. A kit for separating actively translated mRNA from a biological sample comprising:
 - a. one or more chaperone-binding molecules, and
 - b. instructions for use.
29. The kit of claim 28, wherein the kit further comprises a solid support for immobilizing the one or more chaperone-binding molecules.

30. The kit of claim 28, wherein the one or more chaperone binding molecules are one or more antibodies.

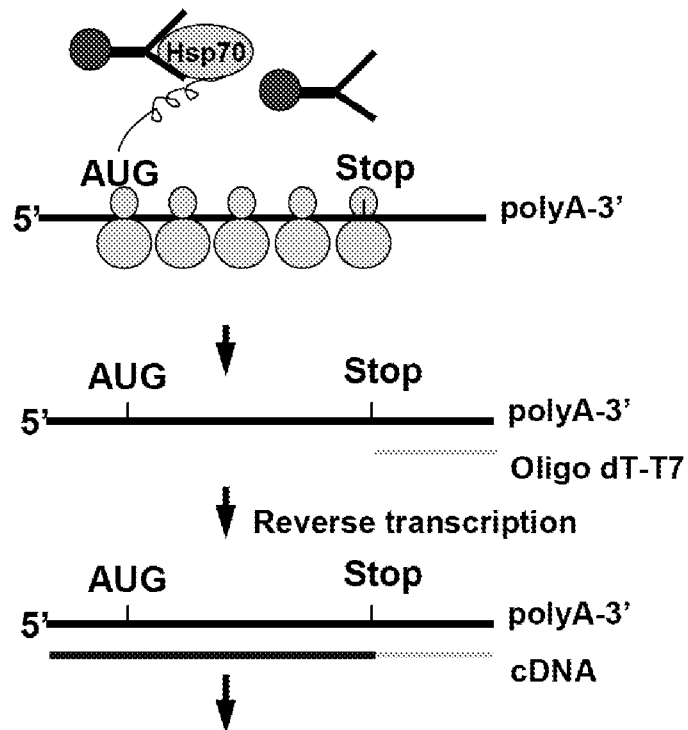
31. The kit of claim 28, wherein the one or more antibodies selectively bind a chaperone protein selected from the group consisting of a HSP40 family chaperone protein, a HSP70 family chaperone protein, a HSP90 family chaperone protein, a HSP110 family chaperone protein, and combinations thereof.

32. The kit of claim 28, wherein the antibody selectively binds to a HSP70 family chaperone protein.

33. The kit of claim 28, wherein the antibody selectively binds to HSC70/HSP73.

34. The kit of claim 28, which further comprises one or more reagents suitable for separating a complex comprising an actively translated mRNA and a chaperone protein from a biological sample.

a.



Gene Expression analysis via qPCR and Microarray

Fig. 1

b.

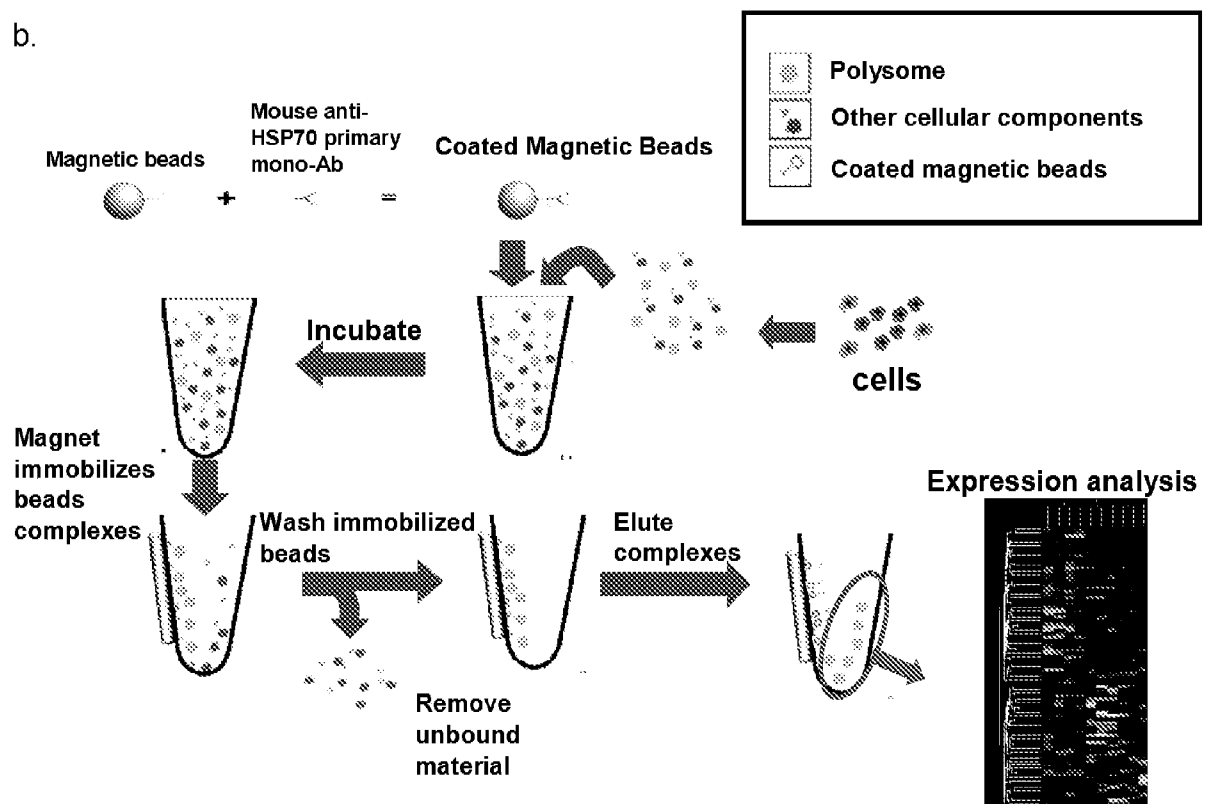


Fig. 1 (cont.)

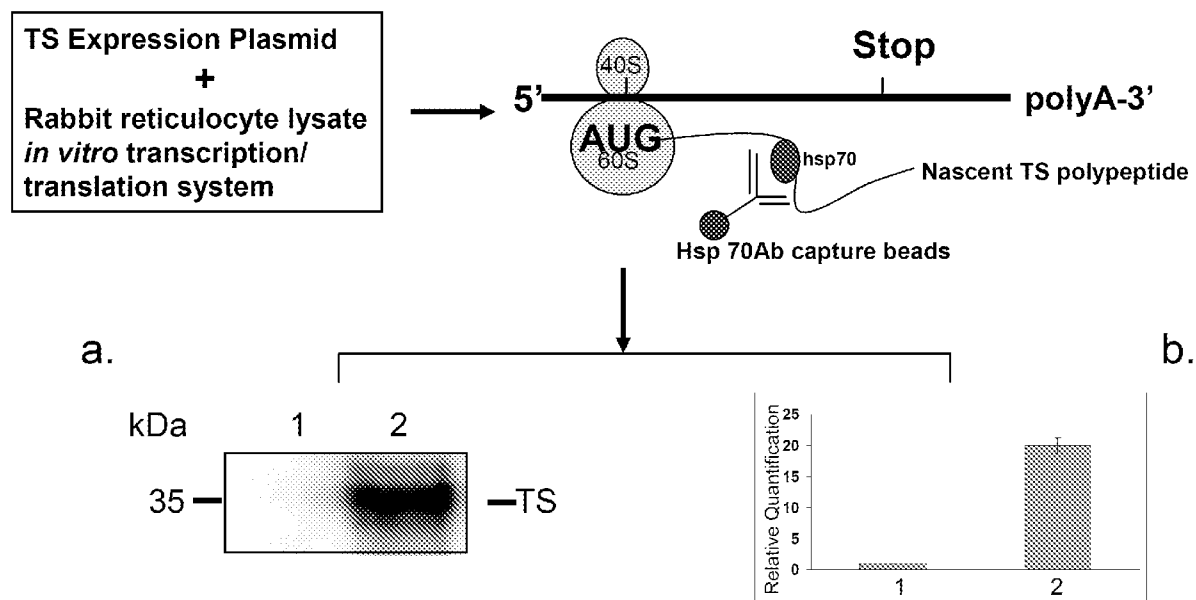
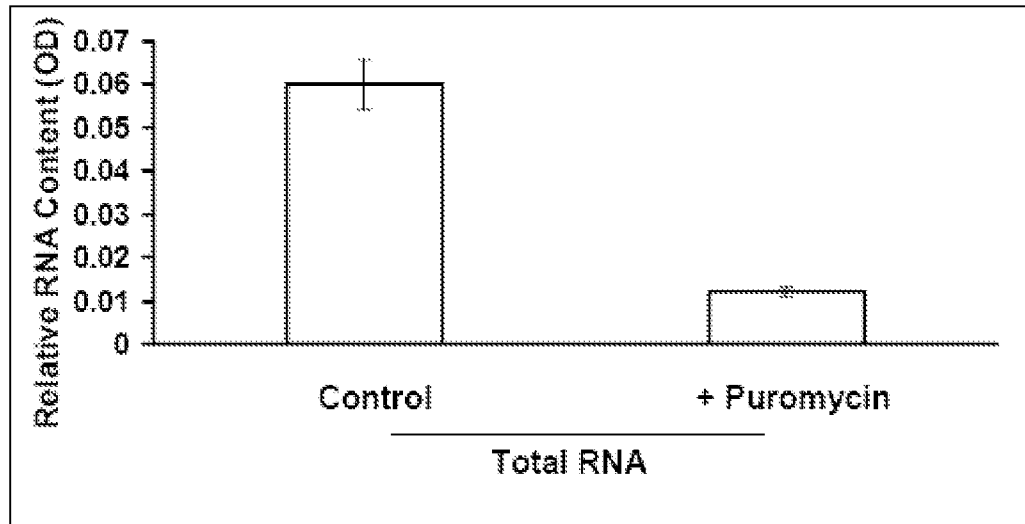


Fig. 2

A.



B.

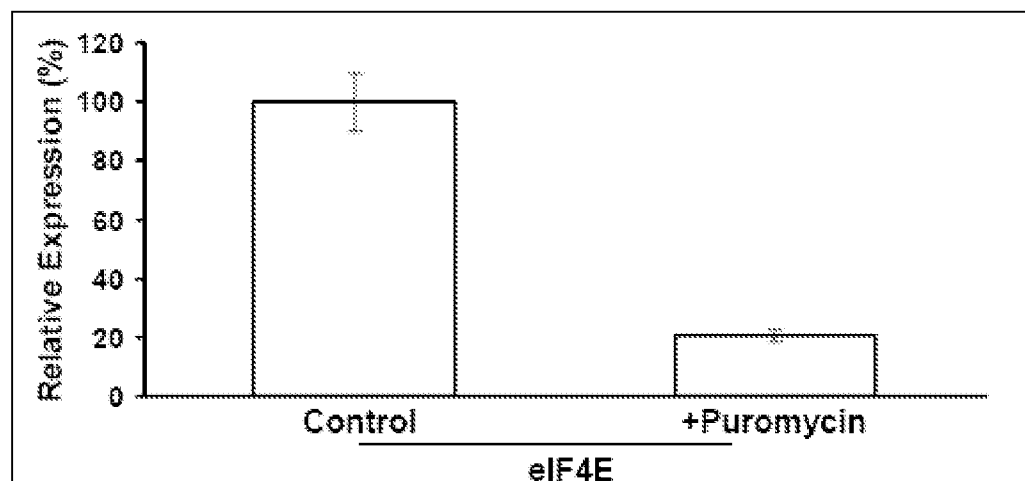
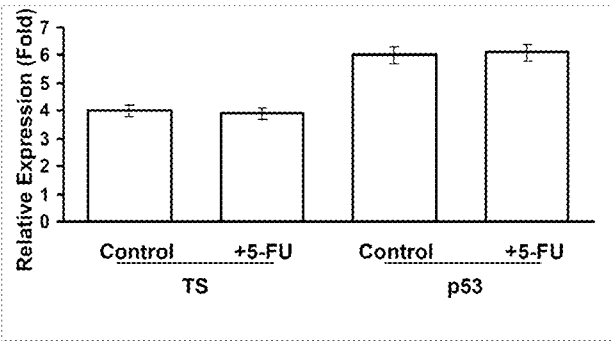
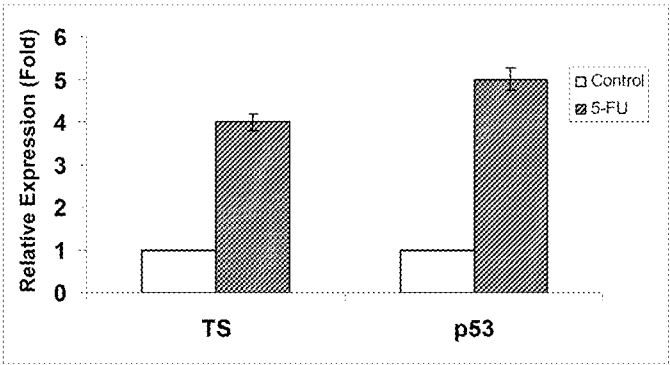


Fig. 3

a.



b.



c.

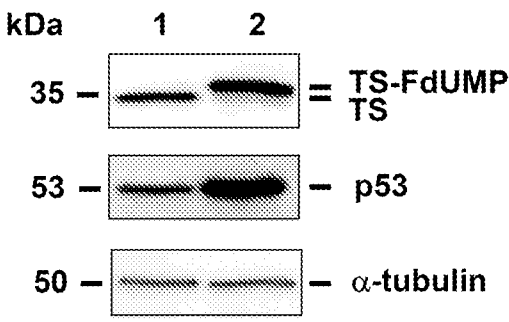
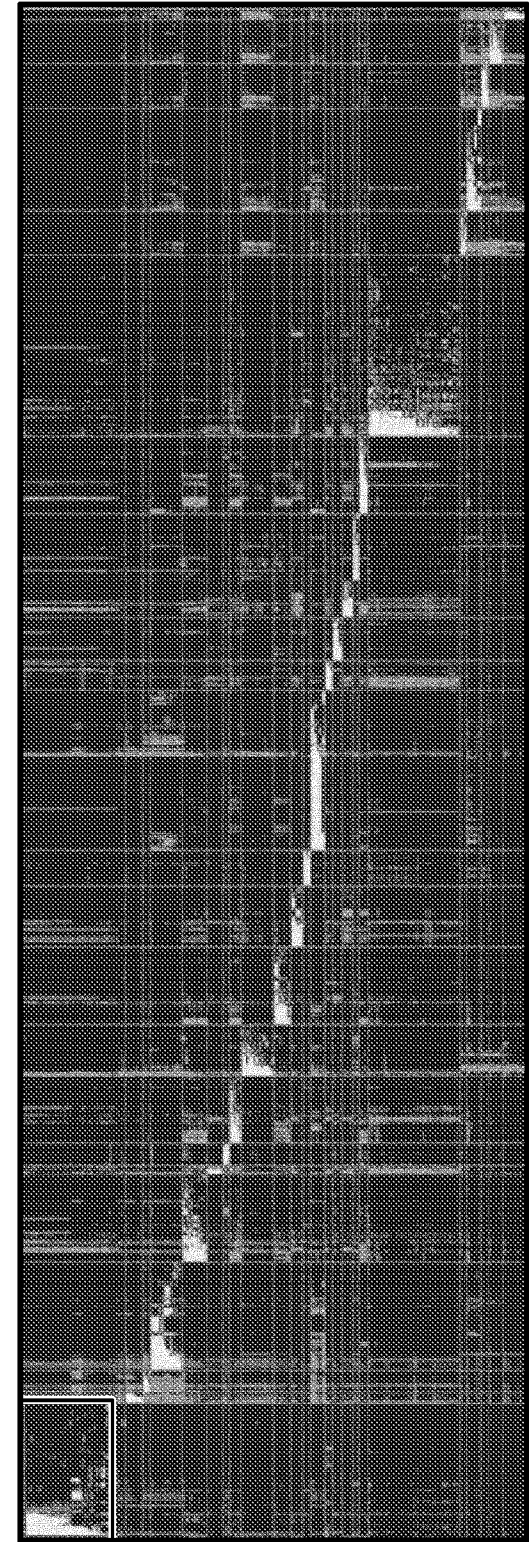


Fig. 4

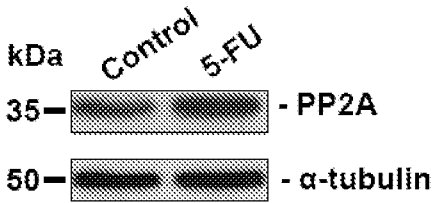


B

● GENE NAMES	○ GENE TERMS	MAP OF REGION OF INTEREST
1 ☐ RIBOSOMAL PROTEIN L23A	☐ EUKARYOTIC TRANSLATION INITIATION	
2 ☐ EUKARYOTIC TRANSLATION INITIATION	☐ SIMILAR TO RPL23AP7 PROTEIN	
3 ☐ SIMILAR TO RPL23AP7 PROTEIN	☐ WILLIAMS - BEUREN SYNDROME CHROM	
4 ☐ WILLIAMS - BEUREN SYNDROME CHROM	☐ EUKARYOTIC TRANSLATION TERMINAT	
5 ☐ EUKARYOTIC TRANSLATION TERMINAT	☐ EUKARYOTIC TRANSLATION INITIATION	
6 ☐ EUKARYOTIC TRANSLATION INITIATION	☐ EUKARYOTIC TRANSLATION INITIATION	
7 ☐ EUKARYOTIC TRANSLATION INITIATION	☐ EUKARYOTIC TRANSLATION INITIATION	
8 ☐ EUKARYOTIC TRANSLATION INITIATION	☐ BASIC LEUCINE ZIPPER AND W2 DOMA	
9 ☐ BASIC LEUCINE ZIPPER AND W2 DOMA	☐ EUKARYOTIC TRANSLATION INITIATION	
10 ☐ EUKARYOTIC TRANSLATION INITIATION	☐ EUKARYOTIC TRANSLATION INITIATION	
11 ☐ EUKARYOTIC TRANSLATION INITIATION	☐ COMPLEMENT COMPONENT 1, O SUBCO	
12 ☐ COMPLEMENT COMPONENT 1, O SUBCO	☐ RIBOSOMAL PROTEIN S14	
13 ☐ RIBOSOMAL PROTEIN S14		

FIG. 5

A.



B.

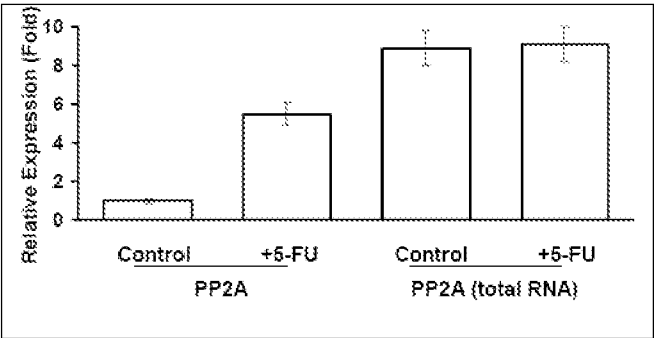


Fig. 6

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/60512

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12Q 1/68 (2011.01)

USPC - 435/6

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8) - C12Q 1/68 (2011.01)

USPC - 435/6

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 435/91.51,333

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Databases: USPTO PubWEST(PGPB,USPT,EPAB,JPAB); Google Scholar

Search terms: antibody, immunoassay, mRNA, sequence, quantify, amplify, hybridize, hsc70, hsp73, microarray, expression profile, lyse, kit, reagent, chaperone

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X - Y	US 2004/0096878 A1 (KEENE et al.) 20 May 2004 (20.05.2004), entire document, especially para [0011]-[0022], [0039]-[0040], [0071], [0084]	1-3, 7-21, 26-30, 34 4-6, 22-25, 31-33
Y	US 2003/0031661 A1 (GRANER et al.) 13 February 2003 (13.02.2003), para [0004]-[0005], [0012]-[0013], [0018], [0031], [0055]-[0057], [0061]	4-6, 22-25, 31-33
A	US 2005/0100947 A1 (WAGNER) 12 May 2005 (12.05.2005), para [0012]-[0022], [0082]	1-34
A	US 2005/0009028 A1 (HEINTZ et al.) 13 January 2005 (13.01.2005), para [0004]-[0005], [0043]-[0064], [0221]-[0240]	1-34

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

07 February 2011 (07.02.2011)

Date of mailing of the international search report

01 MAR 2011

Name and mailing address of the ISA/US

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