

Gene Section

Mini Review

RPL26 (ribosomal protein L26)

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Published in Atlas Database: September 2010

Online updated version : <http://AtlasGeneticsOncology.org/Genes/RPL26ID47470ch17p13.html>

DOI: 10.4267/2042/45029

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Identity

HGNC (Hugo): RPL26

Location: 17p13.1

DNA/RNA

Note

Human RPL26 cDNA was derived from mRNA isolated from human non-small cell lung cancer cell line SW-1573.

Description

RPL26 gene is 5731 bp in length consisting of 4 exons (the first is non-coding) and 3 introns located on the minus strand of chromosome 17p. Exon 2 contains the translation initiator ATG and exon 4 contains the stop codon. The promoter of the RPL26 gene contains an oligopyrimidine tract, TATA-like sequence and a possible binding site for Ets protein family members. Transcription starts at a C-residue within the oligopyrimidine tract.

Transcription

RPL26 mRNA transcript is 602 bp in length.

It has been reported that ribosomal protein L26 mRNA is preferentially expressed in normal early placenta (NEP) compared to L26 mRNA levels in gestational trophoblastic diseases (GTDs).

Pseudogene

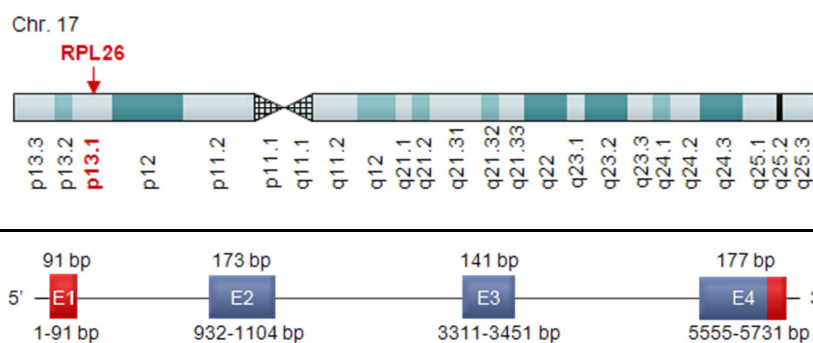
36 human pseudogenes (Entrez Gene).

An RPL26 processed pseudogene has been found within the intron of a functional RPS2 gene.

Protein

Description

Eukaryotic ribosomes consist of a small 40S and large 60S subunit. These ribosomal subunits are composed of 4 ribosomal RNAs and over 80 ribosomal proteins. RPL26 is a ribosomal protein associated with the large 60S subunit of the ribosome and contains a KOW motif, a conserved RNA-binding motif present in many ribosomal proteins.



RPL26 gene. Exons are represented by boxes (red corresponds to the 5' and 3'UTR; blue corresponds to the protein encoding sequence). The size of each exon is shown above the exon and the position of the exon within the gene is shown below each exon.



RPL26 protein. KOW: conserved RNA binding motif.

Expression

Widely expressed.

Localisation

RPL26 protein is primarily localized in the cytoplasm, to a lesser extent, it is found in the nucleoplasm and nucleolus.

Function

Ribosome biogenesis/stability: ribosome biogenesis is associated with proliferation, cell growth and stress responses. Eukaryotic ribosomes consist of a 40S and 60S subunit that are composed of 4 ribosomal RNAs (rRNAs) and approximately 80 ribosomal proteins, ribosomal protein L26 is associated with the 60S subunit of the ribosome. The ratio of rRNAs to ribosomal proteins is tightly regulated within the cell. An excess or reduction in either component can disrupt ribosome assembly. In a recent study investigating the role of ribosomal proteins in mammalian biogenesis, several ribosomal proteins, including RPL26, were individually depleted in HeLa cells using siRNAs. RPL26 knockdown resulted in a decrease in the amount of 60S ribosomal subunit as well as fully assembled ribosomes and polysomes. Also, knockdown of RPL26 resulted in a significant decrease in synthesis of 28S rRNA (associated with 60S subunit) and interestingly 18S rRNA (associated with 40S subunit). This work underscores the importance of RPL26, amongst other ribosomal proteins, in ribosome biogenesis.

Translational regulation of mRNA: protein stability has largely been attributed to increases in p53 protein levels following DNA damage however, more recent reports show an increase in translation of p53 mRNA also contributes to p53 protein levels and is necessary for optimal induction of p53 following irradiation. In particular, the RPL26 protein binds to the 5'UTR of p53 mRNA following irradiation enhancing the association of p53 mRNA with polysomes thereby increasing translation of p53 mRNA. Furthermore, RPL26-mediated enhancement of p53 translation not only resulted in an increase in p53 protein levels but also in the transactivation of downstream p53 targets as demonstrated by the induction of G1 cell-cycle arrest and enhanced apoptosis.

More recently, it has been shown that RPL26 binding to p53 mRNA following DNA damage requires not only the 5'UTR of p53 mRNA but also the 3'UTR. The interaction between complementary sequences found

within the 5' and 3'UTR of p53 mRNA creates a double-stranded RNA structure necessary for RPL26 binding to p53 mRNA. Disruption of this double-stranded RNA structure, either by base mutations in the two complementary UTR sequences or with a single-stranded oligonucleotide targeting the 5'-3'UTR base pairing, abolishes binding of RPL26 to the p53 mRNA, RPL26-enhancement of p53 translation and p53-mediated apoptosis.

Ribosomal proteins are an integral component of protein synthesis however, evidence is emerging that ribosomal proteins have additional functions outside of protein synthesis. Translational regulation of RPL26 mRNA has been shown to be an important feature of LPS-activation of human dendritic cells (DCs). During the early phase of DC maturation via LPS-activation, RPL26 mRNA is translated while during late phase of DC maturation, RPL26 mRNA is translationally down-regulated as demonstrated by a reduction in polysomal-bound RPL26 mRNA and overall RPL26 protein levels. Transcription of the RPL26 gene remained unchanged in all phases of LPS-activated DC maturation.

Interaction with MDM2: regulation of p53 protein levels within the cell has largely been attributed to changes in p53 half-life. In the absence of DNA damage, p53 protein levels are kept low via p53 interaction with MDM2, an E3-ubiquitin ligase that targets p53 for proteasomal degradation. After DNA damage, MDM2-mediated proteasomal degradation of p53 is abrogated allowing p53 protein levels to rapidly accumulate. Recently it has been reported that MDM2 can also regulate p53 protein levels by targeting RPL26-mediated translation of p53 mRNA. In the absence of DNA damage, MDM2 binds to and polyubiquitinates RPL26 targeting the RPL26 protein for proteasomal degradation thereby attenuating RPL26-enhancement of p53 translation. Following DNA damage by irradiation, the inhibitory effect of MDM2 on RPL26-enhancement of p53 translation is abrogated resulting in RPL26-mediated translation of p53 mRNA and accumulation of p53 protein.

In addition to translational regulation of p53 mRNA, it has also been reported that overexpressed RPL26 can regulate p53 protein stability through interaction with MDM2. The interaction of RPL26 with MDM2 stabilizes total p53 protein levels by blocking MDM2-mediated ubiquitination of p53 protein and its subsequent proteasomal degradation.

Homology

RPL26, a member of the L24P family of ribosomal proteins, is an evolutionary conserved protein found in all eukaryotes including *M. musculus*, *R. norvegicus*, *D. melanogaster*, *C. elegans*, *S. pombe*, *S. cerevisiae*.

HomoloGene: 113207. Gene conserved in Eukaryota (HomoloGene).

Mutations

Note

No human RPL26 mutations have been reported. A cell line derived from a UV-induced murine tumor with both alleles of the RPL26 gene harboring different point mutations (P22S and H96Y) has been reported.

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This article should be referenced as such:

Boggs K, Kastan M. RPL26 (ribosomal protein L26). *Atlas Genet Cytogenet Oncol Haematol*. 2011; 15(6):470-472.
