GAS5 (growth arrest-specific 5 (non-protein coding))

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Identity

Other names: NCRNA00030; SNHG2
HGNC (Hugo): GAS5
Location: 1q25.1

Note: GAS5 is also designed as small nucleolar RNA host gene (non-protein coding) 2 and non-protein coding RNA 30.
1q25 locus displays abnormalities in a number of cancers, melanoma, prostate, breast and several types of leukaemia and lymphoma. The GAS5 gene was isolated from NIH 3T3 cells using subtraction hybridisation, in a screen intended to isolate potential tumor suppressor genes. The functions of GAS5 is not well known as yet, however, emerging evidence implicates this gene in apoptosis, autoimmune disease, leukemias and lymphomas, and other cancers.

DNA/RNA

Description

nucleolar RNA (snoRNA) host gene similar to UHG (U22 host gene) which encode, within the 11 introns of the human GAS5 gene, ten box C/D snoRNAs predicted to play a role in the 2'-O-methylation of rRNA. Its 5' end sequence contains an oligopyrimidine tract characteristic of the 5'-TOP class of genes.

**Transcription**

The length of GAS5 transcript is 651 bp (NR_002578 in GenBank). The 5' end sequence of the GAS5 transcript contains an oligopyrimidine tract characteristic of the 5'-TOP class of genes. GAS5 transcripts display several patterns of alternate splicing. The initial GAS5 transcript is subject to complex post-transcriptional processing resulting in several splice variants. However its putative open reading frame is small and poorly conserved during even relatively short periods of evolution, as demonstrated by a number of disruptions caused by frameshift mutations in several mouse strains, and by an interruption by a stop codon after the first 13 amino acids in rat GAS5. The diagram above shows some of GAS5 splice variants which are reported to affect cell fate in different ways.

**Protein**

Note

GAS5 exons do not encode a polypeptide product.

**Mutations**

Note

Chromosomal rearrangements involving GAS5 have been identified in a human B-cell lymphoma where GAS5 gene becomes fused to the BCL6 gene. GAS5 is also involved in a chromosomal rearrangement with Notch1 in radiation-induced murine thymic lymphoma.

**Regulation of cell growth**

Note

The GAS5 gene was isolated from NIH 3T3 cells using subtraction hybridisation, in a screen intended to isolate potential tumor suppressor genes. GAS5 is reported to be ubiquitously expressed during mouse development and adult life, and also to be expressed only at low levels in actively growing Friend leukemia and NIH 3T3 cells, with substantially increased abundance in cells grown to saturation density. The RNA levels of GAS5 appear to be regulated primarily through changes in its rate of degradation rather than through changes in its transcription rate. GAS5 RNA abundance was also found to be increased by amino acid deprivation. Studies also have shown that GAS5 is necessary and sufficient for growth arrest in both untransformed and leukaemic lymphocytes.

**Systemic lupus erythematosus**

**Note**

The GAS5 gene is located in the disease susceptibility locus in mouse BXSB strain, which develops glomerulonephritis associated with systemic lupus erythematosus (SLE). Subsequent studies involving genetic analysis of a mouse model of SLE have indicated that GAS5 may well be involved in its pathology. Besides, the human chromosomal locus 1q25 at which the GAS5 gene is encoded has been associated with SLE in genetic studies in humans.

**Apoptosis/cell cycle regulation**

**Note**

A fragment of GAS5 cDNA has been isolated from a retroviral cDNA expression library by using an unbiased functional screen for genes that control apoptosis in lymphocytes. Further studies have shown that GAS5 plays an essential role in normal growth arrest in both T-cell lines and non-transformed lymphocytes. Overexpression of GAS5 causes both an enhancement in apoptosis and a decrease in the rate of progression through the cell cycle in leukaemic T cell lines and primary lymphocytes. Consistent with this, downregulation of endogenous GAS5 inhibits apoptosis and maintains a more rapid cell cycle, indicating that GAS5 expression is both essential and sufficient for normal growth arrest in T-cell lines as well as human peripheral blood T-cells. Overexpression of certain GAS5 transcripts is reported to induce growth arrest and apoptosis in several mammalian cell lines.

**Oncogenesis**

**Note**

GAS5 is encoded at 1q25, a locus displaying abnormalities in a number of cancers, e.g. melanoma, prostate, breast, and several types of leukaemia and lymphoma. Gene expression analysis has shown that GAS5 is up-regulated 3.3-fold (the greatest up-regulation for any gene in the whole-genome array) by oncogenic kinases associated with myeloproliferative disorders. Chromosomal rearrangements involving GAS5 have also been identified in a human B-cell lymphoma. GAS5 expression levels are reported to regulate both the induction of apoptosis and cell cycle arrest in T-cell lines and non-transformed lymphocytes, suggesting that it may be very significant in the development of leukaemia and lymphoma. Overexpression of certain GAS5 transcripts is reported to induce growth arrest and apoptosis in several human cell lines, including human breast cancer cell lines. GAS5 expression is significantly downregulated in breast cancer tissue compared with those found in untransformed breast epithelial tissue from the same patients, a clear reduction of more than 65% was
observed in this study, suggesting that the reduction in GAS5 expression is an early event in oncogenesis.

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