Gene Section
Short Communication

SRSF1 (serine/arginine-rich splicing factor 1)

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Identity

Other names: ASF, FLJ53078, MGC5228, SF2, SF2p33, SRS1, SRp30a
HGNC (Hugo): SRSF1
Location: 17q22

DNA/RNA

Genomic structure of the SRSF1 gene. The black area indicates the coding sequence.

Description

The SRSF1 locus spans 6424 bp on the minus (-) strand of the long arm of chromosome 17 and is composed of 4 exons.

Transcription

ASF-1 (SF2) contains 4 exons (248 aa). Two additional cDNAs generated by alternative 3' splice-site use or by intron retention have been described and are designated ASF-2 (292 aa) and ASF-3 (201 aa), respectively. However, ASF/SF2 is the only isoform expressed at detectable levels.

Pseudogene

No known pseudogenes.

Protein

Description

248 amino acids, 28 kDa.

Schematic diagram of SF2/ASF protein. SF2/ASF has a modular structure with two RNA recognition motifs (RRM) that provide RNA-binding specificity and one arginine/serine-rich domain (RS), involved in protein-protein interactions that facilitate recruitment of the spliceosome. The RS domain acts also as a nuclear localization signal, controlling the subcellular localization of SF2/ASF. The protein can be phosphorylated in Ser residues in the C-terminal RS domain.

Expression

SF2/ASF is constitutively expressed in all cell types. However, there are differences in expression levels between cell types and organs. Moreover, in some pathological conditions the expression levels are altered.

Localisation

SF2/ASF is a shuttling protein with a high mobility between the nucleus and the cytoplasm. In the nucleus, SF2/ASF is concentrated in speckles and when transcription is activated it accumulates at the sites of transcription.

Function

SF2/ASF modulates both constitutive and alternative pre-mRNA splicing. The function of SF2/ASF in splicing depends on the pre-mRNA sequence and the cellular context. Cis-acting sequences and trans-acting factors modulate SF2/ASF activity. For example, SF2/ASF antagonizes the activity of hnRNP A/B proteins in splice site selection. An excess of hnRNP A1 favors distal 5' splice sites, whereas SF2/ASF promotes the use of proximal 5' splice sites.
SF2/ASF is also involved in transcription, mRNA export, nonsense-mediated mRNA decay, and translation.

**Homology**

SF2/ASF shares a high homology with other members of the SR family. SR proteins are conserved across vertebrates and invertebrates. They contain one or two copies of an RNA recognition motif (RRM) at the amino-terminus, spaced by a series of glycine residues that may form a flexible hinge, and a carboxy-terminal highly charged SR domain.

**Mutations**

**Note**
No mutations have been reported. Gene amplification has been found in some tumor types.

**Implicated in**

**Various cancers**

**Note**
SF2/ASF acts as an oncogene. SF2/ASF is upregulated in various human tumors, including lung, colon, kidney, liver, pancreas, ovary, cervix, and breast. Upregulation is sometimes associated with gene amplification. Overexpression of SF2/ASF is sufficient to transform immortal rodent fibroblasts. mTORC1 activation may be essential for SF2/ASF-mediated transformation. SF2/ASF-bound mRNAs recruit the mTOR kinase, resulting in the phosphorylation and release of 4E-BP, leading to translation initiation. Clinical tumors with SF2/ASF up-regulation may be especially sensitive to mTOR inhibitors.

**Non-small cell lung cancer (NSCLC)**

**Note**
SF2/ASF and survivin expression are involved in non-small cell lung cancer progression. SF2/ASF is overexpressed in lung cancer cell lines and human NSCLC specimens. SF2/ASF controls the expression of survivin through the activation of the mTOR pathway.

**Prostate cancer**

**Note**
Cyclin D1b oncogene is induced by SF2/ASF. SF2/ASF associates with cyclin D1b mRNA, an alternative splicing of the CCND1 transcript with enhanced oncogenic functions. SF2/ASF expression correlates with cyclin D1b in human prostate cancer.

**Cystic fibrosis**

**Note**
Aberrant regulation of CFTR exon 9 alternative splicing by splicing factors may be associated with cystic fibrosis. SF2/ASF binds to an intronic splicing silencer of exon 9 of CFTR and promotes exon exclusion.

**Cardiac remodeling**

**Note**
SF2/ASF has a role in cardiac remodeling. ASF/SF2 is a key regulator of alternative splicing events during postnatal heart remodeling.

**Retroviral splicing**

**Note**
SF2/ASF regulates retroviral splicing. SF2/ASF has been implicated in the regulation of retroviral splicing in Rous sarcoma virus, HIV-1 and HPV-16.

**Cell motility**

**Note**
SF2/ASF activates epithelial to mesenchymal transition. DeltaRon, a splicing isoform of the tyrosine kinase receptor Ron, increases motility. DeltaRon is generated by the skipping of exon 11. SF2/ASF, by controlling the production of DeltaRon, activates epithelial to mesenchymal transition, leading to cell locomotion.

**References**


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