SRSF3 (serine/arginine-rich splicing factor 3)

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Identity

Other names: SFRS3, SRp20
HGNC (Hugo): SRSF3
Location: 6p21.31

DNA/RNA

Description
SRSF3 gene contains 6 exons and spans 10155 bp on the plus (+) strand of the short arm of chromosome 6.

Transcription
SRSF3 mRNA is in size of 3144 nts and encodes a protein with 164 amino acid residues.
By including an alternative exon between exon 3 and exon 4, SRSF3 pre-mRNA could generate additional isoform of SRSF3 transcript.

Pseudogene
No.

Protein

Description
164 amino acid residues, 20 kDa.

Expression
Expression of SRSF3 varies significantly in different cell types.
For example, the expression of SRSF3 is abundant in the undifferentiated or intermediately differentiated keratinocytes in the basal and parabasal layers, but drops significantly in terminally differentiated keratinocytes in the superficial layers of the cervix or skin.
In general, normal cells like muscle or nerve cells have no or little expression of SRSF3.
In contrast, malignant tumor cells express remarkable amount of SRSF3 when compared to their normal counterparts.

Localisation
SRSF3 is a shuttling protein between nucleus and cytoplasm.

Function
SRSF3 is a splicing factor and involved in the regulation of RNA splicing.
It affects alternative splicing by interacting with RNA cis-elements in a concentration and cell differentiation-dependent manner.

Diagram of genomic structure of SRSF3 gene. The numbers above the diagram are the nucleotide positions in SRSF3 gene. The open boxes and broken lines represent exons and introns, respectively.
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Diagram of protein structure of SRSF3. The numbers below the diagram are the amino acid positions in SRSF3 protein. SRSF3 has an RNA recognition motifs (RRM) in the N-terminus and an arginine/serine-rich domain (RS) at the C-terminus. RRM motif identifies and binds specific RNA sequences. RS domain interacts with other proteins and facilitates recruitment of the spliceosomal components. The serine residues of the RS domain can be phosphorylated.

Moreover, SRSF3 plays important roles in RNA export from nuclear to cytoplasm, termination of transcription, alternative RNA polyadenylation, and protein translation. SRSF3 is required for embryonic development and cell cycle progression. SRSF3 at increased expression is tumorigenic and is required for tumor initiation, progression, and maintenance.

Alternative splicing of pre-mRNA
SRSF3 controls viral early to late switch by regulation of gene expression of bovine papillomavirus type 1 and human papillomavirus through interaction with A/C-rich RNA elements (Jia et al., 2009). SRSF3 promotes the inclusion of exon 4 of its own mRNA and reduces the expression of full length SRSF3 protein (Jumaa and Nielsen, 1997). SRSF3 activates the inclusion of exon 10 of PK-M gene to promote the expression of oncogenic M2 isoform (Wang et al., 2012). SRSF3 inhibits the inclusion of a fibronectin cassette exon in the mature mRNA by interacting with RNA polymerase II C-terminal domain (de la Mata and Kornblihtt, 2006).

Termination of transcription
SRSF3 plays a role in termination of transcription by binding to RNA downstream of the cleavage site, facilitating its degradation, and the release of Pol II from template DNA (Cui et al., 2008).

Alternative polyadenylation
The 3'-terminal exon 4 of calcitonin pre-mRNA contains an alternative polyadenylation site. SRSF3 affects the inclusion of exon 4 and alternative polyadenylation by the interaction with CstF (Lou et al., 1998).

RNA export
SRSF3 associates with TAP promoting the export of intronless mRNA of histone H2a gene by interacting with a 22-nt RNA element (Huang et al., 2003; Huang and Steitz, 2001).

Protein translation
SRSF3 is required for poliovirus translation initiation. SRSF3 binds to internal ribosome entry site (IRES) of a viral RNA by interaction with PCBP2 (Bedard et al., 2007).

Homology
Human SRSF3 protein is highly conserved in chimpanzee, dog, sheep, cow, mouse, rat, chicken, zebrafish and so on. SRSF3 is the smallest member of SR (serine/arginine-rich) family and shares a high homology with other members. All of SR proteins contain at least one RRM and one downstream RS domain enriched in repeating arginine-serine dipeptides.

Mutations
Note
There is one mutation which causes amino acid residue change according to NCBI dbSNP database.

Implicated in
Cancer
Note
SRSF3 is a protooncogene. Overexpression of SRSF3 has been found in various cancers, including cervix, lung, breast, stomach, skin, bladder, colon, liver, thyroid, and kidney; and in various soft tissue tumors, including B-cell lymphoma, rhabdomyosarcoma, hemangioendothelioma, hemangiopericytoma, neurofibroma, neurilemmoma, liposarcoma, leiomyosarcoma, histiocytoma, and synovial sarcoma. SRSF3 at overexpression has transformation activity for MEF/3T3 cells, a mouse embryonic fibroblast cell line. SRSF3 controls cell cycle progression and thereby cell proliferation presumably by regulating the expression of forkhead box transcription factor M1 (FoxM1), PLK1 and Cdc25B.

References
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