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Gene Section
Mini Review

SCAF1 (SR-related CTD-associated factor 1)

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Identity

Other names: FLJ00034, SCAF, SFRS19, SRA1, SR-A1,

HGNC (Hugo): SCAF1

Location: 19q13.33

Local order: Telomere to centromere.

Note: The first name of this gene, discovered and cloned by Scorilas et al. was SR-A1. After the establishment of the name "SRA1" for steroid receptor RNA activator 1, the official name of SR-A1 gene has changed into SCAF1, to avoid confusion.

DNA/RNA

Description

Spanning 16.5 kb of genomic DNA, the SCAF1 gene consists of 11 exons and 10 intervening introns (Scorilas et al., 2001).

Transcription

The unique transcript of SCAF1 gene is 4313 bp.

The human SCAF1 gene was shown to be expressed widely in many normal tissues, but its mRNA levels vary a lot. The highest levels of SCAF1 transcripts were detected in the fetal brain and fetal liver and the lowest in salivary gland, skin, heart, uterus and ovary.
In the mammary and prostate gland, SCAF1 mRNA transcripts are constitutively present at relatively high levels.
The mRNA levels of SCAF1 appear to increase in cancer cell lines treated with various steroid hormones, including estrogens, androgens and glucocorticoids, and to a lesser extent with progestins (Scorilas et al., 2001).

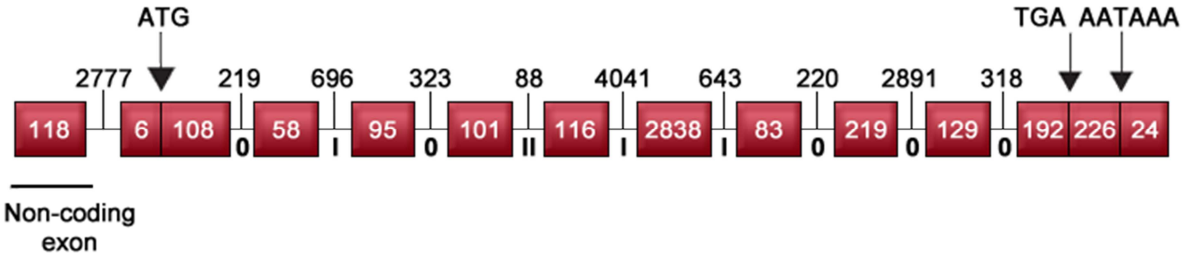
Pseudogene

Not identified so far.

Protein

Description

The SCAF1 protein is composed of 1312 amino acids, with a calculated molecular mass of 139.1 kDa and a theoretical isoelectric point of 9.31.



Schematic representation of the SCAF1 gene. Exons are shown as boxes and introns as connecting lines. Arrows show the positions of the start codon, stop codon, and polyadenylation signal. Roman numerals indicate intron phases. The intron phase refers to the location of the intron within the codon; I denotes that the intron occurs after the first nucleotide of the codon, II that the intron occurs after the second nucleotide, and 0 that the intron occurs between distinct codons. The numbers inside boxes indicate exon lengths and the vertical connecting lines show the intron lengths (in bp). Figure is not drawn to scale.

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   1 MEEEDESRGK TEESGEDRGD GPPDRDPTLS PSAFILRAIQ QAVGSSLQGD LPNDKDGSRC
  61 HGLRWRRCRS PRSEPRSQES GGTDTATVLD MATDSFLAGL VSVLDPPDTW VPSRLDLRPG
 121 ESEDMLELVA EVRIGDRDPI PLPVPSLLPR LRAWRTGKTV SPQSNSSRPT CARHLTLGTG
 181 DGGPAPPPAP SSASSSPSPS PSSSSPSPPP PPPPPAPPAP PAPRFDIYDP FHPTDEAYSP
 241 PPAPEQKYDP FEPTGSNPSS SAGTPSPEEE EEEEEEEEEE EEDEEEEEGL SQSISRISET
 301 LAGIYDDNSL SQDFPGDESP RPDAQPTQPT PAPGTPPQVD STRADGAMRR RVFVVGTEAE
 361 ACREGKVSVE VVTAGGAALP PPLLPPGDSE IEEGEIVQPE EEPRLALSLF RPGGRAARPT
 421 PAASATPTAQ PLPQPPAPRA PEGDDFLSLH AESDGEGALQ VDLGEPAPAP PAADSRWGGL
 481 DLRRKILTQR RERYRQRSPS PAPAPAPAAA AGPPTRKKSR RERKRSGEAK EAASSSSGTQ
 541 PAPPAPASPW DSKKHRSRDR KPGSHASSSA RRRSRSRSRS RSTRRRSRST DRRRGGSRRS
 601 RSREKRRRRR RSASPPPATS SSSSSRRERH RGKHRDGGGS KKKKKRSRSR GEKRSGDGSE
 661 KAPAPAPPPS GSTSCGDRDS RRRGAVPPSI QDLTDHDLFA IKRTITVGRL DKSDPRGPSP
 721 APASSPKREV LYDSEGLSGE ERGGKSSQKD RRRSGAASSS SSSREKGSRR KALDGGDRDR
 781 DRDRDRDRDR SSKKARPPKE SAPSSGPPPK PPVSSGSGSS SSSSSCSSRK VKLQSKVAVL
 841 IREGVSSTTP AKDAASAGLG SIGVKFSRDR ESRSPFLKPD ERAPTEMAKA APGSTKPKKT
 901 KVKAKAGAKK TKGTKGKTKP SKTRKKVRSG GGSGGSGGQV SLKKSKADSC SQAAGTKGAE
 961 ETSWSGEERA AKVPSTPPPK AAPPPPALTP DSQTVDSSCK TPEVSFLPEE ATEEAGVRGG
1021 AEEEEEEEEE EEEEEEEEEQ QPATTTATST AAAAPSTAPS AGSTAGDSGA EDGPASRVSQ
1081 LPTLPPPMPW NLPAGVDCTT SGVLALTALL FKMEEANLAS RAKAQELIQA TNQILSHRKP
1141 PSSLGMTPAP VPTSLGLPPG PSSYLLPGSL PLGGCGSTPP TPTGLAATSD KREGSSSSEG
1201 RGDTDKYLKK LHTQERAVEE VKLAIKPYYQ KKDITKEEYK DILRKAVHKI CHSKSGEINP
1261 VKVSNLVRAY VQRYRYFRKH GRKPGDPPGP PRPPKEPGPP DKGGPGLPLP PL
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Schematic representation of the amino acid sequence of the SCAF1 protein. The Arg/Ser-rich domain is shown in bold and underlined, and the CTD-binding domain is double-underlined. Additionally, the SCAF1 protein contains two areas with negatively charged polyglutamic acid (E) stretches, shown as underlined with dashes, and an Arg/Asp-rich motif, which is normally underlined. Various putative post-translational modification sites have also been identified, including numerous potential sites for either O- or N-glycosylation, and several possible sites of phosphorylation by cAMP-dependent protein kinase (PKA), protein kinase C (PKC), and casein kinase 2.

The SCAF1 protein contains an Arg/Ser-rich domain (SR) as well as a CTD-binding domain, present only in a subset of Arg/Ser-rich splicing factors.

Through interactions with the pre-mRNA and the C-terminal domain (CTD) of the large subunit of RNA polymerase II, Arg/Ser-rich proteins have been shown to regulate alternative splicing. In addition, we identified two areas with negatively charged polyglutamic acid (E) stretches and an Arg/Asp-rich motif in the SCAF1 protein. This motif is also present in a number of other RNA-binding proteins such as the U1-70 K, the RD RNA-binding protein and the 68 kDa human pre-mRNA cleavage factor I_m.

Examination of the hydrophobicity profile of the SCAF1 protein did not reveal regions with long stretches of hydrophobic residues.

SCAF1 is predicted to be a nuclear protein with no transmembrane region.

Various putative post-translational modification sites have been identified, including numerous potential sites for either O- or N-glycosylation, and several possible sites of phosphorylation by cAMP-dependent protein kinase (PKA), protein kinase C (PKC), and casein kinase 2 (Scorilas et al., 2001).

Expression

Currently, there are no data concerning the in vivo expression of the human SCAF1 protein.

Localisation

The SCAF1 protein is predicted to be localized to the nucleus.

Function

SCAF1 interacts with the CTD domain of the RNA polymerase II polypeptide A (POLR2A) and may be involved in pre-mRNA splicing.

Homology

Human SCAF1 shares 85% amino acid identity and 91% similarity with the mouse and rat Scaf1 protein. Moreover, it shows 25% identity and 48% similarity with the human PHRF1 protein ("PHD and RING finger domain-containing protein 1", also known as "CTD-binding SR-like protein rA9"), and to a lesser extent with other Arg/Ser-rich splicing factors.

Mutations

No germinal or somatic mutations associated with cancer have been identified so far.

Implicated in

Breast and ovarian cancer

Prognosis

Expression analysis of the SCAF1 gene has showed that SCAF1 mRNA expression may be considered as a new unfavorable prognostic marker for breast and ovarian cancer. Expression of the SCAF1 gene in breast cancer tissues is influenced by the tumor size and the existence of lymph node metastases. Furthermore, high SCAF1 expression is a significant independent prognostic marker of disease-free survival (DFS), and low mRNA expression of the gene is associated with long DFS and overall survival (OS).
Regarding SCAF1 gene expression in ovarian cancer, it is positively related to the histological grade and stage of the disease, the size of the tumor, and the debulking success. Additionally, high SCAF1 expression is a significant independent prognostic marker of OS, and low mRNA expression of the gene is related to long DFS and OS.

Colon cancer

Prognosis

SCAF1 mRNA expression seems also to be associated with colon cancer progression, since its expression is higher at the initial stages of tumorigenesis and is reduced as cancer progresses.

Leukemia

Prognosis

Alterations of SCAF1 mRNA expression have been noticed in the human acute promyelocytic leukemia cell line HL-60, after treatment with cisplatin and bleomycin. mRNA levels of SCAF1 are modulated in both cases as a response to apoptosis induction by each drug, with up-regulation in bleomycin-induced apoptosis and down-regulation in cisplatin-induced apoptosis in HL-60 cells. This differential response of SCAF1 mRNA levels to apoptosis induced by each drug may be due to distinct apoptotic pathways and therefore to distinct cellular needs for the splice variants of specific genes.

Cytogenetics

No cytogenetic abnormalities have been identified so far.

Hybrid/Mutated gene

Not identified so far.

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