

Gene Section

Mini Review

SOCS1 (suppressor of cytokine signaling 1)

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Identity

Hugo: SOCS1

Other names: JAB (JAK binding protein); CIS1 (cytokine-inducible SH2 protein 1); SSI1 (STAT-induced STAT inhibitor); TIP3 (Tec-interacting protein 3); CISH1; SSI-1

Location: 16p13.13

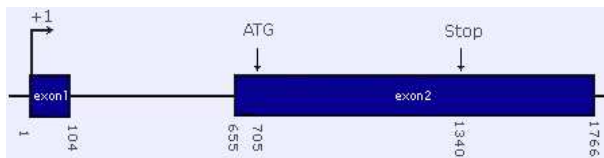
DNA/RNA

Description

The SOCS1 gene is divided in 2 exons. The exon 1 contains the 5'untranslated region. The exon 2 contains part of 5'untranslated region, the translation initiation ATG, the stop codon, and the 3'untranslated region.

Transcription

The 1216 bases of human SOCS1 mRNA contains an open reading frame of 633 bases, resulting in a protein of 211 amino acid residues.



The sequence numbering shown under the central diagram are according to Genebank accession no. NC000016 for SOCS1 DNA.

Protein

Description

The SOCS1 is a member of the STAT-induced STAT inhibitor (SSI), also known as suppressor of cytokine signaling (SOCS), family. The SSI family members are cytokine-inducible negative regulators of cytokine

signaling. The SOCS1 possesses tumor suppressor function.

Localisation

Cytoplasmic.

Function

The SOCS1 functions downstream of cytokine receptors, and takes part in a negative feedback loop to attenuate cytokine signaling. The SOCS1 is rapidly induced following stimulation by several type I and type II cytokines, and it attenuates their signaling by its ability to bind and inhibit all four of the Janus family of intracellular tyrosine kinases (JAKs). The SOCS1 functions as a negative regulator in TNF-induced inflammation and activation of c-jun N-terminal kinase by mediating ASK1 degradation in endothelial cells.

The SOCS-1 is found to colocalize and biochemically copurify with the microtubule organizing complex (MTOC) and its associated 20S proteasome. The SOCS-1 SH2 domain is required for the localization of SOCS-1 to the MTOC and targets Jak1 to a perinuclear distribution resembling the MTOC-associated 20S proteasome.

Mutations

Note: Mutations of the tumor suppressor gene SOCS-1 in classical Hodgkin lymphoma and primary mediastinal B-cell lymphoma are frequent.

Somatic

191-218del (V64S, out-of-frame), 349-359del (V117, out-of-frame), 393-417del (Q131H, delA132-H136), 431-512del (F144C, out-of-frame), 435-446del (D145E, delC146-E149), 448C>G (L150V)

The sequence numberings are according to the Genebank accession number NM_003745 for SOCS1 mRNA.

Implicated in

Various cancers and diseases

Note: Aberrant methylation in the CpG island of SOCS1.

Disease

Hepatocellular carcinoma, hepatoblastoma, hepatitis C virus-associated chronic hepatitis and liver cirrhosis, brain tumor, head and neck squamous cell carcinoma, gastric carcinoma, pancreatic cancer, colorectal cancer, acute myeloid leukemia, multiple myeloma, myelodysplastic syndrome, chronic myeloid leukemia.

Oncogenesis

Loss-of-expression by aberrant DNA methylation.

Hodgkin lymphoma, primary mediastinal B-cell lymphoma

Note: Somatic origin.

Oncogenesis

Loss-of-function mutations.

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