

Gene Section

Mini Review

SOCS2 (suppressor of cytokine signaling 2)

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Identity

Hugo: SOCS2

Other names: CIS-2, Cytokine-inducible SH2 protein 2; CIS2, STAT induced STAT inhibitor-2; Cish2, STAT-induced STAT inhibitor 2; SOCS-2, suppressor of cytokine signaling 2; SSI-2, suppressor of cytokine signaling-2; SSI2; STATI2

Location: 12q21.33

Local order: By cytogenetic and radiation hybrid mapping, SOCS-2 has been mapped to chromosome 12q21.3-q23 (Yandava et al., 1999).

DNA/RNA

Description

6,38 kb; 3 exons. Mouse SOCS2 gene is composed of 3 exons and 2 introns (Metcalf et al., 2000). Human SOCS-2 is a functioning gene that comprises 3 exons spanning roughly 6,38 kb of genomic DNA.

Transcription

2210 bp mRNA. 1 protein (22.2 kDa; 198 aa). Although constitutively expressed SOCS2 mRNA has been detected in several tissues and cell types, its expression is, in general, induced by stimulation with different cytokines and hormones (Rico-Bautista et al., 2006). SOCS2 promoter analysis indicates the presence of AhR and STAT5 binding sites that confer responsiveness to dioxin (Boverhof et al., 2004) and GH (Vidal et al., 2006), respectively.

Protein

Description

22.2 kDa; 198 aa.

Expression

SOCS mRNA and protein levels are constitutively low in unstimulated cells, but their expression is rapidly induced upon cytokine stimulation, thereby creating a negative feedback loop. Its expression is, in general, induced by stimulation with different cytokines and hormones (Rico-Bautista et al., 2006).

Localisation

Intracellular, cytoplasm.

Function

SOCS mechanisms of action rely on their ability to bind tyrosine phosphorylated proteins through their SH2 domains, but also to bind Elongin BC through their SOCS box domains. SOCS family proteins form part of a classical negative feedback system that regulates cytokine signal transduction (Rico-Bautista et al., 2006). SOCS2 appears to be a negative regulator in the growth hormone/IGF1 signaling pathway (Metcalf et al., 2000). SOCS2 appear to be involved in regulating protein turnover, targeting proteins for proteasome-mediated degradation (Rico-Bautista et al., 2004).

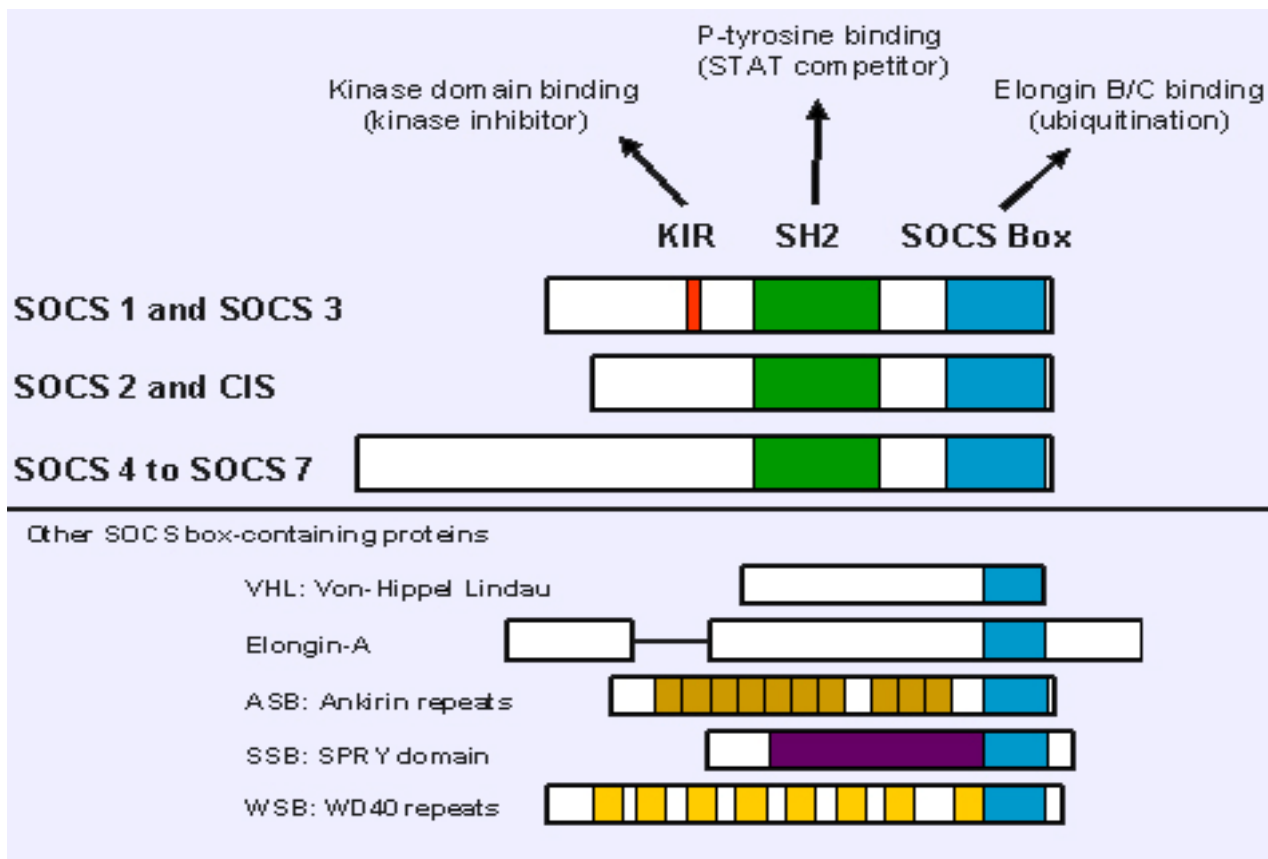


Diagram representing the structure of SOCS proteins. At least eight proteins belonging to the SOCS family of proteins are shown (upper panel). They are characterized by the presence of an SH2 central domain and the SOCS box domain at the C-terminus. A small domain called kinase inhibitory region (KIR), only found in SOCS1 and SOCS3, is shown as a small box at the N-terminal region. SOCS proteins can interact with phosphotyrosine phosphorylated proteins through their SH2 domain and with Elongin BC through their SOCS box domain. Other proteins containing a SOCS box domain but lacking a SH2 domain are also shown (lower panel). Adapted from Elliott and Johnston (Elliott and Johnston, 2004) with modifications.

Mutations

Note: SNP: increasing the risk of type 2 diabetes.

Implicated in

Diabetes

Note: Susceptibility to type 2 diabetes (Kato et al., 2006).

Metabolism

Note: SOCS2 null mice are giants but not obese (Metcalf et al., 2000). SOCS2 deficient mice have some metabolic characteristics that can be related to the enhanced GH actions (Rico-Bautista et al., 2005).

Bone

Note: Analysis of SOCS2 null mice have revealed that the absence of SOCS2 induces a reduction in the trabecular and cortical volumetric bone mineral density (Lorentzon et al., 2005). SOCS2 induces the

differentiation of C2C12 mesenchymal cells into myoblasts or osteoblasts (Ouyang et al., 2006).

Neural development

Note: SOCS2 plays a critical role in neuronal development, growth, and stem cell differentiation (Turnley et al., 2002).

Cancer

Note: SOCS2 has been associated with cancer such as myeloid leukaemia, pulmonary adenocarcinoma, and ovarian cancer, breast cancer, and anal cancer.

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