

Gene Section

Mini Review

SMAD2 (mothers against decapentaplegic homolog 2 (Drosophila))

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Published in Atlas Database: July 2004

Online updated version: <http://AtlasGeneticsOncology.org/Genes/SMAD2ID370.html>
DOI: 10.4267/2042/38110

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Identity

Other names: MADH2; MADR2; JV18-1; JV18

HGNC (Hugo): SMAD2

Location: 18q21.1



Probe(s) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Description

The gene encompasses 90 kb of DNA; 12 exons.

Transcription

2285 nucleotides mRNA. Alternative splicing was described.

Protein

Description

467 amino acids; 52 kDa protein. A short 438 amino acids isoform was also described. Smad2 belongs to the Darwin proteins family which are composed of two conserved amino- and carboxyl-terminal domains known as MH1 and MH2, respectively.

Expression

High expression levels in skeletal muscle, heart and placenta.

Function

Smad2 is an intracellular mediator of TGF-beta family and activin type 1 receptor. Smad2 mediate TGF-beta signaling to regulate cell growth and differentiation. Smad2 is released from cytoplasmic retention by TGF-beta receptor-mediated phosphorylation. The phosphorylated Smad2 then forms a heterodimeric complex with Smad4, and this complex translocates from cytoplasm into nucleus. By interacting with DNA-binding proteins, Smad complexes then positively or negatively regulate the transcription of target genes.

Homology

With the other members of the Darwin/Smad family.

Implicated in

Disease

Colorectal cancers

Oncogenesis

Smad2 was proposed to be a tumor suppressor gene that may function to disrupt TGF-beta signaling. Inactivating mutations in Smad2 have been found in various cancer including colorectal carcinomas. The majority of tumor-derived mutations cluster in the carboxy-terminal MH2 domain, and some of these have been shown to disrupt TGF-beta signaling by blocking receptor-dependent phosphorylation or by preventing heterodimeric interactions between Smads. A mutation at position 133 in the amino-terminal MH1 domain has also been associated with colorectal carcinoma. Nevertheless, loss of Smad2 activation and/or expression was related to occur in less than 10% of colorectal cancers.

To be noted

Smad2 gene has also been found altered in lung carcinomas, cervical carcinomas and hepatocellular carcinomas.

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This article should be referenced as such:

Saffroy R, Lemoine A, Debuire B. SMAD2 (mothers against decapentaplegic homolog 2 (Drosophila)). *Atlas Genet Cytogenet Oncol Haematol.* 2004; 8(3):249-250.
