JAG2 (human jagged2)
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Identity
Hugo: JAG2
Other names: HJ2; Jagged2
Location: Human Jagged2 (jag2), a ligand for Notch receptor, was mapped in the chromosomal region 14q32.

DNA/RNA
Description
Human Jagged2 gene contains approximately 5,077 bps including 26 exons and a putative promoter region. In addition to a TATA box and a CAC binding site, the promoter region also contains several transcription factor binding sites like NF-kappaB, E47, E12, E2F etc. JAG2 gene has a structural similarity (overall 62% at nucleotide level) with JAG1, though JAG1 is located at chromosomal region 20p12.

Protein
Description
The predicted JAG2 protein is approximately 1,238-amino acid long. It has several recognizable motifs, including a signal peptide, 16 EGF-like repeats, a transmembrane domain, and a short cytoplasmic domain.

Expression
In human, JAG2 is expressed at high levels in the heart, the skeletal muscle and the pancreas.

Implicated in
Multiple Myeloma
Disease
The NOTCH ligand, JAG2, has been found to be overexpressed in malignant plasma cells from multiple myeloma (MM) patients and cell lines but not in nonmalignant plasma cells from tonsils, bone marrow from healthy individuals, or patients with other malignancies. Since MM cells have been shown to induce IL-6 expression in stromal cells in a largely cell contact-dependent manner, it has been concluded that MM cells induce production of IL-6 in stromal cells through overexpression of JAG2. Once secreted, IL-6 enhances proliferation of myeloma cells in a paracrine fashion.

Oncogenesis
The induction of IL-6 secretion has been blocked in vitro by interference with anti-Notch-1 monoclonal antibodies raised against the binding sequence of Notch-1 with JAG2. Taken together, these results indicate that JAG2 over expression may be an early event in the pathogenesis of multiple myeloma involving IL-6 production.
Schematic representation of the physiological activation of NOTCH, with Cell 1 (MM plasma cell) expressing JAG2 and Cell 2 (Stromal cell) NOTCH.

A: JAG2 binds NOTCH via cell-to-cell contact.
B: Binding of JAG2 induces a proteolytic cleavage of the intracellular part of NOTCH (NOTCH-IC).
C: Once cleaved, NOTCH-IC is translocated into the nucleus.
D: Once in the nucleus, NOTCH-IC will be able to bind to downstream effectors such as CBF1, to activate, for example, the IL-6 gene transcription.

References

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