Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

SEMA3B (sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B)

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Identity

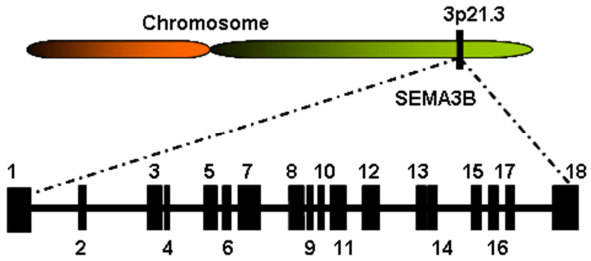
Other names: FLJ34863; LUCA-1; SEMA5; SEMAA; SemA; semaV

HGNC (Hugo): SEMA3B

Location: 3p21.31

DNA/RNA

Note
SEMA3B was first discovered as a secreted member of the semaphorin/collapsing family (contains a highly conserved semaphorin domain) and it has a role in axonal guidance.



Description

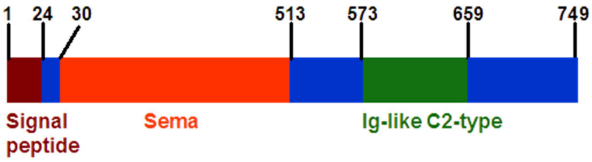
DNA size 11.53kb; mRNA size 9534 bp 18 exons.

Protein

Description

749 amino acids; region 1-24 (24) is a signal peptide, 30-513 (484) is the sema domain and 573-659 (87) is the Ig-like C2-type domain.

Isoforms: two isoforms have been identified.
- Isoform 1 (identifier: Q13214-1): this isoform has been chosen as the 'canonical' sequence.
- Isoform 2 (identifier: Q13214-2): the sequence of this isoform differs from the 'canonical' sequence, amino acid residues from 332-332 are missing.



Expression

It is expressed abundantly, but expressed differentially in neural and non-neural tissues.

Localisation

Secreted.

Function

SEMA3B belongs to the semaphorin/collapsing group of family (contains a highly conserved 749 amino acid semaphoring domain at NH_2-terminal). SEMA3B involves in diverse processes such as immune modulation, organogenesis, neuronal apoptosis and drug resistance. SEM3B also plays a critical role in axonal guidance during neuronal development. SEMA3B can act as a tumour suppressor by inducing apoptosis either by its expression in tumour cells or when applied as a soluble ligand. SEM3B induced apoptosis is associated with increase in cytochrome c release and caspase-3 cleavage, as well as increased phosphorylation of several proapoptotic proteins, including glycogen synthase kinase-3beta, FKHR and

MDM-2. The common method of inactivation of SEMA3B is by allelic loss and gene inactivation via promoter methylation and consequently, expression level of SEM3B is reduced in tumor cells.

Homology

The percent identity below represents identity of SEMA3B over an aligned region in UniGene.
Pan troglodytes 98.54%, Bos taurus 90.24%, Rattus norvegicus 89.19%, Canis lupus familiaris 88.72%, Mus musculus 88.65%.

Mutations

Note
A missense mutation in SEMA3B is reported in African-American and Latino-American population.

Implicated in

Gallbladder carcinoma (GBC)

Note
SEMA3B believes to play a role in gallbladder carcinoma (GBC), which is a highly malignant neoplasm in the Chilean females. A very high frequency (46/50, 92%) of abnormal promoter methylation that causes epigenetic inactivation of SEMA3B and the loss of heterozygosity at 3p21.3 (14/32, 44%) region (that contains SEMA3B gene) was detected among the Chilean females with GBC. Therefore, SEMA3B gene alterations may play a role in GBC pathogenesis via a two-hit mechanism, including allelic loss and abnormal promoter methylation.

Nasopharyngeal carcinoma

Note
SEMA3B is associated with nasopharyngeal carcinoma (NPC), as evident from both loss of heterozygosity analysis and functional studies. 21 primary NPC tumors and 2 NPC cell lines (CNE2 and SUNE1) screened for mutations by PCR-sequencing and two missense polymorphisms including Thr415Ile and lle242Met were found in SEMA3B. For the Thr415Ile polymorphism, the Ile allele type which leads to SEMA3B function defects was predominant in NPC with the allele frequency of 64% (27/42). SEMA3B mRNA is expressed in non-neoplastic nasopharyngeal epithelia, but found absent or down-regulated in 76% (16/21) of primary NPC tumors. Thus, high frequency of SEMA3B expression alterations suggests that the inactivation of this gene was strongly associated with NPC.

Neuroblastoma

Note
In neuroblastoma, significantly higher percentage of methylated CpG sites in the SEMA3B promoter was detected in tumors exhibiting 3p loss (95%), relative to tumors without loss (52%), suggesting a two-hit mechanism of allele inactivation. Additionally, low levels of SEMA3B expression were also seen in tumors with unmethylated SEMA3B promoters (n = 4). However, SEMA3B was upregulated in the SK-N-BE neuroblastoma cell line following induction of differentiation with retinoic acid and interestingly, higher levels of SEMA3B expression was found in differentiated tumors with favorable histopathology (n = 19) than in tumors with unfavorable histology (n = 22). The association of SEMA3B expression with neuroblastoma differentiation suggests that this TSG may play a role in neuroblastoma pathobiology and SEMA3B expression profile suggests that transcriptional regulation of this locus is complex.

Colorectal carcinoma

Disease
SEMA3B was also found frequently downregulated in colorectal cancer, which suggests that SEMA3B is involved in the suppression of colon tumor growth. However, the molecular mechanism through which SEM3B suppresses colorectal cancer is not clear.

Breast cancer

Disease
Expression of SEMA3B induces apoptosis in breast cancer cells. SEMA3B induces apoptosis through the neuropilin-1 (Np-1) receptor by inactivating the Akt signaling pathway.

Ovarian cancer

Note
Decreased expression of SEMA3B and loss of heterozygosity (LOH) at SEMA gene loci also account for ovarian cancer progression. Patients with a high vascular endothelial growth factor/SEMA (VEGF/SEMA) ratio showed poor survival than those with a low VEGF/SEMA ratio.

Lung cancer

Note
A single nucleotide alteration in the SEMA3B leads to amino acid substitution T415I and this variant protein has a reduced ability to act as a tumour suppressor. Thr to Ile substitution alters the structure of protein by altering its conformation and affects binding of SEMA3B with neuropilin receptors-1 (NRP-1) and NRP-2. The variant Ile allele occurs at an allele frequency of 0.18 in African-American and 0.39 in Latino-American population.

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