Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section

Mini Review

GNB2L1 (guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1)

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Identity

Hugo: GNB2L1
Other names: Gnb2-rs1; H12.3; HLC-7; PIG21 (proliferation-inducing gene 21); RACK1 (Receptor for activated kinase C); lung cancer oncogene 7; protein homologous to chicken B complex protein, guanine nucleotide binding
Location: 5q35.3
Note: Aberrations on 5q35.3 are reported to be associated with asbestos-related lung cancer. 5q35.3 also displays high frequency of deletions in non small lung carcinoma.

DNA/RNA

Description

The gene spans approximatively 6.9 kb. Orientation minus strand. Number of exons: 10.

Transcription

The length of GNB2L1 transcript is 951 bp.

Protein

Description

GNB2L1 encodes a cytosolic protein with a molecular mass of approximatively 35 kDa (317 amino acids). The protein has seven internal Trp-Asp 40 (WD40 domain) repeats. The WD40 repeats of RACK1/GNB2L1 are predicted to form a seven-bladed propeller structure, where each blade is composed of a four-stranded anti-parallel beta-sheet. The highly conserved WD repeat sequence of RACK1/GNB2L1 is found in a number of eukaryotic proteins and is implicated in a wide variety of functions including adaptor/regulatory modules in signal transduction, pre-mRNA processing and cytoskeleton assembly.

Expression

GNB2L1 is ubiquitously expressed in the tissues of higher mammals and humans including brain, liver, and spleen.

Localisation

GNB2L1 is a cytosolic protein.

Function

GNB2L1 was originally identified as an anchoring protein for protein kinase C beta (PKCbeta), which it stabilises in the active state and anchors to membranes or functional sites. However, evidence has accumulated to support a central role of RACK1/GNB2L1 in critical biological responses. In addition to binding specifically to the active form of PKCbeta isoforms, GNB2L1 also interacts with several other important signaling proteins including the Src kinase family, integrin beta1, integrin beta2, integrin beta3 and integrin beta5, beta-spectrin and dynamin, RasGAP, the androgen receptor, insulin-like growth factor 1 receptor (IGF-1r), Epstein-Barr virus trans-activator protein BZLF1, p73 and pRB.
This suggests that GNB2L1 may act as an anchor or adaptor protein, recruiting other proteins to various transmembrane receptors, providing a platform for protein-protein interactions and acting as the focus for several cell-signaling pathways. Accordingly, a number of cellular functions have been attributed to GNB2L1, e.g. in cell growth, adhesion, protrusion and chemotactic migration.
GNB2L1 might also have an effect on brain function; a reduction in GNB2L1 levels by around 50% has been reported in the brains of aged rats compared with adult or middle aged rat brains. GNB2L1 is also reported to be involved in number of functions in the nervous system. These include neurite growth, dendritic transport, glutamatergic and dopaminergic

neurotransmissions and functioning of GABAA receptors.
In addition, up-regulation of GNB2L1 in lymphocytes results in suppression of apoptosis, indicating that it also plays an important role in the regulation of apoptosis. It is also reported that GNB2L1 inhibits the effects of adenovirus E1a on yeast, Saos osteosarcoma and HeLa cells, including the induction of apoptosis.
In addition, GNB2L1 over-expression was reported to protect PC-12 cell survival on withdrawal of Nerve Growth Factor.

Homology

GNB2L1 is homologous to the G protein beta subunit, having 42% identity with many conserved amino acid substitutions.

Mutations

Note: Mutations in the GNB2L1 gene have not been found in 274 samples from somatic cancer. However, GNB2L1 is reported to be up-regulated in angiogenesis and in human carcinomas.

Implicated in

Brain pathologies and ageing

Disease

Changes in GNB2L1 levels were found in a number of brain pathologies and during ageing. GNB2L1 levels were significantly decreased in the cortex of patients with Down Syndrome, all of who develop Alzheimer's disease as young adults. Association of GNB2L1 with PKC was put forward as a putative cause of the increase in PKC activity observed in the frontal cortex of subjects with bipolar disorder.

Angiogenesis and tumor growth

Oncogenesis

GNB2L1 might contribute to angiogenesis and tumor growth, since it was shown to be up-regulated during angiogenesis in vitro and in vivo, and was also expressed in tumor angiogenesis. GNB2L1 expression was higher in human non-small cell lung and colon carcinomas than in the corresponding normal tissues.

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