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Gene Section

Mini Review

SH3GL2 (SH3-domain GRB2-like 2)

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Identity

Other names: CNSA2; EEN-B1; Endophilin-1; FLJ20276; FLJ25015; OTTHUMP00000021084; SH3D2A; SH3P4

HGNC (Hugo): SH3GL2

Location: 9p22.2

Local order: Next to ADAMTSL1 and FAN154A.

DNA/RNA

Description

10 exons; spans 217.93kb.

Transcription

mRNA of 2483 and 2417bp (there are two transcripts).

Protein

Description

352 amino acids; 39.96kDa and 330 amino acids; 37.51kDa.

Expression

Highest expression found in brain followed by pituitary gland and kidney. Expression has also been reported in bladder, eye, heart, cervix, breast, head and neck tissues etc.

Localisation

Cytoplasmic (diffuse cytoplasmic distribution in resting cells and a colocalization with EGF receptor in endocytic vesicles after EGF stimulation).

Function

SH3GL2 is a presynaptic protein that binds to dynamin, a GTPase that is implicated in endo-cytosis and recycling of synaptic vesicles. SH3GL2 by its LPAAT activity may induce negative membrane curvature by converting an inverted cone shaped lipid to a cone shaped lipid in the cytoplasmic leaflet of the bilayer. Through this action, SH3GL2 works with dynamin to mediate synaptic vesicle invagination from the plasma membrane and fission. SH3GL2 in complex with CBL and CIN85 participates in activated EGF receptor (Stimulated by EGF) endocytosis from the membrane surface and its subsequent lysosomal degradation.

The SH3 domain of SH3GL2 binds to a 24 amino acid proline rich domain (PRD) in the third intracellular loop of the G-protein coupled-1-adrenergic receptor. SH3GL2 overexpression increased isoproterenol-induced receptor inter-nalization by 25% and decreased coupling of receptor to the G-protein.

The SH3 domain of SH3GL2 also binds to a proline rich domain within the cytoplasmic tail of metallo-protease disintegrins, transmembrane glycoproteins acting in cell adhesion and growth factor signaling. SH3GL2 binds preferentially to the pro-form found in the trans-Golgi network. Therefore SH3GL2 binding may regulate intracellular transit and maturation of metalloprotease disintegrin.

Rat germinal centre kinse-like kinase (rGLK), a serine/threonine cytosolic kinase, interacted with SH3GL2. rGLK modulated c-Jun N-terminal kinase (JNK) activity by phosphorylation and binds to the SH3 domain of SH3GL2 through a C-terminal proline rich domain. Coexpression of rGLK and full length SH3GL2 increased JNK activity two fold, whereas coexpression with the SH3 domain of SH3GL2 abrogated rGLK-induced JNK activation. SH3GL2, therefore, modulated the mitogen-activated protein kinase pathway through physical association with rGLK.

Homology

SH3GL2 contains a C-terminal SH3 domain, which shares 92% and 84% amino acid sequence homology with the SH3 domain of SH3GL3 and SH3GL1, respectively. The SH3 domain of SH3GL2 also shows high homology to the C-terminal SH3 domain of GRB2.

Mutations

Somatic

In SH3GL2, mutation in SH3 domain has only been reported.

Implicated in

Sporadic cancer

Disease

Reduced expressions of SH3GL2 due to different types of molecular alterations are involved in tumor formation in head and neck, breast and gastric tissues.

Prognosis

The prognostic significance of down regulation of SH3GL2 in sporadic tumors is not understood clearly.

Cytogenetics

Chromosomal deletions, chromosomal gain or amplification and chromosomal breakpoints are frequent.

Oncogenesis

LOH on 9p22 is one of the most frequent events identified in head and neck tumor, breast carcinoma, pituitary adenoma, neuroblastoma etc. However, promoter methylation appears to be another common mechanism of SH3GL2 inactivation.

Alzheimer disease

Disease

The increased expression level of SH3GL2 in neuron is linked to an increase in the activation of the stress kinase c-Jun N-terminal kinase with the subsequent death of the neuron.

Prognosis

SH3GL2 overexpression is now considered as a new indicator of the progression of Alzhemier disease.

Cytogenetics

Increase in aneuploidy or aberration, but chromosomal loss or gain in aneuploid cell was not specific. In some forms of Alzheimer disease, a specific type of aneuploidy-trisomy 21 mosaicism has been reported.

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