RAP1GAP (RAP1 GTPase activating protein)

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Identity

Other names: RAPGAP; RAP1GA1; KIAA0474; RAP1GAP1; RAP1GAPII
HGNC (Hugo): RAP1GAP
Location: 1p36.12
Local order: From centromere to telomere: NBPF3, ALPL, RAP1GAP, USP48, HSPG2.

DNA/RNA

Description
25 exons encompassing about 73 kb of genomic DNA.

Transcription
About 3.334 kb mRNA, and has three transcript variant, RAP1 GTPase activating protein isoform a, b, c.

Protein

Description
663 amino acids; homodimer and heterodimer with RAP1B.

Expression
Significant expression seen in the brain, kidney and pancreas. Abundant in the cerebral cortex and expressed at much lower levels in the spinal cord. Not detected in the lymphoid tissues. (according to Swiss-Prot).

Localisation
Golgi apparatus membrane; Peripheral membrane protein (according to Swiss-Prot).

Function

GT.Pase activator for the nuclear Ras-related regulatory protein Rap1, converting it to the putatively inactive GDP-bound state (according to Swiss-Prot); Regulation of small GTPase-mediated signal transduction.

Homology

The RAP1GAP gene is conserved in cow, mouse, rat, zebrafish, fruit fly, mosquito, and C. elegans.

Implicated in

Solid tumors

Disease
Papillary thyroid cancer, pancreatic cancer, prostate cancer, melanoma tumors

Oncogenesis

Rap1GAP, which acts as a GTPase activator for the nuclear Ras-related regulatory protein Rap1, was a specific negative regulator of Rap1, and the monomeric G protein Rap1 has been implicated in cancer tumorigenesis. It signals to pathways involved in cell adhesion, migration, and survival. Loss of Rap1GAP was discovered in papillary thyroid cancer, pancreatic cancer, prostate cancer, melanoma tumors, and their cell lines, all of them exhibited increased Rap1 activity, that activation of Rap1 promotes cell proliferation and migration potentiality through the mitogen-activated protein kinase pathway and integrin activation. As a putative tumor suppressor gene, Rap1GAP inhibits tumor growth but induces MMP2- and MMP9-mediated squamous cell carcinoma invasion and tumor progression, suggesting a role for this protein as a biomarker for early N-stage, aggressive squamous cell carcinomas.
**Myelodysplastic syndrome (MDS)**

Disease

The expression level of Rap1GAP in MDS patients significantly increased as compared with patients with non-malignant blood diseases or acute myeloid leukemia (AML). Among MDS patients, the expression level of Rap1GAP in MDS-refractory anemia (RA) was significantly higher than that in MDS-refractory anemia with excess of blasts (RAEB). On the other hand, inhibiting Rap1 activity by expression of Rap1GAP increased leukocyte transendothelial migration, providing physiological relevance to the hypothesis that Rap1 augments barrier function of inter-endothelial cell junctions, implying the relevance of Rap1GAP in the regulation of haematogenesis.

**References**


This article should be referenced as such: