ARHGEF12 (Rho guanine nucleotide exchange factor (GEF) 12)

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Identity

Other names: LARG (Leukemia Associated Rho Guanine nucleotide exchange factor); KIAA0382
HGNC (Hugo): ARHGEF12
Location: 11q23
Local order: Telomeric to MLL.

DNA/RNA

Transcription
9501 bp mRNA; 4634 bp open reading frame.

Protein

Description
The gene encodes a guanine nucleotide exchange factor; 1544 amino acids; NH2- PDZ domain, Lsc homology (LH) domain, bipartite nuclear localization signal, Dbl homology (DH) domain, and a pleckstrin homology (PH) domain –COOH.

Expression
Wide (leukocytes, spleen, prostate, testis, ovary, small intestine, colon, thymus).

Function
PDZ domains are involved in protein-protein interactions in transmembrane signaling pathways; LH domains bind G proteins; nuclear localization signals are implicated in translocation of proteins from the cytoplasm to the nucleus; DH domains are responsible for the nucleotide exchange activity of guanine nucleotide exchange (GEF) toward Rho GTPases, PH domains function in membrane localization; Rho GEF are regulators of GTPases, and have oncogenic properties.

Homology
Member of the family of Rho GEF factors, like dbl, vav, tiam, and BCR.

Implicated in

Acute non lymphocytic leukemia (ANLL) with apparently normal cromosomes 11 --> MLL-LARG

Note
Poorly defined: only 1 case to date, a 38 year old male patient with occupational exposure; M4-ANLL; CR; death unrelated to the leukemia.

Cytogenetics
The case was 51,XY,+8,+19,+3mar; the interstitial deletion at 11q23 resulting in MLL-LARG fusion cannot be seen at the chromosome level.

Hybrid/Mutated gene
5’ MLL fused at exon 6 with the 3’ end of almost the entire LARG; LARG is oriented in a 5’ to 3’direction, like MLL.

Abnormal protein
Excludes the NH2- PDZ domain of LARG, and includes most of LARG, from the Lsc homology (LH) domain to COOH.
### References


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