

## Gene Section

### Short Communication

# 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; NH<sub>2</sub>- 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 chromosomes 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 NH<sub>2</sub>- PDZ domain of LARG, and includes most of LARG, from the Lsc homology (LH) domain to COOH.

## References

Kourlas PJ, Strout MP, Becknell B, Veronese ML, Croce CM, Theil KS, Krahe R, Ruutu T, Knuutila S, Bloomfield CD, Caligiuri MA. Identification of a gene at 11q23 encoding a guanine nucleotide exchange factor: evidence for its fusion with MLL in acute myeloid leukemia. Proc Natl Acad Sci U S A. 2000 Feb 29;97(5):2145-50

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