Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

LRIG1 (leucine-rich repeats and immunoglobulin-like domains 1)

Dongsheng Guo, Baofeng Wang

Dept of Neurosurgery, Tongji Hospital, Huazhong University of Science and Technology, Wuhan, Hubei, 430030, People's Republic of China (DG, BW)

Published in Atlas Database: December 2010

Online updated version : http://AtlasGeneticsOncology.org/Genes/LRIG1ID41198ch3p14.html
DOI: 10.4267/2042/46009

Identity

Other names: DKFZp586O1624; LIG-1; LIG1

HGNC (Hugo): LRIG1

Location: 3p14.1

DNA/RNA

Description

Genomic DNA encoding LRIG1 spans a region of 122.89 kilobases on chromosome 3, at 3p14. LRIG1 gene is encoded on the reverse strand.

Transcription

The pre-mRNA comprises 19 exons.
Coding sequence: 4812 bp.

Protein

Description

LRIG1 is a transmembrane cell-surface protein consisting of 1093 amino acids. LRIG1 contains extracellular part containing 15 leucine-rich repeats (LRR) and three C2-type immunoglobulin-like domains, a transmembrane region, and a cytoplasmic tail. LRIG1 can be cut into soluble LRIG1 ectodomain by proteolytic processing, which also is a functional molecule.

Expression

LRIG1 is expressed ubiquitously in various epithelial cells, endothelial cells, heart, smooth and striated muscles, and in large neurons.

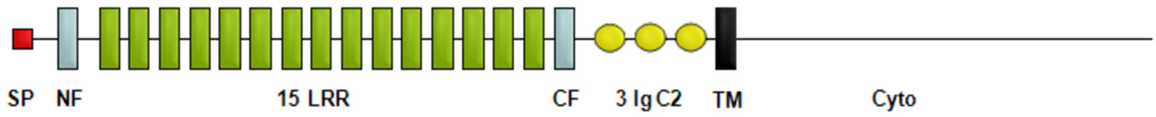
Localisation

Differential subcellular distribution in a cell type-specific manner.

Function

LRIG1 acts as a suppressor of receptor tyrosine kinases, such as epidermal growth factor receptor (EGFR) family, MET (hepatocyte growth factor receptor), and RET. The interaction of the extracellular LRR domain and immunoglobulin-like domains of LRIG1 with the extracellular parts of the human EGFR results in recruitment of c-Cbl to the cytoplasmic domains, and induction of EGFR degradation. LRIG1 is involved in signal transduction, cell proliferation, cell apopotosis, cell cycle, cell migration, and cell invasion. LRIG1 as a putative tumor suppressor gene often be down-regulated in various human tumors.
Soluble ectodomain of LRIG1 protein can modulate EGFR signaling and its growth-promoting activity in a paracrine fashion.

LRIG1 gene. Exons are represented by red boxes (in scale). Exons 1 to 19 are from the 5' to 3' direction.



LRIG1 protein. SP: signal peptide; NF: N-terminal cysteine-rich flanking domain; LRR: leucine-rich repeat; CF: C-terminal cysteine-rich flanking domain; Ig C2: C2-type immunoglobulin-like domains; TM: transmembrane domain; Cyto: cytoplasmic domain.

Implicated in

Ependymoma

Note

Higher cytoplasmic immunoreactivity of LRIG1 correlates with older patient age and higher LRIG1 nuclear immunoreactivity with lower WHO grade.

Prostate cancer

Note

High LRIG1 expression is significantly associated with short overall and prostate cancer-specific survival for 256 Swedish patients analysed. In contrast, in the U.S. series, high LRIG1 expression is significantly associated with longer overall survival.

Renal cell carcinoma (RCC)

Note

LRIG1 expression is generally downregulated in conventional and papillary RCC but not in chromophobic RCC.

Cutaneous squamous cell carcinoma (SCC)

Note

LRIG-1 expression is highest in well-differentiated lesions of cutaneous SCC. LRIG-1 expression intensity of tumor cells is significantly correlated with histologic differentiation of SCC. The SCC patients have significant survival benefits in the high LRIG-1 expression groups compared with low LRIG-1 expression groups.

Breast tumor

Note

LRIG1 protein levels are significantly suppressed in the majority of human breast tumors expressing ErbB2.

Cervical squamous cell carcinoma

Note

LRIG1 appears to be a significant prognosis predictor in early-stage cervical cancer, independent of the other tumor markers.

Astrocytic tumor

Note

Perinuclear staining of LRIG1 is associated with low WHO grade and better survival of the patients.

Psoriasis

Note

In psoriasis, LRIG1 is mostly absent from the cell surfaces in the spinous layers.

References

Nilsson J, Vallbo C, Guo D, Golovleva I, Hallberg B, Henriksson R, Hedman H. Cloning, characterization, and expression of human LIG1. Biochem Biophys Res Commun. 2001 Jun 29;284(5):1155-61

Nilsson J, Starefeldt A, Henriksson R, Hedman H. LRIG1 protein in human cells and tissues. Cell Tissue Res. 2003 Apr;312(1):65-71

Thomasson M, Hedman H, Guo D, Ljungberg B, Henriksson R. LRIG1 and epidermal growth factor receptor in renal cell carcinoma: a quantitative RT--PCR and immunohistochemical analysis. Br J Cancer. 2003 Oct 6;89(7):1285-9

Guo D, Holmlund C, Henriksson R, Hedman H. The LRIG gene family has three vertebrate paralogs widely expressed in human and mouse tissues and a homolog in Ascidiacea. Genomics. 2004 Jul;84(1):157-65

Gur G, Rubin C, Katz M, Amit I, Citri A, Nilsson J, Amariglio N, Henriksson R, Rechavi G, Hedman H, Wides R, Yarden Y. LRIG1 restricts growth factor signaling by enhancing receptor ubiquitylation and degradation. EMBO J. 2004 Aug 18;23(16):3270-81

Laederich MB, Funes-Duran M, Yen L, Ingalla E, Wu X, Carraway KL 3rd, Sweeney C. The leucine-rich repeat protein LRIG1 is a negative regulator of ErbB family receptor tyrosine kinases. J Biol Chem. 2004 Nov 5;279(45):47050-6

Ye F, Guo DS, Niu HQ, Tao SZ, Ou YB, Lu YP, Lei T. [Molecular mechanism of LRIG1 cDNA-induced apoptosis in human glioma cell line H4]. Ai Zheng. 2004 Oct;23(10):1149-54

Tanemura A, Nagasawa T, Inui S, Itami S. LRIG-1 provides a novel prognostic predictor in squamous cell carcinoma of the skin: immunohistochemical analysis for 38 cases. Dermatol Surg. 2005 Apr;31(4):423-30

Guo D, Nilsson J, Haapasalo H, Raheem O, Bergenheim T, Hedman H, Henriksson R. Perinuclear leucine-rich repeats and immunoglobulin-like domain proteins (LRIG1-3) as prognostic indicators in astrocytic tumors. Acta Neuropathol. 2006 Mar;111(3):238-46

Jensen KB, Watt FM. Single-cell expression profiling of human epidermal stem and transit-amplifying cells: Lrig1 is a regulator of stem cell quiescence. Proc Natl Acad Sci U S A. 2006 Aug 8;103(32):11958-63

Yang WM, Yan ZJ, Ye ZQ, Guo DS. LRIG1, a candidate tumour-suppressor gene in human bladder cancer cell line BIU87. BJU Int. 2006 Oct;98(4):898-902

Goldoni S, Iozzo RA, Kay P, Campbell S, McQuillan A, Agnew C, Zhu JX, Keene DR, Reed CC, Iozzo RV. A soluble ectodomain of LRIG1 inhibits cancer cell growth by attenuating basal and ligand-dependent EGFR activity. Oncogene. 2007 Jan 18;26(3):368-81

Guo D, Han L, Shu K, Chen J, Lei T. Down-regulation of leucine-rich repeats and immunoglobulin-like domain proteins

(LRIG1-3) in HP75 pituitary adenoma cell line. J Huazhong Univ Sci Technolog Med Sci. 2007 Feb;27(1):91-4

Hedman H, Henriksson R. LRIG inhibitors of growth factor signalling - double-edged swords in human cancer? Eur J Cancer. 2007 Mar;43(4):676-82

Ljuslinder I, Golovleva I, Palmqvist R, Oberg A, Stenling R, Jonsson Y, Hedman H, Henriksson R, Malmer B. LRIG1 expression in colorectal cancer. Acta Oncol. 2007;46(8):1118-22

Shattuck DL, Miller JK, Laederich M, Funes M, Petersen H, Carraway KL 3rd, Sweeney C. LRIG1 is a novel negative regulator of the Met receptor and opposes Met and Her2 synergy. Mol Cell Biol. 2007 Mar;27(5):1934-46

Karlsson T, Mark EB, Henriksson R, Hedman H. Redistribution of LRIG proteins in psoriasis. J Invest Dermatol. 2008 May;128(5):1192-5

Ledda F, Bieraugel O, Fard SS, Vilar M, Paratcha G. Lrig1 is an endogenous inhibitor of Ret receptor tyrosine kinase activation, downstream signaling, and biological responses to GDNF. J Neurosci. 2008 Jan 2;28(1):39-49

Lindström AK, Ekman K, Stendahl U, Tot T, Henriksson R, Hedman H, Hellberg D. LRIG1 and squamous epithelial uterine cervical cancer: correlation to prognosis, other tumor markers, sex steroid hormones, and smoking. Int J Gynecol Cancer. 2008 Mar-Apr;18(2):312-7

Miller JK, Shattuck DL, Ingalla EQ, Yen L, Borowsky AD, Young LJ, Cardiff RD, Carraway KL 3rd, Sweeney C. Suppression of the negative regulator LRIG1 contributes to ErbB2 overexpression in breast cancer. Cancer Res. 2008 Oct 15;68(20):8286-94

Stutz MA, Shattuck DL, Laederich MB, Carraway KL 3rd, Sweeney C. LRIG1 negatively regulates the oncogenic EGF receptor mutant EGFRvIII. Oncogene. 2008 Sep 25;27(43):5741-52

Yi W, Haapasalo H, Holmlund C, Järvelä S, Raheem O, Bergenheim AT, Hedman H, Henriksson R. Expression of leucine-rich repeats and immunoglobulin-like domains (LRIG) proteins in human ependymoma relates to tumor location, WHO grade, and patient age. Clin Neuropathol. 2009 Jan-Feb;28(1):21-7

Thomasson M, Wang B, Hammarsten P, Dahlman A, Persson JL, Josefsson A, Stattin P, Granfors T, Egevad L, Henriksson R, Bergh A, Hedman H. LRIG1 and the liar paradox in prostate cancer: a study of the expression and clinical significance of LRIG1 in prostate cancer. Int J Cancer. 2011 Jun 15;128(12):2843-52

Yi W, Holmlund C, Nilsson J, Inui S, Lei T, Itami S, Henriksson R, Hedman H. Paracrine regulation of growth factor signaling by shed leucine-rich repeats and immunoglobulin-like domains 1. Exp Cell Res. 2011 Feb 15;317(4):504-12

This article should be referenced as such:

Guo D, Wang B. LRIG1 (leucine-rich repeats and immunoglobulin-like domains 1). Atlas Genet Cytogenet Oncol Haematol. 2011; 15(8):625-627.