

Gene Section

Short Communication

PSIP1 (PC4 and SFRS1 interacting protein 1)

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Identity

Hugo: PSIP1

Other names: LEDGF (lens epithelium-derived growth factor); p75; p52

Location: 9p22.3

DNA/RNA

Description

The gene contains at least 15 exons and 14 introns.

Transcription

Two alternative splice variants: p75 and p52.

Protein

Description

530 amino acids (p75), 333 amino acids (p52);
N-term - PWWP (proline - tryptophan - tryptophan - proline) domain - NLS (nuclear localization signal) - AT-hook-like - Coiled coil - IBD (integrase binding domain) - HTH1 (helix-turn-helix DNA binding motif) - HTH2 - C-term.

Expression

Expression of PSIP1 has been reported to be increased in human breast and bladder cancer, prostate tumors and benign prostate hyperplasia.

Localisation

Nuclear.

Function

Transcriptional regulation of stress-associated genes, mRNA splicing and cell survival. The involvement of PSIP1 (LEDGF) has been reported in human immunodeficiency virus type-1 (HIV-1) integration, autoimmune disorders, and neurogenesis. Recent data

reveal LEDGF as an oncogenic protein that controls a caspase-independent lysosomal cell death pathway.

Homology

PSIP1 belongs to the hepatoma-derived growth factor (HDGF) family of proteins that contain a well conserved N-terminal amino acid sequence known as the HATH (homologous to amino terminus of HDGF) region.

Implicated in

t(9;11)(p22;p15) NUP98-PSIP1

Note: acute non lymphoblastic leukemia (ANLL), one case of transformed chronic myeloid leukemia (CML-BC).

Hybrid/Mutated Gene

5'NUP98 - 3'PSIP1.

Abnormal Protein

Fuses the GLFG repeat domains of NUP98 to the COOH-terminus of PSIP1.

References

Ahuja HG, Hong J, Aplan PD, Tcheurekdjian L, Forman SJ, Slovak ML. t(9;11)(p22;p15) in acute myeloid leukemia results in a fusion between NUP98 and the gene encoding transcriptional coactivators p52 and p75-lens epithelium-derived growth factor (LEDGF). *Cancer Res* 2000;60:6227-6229.

Singh DP, Kimura A, Chylack LT, Shinohara T. Lens epithelium-derived growth factor (LEDGF/p75) and p52 are derived from a single gene by alternative splicing. *Gene* 2000;242:265-273.

Hussey DJ, Moore S, Nicola M, Dobrovic A. Fusion of the NUP98 gene with the LEDGF/p52 gene defines a recurrent acute myeloid leukemia translocation. *BMC Genet* 2001;2:20.

Wu X, Daniels T, Molinaro C, Lilly MB, Casiano CA. Caspase cleavage of the nuclear autoantigen LEDGF/p75 abrogates its pro-survival function: implications for autoimmunity in atopic disorders. *Cell Death Differ* 2002;9:915-925.

Cherepanov P, Maertens G, Proost P, Devreese B, Van Beeumen J, Engelborghs Y, De Clercq E, Debysers Z. HIV-1 integrase forms stable tetramers and associates with LEDGF/p75 protein in human cells. *J Biol Chem* 2003;278:372-381.

Daniels T, Zhang J, Gutierrez I, Elliot ML, Yamada B, Heeb MJ, Sheets SM, Wu X, Casiano CA. Antinuclear autoantibodies in prostate cancer: immunity to LEDGF/p75, a survival protein highly expressed in prostate tumors and cleaved during apoptosis. *Prostate* 2005;62:14-26.

Grand FH, Koduru P, Cross NC, Allen SL. NUP98-LEDGF fusion and t(9;11) in transformed chronic myeloid leukemia. *Leuk Res* 2005;29:1469-1472.

Morerio C, Acquila M, Rosanda C, Rapella A, Tassano E, Micalizzi C, Panarello C. t(9;11)(p22;p15) with NUP98-LEDGF fusion gene in pediatric acute myeloid leukemia. *Leuk Res* 2005;29:467-470.

Singh DP, Kubo E, Takamura Y, Shinohara T, Kumar A, Chylack LT Jr, Fatma N. DNA binding domains and nuclear

localization signal of LEDGF: contribution of two helix-turn-helix (HTH)-like domains and a stretch of 58 amino acids of the N-terminal to the trans-activation potential of LEDGF. *J Mol Biol* 2006;355:379-394.

Sutherland HG, Newton K, Brownstein DG, Holmes MC, Kress C, Semple CA, Bickmore WA. Disruption of Ledgf/Psip1 results in perinatal mortality and homeotic skeletal transformations. *Mol Cell Biol* 2006;26:7201-7210.

Daugaard M, Kirkegaard-Sørensen T, Ostenfeld MS, Aaboe M, Høyer-Hansen M, Orntoft TF, Rohde M, Jäättelä M. Lens epithelium-derived growth factor is an Hsp70-2 regulated guardian of lysosomal stability in human cancer. *Cancer Res* 2007;67:2559-2567.

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