Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section

Mini Review

PLCB1 (phospholipase C, beta 1 (phosphoinositide-specific))

Matilde Y Follo, Vincenza Rita Lo Vasco, Giovanni Martinelli, Giandomenico Palka, Lucio Cocco

Cellular Signalling Laboratory, Department of Anatomical Sciences, University of Bologna, Via Irnerio, 48 I-40126 Bologna, Italy

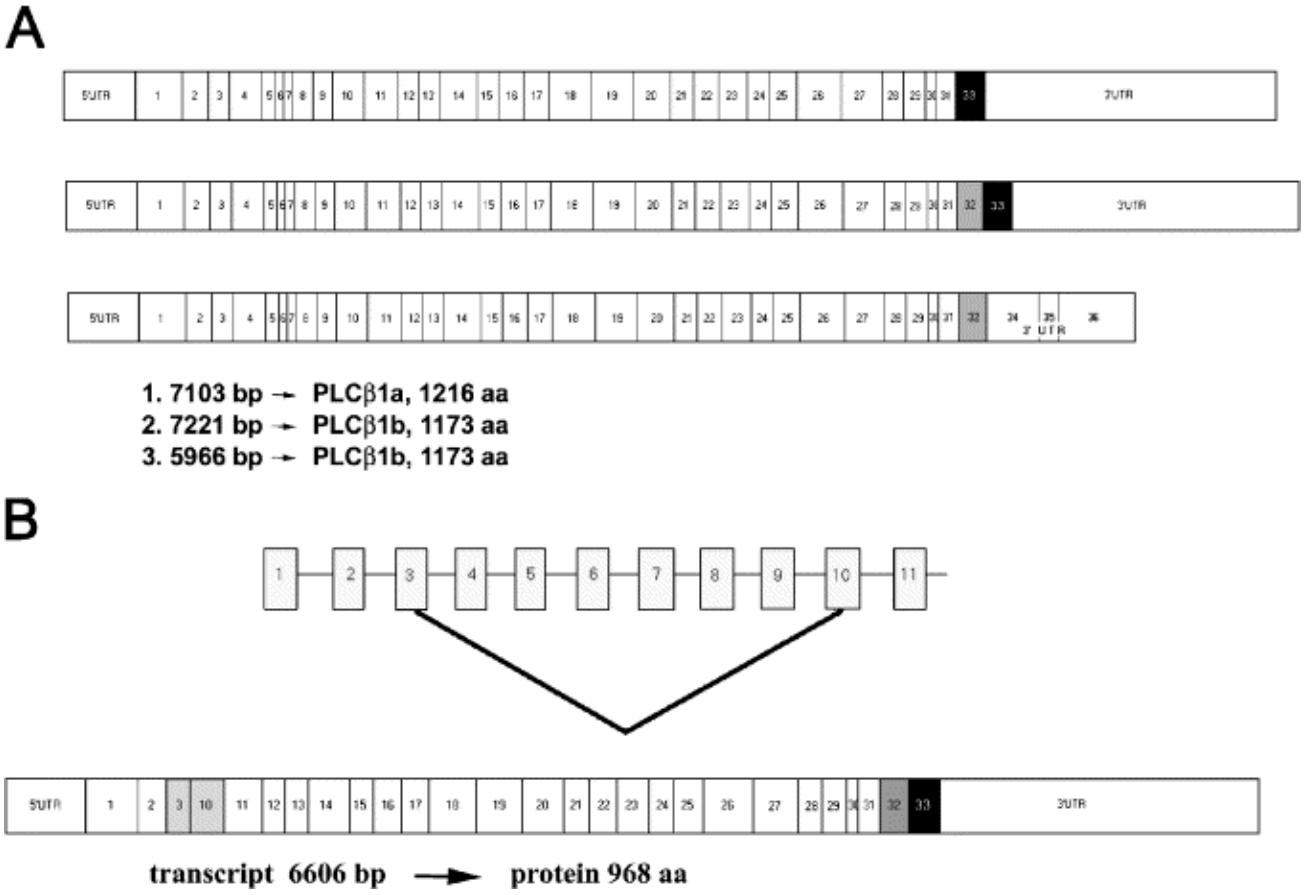
Published in Atlas Database: December 2005

Online updated version: http://AtlasGeneticsOncology.org/Genes/PLCB1ID41742ch20p12.html
DOI: 10.4267/2042/38314

Identity

Hugo: PLCB1
Other names: PLC-I; PI-PLC; PLC-154
Location: 20p12.3

Local order: between the markers D20S917 and D20S177.



Panel A: structure of PLCB1a and PLCB1b human cDNAs. Upper, PLCB1a; middle, PLCB1b; lower, PLCB1b with different 3'- UTR.
Panel B: structure of the splicing variant lacking exons 4-9.

DNA/RNA

Description

33 small exons and introns spanning about 250 kbp.

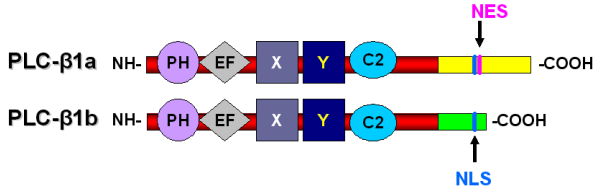
Transcription

By alternative splicing at the 3-prime end the gene produces 2 variants: PLCB1a (1.216 aminoacids, 6705 bp mRNA) and PLCB1b (1.173 aminoacids, 6823 bp mRNA). An additional exon at the 5-prime end was identified, which gives a smaller isoform, and another PLCB1b isoform, which is produced by using an alternative 3'-UTR.

Pseudogene

No known pseudogenes.

Protein



PH = Pleckstrin Homology Domain;
EF = EF-Hand Domain;
X and Y = Catalytic Domain;
C2 = Calcium-binding Domain;
NLS = Nuclear Localisation Signal (common to both isoforms);
NES = Nuclear Export Signal

Description

PLC beta1 contains a PH-domain at the NH2-terminus, which is present in many signalling proteins, that binds to polyphosphoinositides and to inositol phosphates. Two additional modules are also present: an EF-hand domain, located between the PH and X domains, and a C2 domain, which is sometimes represented as part of an extended Y domain.

Expression

PLC beta1 is ubiquitous at different levels of expression: higher signal intensities were observed in some CNS areas, such as the amygdala, caudate nucleus, and hippocampus, and PLCB1a appeared to be expressed at slightly higher levels in most tissues. PCR analysis of embryonic and adult rat tissues indicated restricted expression of both isoforms to embryonic and adult brain, with lower levels of expression in lung and testis.

Localisation

By using confocal immunolocalization of endogenous or transfected epitope-tagged PLC beta1, for subcellular localisation it has been shown that PLCB1a is within the cytoplasm and at the plasma membrane but localises also in the nucleus. PLCB1b is almost completely nuclear.

Function

Phospholipase C-beta (PLC beta) catalyzes the generation of inositol 1,4,5-trisphosphate (IP3) and diacylglycerol (DAG) from phosphatidylinositol 4,5-bisphosphate (IP2), a key step in the intracellular transduction of many extracellular signals. PLCB1 is one of several mammalian PLCB isoforms which differ in their function and expression patterns in vivo. PLC beta1 protein is present in the nucleus and is involved in the control of the cell cycle.

Homology

96% with bovine PLC beta1; The amino acid sequences of PLC isozymes are relatively not conserved except for two regions, known as the X and Y domains that form the catalytic core which is 60% homologous among all mammalian isozymes.

Mutations

Note: Until now only deletions have been relevated by using FISH analysis.

Implicated in

Myelodysplastic Syndrome

Note: Transition from Myelodysplastic Syndrome to Acute Myeloid Leukemia.

Disease

In patients with normal GTG banding karyotype affected by Myelodysplastic Syndrome (MDS) (9 patients) and with Acute Myeloid Leukemia (AML) (6 patients), a monoallelic loss of the PLCB1 gene was detected. All the MDS patients, even though with normal karyotype, belonged to the high-risk group as scored by IPSS and FAB classifications. Out of 9 MDS patients with normal karyotype 4 had monoallelic deletion of the PLC beta1 gene, and all 4 died within 1 to 6 months after developing AML, compared to survival of over 30 months in the 5 MDS patients without the deletion. Two of 6 AML patients with normal karyotype had a monoallelic deletion of the PLCB1 gene; these 2 patients had a reduced survival (1 to 12 months) compared to the AML patients without the deletion (20 to 29 months). These evidences suggest a possible role for PLC beta1 in the progression of MDS to AML in high-risk patients.

Prognosis

Worse in patients having the deletion of the PLC beta1 gene.

Cytogenetics

FISH performed using a 115.000 bp probe (PAC clone 881E24) spanning from exon 19 to 32 of the gene.
FISH analysis, using KIAA 0581, i.e., part of human PLC beta1 cDNA, of human metaphases showing

signals on both chromosomes 20 at band p12. (a) Q-Like banding; (b) fluorescence signals detected by FISH; (c) a partial karyotype along with a human chromosome 20 ideogram. (d) A schematic representation of the 1.9 cM interval, flanked by microsatellite markers D20S917 and D20S977, to which human PLC beta1 maps.

Oncogenesis

PLC beta1 is a key player in the control of cell cycle, namely the physiological progression through the G1 phase, in that the nuclear PLC beta1 evoked signalling targets the cyclin D3/cdk4 complex which phosphorylates retinoblastoma protein (pRb) that in turn activates the transcription factor E2F-1. Possibly alterations of this pathway could be involved in malignancies.

References

Nagase T, Ishikawa K, Miyajima N, Tanaka A, Kotani H, Nomura N, Ohara O. Prediction of the coding sequences of unidentified human genes. IX. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro. DNA Res 1998;5:31-39.

Caricasole A, Sala C, Roncarati R, Formenti E, Terstappen GC. Cloning and characterization of the

human phosphoinositide-specific phospholipase C-beta 1 (PLC-beta 1). Biochim Biophys Acta 2000; 1517:63-72.

Peruzzi D, Calabrese G, Faenza I, Manzoli L, Matteucci A, Gianfrancesco F, Billi AM, Stuppia L, Palka G, Cocco L. Identification and chromosomal localisation by fluorescence in situ hybridisation of human gene of phosphoinositide-specific phospholipase C beta-1. Biochim Biophys Acta 2000;1484:175-182.

Peruzzi D, Aluigi M, Manzoli L, Billi AM, Di Giorgio FP, Morleo M, Martelli AM, Cocco L. Molecular characterization of the human PLC beta-1 gene. Biochim Biophys Acta 2002;1584:46-54.

Lo Vasco VR, Calabrese G, Manzoli L, Palka G, Spadano A, Morizio E, Guanciali-Franchi P, Fantasia D, Cocco L. Inositide-specific phospholipase c beta-1 gene deletion in the progression of myelodysplastic syndrome to acute myeloid leukemia. Leukemia 2004;18:1122-1126.

This article should be referenced as such:
Follo MY, Lo Vasco VR, Martinelli G, Giandomenico Palka G, Cocco L. PLCB1 (phospholipase C, beta 1 (phosphoinositide-specific)). Atlas Genet Cytogenet Oncol Haematol.2006; 10(3):154-156.