

BACKGROUND

PtdIns (4,5) P_2 is positioned at the crossroads of many of these signaling cascades, as it may be metabolized by phospholipase C to generate Ins (1,4,5) P_3 and 1,2-diacylglycerol, further phosphorylated at the 3-position of the inositol ring by PI 3-kinase to generate PtdIns (3,4,5) P_3 or used directly as a messenger molecule by binding to proteins containing PH (pleckstrin homology), PX (phox homology), FERM (band 4.1, ezrin, radixin, moesin) or comparable domains. PtdIns (4,5) P_2 seems to be synthesized in a highly site-specific manner at distinct subcellular locales where it is directly utilized as a signaling molecule, thereby modulating the activity, conformation, assembly or disassembly of proteins at these sites. The spatial and temporal metabolism of PtdIns (4,5) P_2 has emerged as a crucial regulator of multiple cellular processes, including actin reorganization, focal-adhesion dynamics, endocytosis and exocytosis, nuclear signaling pathways and gene expression.¹

Most cellular PtdIns (4,5) P_2 generation is fulfilled by the alpha, beta and gamma isoforms of the type I PIPKs (PtdIns4P 5-kinases) (also called "PIP5K1A," "PIP5K1B," and "PIP5K1C," respectively), although PIP5K types II enzymes also synthesize PtdIns (4,5) P_2 . Of these three homologues, PIP5K1C/PIP5Kgamma is thought to be the main enzyme responsible for PtdIns (4,5) P_2 synthesis in the brain, which plays important role in synaptic transmission.² Although retaining high homology within the lipid kinase domain, each isoform exhibits a distinct subcellular localization pattern and functional specificity. It is believed that the N- and C-terminal sequence divergence of each PIP5KI isoform contributes to this diversity in targeting and function. PIP5KIalpha participates in both nuclear and cytoplasmic PtdIns (4,5) P_2 generation, where it has been implicated in the regulation of RNA polyadenylation machinery and growth-factor-induced reorganization of the cytoskeletal superstructure. The cellular roles of PIP5Kibeta are less defined, but a function for PIP5Kibeta in actin assembly and endocytosis has been suggested. PIP5K1C/PIP5Kgamma is a workhorse for site-specific PtdIns (4,5) P_2 generation in a plethora of cytoplasmic processes.³ PIP5K1C/PIP5Kgamma is a fundamental regulator of the assembly and disassembly of sites of cell-matrix and cell-cell interaction termed focal adhesions and adherens junctions respectively. Importantly, the human PIP5K1C/PIP5Kgamma is known to encode at least two alternative splice variants, PIPKgamma640 and PIPKgamma668. This 28-amino-acid extension at C-terminus has been demonstrated to confer specific subcellular targeting and function on PIP5K1C/PIP5Kgamma 668, where it consequently regulates focal adhesion dynamics, EGF-stimulated directional migration, basolateral targeting of E-cadherin, and endocytosis of the transferrin receptor. Aside from mediating specific protein-protein interactions,

this extension also affords several methods of regulating PIP5K1C/PIP5Kgamma668 activity, as it is tyrosine- and serine-phosphorylated by Src and cyclin-dependent kinase respectively. In addition, PIP5K1C/PIP5Kgamma can be directly phosphorylated by EGFR. In the absence of a specific C-terminal extension, PIP5K1C/PIP5Kgamma 640 also plays a specific cellular role, as it is the major contributor of the PtdIns (4,5) P_2 utilized in G-protein-coupled-receptor-mediated Ins (1,4,5) P_3 generation.⁴ PIP5K1C/PIP5Kgamma deficiency affects various signaling pathways including PI3-kinase pathway, which leads to phosphorylation of PtdIns(4,5) P_2 and to generation of PtdIns (3,4,5) P_3 . PI3-kinase catalyzed synthesis of PtdIns (3,4,5) P_3 was diminished in the LCCS3 patents and PIP5Kgamma(-/-) mice as a result of reduced synthesis of its precursor, PtdIns (4,5) P_2 .⁵

References:

1. Di Paolo, G. et al: Nature 431:415-22, 2004
2. Akiba, Y. et al: Gene Exp. Patterns 1:123-33, 2002
3. van den Bout, I. & Divecha, N.: J. Cell Sci. 122:3837-50, 2009
4. Schill, N.J. & Anderson, R.A. : Biochem. J. 422(Pt.3) :473-82, 2009
5. Narkis, G. et al: Am. J. Hu. Genet. 81:530-9, 2007

TECHNICAL INFORMATION

Source:

PIP5K1C/PIP5Kgamma antibody is a rabbit antibody raised against recombinant human PIP5K1C proteins.

Specificity and Sensitivity:

This antibody detects endogenous PIP5K1C proteins without cross-reactivity with other family members.

Storage Buffer: Rabbit IgG in phosphate buffered saline (without Mg²⁺ and Ca²⁺), pH 7.4, 150mM NaCl, 0.02% sodium azide and 50% glycerol.

Storage:

Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

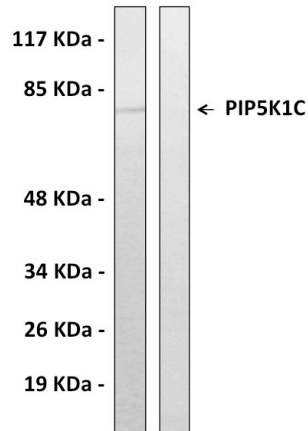
APPLICATIONS

Application:	*Dilution:
WB	1:500-1:1000
IP	n/d
IHC	n/d
ICC	n/d
FACS	n/d
ELISA	1:20000

**Optimal dilutions must be determined by end user.*



QUALITY CONTROL DATA



Immunoblotting analysis of extracts from A549 cells, using Anti-PIP5K1C antibody. The lane on the left was treated with the Anti-PIP5K1C antibody. The lane on the right (negative control) was treated with both Anti-PIP5K1C antibody and the synthesized immunogen peptide.

