Phosphoinositide-specific phospholipase C (E.C. 3.1.4.11)

Overview: Phosphoinositide-specific phospholipase C (PLC) catalyses the hydrolysis of phosphatidylinositol 4,5-bisphosphate to inositol 1,4,5-trisphosphate and 1,2-diacylglycerol, each of which have major second messenger functions. Two domains, X and Y, essential for catalytic activity, are conserved in the different forms of PLC. Isoforms of PLC-β (ENSF00000000466) are activated primarily by 7TM receptors through members of the $G_{q/11}$ family of G proteins. The receptor-mediated activation of PLC-γ involves their phosphorylation by tyrosine kinases in response to activation of a variety of growth factor receptors and immune system receptors. PLC-ε1 may represent a point of convergence of signalling via both 7TM and catalytic receptors. Ca^{2+} ions are required for catalytic activity of PLC isoforms and have been suggested to be the major physiological form of regulation of PLC-δ activity. PLC has been suggested to be activated non-selectively by the small molecule *m*-3M3FBS (Bae *et al*., 2003), although this mechanism of action has been questioned (Krjukova *et al*., 2004). The aminosteroid U73122 has been described as an inhibitor of phosphoinositide-specific PLC (Smith *et al*., 1990), although its selectivity among the isoforms is untested and it has been reported to occupy the H_1 histamine receptor (Hughes *et al*., 2000).

Nomenclature	β1	β2	β3	β4
Other names	PLC-I, PLC-154, KIAA0581	–	–	–
Ensembl ID	ENSG00000182621	ENSG00000137841	ENSG00000149782	ENSG00000101333
Endogenous activators	Gαq (Smrcka *et al*., 1991; Hepler *et al*., 1993), Gα11 (Hepler *et al*., 1993), G$\beta\gamma$ (Park *et al*., 1993)	Gα16 (Lee *et al*., 1992), G$\beta\gamma$ (Camps *et al*., 1992; Park *et al*., 1993), rac2 (Illenberger *et al*., 2003a; b)	Gαq (Lee *et al*., 1992), G$\beta\gamma$ (Carozzi *et al*., 1993; Park *et al*., 1993)	Gαq (Jhon *et al*., 1993)

Nomenclature	γ1	γ2	δ1	δ3	δ4
Other names	PLC-II, PLC-148	PLC-IV	PLC-III	–	–
Ensembl ID	ENSG00000124181	ENSG00000197943	ENSG00000187091	ENSG00000161714	ENSG00000115556
Endogenous activators	PtdIns 3,4,5-P_3 (Bae *et al*., 1998)	PtdIns 3,4,5-P_3 (Bae *et al*., 1998)	Transglutaminase II (Murthy *et al*., 1999), p122-RhoGAP (Homma and Emori, 1995), spermine (Haber *et al*., 1991), G$\beta\gamma$ (Park *et al*., 1993)	–	–
Inhibitors	–	Rac1, rac2, rac3 (Piechulek *et al*., 2005; Walliser *et al*., 2008)	Sphingomyelin (Pawelczyk and Lowenstein, 1992)	–	–

PLC-δ2 has been cloned from bovine sources (Meldrum *et al*., 1991).

Nomenclature	ε1	ζ1	η1	η2
Other names	Pancreas-enriched PLC	Testis-development protein NYD-SP27	–	–
Ensembl ID	ENSG00000138193	ENSG00000139151	ENSG00000114805	ENSG00000149527
Endogenous activators	Ras (Song *et al*., 2001), Rho (Wing *et al*., 2003)	–	–	G$\beta\gamma$ (Zhou *et al*., 2005)

A series of PLC-like proteins (PLCL1 ENSG00000115896; PLCL2 ENSG00000154822 and PLCL3 ENSG00000114805) form a family (ENSF00000000386) with PLCδ and PLCζ1 isoforms, but appear to lack catalytic activity.

Abbreviations: ***m*-3M3FBS**, 2,4,6-trimethyl-*N*-(*meta*-3-trifluoromethylphenyl)-benzenesulphonamide; **PtdIns 3,4,5-P_3**, phosphatidylinositol 3,4,5-trisphosphate; **U73122**, 1-(6-[[(17β)-3-methoxyestra-1,3,5[10]-trien-17-yl}amino]hexyl)-1*H*-pyrrole-2,5-dione

Further Reading

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