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Phosphatidylinositol kinases (version 2020.2) in the IUPHAR/BPS Guide to Pharmacology Database

Mohib Uddin[1]

1. AstraZeneca, Sweden

Abstract

Phosphatidylinositol may be phosphorylated at either 3- or 4- positions on the inositol ring by PI 3-kinases or PI 4-kinases, respectively.

Phosphatidylinositol 3-kinases

Phosphatidylinositol 3-kinases (PI3K, provisional nomenclature) catalyse the introduction of a phosphate into the 3-position of phosphatidylinositol (PI), phosphatidylinositol 4-phosphate (PIP) or phosphatidylinositol 4,5-bisphosphate (PIP_2). There is evidence that PI3K can also phosphorylate serine/threonine residues on proteins. In addition to the classes described below, further serine/threonine protein kinases, including ATM (Q13315) and mTOR (P42345), have been described to phosphorylate phosphatidylinositol and have been termed PI3K-related kinases. Structurally, PI3Ks have common motifs of at least one C2, calcium-binding domain and helical domains, alongside structurally-conserved catalytic domains. wortmannin and LY 294002 are widely-used inhibitors of PI3K activities. wortmannin is irreversible and shows modest selectivity between Class I and Class II PI3K, while LY294002 is reversible and selective for Class I compared to Class II PI3K.

Class I PI3Ks (EC 2.7.1.153) phosphorylate phosphatidylinositol 4,5-bisphosphate to generate phosphatidylinositol 3,4,5-trisphosphate and are heterodimeric, matching catalytic and regulatory subunits. Class IA PI3Ks include p110α, p110β and p110δ catalytic subunits, with predominantly p85 and p55 regulatory subunits. The single catalytic subunit that forms Class IB PI3K is p110γ. Class IA PI3Ks are more associated with receptor tyrosine kinase pathways, while the Class IB PI3K is linked more with GPCR signalling.

Class II PI3Ks (EC 2.7.1.154) phosphorylate phosphatidylinositol to generate phosphatidylinositol 3-phosphate (and possibly phosphatidylinositol 4-phosphate to generate phosphatidylinositol 3,4-bisphosphate). Three monomeric members exist, PI3K-C2α, β and β, and include Ras-binding, Phox homology and two C2domains.

The only **class III PI3K** isoform (EC 2.7.1.137) is a heterodimer formed of a catalytic subunit (VPS34) and regulatory subunit (VPS15).

Phosphatidylinositol 4-kinases

Phosphatidylinositol 4-kinases (EC 2.7.1.67) generate phosphatidylinositol 4-phosphate and may be divided into higher molecular weight type III and lower molecular weight type II forms.

Contents

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Database links

Phosphatidylinositol kinases
http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=781

Enzymes

PI4KIIIα/PIK4CA(phosphatidylinositol 4-kinase alpha)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2148

PI3Kα(phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2153

PI4KIIIβ/PIK4CB(phosphatidylinositol 4-kinase beta)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2149

PI3Kβ(phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit beta)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2154

PI4KIIα/PI4K2A(phosphatidylinositol 4-kinase type 2 alpha)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2498

PI3Kγ(phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit gamma)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2156

PI4KIIβ/PI4K2B(phosphatidylinositol 4-kinase type 2 beta)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2499

PI3Kδ(phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit delta)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2155

p85α/PIK3R1(phosphoinositide-3-kinase regulatory subunit 1)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2503

p85β/PIK3R2(phosphoinositide-3-kinase regulatory subunit 2)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2504

p55γ/PIK3R3(phosphoinositide-3-kinase regulatory subunit 3)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2505

p150/VPS15/PIK3R4(phosphoinositide-3-kinase regulatory subunit 4)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2157

p101/PIK3R5(phosphoinositide-3-kinase regulatory subunit 5)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2506

p87/PIK3R6(phosphoinositide-3-kinase regulatory subunit 6)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2507

C2α/PIK3C2A(phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 alpha)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2150

C2β/PIK3C2B(phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 beta)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2151

C2γ/PIK3C2G(phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 gamma)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2288

VPS34(phosphatidylinositol 3-kinase catalytic subunit type 3)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2152

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