PI3K phosphorylates PIP2 to PIP3

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

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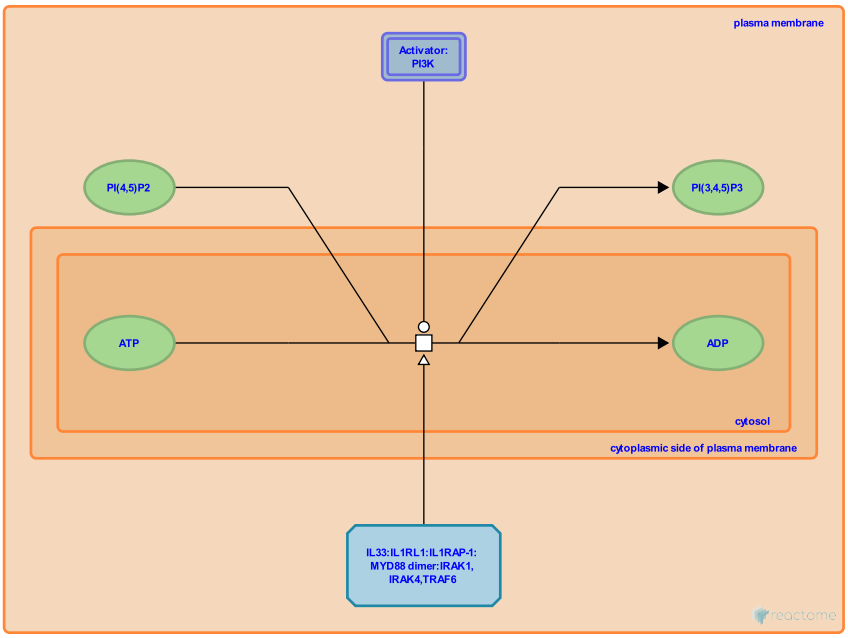
Stable identifier: R-HSA-2316434

Type: transition

Compartments: cytosol, plasma membrane



A number of different extracellular signals converge on PI3K activation. PI3K can be activated downstream of receptor tyrosine kinases (RTKs) such as FGFR (Ong et al. 2001, Eswarakumar et al. 2005), KIT (Chian et al. 2001, Ronnstrand 2004, Reber et al. 2006), PDGF (Coughlin et al. 1989, Fantl et al. 1992, Heldin et al. 1998), insulin receptor IGF1R (Hadari et al. 1992, Kooijman et al. 1995), and EGFR and its family members (Rodrigues et al. 2000, Jackson et al. 2004, Kainulainen et al. 2000, Junttila et al. 2009). Other proteins, such as CD28 (Pages et al. 1996, Koyasu 2003, Kane and Weiss, 2003) and TRAT1 (Bruyns et al. 1998, Koyasu 2003, Kolsch et al. 2006), can also trigger PI3K activity.

In unstimulated cells, PI3K class IA exists as an inactive heterodimer of a p85 regulatory subunit (encoded by PIK3R1, PIK3R2 or PIK3R3) and a p110 catalytic subunit (encoded by PIK3CA, PIK3CB or PIK3CD). Binding of the iSH2 domain of the p85 regulatory subunit to the ABD and C2 domains of the p110 catalytic subunit both stabilizes p110 and inhibits its catalytic activity. This inhibition is relieved when the SH2 domains of p85 bind phosphorylated tyrosines on activated RTKs or their adaptor proteins. Binding to membrane-associated receptors brings activated PI3K in proximity to its membrane-localized substrate, PIP2 (Mandelker et al. 2009, Burke et al. 2011).

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Editions

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