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Phosphoinositides originally gained fame as precursors for specific second messengers involved in signal transduction. Both phospholipase C and phosphoinositide 3-kinases use phosphatidylinositol bisphosphate (PIP2) as a substrate leading to the generation of the second messengers, inositol 1,4,5 trisphosphate (IP3), diacylglycerol and phosphatidylinositol trisphosphate (PIP3). Laterly, they have taken centre stage in controlling many essential processes at virtually every single membrane. Phosphoinositides regulate many aspects of membrane traffic including exocytosis, endocytosis, phagocytosis, cytokinesis as well as actin dynamics.

Phosphoinositides are phosphorylated derivatives of phosphatidylinositol (PI). Phosphorylation of the inositol ring of phosphatidylinositol gives rise to seven distinct phosphoinositide species with highly specific regulatory functions. Each phosphoinositide species has its own unique subcellular distribution and most organelles appear to be enriched in a specific phosphoinositide; for example, PI(4,5)P2 is abundant at the plasma membrane, while PI(4)P is enriched at the Golgi apparatus. Thus, phosphoinositides can contribute to compartmental identity. This is mainly determined by the complement of the lipid kinases present at the different organelles.

Phosphatidylinositol is the precursor for all the phosphorylated derivatives and is synthesised at the endoplasmic reticulum. Membrane lipids are insoluble in the aqueous environment and thus trafficking of PI to different organelles can only occur by vesicular transport or by protein-mediated transport. Vesicular transport implies bulk transport of total phospholipids and would not be selective for a specific lipid. Transport proteins on the other hand specifically bind and transfer phosphatidylinositol (Phosphatidylinositol transport proteins; PITP) and have been identified in many eukaryotes. Phosphatidylinositol transfer proteins (PITPs), comprising five members in the human genome are implicated in the non-vesicular traffic of phosphatidylinositol (PI) between intracellular membranes and the plasma membrane. Three members of the PITP family (PITPa, PITPb, and RdgBb (retinal degeneration type B) alt. name PITPNC1) are present as single domain proteins and two (RdgBaI and RdgBaII alt. name PITPNM1 and PITPNM2) are present as multidomain proteins with the PITP domain located at the N-terminus. The hallmark of PITP proteins is to extract PI molecules from a membrane, sequester in its binding pocket and deposit the lipid to membranes. PITPs regulate the synthesis of phosphoinositides (PPIs) either by delivery of the substrate, PI to specific membrane compartments or by potentiating the activities of the lipid kinases, or both. The common requirement for the diverse functions for all PITPs is their ability to bind PI and coupling its function to phosphoinositide-dependent pathways. Studies with the single domains PITPs demonstrate that they participate in phospholipase C signalling as well as in membrane traffic

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Lipid Transfer Proteins in Phosphoinositide Signalling and Membrane Traffic

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Thursday, April 3, 2014 at 4 p.m.
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Lecture is open to all

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