

The phosphoinositide 3-kinase signaling network in lymphocytes.

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Phosphoinositide 3-kinases play critical roles in normal and cancer cell biology through phosphorylation of the D3 position of the inositol headgroup in membrane lipids. Enzymatic activation of phosphoinositide 3-kinases and targeting to the plasma membrane is controlled by membrane receptors such as lymphocyte antigen receptors. Active PI3Ks generate several types of D3 phosphoinositides (PI), including PI(3,4,5)P₃ and PI(3,4)P₂. The accumulation of these different PI species is further controlled by inositol phosphatases including the D3 PI phosphatase PTEN and the D5 phosphatase SHIP. PI(3,4,5)P₃ and PI(3,4)P₂ have distinct regulation, distinct protein binding partners and distinct functions in cell biology. Studies in transformed lymphocyte and animal models indicate that PI(3,4)P₂ binding partners may serve in both negative feedback to limit signaling and mitogenesis and in a positive capacity to orchestrate cytoskeletal dynamics required for cell adhesion and migration.