SAC1 encodes a lipid phosphatase that is involved in many cellular processes, such as cell wall maintenance and membrane and protein trafficking, through regulating levels of phosphotidylinositolphosphates. Although Sac1p is able to dephosphorylate PtdIns[3]P, PtdIns[4]P, and PtdIns[3,5]P2 in vitro, the role of Sac1p in processes involving PtdIns[4]P has been the primary focus of in vivo studies. Sac1p specifically acts upon PtdInsP produced by the PtdIns 4-kinase Stt4p and acts as antagonist to the PtdIns 4-kinase Pik1p. Sac1p is a type II transmembrane protein that localizes to the Golgi and the ER. This subcompartmentalization of the phosphatase determines which processes it regulates. Golgi-localized Sac1p is involved in Golgi trafficking and cell wall maintenance, while ER-localized Sac1p participates in ATP uptake into the ER, ER-based secretion and protein processing, and vacuolar function. Localization of Sac1p is regulated by growth conditions as well as interactions with proteins such as Dpm1p. Expression of SAC1 is regulated in response to changing levels of PtdIns[4]P. SAC1 was originally identified as a suppressor of the temperature-conditional act1-1 allele, and thus some of the phenotypes seen in the sac1 mutant are similar to those of actin mutants, such as defects in actin cytoskeleton polarization and abnormal chitin deposition. sac1 null phenotypes also include cold sensitivity, inositol auxotrophy, fragmented vacuoles, accumulation of lipid droplets, elevated levels of PtdIns[4]P, calcofluor white sensitivity, and constitutively-activated unfolded protein response. Sac1p is the founding member of a family of PtdIns phosphatases that share a catalytic domain known as the Sac1-like domain. In S. cerevisiae, this family includes the phosphatases Fig4p, Inp51p, Inp52p, and Inp53p, all of partially overlapping function. All of the Sac1-like domain containing proteins are highly conserved from yeast to human; mammalian members of this protein family include synaptojanin-1and synaptojanin -2.About Phosphatidylinositol Phosphate Biosynthesis The phosphorylated products of phosphatidylinositol, collectively referred to as phosphoinositides or phosphatidylinositol phosphates, are membrane-bound lipids that function as structural components of membranes, as well as regulators of many cellular processes in eukaryotes, including vesicle-mediated membrane trafficking, cell wall integrity, and actin cytoskeleton organization. PtdInsPs are also precursors of the water-soluble inositol phosphates, an important class of intracellular signaling molecules. The inositol ring of the membrane phospholipids and the water-soluble IPs are readily phosphorylated and dephosphorylated at a number of positions making them well suited as key regulators. PtdIns can be phosphorylated at one or a combination of positionson the inositol headgroup, generating a set of unique stereoisomers that have specific biological functions. These stereoisomers have been shown to be restricted to certain membranes. Phosphatidylinositol 4-phosphateis the major PtdInsP species of the Golgi apparatus, where it plays a role in the vesicular trafficking of secretory proteins from the Golgi to the plasma membrane. Phosphatidylinositol 4,5-bisphosphateis the major species found at the plasma membrane and is involved in the regulation of actin cytoskeleton organization, as well as cell wall integrity, and heat shock response pathways. Phosphatidylinositol 3-phosphateis found predominantly at endosomal membranes and in multivesicular bodies, where it plays a role in endosomal and vacuolar membrane trafficking. Phosphatidylinositol 3,5-bisphosphateis found on vacuolar membranes where it plays an important role in the MVB sorting pathway. Phosphorylation and dephosphorylation of the inositol headgroups of PtdInsPs at specific membrane locations signals the recruitment of certain proteins essential for vesicular transport. PtdInsPs recruit proteins that contain PtdInsP-specific binding domains, such as the well-studied pleckstrin homologydomain that recognizes the phosphorylation pattern of specific PtdInsP inositol headgroups. A number of kinases and phosphatases are involved in the generation and interconversions of PtdInsPs, the majority of which have been well conserved during evolution. The PtdInsP kinases, in contrast to the lipid phosphatases, have a higher degree of specificity. While each kinase appears to phosphorylate only one substrate, many of the lipid phosphatases can dephosphorylate a number of substrates.