



Model for the PtdIns(3)P - PtdIns(3,5)P₂ interconversion on mammalian endosomal membranes through a multiprotein PAS complex. The PAS complex is comprised of the kinase PIKfyve, the PtdIns(3,5)P₂-specific phosphatase Sac3, and the scaffold ArPIKfyve. The evolutionarily conserved domains in the PIKfyve middle region interact with the ArPIKfyve-Sac3 subcomplex, formed via the C-termini of an ArPIKfyve homooligomer and the C-terminus of a Sac3 monomer. These interactions allow PIKfyve to acquire “activated” conformation to increase local synthesis of PtdIns(3,5)P₂ and recruitment of PtdIns(3,5)P₂ effectors. The increase in PtdIns(3,5)P₂ is counterbalanced by Sac3, which when incorporated in the PAS complex retains its activity for PtdIns(3,5)P₂ hydrolysis. The concerted action of the two enzymes coordinate dynamic endosome remodeling in parallel with fission and fusion events.