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A steep phosphoinositide phosphate gradient critical for fungal filamentous growth.

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Membrane phosphoinositide phosphates, such as phosphatidylinositol 4,5-bisphosphate – $PI(4,5)P_2$ and phosphatidylinositol 3,4,5-triphosphate – $PI(3,4,5)P_3$, despite being relatively minor components of membranes play a central role in cell polarity, directional growth, movement and, in particular, actin cytoskeleton organization. These responses are mediated by a variety of small G proteins, which are conserved from yeast to humans. In the budding yeast *Saccharomyces cerevisiae* and the opportunistic human pathogen *Candida albicans,* neither $PI(3,4,5)P_3$ nor PI-3-kinase homologs have been found, raising the possibility that the $PI(4,5)P_2$ fulfills some of the functions of $PI(3,4,5)P_3$ and is required for polarized growth and morphological changes. In *S. cerevisiae* a single PI(4)P-5-kinase, encoded by *MSS4*, is required for $PI(4,5)P_2$ synthesis and three PI-4-kinases (encoded by *LSB6*, *STT4* and *PIK1*) synthesize PI(4)P. In this yeast the Mss4, Stt4 and Pik1 kinases are required for viability, organization of the actin cytoskeleton and membrane traffic. In budding yeast, Mss4 and Stt4 are found at the plasma membrane, whereas Pik1 is localized to the Golgi. We have been examining the roles of PI(4)P and $PI(4,5)P_2$ in *C. albicans* invasive filamentous growth in response to different stimuli.

In *C. albicans* the switch from yeast to a filamentous form is important for pathogenicity and requires a dramatic reorganization of the actin cytoskeleton. We have been using strains in which the levels of these critical lipid kinases can be manipulated. In addition, using different fluorescent lipid associated reporters (FLAREs), we have been following the distribution of PI(4)P and $PI(4,5)P_2$ during the transition from budding to filamentous growth. I will discuss the different lipid asymmetries that occur during the distinct growth states as well as how these asymmetric distributions are generated and maintained in time and space.