Cycling and Recycling - New Insights into the Mechanisms of Cell Polarization

Tina Freisinger, Ben Klünder, Jared L. Johnson, Charles Boone, Richard A. Cerione, Erwin Frey, and Roland Wedlich-Söldner

Polarity establishment in many cells is driven by feedback loops that amplify stochastic fluctuations in the distribution of the central polarity regulators. We found that a combination of actin and Guanine nucleotide Dissociation Inhibitor (GDI) dependent recycling of the GTPase Cdc42 is required to achieve rapid, robust and unique polarization during yeast budding. Importantly, the two recycling pathways were coordinated by the GTPase cycle of Cdc42. While actin-driven endocytosis and transport were specifically regulated by the GTP-bound form of Cdc42, membrane extraction by the GDI was tightly coupled to the cycle speed of the GTPase. A detailed mathematical model was able to recapitulate all measured parameters and could accurately predict defects associated with changes in Cdc42 activation and recycling.