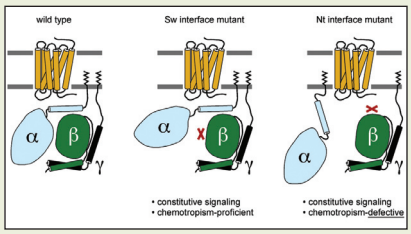
INCYTES from MBC
January, Vol. 19, No. 1



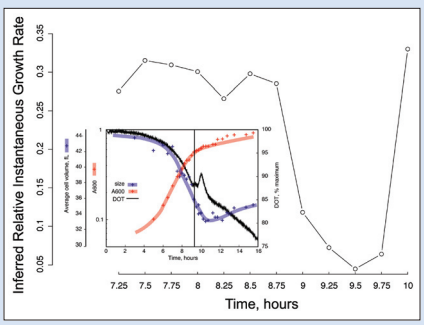
Distinct Roles for Two Gα-Gβ Interfaces in Cell Polarity Control by a Yeast Heterotrimeric G Protein

Shelly C. Strickfaden and Peter M. Pryciak

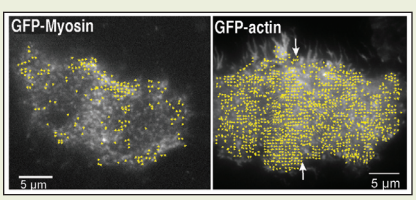
Cell polarization in budding yeast is controlled by extracellular chemoattractants called mating pheromones, which bind to G protein–coupled receptors (GPCRs) to activate a heterotrimeric G protein (Gαβγ) and a downstream MAP kinase cascade. To compare the roles of these signaling modules in cell polarity control, the authors developed tools for independent activation of the MAP kinase pathway. MAP kinase signaling alone could induce cell asymmetry. However, proper control of cell polarity required continuous communication between the GPCR and the Gαβγ module, perhaps to regulate Gαβγ in a spatially asymmetric manner. Interactions between Gα and Gβ occur via two interfaces: the N-terminal (Nt) interface and the Switch (Sw) interface. Analysis of Gβ subunit mutants revealed that different polarity phenotypes were obtained depending on which Gα-Gβ interface was disrupted. The results suggest that the Sw interface controls signaling, while the Nt interface facilitates directional responses through receptor-Gαβγ coupling. A partially dissociated Gαβγ heterotrimer, where only one interface is released, could facilitate polarization by allowing activated Gβγ to remain in regulatory communication with the GPCR.

Coordination of Growth Rate, Cell Cycle, Stress Response, and Metabolic Activity in Yeast

Matthew J. Brauer, Curtis Huttenhower, Edoardo M. Airoldi, Rachel Rosenstein, John C. Matese, David Gresham, Viktor M. Boer, Olga G. Troyanskaya, and David Botstein



The most fundamental system-level challenge for cell physiology is the achievement of balanced growth in the face of a fluctuating environment. The authors have used yeast chemostat cultures at six different growth rates under six different nutrient limitations to comprehensively and quantitatively study the relation between growth rate and genome-wide gene expression, cell cycle progression, and glucose metabolism. The expression of ~27% of all yeast genes is linearly correlated with growth rate, and there is a linear relationship between growth rate and the fraction of the cell population in the G0/G1 cell cycle phase, independent of limiting nutrient. Many (but not all) genes associated with stress response are strongly correlated with growth rate. Surprisingly, batch and steady-state cultures limited by auxotrophic requirements waste excess glucose, whereas those limited by phosphate, sulfate, or ammonia do not; this phenomenon is reminiscent of the "Warburg effect" in cancer cells. Using a simple quantitative model, the authors define, even for batch cultures in which the growth rate is changing, an "instantaneous growth rate." This concept is useful in interpreting the system-level connections among growth rate, metabolism, stress, and the cell cycle.



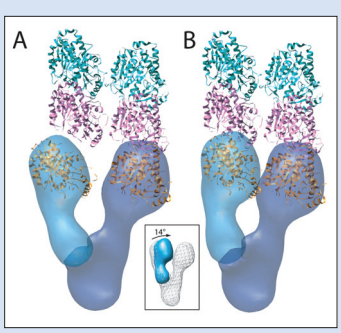
Distinct Pathways for the Early Recruitment of Myosin II and Actin to the Cytokinetic Furrow

Mian Zhou and Yu-Li Wang

Many models of cortical ingression during cytokinesis involve global, coupled movements of actin and myosin II filaments into the equatorial region. To test these models, the authors used total internal reflection fluorescence microscopy to obtain high-resolution videos of cortical myosin II and actin during early cytokinesis. Structural movements were analyzed with spatial-temporal image correlation spectroscopy, and domains of assembly/disassembly were identified with a new algorithm termed temporal differential microscopy. Contrary to the predictions of previous models, no directional flow of cortical myosin II was detected. Instead transient myosin assembly was observed throughout the cortex, while disassembly was suppressed along the equator, resulting in an equatorial concentration of myosin II. In contrast, actin filaments showed a striking myosin II–dependent flux toward the equator, as well as de novo equatorial assembly. These results indicate that cortical reorganization during cytokinesis involves both regulated assembly and disassembly and argue against mechanisms coupled to global cortical movements such as polar relaxation.

The Structure of the γ-Tubulin Small Complex: Implications of Its Architecture and Flexibility for Microtubule Nucleation

Justin M. Kollman, Alex Zelter, Eric G.D. Muller, Bethany Fox, Luke M. Rice, Trisha N. Davis, and David A. Agard



Microtubules do not grow spontaneously under intracellular conditions, but are nucleated by complexes containing γ-tubulin, a mechanism that allows spatial and temporal control of the microtubule cytoskeleton. The authors have used single particle electron microscopy to determine the structure of the core nucleation complex, γ-tubulin small complex (γ-TuSC). γ-TuSC is Y shaped, with one γ-tubulin located at the tip of each arm. One of the arms is flexibly attached to the rest of the complex, resulting in variation of the relative positions of the γ-tubulins. Rather than having the γ-tubulins positioned laterally as in the microtubule lattice, within the γ-TuSC they are held apart in a microtubule-incompatible conformation. This likely serves to suppress the intrinsic nucleating activity of γ-tubulin until the γ-TuSC is incorporated into higher-order complexes or localized at microtubule organizing centers. The authors propose that further movement of the flexibly attached arm is required to bring the γ-tubulins together to participate in microtubule-like interactions, providing a template for microtubule growth. ■