Contents

BRIEF REPORTS

A conserved signaling network monitors delivery of sphingolipids to the plasma membrane in budding yeast
Jesse Clarke, Noah Dephoure, Ira Horecka, Steven Gygi, and Douglas Kellogg
2589–2599

In budding yeast, signals generated in response to membrane growth are required for cell cycle progression. A mass spectrometry screen for signals triggered by an arrest of membrane growth identified sphingolipid signaling pathways. Delivery of sphingolipids to the plasma membrane could generate signals that control cell growth and the cell cycle.

Reconstituted IMPDH polymers accommodate both catalytically active and inactive conformations
Sajitha A. Anthony, Anika L. Burrell, Matthew C. Johnson, Krisna C. Duong-Ly, Yin-Ming Kuo, Jacqueline C. Simonet, Peter Michener, Andrew Andrews, Justin M. Kollman, and Jeffrey R. Peterson
2600–2608

The metabolic enzyme IMPDH assembles into octamers that can polymerize and form micron-scale structures in cells. Octamers can adopt active, expanded or inactive, compressed conformations driven by allosteric nucleotide and substrate binding. Both forms are accommodated within polymers, and polymerization alone does not alter catalytic activity.

ARTICLES

Biosynthesis and Biodegradation

Coi1 is a novel assembly factor of the yeast complex III–complex IV supercomplex
Ravi K. Singhal, Christine Kruse, Juliana Heidler, Valentina Strecker, Klaus Zwicker, Lea Düsterwald, Benedikt Westermann, Johannes M. Herrmann, Ilka Wittig, and Doron Rapaport
2609–2622

Coi1 was identified as an important assembly factor for mitochondrial complex III, complex IV, and their supercomplexes. Deletion of COI1 in yeast cells results in severe growth defect, reduced membrane potential, hampered respiration, and altered assembly of complexes III and IV as well as their supercomplexes.

Cell Biology of Disease

Neuroprotective astrocyte-derived insulin/insulin-like growth factor 1 stimulates endocytic processing and extracellular release of neuron-bound Aβ oligomers
2623–2636

Findings reveal a novel basis for protecting CNS neurons against Aβ oligomers (AβOs), neurotoxins believed to instigate neural damage leading to Alzheimer's dementia. Results with spatially separated cocultures of astrocytes and hippocampal neurons show an exosome-like mechanism by which insulin/IGF1 from astrocytes clear bound AβOs from neuronal surfaces.

Cell Physiology

The SAGA complex, together with transcription factors and the endocytic protein Rvs167p, coordinates the reprofilig of gene expression in response to changes in sterol composition in Saccharomyces cerevisiae
Gisèle Dewhurst-Manidor, Daniel Abegg, Fabrice P. A. David, Jacques Rougemont, Cameron C. Scott, Alexander Adibekian, and Howard Riezman
2637–2649

The SAGA complex, together with transcription factors and Rvs167p, coordinates sterol-dependent transcription changes. In ergosterol mutants the SAGA complex increases its occupancy on ergosterol biosynthesis and anaerobic gene promoters, recruits the SWI/SNF complex, and binds to transcription factors and Rvs167p. Genes encoding stress proteins and basic amino acid synthesis are also affected even though promoter occupancy is not changed.
Cytoskeleton

Force-induced transcellular tunnel formation in endothelial cells
Win Pin Ng, Kevin D. Webster, Caroline Stefani, Eva M. Schmid, Emmanuel Lemichez, Patricia Bassereau, and Daniel A. Fletcher

Transcellular tunnels in endothelial cells can be formed by leukocytes and pathogens as a way of crossing the endothelial barrier. Using force microscopy and fluorescence microscopy, we find that the actin cytoskeleton provides the primary mechanical barrier to transcellular tunnel formation, which can be overcome by force or by toxins.

Mechanical signals activate p38 MAPK pathway-dependent reinforcement of actin via mechanosensitive HspB1
Laura Hoffman, Christopher C. Jensen, Masaaki Yoshigi, and Mary Beckerle

Mechanical force induces protein phosphorylations, subcellular redistributions, and actin remodeling. We show that mechanical activation of the p38 MAPK pathway leads to phosphorylation of HspB1 (hsp25/27), which redistributes to cytoskeletal structures, and contributes to the actin cytoskeletal remodeling induced by mechanical stimulation.

Membrane Trafficking

Role of clathrin in dense core vesicle biogenesis
Bhavani S. Sahu, Paul T. Manna, James R. Edgar, Robin Antrobus, Sushil K. Mahata, Alessandro Bartolomucci, Georg H. H. Borner, and Margaret S. Robinson

Knocking down clathrin in PC12 cells not only affects the maturation of dense core vesicles, it also renders them essentially incapable of secretagogue-induced exocytosis.

The golgin protein Coy1 functions in intra-Golgi retrograde transport and interacts with the COG complex and Golgi SNAREs
Nadine S. Anderson, Indrani Mukherjee, Christine M. Bentivoglio, and Charles Barlowe

Yeast Coy1 and its human homologue CASP belong to the golgin family of extended coiled-coil proteins that underlie the structure and function of the Golgi complex. Here Coy1 is shown to operate in intra-Golgi retrograde transport through direct interactions with the COG complex and specific Golgi SNARE proteins.

Basolateral delivery of the type I transforming growth factor beta receptor is mediated by a dominant-acting cytoplasmic motif
Xueqian Yin, Jeong-Han Kang, Mahefatiana Andrianifahanana, Youli Wang, Mi-Yeon Jung, Danielle M. Hernandez, and Edward B. Leof

A novel motif within the cytoplasmic tail of the type I TGF-β receptor (TβRI) controls basolateral delivery. While this element functions independent of TβRI recycling and heteromeric TGF-β receptor trafficking, it can dominantly direct an apically expressed receptor to the basolateral membrane in polarized epithelial cells.

Sphingolipids facilitate age asymmetry of membrane proteins in dividing yeast cells
Pushpendra Singh, Sree Kumar Ramachandran, Jin Zhu, Byoung Choul Kim, Debojyoti Biswas, Taekjip Ha, Pablo A. Iglesias, and Rong Li

Asymmetrically dividing yeast cells segregate determinants of aging, and sphingolipids play a role in restricting the diffusion, and thus the mixing, of young and aged plasma membrane proteins.

Neurodegeneration-associated mutant TREM2 proteins abortively cycle between the ER and ER–Golgi intermediate compartment
Daniel W. Sirkis, Renan E. Aparicio, and Randy Schekman

Mutations in the microglial cell surface receptor TREM2 are associated with multiple forms of neurodegeneration. Several of these mutant forms of TREM2 were thought to be retained in the endoplasmic reticulum (ER), but careful analysis reveals that they engage in an abortive cycling pathway between the ER and ER–Golgi intermediate compartment.

Methods

Superresolution microscopy of the β-carboxysome reveals a homogeneous matrix
Matthew J. Niederhuber, Talley J. Lambert, Clarence Yapp, Pamela A. Silver, and Jessica K. Polka

Application of 3D-structured illumination microscopy to study the protein organization of the β-carboxysome in Synechococcus elongatus reveals new structural details of this bacterial microcompartment and the feasibility of using superresolution microscopy to study nanometer-scaled protein organization in vivo.