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Fracture faces of frozen membranes: 50th anniversary
Daniel Branton 421–423

MBoC PERSPECTIVE ON CELL BIOLOGY AND HUMAN HEALTH

From CFTR biology toward combinatorial pharmacotherapy: expanded classification of cystic fibrosis mutations

BRIEF REPORTS

Mechanisms of JAK/STAT pathway negative regulation by the short coreceptor Eye Transformer/Latrán
Katherine H. Fisher, Wojciech Stec, Stephen Brown, and Martin P. Zeidler 434–441

The short receptor Et/Lat negatively regulates Drosophila JAK/STAT signaling. It binds to intracellular components and the Domeless receptor but cannot bind ligands, thus generating a signaling-incompetent complex. Et/Lat is also more stable than Dome. The study provides insights into how short receptors negatively regulate signaling.

Roles of septins in prospore membrane morphogenesis and spore wall assembly in Saccharomyces cerevisiae
Lydia R. Heasley and Michael A. McMurray 442–450

In mitotically dividing cells, septin proteins form cytoskeletal filaments that function in cell morphogenesis and division. Gametogenesis in yeast couples meiosis with a fundamentally different form of cytokinesis involving de novo membrane synthesis. Budding yeast septins are critical for spore membrane extension and wall assembly.

ARTICLES

Cell Biology of Disease

Cells activated for wound repair have the potential to direct collective invasion of an epithelium
Brigid M. Bleaken, A. Sue Menko, and Janice L. Walker 451–465

Studies using a clinically relevant injury invasion model reveal that cells critical to wound repair are inherently invasive, acting as leaders to direct the collective invasion of a wounded epithelium. This model is a valuable tool with which to study leader cell–directed invasion and help understand how mechanisms of wound healing are hijacked to cause disease.

A Highlights from MBoC Selection

APC binds the Miro/Milton motor complex to stimulate transport of mitochondria to the plasma membrane
Kate M. Mills, Mariana G. Brocardo, and Beric R. Henderson 466–482

The role of adenomatous polyposis coli (APC) tumor suppressor at mitochondria is unclear. We show that APC associates with the Miro/Milton/kinesin complex to stimulate anterograde transport of mitochondria. This identifies the first regulatory role of APC in organelle transport. APC cancer mutations block this activity.
Epithelial Sel1L is required for the maintenance of intestinal homeostasis
Shengyi Sun, Rohan Lourie, Sara B. Cohen, Yewei Ji, Julia K. Goodrich, Angela C. Poole, Ruth E. Ley, Eric Y. Denkers, Michael A. McGuckin, Qiaoming Long, Gerald E. Duhamel, Kenneth W. Simpson, and Ling Qi

Endoplasmic reticulum (ER)-associated degradation (ERAD) clears misfolded proteins in the ER. Epithelial ERAD plays an indispensable role in Paneth cell biology and the maintenance of small intestine homeostasis. The findings implicate Sel1L-Hrd1 ERAD as a novel therapeutic target for Crohn’s disease.

Cell Interactions
A role of the sphingosine-1-phosphate (S1P)–S1P receptor 2 pathway in epithelial defense against cancer (EDAC)
Sayaka Yamamoto, Yuta Yako, Yoichiro Fujioka, Mihoko Kajita, Takeshi Kameyama, Shunsuke Kon, Susumu Ishikawa, Yusuke Ohba, Yusuke Ohno, Akio Kihara, and Yasuyuki Fujita

Normal epithelial cells have an ability to sense and actively eliminate neighboring transformed cells, a process called epithelial defense against cancer (EDAC). Exogenous S1P plays a crucial role in EDAC; the S1P–S1PR2 pathway regulates Rho–Rho kinase–filamin in the surrounding normal cells, promoting apical extrusion of RasV12-transformed cells from epithelia.

Cell Motility
Nerve growth factor stimulates axon outgrowth through negative regulation of growth cone actomyosin restraint of microtubule advance

Nerve growth factor (NGF) stimulation of embryonic mouse sensory axon outgrowth is MII dependent. NGF regulates two actomyosin processes: transverse actin bundling and peripheral retrograde (radial) network actin flow. These two processes oppose microtubule advance and differentially involve MIIA and MIIB, respectively.

Cell Physiology
hnRNP-Q1 represses nascent axon growth in cortical neurons by inhibiting Gap-43 mRNA translation
Kathryn R. Williams, Damian S. McAninch, Snezana Stefanovic, Lei Xing, Megan Allen, Wenqi Li, Yue Feng, Mihaela Rita Mihailescu, and Gary J. Bassell

A novel posttranscriptional mechanism for regulating the neuronal protein GAP-43 is reported. The mRNA-binding protein hnRNP-Q1 represses Gap-43 mRNA translation by a mechanism involving a 5’ untranslated region G-quadruplex structure, which affects GAP-43 function, as demonstrated by a GAP-43–dependent increase in neurite length and number with hnRNP-Q1 knockdown.

Cytoskeleton
By moonlighting in the nucleus, villin regulates epithelial plasticity
Srinivas Pattank, Sudeep P. George, Eric Pham, Swati Roy, Kanchan Singh, John M. Mariadason, and Seema Khurana

Nuclear villin regulates the expression and activity of Slug, a key transcriptional regulator of epithelial–mesenchymal transition, by directly interacting with its transcriptional corepressor, ZBRK1. Villin accumulates in the nucleus during wound repair, and altering the cellular microenvironment by hypoxia increases the nuclear villin.

An ensemble of specifically targeted proteins stabilizes cortical microtubules in the human parasite Toxoplasma gondii
Jun Liu, Yudou He, Imaan Benmerzouga, William J. Sullivan, Jr., Naomi S. Morissette, John M. Murray, and Ke Hu

The human parasite Toxoplasma gondii has 22 regularly spaced microtubules associated with the cortex. This work defines the differential localization of associated proteins, explores the biophysical constraints on specific targeting along the cortical microtubules, and investigates the function of these proteins in stabilizing the polymers.
Membrane Trafficking

Munc13-4 interacts with syntaxin 7 and regulates late endosomal maturation, endosomal signaling, and TLR9-initiated cellular responses

Jing He, Jennifer L. Johnson, Jlenia Monfregola, Mahalakshmi Ramadass, Kersi Pestonjamasp, Gennaro Napolitano, Jinzhong Zhang, and Sergio D. Catz

Munc13-4 regulates late endosome maturation and Toll-like receptor 9–dependent endosome-initiated signaling through a mechanism that involves interaction with the endocytic SNAREs syntaxin 7 and VAMP8. The results thus provide new mechanistic insight into endosomal maturation and function.

A Highlights from MBoC Selection

The alternate AP-1 adaptor subunit Apm2 interacts with the Mill regulatory protein and confers differential cargo sorting

Shawn T. Whitfield, Helen E. Burston, Björn D. M. Bean, Nandini Raghuram, Lymarie Maldonado-Báez, Michael Davey, Beverly Wendland, and Elizabeth Conibear

Adaptor complexes are important for cargo sorting in clathrin-coated vesicles. The μ adaptor subunits Apm1 and Apm2 create functionally distinct versions of the yeast AP-1 complex. A novel regulatory protein is identified that selectively binds Apm2-containing complexes and contributes to their membrane recruitment.