Contents

EDITORIAL

MBoC celebrates its first 20 years
D. Drubin 4143

MBoC 20TH ANNIVERSARY FAVORITE

An MBoC Favorite: Mitochondrial transmission during mating in *Saccharomyces cerevisiae* is determined by mitochondrial fusion and fission and the intramitochondrial segregation of mitochondrial DNA
T. D. Fox 4144

ASCB AWARD ESSAYS

Building a path in cell biology
G. Voeltz and I. Cheeseman 4145–4147

Being at the right place at the right time
S. G. Martin 4148–4150

A career at the interface of cell and developmental biology: a view from the crest
M. E. Bronner 4151–4153

A passion for the science of the human genome
G. M. Dunston 4154–4156

Membranes, viruses, detergents, and endosomes
A. Helenius 4157–4159

PERSPECTIVES

Why we need more basic biology research, not less
D. Botstein 4160–4161

An expanding role for cell biologists in drug discovery and pharmacology
P. K. Sorge and B. Schoeberl 4162–4164

Living matter—nexus of physics and biology in the 21st century
M. L. Gardel 4165–4166

Bringing the physical sciences into your cell biology research
D. N. Robinson and P. A. Iglesias 4167–4170

Political advocacy by the American Society for Cell Biology and its partners
T. D. Pollard 4171–4174

ARTICLES

Cell Biology of Disease

A zebrafish model of PMM2-CDG reveals altered neurogenesis and a substrate-accumulation mechanism for N-linked glycosylation deficiency

PMM2-CDG patients have phosphomannomutase (Pmm2) deficiency, with developmental and N-linked glycosylation defects attributed to depletion of mannose-1-phosphate and downstream lipid-linked oligosaccharides (LLOs). This, the first PMM2-CDG zebrafish model, shows, unexpectedly, that accumulation of the Pmm2 substrate mannose-6-phosphate explains LLO deficiency.
Proinflammatory cytokine secretion is suppressed by TMEM16A or CFTR channel activity in human cystic fibrosis bronchial epithelia


Functional expression of either CFTR or the calcium-activated chloride channel TMEM16A attenuates expression and secretion of the proinflammatory cytokines IL-6, IL-8, and CXCL1/2 in respiratory epithelia. Thus augmented proinflammatory cytokine secretion caused by defective anion transport may contribute to lung inflammation in cystic fibrosis.

Cell Cycle

Hect E3 ubiquitin ligase Tom1 controls Dia2 degradation during the cell cycle

D.-H. Kim and D. M. Koepp

This study identifies the degradation pathway for the F-box protein Dia2, which plays an important role in maintaining genomic integrity. The Hect domain E3 ligase Tom1 recognizes a stretch of positively charged residues in Dia2, leading to Dia2 degradation by the ubiquitin proteasome system. Failure to degrade Dia2 disrupts cell cycle dynamics.

Cell Interactions

The tyrosine phosphatase SHP2 regulates recovery of endothelial adherens junctions through control of β-catenin phosphorylation

I. Timmerman, M. Hoogenboezem, A. M. Bennett, D. Geerts, P. L. Hordijk, and J. D. van Buul

Reconstitution of the endothelial barrier involves SHP2-mediated dephosphorylation of VE-cadherin-associated β-catenin, leading to reassembly of adherens junctions and thereby closing the gaps between endothelial cells.

Cytoskeleton

BICD2, dynactin, and LIS1 cooperate in regulating dynein recruitment to cellular structures


This study dissects the recruitment of dynein and dynactin to cargo by a conserved motor adaptor BICD2. It is shown that dynein, dynactin, and BICD2 form a triple complex in vitro and in vivo. Investigation of the properties of this complex by direct visualization of dynein in live cells shows that BICD2-induced dynein transport requires LIS1.

Mammalian SEPT9 isoforms direct microtubule-dependent arrangements of septin core heteromers

M. E. Sellin, S. Stenmark, and M. Gullberg

Cell type–specific alternative splicing results in six confirmed mammalian SEPT9 isoforms. SEPT9 expression levels dictate the hexamer-to-octamer ratio of septin core heteromers, and isoform compositions and expression levels together determine higher-order arrangements of septin filaments.

Membrane Trafficking

SLAC, a complex between Sla1 and Las17, regulates actin polymerization during clathrin-mediated endocytosis

D. Feliciano and S. M. Di Pietro

During endocytosis, actin polymerization nucleated by the Arp2/3 complex provides force needed to drive internalization. Las17 is the strongest activator of the Arp2/3 complex in yeast cells. This study shows that Las17 is associated into a stable complex with Sla1, an adaptor that inhibits Las17 activity both in vitro and in vivo.

Nuclear Functions

Human RECQL5 participates in the removal of endogenous DNA damage


Five human RecQ helicases are involved in genome maintenance. RECQL5, one of the important members of this helicase family, is involved in DNA single-strand break repair and base excision DNA repair.
The Hog1 SAPK controls the Rtg1/Rtg3 transcriptional complex activity by multiple regulatory mechanisms
C. Ruiz-Roig, N. Noriega, A. Duch, F. Posas, and E. de Nadal

The retrograde (RTG) pathway transcription factors Rtg1 and Rtg3 are shown to be targets of the Hog1 stress-activated protein kinase (SAPK). Hog1 acts on the RTG complex at multiple levels to mediate gene expression upon stress. The SAPK is required for the nuclear accumulation of the complex, the recruitment of the complex at RTG-responsive promoters, and the regulation of Rtg3 transcriptional activity.

Sub1 associates with Spt5 and influences RNA polymerase II transcription elongation rate
A. García, A. Collin, and O. Calvo

The transcriptional coactivator Sub1 is a functional component of the PIC implicated in several steps of mRNA metabolism. Sub1 directly and specifically influences the transcription elongation rate by an interaction with the elongation factor Spt5. The results provide a novel mechanistic insight into the process of elongation by RNAPII.

The methyltransferase adaptor protein Trm112 is involved in biogenesis of both ribosomal subunits
R. Sardana and A. W. Johnson

This study shows that Trm112 interacts with and is required for the presence of 18S rRNA methyltransferase Bud23. Also shown is the involvement of Trm112 in 60S biogenesis, thus extending the known functions of Trm112 from tRNA and translation factor methylation to roles in biogenesis of both ribosomal subunits.

Signaling
Nucleolar AATF regulates c-Jun–mediated apoptosis
S. E. Ferraris, K. Isoniemi, E. Torvaldson, J. Anckar, J. Westermarck, and J. E. Eriksson

The AP-1 transcription factor c-Jun is essential for stress-induced apoptosis in several models. The apoptosis-antagonizing transcription factor is a novel nucleolar stress sensor, which is required as a cofactor for c-Jun–mediated apoptosis.

CORRECTION
UHRF1 phosphorylation by cyclin A2/cyclin-dependent kinase 2 is required for zebrafish embryo genesis

UHRF1 phosphorylation by cyclin A2/cyclin-dependent kinase 2 is required for zebrafish embryogenesis