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ARTICLES

Cell Biology of Disease
Small-molecule agonists of mammalian Diaphanous–related (mDia) formins reveal an effective glioblastoma anti-invasion strategy
3704–3718
Formin agonists impede the most dangerous aspect of glioblastoma—tumor spread into surrounding healthy tissue. Formin activation impairs a novel aspect of the transformed cell and informs the development of antitumor strategies for a cancer needing a more effective therapy.

Proteasomal degradation of preemptive quality control (pQC) substrates is mediated by an AIRAPL–p97 complex
I. Braunstein, L. Zach, S. Allan, K.-U. Kalies, and A. Stanhill
3719–3727
The preemptive quality control (pQC) pathway participates in the unfolded protein response regulating ER homeostasis, yet many components are not known. The role of p97 and its adaptor, AIRAPL, in proteasomal processing of pQC substrates is shown, and an insulin-processing mutant (R6C) is identified as a pQC substrate.

Meis3 is required for neural crest invasion of the gut during zebrafish enteric nervous system development
R. A. Unbe and M. E. Bronner
3728–3740
Loss of Meis3 leads to defects in enteric neural crest cell migration, number, and proliferation during colonization of the gut. This leads to colonic aganglionosis, in which the hindgut is devoid of neurons, identifying it as a novel candidate factor in the etiology of Hirschsprung’s disease during enteric nervous system development.
**Cell Cycle**

**A Highlights from MBoC Selection**

**Centrin 3 is an inhibitor of centrosomal Mps1 and antagonizes centrin 2 function**


Cetn3 inhibits Mps1 kinase activity in vitro and at centrosomes by blocking activating autophosphorylation and can prevent Mps1 from phosphorylating Cetn2 even when Mps1 is present at 10-fold molar excess. Cetn3 also prevents incorporation of Cetn2 into centrioles, but mimicking phosphorylation of Cetn2 bypasses the inhibitory effects of Cetn3.

**Phosphorylation of the Scc2 cohesin deposition complex subunit regulates chromosome condensation through cohesin integrity**

J. Woodman, M. Hoffman, M. Dzieciatkowska, K. C. Hansen, and P. C. Megee

Cohesin deposition requires the Scc2/Scc4 complex. Scc2 is phosphorylated, and mutations that mimic constitutive phosphorylation lead to inviability and chromosome condensation defects, likely due to reduced Mcd1 levels resulting from compromised cohesin integrity. Thus phosphorylation of Scc2 has important consequences for chromosome integrity.

**Dynamic changes in CCAN organization through CENP-C during cell-cycle progression**


Dynamic changes in CCAN organization during progression of the cell cycle are examined in chicken DT40 cells. CENP-C166-324 is sufficient for interphase centromere localization through association with CENP-L-N, and CENP-C643-864 is essential for mitotic centromere localization through binding to CENP-A nucleosomes.

**Cell Physiology**

**Global analysis of asymmetric RNA enrichment in oocytes reveals low conservation between closely related Xenopus species**

M. Claußen, T. Lingner, C. Pommerenke, L. Opitz, G. Salinas, and T. Pieler

Subcellular localization of mRNAs contributes to the generation of cellular asymmetries and cell fate determination. A comparative global analysis is given of animally and vegetally enriched RNAs in oocytes from two closely related Xenopus species.

**Cytoskeleton**

**MDM1 is a microtubule-binding protein that negatively regulates centriole duplication**

D. Van de Mark, Dong Kong, J. Loncarek, and T. Stearns

MDM1 is a microtubule-binding protein that localizes to centrioles. 3D-SIM microscopy shows MDM1 to be closely associated with the centriole barrel, likely residing in the centriole lumen. MDM1 overexpression and depletion experiments suggest that MDM1 is a negative regulator of centriole duplication.

**Cordon bleu promotes the assembly of brush border microvilli**

N. E. Grega-Larson, S. W. Crawley, A. L. Erwin, and M. J. Tyska

Microvilli are actin-based protrusions that amplify plasma membrane area and mediate interactions with the extracellular environment. We found that the multifunctional actin regulator cordon bleu promotes the growth of intestinal brush border microvilli. These results provide a new framework for investigating brush border biogenesis.

**Membrane Trafficking**

**p38 MAP kinase–dependent phosphorylation of the Gp78 E3 ubiquitin ligase controls ER–mitochondria association and mitochondria motility**

Lei Li, Guang Gao, J. Shankar, B. Joshi, L. J. Foster, and I. R. Nabi

Epitope mapping of the 3F3A mAb identified p38 MAPK phosphorylation of Ser-538 of the E3 ubiquitin ligase Gp78. p38 MAPK phosphorylation of Ser-538 prevents Gp78-dependent mitofusin degradation, mitochondrial fission, and ER–mitochondria association, defining a novel regulatory mechanism of Gp78 activity at the ER–mitochondria interface.
A Pan1/End3/Sla1 complex links Arp2/3-mediated actin assembly to sites of clathrin-mediated endocytosis
Y. Sun, N. T. Leong, T. Wong, and D. G. Drubin

Eps15-related proteins couple the clathrin-mediated endocytic-site initiation and actin assembly phases and coordinate endocytic-site formation with cargo capture and actin assembly through their interaction with a CIN85-related protein.

Nuclear Functions
Ccq1-Tpz1TPP1 interaction facilitates telomerase and SHREC association with telomeres in fission yeast
B. A. Moser, O. N. Raguimova, and T. M. Nakamura

Through characterization of ccq1 mutants that disrupt Ccq1-Tpz1TPP1 interaction, the authors establish that Ccq1-Tpz1TPP1 interaction contributes to optimal binding of the Ccq1-SHREC complex and is required for Ccq1 Thr93 phosphorylation and telomerase recruitment.

Signaling

A Highlights from MBoC Selection
PTP1B-dependent regulation of receptor tyrosine kinase signaling by the actin-binding protein Mena

The actin-binding protein Mena regulates RTK signaling after growth factor stimulation in tumor cells by a novel mechanism. The alternatively spliced MenaINV isoform disrupts this attenuation to drive sensitivity to growth factors, resistance to targeted inhibitors, and ultimately tumor invasion and metastasis.

Sorting nexin 9 differentiates ligand-activated Smad3 from Smad2 for nuclear import and transforming growth factor β signaling
M. C. Wilkes, C. E. Repellin, Jeong-Han Kang, M. Andrianifahanana, Xueqian Yin, and E. B. Leof

Sorting nexin 9 (SNX9) is shown to differentiate Smad3 from Smad2 nuclear delivery by mediating the association of phosphorylated Smad3 with importin 8 and the nuclear membrane. While the absence of SNX9 had negligible effects on transforming growth factor β receptor activity or Smad2 signaling, Smad3-dependent targets and phenotypes were inhibited.