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ARTICLES

Biosynthesis and Biodegradation

VWA domain of S5a restricts the ability to bind ubiquitin and Ubl to the 26S proteasome
R. Piterman, I. Braunstein, E. Isakov, T. Ziv, A. Navon, S. Cohen, and A. Stanhill

The only stoichiometric proteasomal subunit found to reside outside the proteasome is the ubiquitin receptor S5a. S5a-dependent binding of substrates and shuttle factors is restricted to occur only on the proteasome, thus increasing efficiency of substrate degradation by the 26S proteasome.

A discrete pathway for the transfer of intermembrane space proteins across the outer membrane of mitochondria
A. Gornicka, P. Bragoszewski, P. Chrosicki, L.-S. Wenz, C. Schulz, P. Rehling, and A. Chacinska

The TOM translocase serves as a portal for proteins destined to the mitochondrial membranes and matrix. This study determines how proteins targeted to the MIA pathway arrive in the intermembrane space. A different mode of the transport across the outer membrane for intermembrane space proteins with the help of Tom40 is postulated.

Cell Biology of Disease

Formation of α-synuclein Lewy neurite–like aggregates in axons impedes the transport of distinct endosomes

Pathological α-synuclein inclusions in axons impair transport of Rab7 and TrkB receptor-containing endosomes, as well as autophagosomes. Transport of synaptophysin and mitochondria is unaltered. Selective defects in axonal transport may contribute to the etiology of Parkinson’s disease and have important implications for treatment.

Alternative splicing of human NT5E in cirrhosis and hepatocellular carcinoma produces a negative regulator of ecto-5’-nucleotidase (CD73)
N. T. Snider, P. J. Altshuler, S. Wan, T. H. Welling, J. Cavalcoti, and M. B. Omary

Alternative splicing of human NT5E generates CD73S, an endoplasmic reticulum–associated and dimerization-deficient glycoprotein that lacks enzymatic activity. CD73S functions as a negative regulator of canonical CD73 by promoting its proteasomal degradation, which may have significance in chronic liver disease and liver cancer.

Cell Cycle

Chromosomal attachments set length and microtubule number in the Saccharomyces cerevisiae mitotic spindle
N. J. Nannas, E. T. O’Toole, M. Winey, and A. W. Murray

Altering the number of kinetochores revealed that chromosomal attachments set the length of the metaphase spindle and the number of microtubules within it. Reducing the number of kinetochores increases length, whereas adding extra kinetochores shortens it, suggesting that kinetochore-generated inward forces help set spindle length in budding yeast.
A Highlights from MBoC Selection  An astral simulacrum of the central spindle accounts for normal, spindle-less, and anucleate cytokinesis in echinoderm embryos
Kuan-Chung Su, W. M. Bement, M. Petronczki, and G. von Dassow  4049–4062

Live imaging of Ect2 and Cyk4 in echinoderm embryos shows successive recruitment to central spindle, astral microtubules, and the cleavage furrow not only in normal cells, but also between paired asters in toroidal or anucleate cells. This suggests that a common signaling ensemble underlies all functional cytokinetic furrow induction events.

Identification of a mitotic Rac-GEF, Trio, that counteracts MgcRacGAP function during cytokinesis
A. Cannet, S. Schmidt, B. Delaval, and A. Debant  4063–4071

Inactivation of Rac1 by MgcRacGAP at the cleavage plane is essential to ensure cytokinesis. Trio activates Rac1 in dividing cells, and its depletion rescues the cytokinesis failure induced by MgcRacGAP. This work identifies for the first time a GEF-activating Rac1 in dividing cells that counteracts MgcRacGAP function in cytokinesis.

Cell Motility

GSK3 and Polo-like kinase regulate ADAM13 function during cranial neural crest cell migration

ADAM13 controls neural crest cell migration by cleaving cadherin-11 and regulating gene expression via its cytoplasmic domain. GSK3 and Polo-like kinases regulate positively the nuclear activity of ADAM13 to promote cell migration in vivo.

Cell Physiology

Increase in cellular triacylglycerol content and emergence of large ER-associated lipid droplets in the absence of CDP-DG synthase function
Yue He, C. Yam, K. Pomraning, J. S. R. Chin, J. Y. Yew, M. Freitag, and S. Oliferenko  4083–4095

Cds1 is an evolutionarily conserved CDP-DG synthase. Fission yeast are used to demonstrate that cells deficient in its function exhibit markedly increased triacylglycerol content and assemble unusual ER-associated lipid droplets that recruit the triacylglycerol synthesis machinery and grow by expansion.

Spatiotemporal dynamics of triglyceride storage in unilocular adipocytes

Real-time fluorescence microscopy is used to investigate the trafficking of metabolizable fluorescent fatty acid in unilocular adipocytes from adipose tissue of nonhuman primates. The study reveals novel cell biological features that may contribute to the mechanism of adipocyte hypertrophy.

Olfactomedin 2, a novel regulator for transforming growth factor-β-induced smooth muscle differentiation of human embryonic stem cell–derived mesenchymal cells
Ning Shi, Xia Guo, and Shi-You Chen  4106–4114


Cytoskeleton

Endothelial cells use dynamic actin to facilitate lymphocyte transendothelial migration and maintain the monolayer barrier
O. L. Mooren, J. Li, J. Nawas, and J. A. Cooper  4115–4129

Actin assembly downstream of WAVE2 in endothelial cells is necessary to engage transmigrating lymphocytes, promote the transcellular route of migration, and close junctional pores after the lymphocyte moves away. In addition, WAVE2 is necessary for endothelial monolayer integrity.

A Highlights from MBoC Selection  Neuromuscular synapse integrity requires linkage of acetylcholine receptors to postsynaptic intermediate filament networks via rapsyn–plectin 1f complexes

P1f, a specific isoform of the cytolinker protein plectin, bridges AChRs to the desmin IF network of myofibers via direct interaction with the AChR-scaffolding protein rapsyn. P1f-mediated IF linkage is crucial for the formation and maintenance of AChR clusters, postsynaptic organization of the NMJ, and body locomotion.
Genetic suppression of a phosphomimic myosin II identifies system-level factors that promote myosin II cleavage furrow accumulation
Yixin Ren, H. West-Foyle, A. Surcel, C. Miller, and D. N. Robinson 4150–4165
Genetic interaction analysis is used to identify new cytokinesis proteins involved in myosin II cleavage furrow accumulation and to demonstrate how different pathways collaborate to drive myosin II to the cleavage furrow. One of these proteins, RMD1, is required for myosin II cleavage furrow localization and acts in parallel with mechanical stress.

Methods
Superresolution imaging reveals structural features of EB1 in microtubule plus-end tracking
Peng Xia, Xing Liu, Bing Wu, Shuyuan Zhang, Xiaoyu Song, P. Y. Yao, J. Lippincott-Schwartz, and Xuebiao Yao 4166–4173
A method is introduced for optically imaging intracellular protein interactions at nanometer spatial resolution in live cells using photoactivatable complementary fluorescent (PACF) proteins. The PACF approach established here will enable the simultaneous visualization of homo- and heterodimeric interactions at the single live-cell level.

Nuclear Functions
Neural crest specification and migration independently require NSD3-related lysine methyltransferase activity
B. T. Jacques-Fricke and L. S. Gammill 4174–4186
Nuclear receptor–binding, SET-domain containing 3 (NSD3) is the first protein methyltransferase essential for early neural crest development. NSD3 is required for neural crest gene expression but not for H3K36 dimethylation of most neural crest genes. NSD3-related methyltransferase activity independently regulates neural crest migration.

HDAC6–ubiquitin interaction controls the duration of HSF1 activation after heat shock
L. Pernet, V. Faure, B. Gilquin, S. Dufour-Guérin, S. Khochbin, and C. Vourc’h 4187–4194
A full response to heat shock depends on the duration of HSF1 activation, which is controlled by the deacetylase HDAC6, known to bind ubiquitin residues, and by AAA ATPase p97/VCP. This new regulatory process relies on the extent of protein ubiquitination and directs the ability of cells to remain protected against heat-dependent apoptosis.

Signaling
Rap1-dependent pathways coordinate cytokinesis in Dictyostelium
K. Plak, I. Keizer-Gunnink, P. J. M. van Haastert, and A. Kortholt 4195–4204
Dictyostelium Rap1 is dynamically activated during cytokinesis and drives cytokinesis progression by coordinating the three major cytoskeletal components: microtubules, actin, and myosin II. Importantly, mutated forms of Rap also affect cytokinesis in other organisms, suggesting a conserved role for Rap in cell division.