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**ASCB ANNUAL MEETING ABSTRACTS**

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**ARTICLES**

**Cell Biology of Disease**

Activation of serum/glucocorticoid-induced kinase 1 (SGK1) underlies increased glycogen levels, mTOR activation, and autophagy defects in Lafora disease
P. K. Singh, S. Singh, and S. Ganesh 3776–3786

Loss of laforin, a protein phosphatase involved in Lafora disease (LD), results in the activation of serum/glucocorticoid-induced kinase 1 (SGK1), increased cellular glycogen accumulation, and autophagy defects. Inhibition of SGK1 restores normal glycogen content and autophagy defects in a cellular model of LD.

Ubiquitination-dependent quality control of hERG K⁺ channel with acquired and inherited conformational defect at the plasma membrane
P. M. Apaja, B. Foo, T. Okiyoneda, W. C. Valinsky, H. Barriere, R. Atanasiu, E. Ficker, G. L. Lukacs, and A. Shrier 3787–3804

The role of the plasma membrane quality control machinery is demonstrated in the development of the long QT syndrome phenotype, caused by acquired and inherited conformational defects of the hERG potassium channel in multiple expression systems, including cardiac myocytes.

Estrogen regulates histone deacetylases to prevent cardiac hypertrophy

Angiotensin II stimulation of HDAC2 production, phosphorylation by CK2, and resulting modulation of target genes, which promote cardiac hypertrophy, are opposed by estrogen/ERβ. Angiotensin II also represses class II HDAC4 and 5 production and stimulates their phosphorylation, which expels them from the nucleus, and estrogen prevents this.

**Cell Cycle**

Stathmin and microtubules regulate mitotic entry in HeLa cells by controlling activation of both Aurora kinase A and Plk1
V. C. Silva and L. Cassimeris 3819–3831

Stathmin depletion, acting partially via microtubules, delays cells during G2 of the cell cycle through reduced activation of both Aurora kinase A and Polo-like kinase 1.

Specific deletion of Cdc42 does not affect meiotic spindle organization/migration and homologous chromosome segregation but disrupts polarity establishment and cytokinesis in mouse oocytes
Zhen-Bo Wang, Zong-Zhe Jiang, Qing-Hua Zhang, Meng-Wen Hu, Lin Huang, Xiang-Hong Ou, Lei Guo, Ying-Chun Ouyang, Yi Hou, C. Brakebusch, H. Schatten, and Qing-Yuan Sun 3832–3841

Oocyte-specific deletion of Cdc42 has little effect on meiotic spindle organization and migration to the cortex but inhibits polar body emission, although homologous chromosome segregation occurs. The failure of cytokinesis is due to loss of polarized Arp2/3 accumulation and actin cap formation, and thus the defective contract ring.
Regulation of mitosis by the NIMA kinase involves TINA and its newly discovered partner, An-WDR8, at spindle pole bodies
Kuo-Fang Shen and S. A. Osmani

Mitosis requires events triggered at spindle pole bodies, including seeding and anchoring of spindle microtubules. Analysis of the NIMA kinase and the mitotic SPB protein TINA extends our understanding of mitotic-specific protein targeting to SPBs and indicates that microtubule anchoring at SPBs involves TINA and its newly identified partner, An-WDR8.

Cell Motility

The Rac-GAP Bcr is a novel regulator of the Par complex that controls cell polarity
A. S. Narayanan, S. B. Reyes, K. Um, J. H. McCarty, and K. F. Tolias

The Par complex (Par3, Par6, and PKCζ) controls cell polarity, which is essential for many biological processes. Here we identify the Rac1 GTPase-activating protein Bcr as an integral member of the Par complex that regulates polarized cell migration by locally restricting both Rac1 and PKCζ function.

Cytoskeleton

Emerin organizes actin flow for nuclear movement and centrosome orientation in migrating fibroblasts
Wakam Chang, E. S. Folker, H. J. Worman, and G. G. Gundersen

Emerin, a nuclear membrane protein, and myosin IIB contribute to nuclear movement by regulating the directionality of nuclear movement and dorsal actin cable flow. Emerin interacts with myosin IIB and is required for its perinuclear localization. The results show that the nuclear envelope actively organizes cytoplasmic polarity.

Membrane Trafficking

Src-mediated caveolin-1 phosphorylation affects the targeting of active Src to specific membrane sites

Biophysical and biochemical studies show that caveolin-1 phosphorylation by Src at Tyr-14, followed by binding of the SH2 domain of activated Src to phospho–Tyr-14, enhances Src–plasma membrane interaction. This targets activated Src preferentially to focal adhesions, providing a mechanism that potentially regulates focal adhesion function.

ER-associated SNAREs and Sey1p mediate nuclear fusion at two distinct steps during yeast mating
J. V. Rogers, T. Arlow, E. R. Inkellis, T. S. Koo, and M. D. Rose

Both SNAREs and Sey1p are required for efficient nuclear fusion during yeast mating. SNAREs appear to act at the step of nuclear envelope fusion, whereas Sey1p remodels the ER network to permit nuclear congression. In addition, SNARE sey1Δ double mutants reveal an Sey1p-independent, SNARE-mediated ER fusion pathway.

Nuclear Functions

The spatial segregation of pericentric cohesin and condensin in the mitotic spindle

The mitotic chromatin spring is organized into a rosette of intramolecular loops of pericentric chromatin by condensin and cohesin. Model convolution reveals that condensin clusters along the spindle axis, while cohesin is dispersed radially along pericentromere loops.

The nuclear basket proteins Mlp1p and Mlp2p are part of a dynamic interactome including Esc1p and the proteasome

Mlp1p and Mlp2p form the basket of the yeast nuclear pore complex (NPC) and contribute to NPC positioning, nuclear stability, and nuclear envelope morphology. The Mlpps also embed the NPC within an extended interactome, which includes protein complexes involved in mRNP biogenesis, silencing, spindle organization, and protein degradation.
Signaling

CCN2 modulates hair follicle cycling in mice
Shangxi Liu and A. Leask 3939–3944

Mesenchymal cells play a role in controlling the number of hair follicles. However, the precise molecules involved are unclear. Absence in mesenchymal cells of the expression of the secreted matricellular protein CTGF/CCN2 results in an increased number of hair follicles, concomitant with increased β-catenin activity.

Theory

Bidirectional coupling between integrin-mediated signaling and actomyosin mechanics explains matrix-dependent intermittency of leading-edge motility
E. S. Welf, H. E. Johnson, and J. M. Haugh 3945–3955

A physicochemical model is used to describe the coupling of adhesion, cytoskeletal, and signaling dynamics during cell migration. Analysis of stochastic simulations predicts relationships between measurable quantities that reflect partitioning of stress between F-actin–bound adhesions, which act as a molecular clutch, and retrograde F-actin flow.

CORRECTION

The nucleolus stress response is coupled to an ATR-Chk1–mediated G2 arrest
H. Ma and T. Pederson 3956