September 5, 2008: 134 (5)

"Coronin Remodels Actin Branches"
[Cover Caption]

Browse Archive

Immediate Early Publication

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In This Issue p695,697
[Full Text] [PDF] [Comments]

Immunology Select p699,701
[Summary] [Full Text] [PDF] [Comments]

Essay

Cancer Cell Metabolism: Warburg and Beyond p703
Peggy P. Hsu and David M. Sabatini
[Summary] [Full Text] [PDF] [Comments]

An Invitation to the Marriage of Metagenomics and Metabolomics p708
Peter J. Turnbaugh and Jeffrey I. Gordon
[Summary] [Full Text] [PDF] [Comments]

Forum

Metabolic Phenotyping in Health and Disease p714
Elaine Holmes, Ian D. Wilson, and Jeremy K. Nicholson
[Summary] [Full Text] [PDF] [Comments]

Previews

A Protein Scaffold Plays Matchmaker for Chordin p718
Richard M. Harland
[Summary] [Full Text] [PDF] [Comments]

Caspase Cleavage Is Not for Everyone p720
Carrie E. Johnson and Sally Kornbluth
[Summary] [Full Text] [PDF] [Comments]

Highways for mRNA Transport p722
Robert H. Singer
[Summary] [Full Text] [PDF] [Comments]

Unresolved ER Stress Inflames the Intestine p724
Averil Ma
[Summary] [Full Text] [PDF] [Comments]

Brown Fat and Skeletal Muscle: Unlikely Cousins? p726
Stephen R. Farmer
[Summary] [Full Text] [PDF] [Comments]

Review

The Meter of Metabolism p728
Carla B. Green, Joseph S. Takahashi, and Joseph Bass
[Summary] [Full Text] [PDF] [Comments]

SnapShot

SnapShot: Nucleic Acid Helicases and Translocases p888

Research Articles

XBP1 Links ER Stress to Intestinal Inflammation and Confers Genetic Risk for Human Inflammatory Bowel Disease p743
Arthur Kaser, Ann-Hwee Lee, Andre Franke, Jonathan N. Glickman, Sebastian Zeissig, Herbert Tilg, Edward E.S. Nieuwenhuis, Darren E. Higgins, Stefan Schreiber, Laurie H. Glimcher, and Richard S. Blumberg
[Summary] [Full Text] [PDF] [Supplemental Data][Comments]

Crossing the Species Barrier by PrP^{Sc} Replication In Vitro Generates Unique Infectious Prions p757
Joaquín Castilla, Dennisse Gonzalez-Romero, Paula Saá, Rodrigo Morales, Jorge De Castro, and Claudio Soto
[Summary] [Full Text] [PDF] [Supplemental Data][Comments]

Chemical and Biological Approaches Synergize to Ameliorate Protein-Folding Diseases p769
Ting-Wei Mu, Derrick Sek Tong Ong, Ya-Juan Wang, William E. Balch, John R. Yates, Laura Segatori, and Jeffery W. Kelly
[Summary] [Full Text] [PDF] [Supplemental Data][Comments]

HIV Envelope-CXCR4 Signaling Activates Cofilin to Overcome Cortical Actin Restriction in Resting CD4 T Cells p782
Alyson Yoder, Dongyang Yu, Li Dong, Subashini R. Iyer, Xuehua Xu, Jeremy Kelly, Juan Liu, Weifeng Wang, Paul J. Vorster, Liane Agulto, David A. Stephany, James N. Cooper, Jon W. Marsh, and Yuntao Wu
[Summary] [Full Text] [PDF] [Supplemental Data][Comments]

Structural Coupling of SH2-Kinase Domains Links Fes and Abl Substrate Recognition and Kinase Activation p793
Panagis Filippakopoulos, Michael Kofler, Oliver Hantschel, Gerald D. Gish, Florian Grebien, Eidarus Salah, Philipp Neudecker, Lewis E. Kay, Benjamin E. Turk, Giulio Superti-Furga, Tony Pawson, and Stefan Knapp
[Summary] [Full Text] [PDF] [Supplemental Data][Comments]

UBXD7 Binds Multiple Ubiquitin Ligases and Implicates p97 in HIF1α Turnover p804
Gabriela Alexandru, Johannes Graumann, Geoffrey T. Smith, Natalie J. Kolawa, Ruihua Fang, and Raymond J. Deshaies
[Summary] [Full Text] [PDF] [Supplemental Data][Comments]

Molecular Basis for the Sorting of the SNARE VAMP7 into Endocytic Clathrin-Coated Vesicles by the ArfGAP Hrb p817
Paul R. Pryor, Lauren Jackson, Sally R. Gray, Melissa A. Edeling, Amanda Thompson, Christopher M. Sanderson, Philip R. Evans, David J. Owen, and J. Paul Luzio
[Summary] [Full Text] [PDF] [Supplemental Data][Comments]

Coronin 1B Antagonizes Cortactin and Remodels Arp2/3-Containing Actin Branches in Lamellipodia p828
Liang Cai, Alexander M. Makhov, Dorothy A. Schafer, and James E. Bear
[Summary] [Full Text] [PDF] [Supplemental Data][Comments]

In Vivo Imaging of *oskar* mRNA Transport Reveals the Mechanism of Posterior Localization p843
Vitaly L. Zimyanin, Katsiaryna Belaya, Jacques Pecreaux, Michael J. Gilchrist, Alejandra Clark, Ilan Davis, and Daniel St

Featured Article

XBP1 Links ER Stress to Intestinal Inflammation and Confers Genetic Risk for Human Inflammatory Bowel Disease p743
Arthur Kaser, Ann-Hwee Lee, Andre Franke, Jonathan N. Glickman, Sebastian Zeissig, Herbert Tilg, Edward E.S. Nieuwenhuis, Darren E. Higgins, Stefan Schreiber, Laurie H. Glimcher, and Richard S. Blumberg
[Summary] [Full Text] [PDF] [Supplemental Data][Comments]

Inflammatory bowel disease (IBD) has been attributed to aberrant mucosal immunity to the intestinal microbiota. The transcription factor XBP1, a key component of the endoplasmic reticulum (ER) stress response, is required for development and maintenance of secretory cells and linked to JNK activation. We hypothesized that a stressful environmental milieu in a rapidly proliferating tissue might instigate a proinflammatory response. We report that Xbp1 deletion in intestinal epithelial cells (IECs) results in spontaneous enteritis and increased susceptibility to induced colitis secondary to both Paneth cell dysfunction and an epithelium that is overly reactive to inducers of IBD such as bacterial products (flagellin) and TNFα. An association of XBP1 variants with both forms of human IBD (Crohn's disease and ulcerative colitis) was identified and replicated (rs35873774; p value 1.6 × 10−5) with novel, private hypomorphic variants identified as susceptibility factors. Hence, intestinal inflammation can originate solely from XBP1 abnormalities in IECs, thus linking cell-specific ER stress to the induction of organ-specific inflammation.

Cover Caption

On the cover: Coronins are highly conserved actin-binding proteins that localize to the leading edge of motile cells. In this issue, Cai et al. (pp. 828–842) describe the mechanism of Coronin 1B function. This protein can target actin filament branches generated by the Arp2/3 complex, replace this complex, and produce a remodeled branch with altered geometry. This activity is antagonized by Cortactin, an actin-binding adaptor protein that protects the branches from disassembly. The illustration is an artistically rendered version of a dual-color kymograph used to demonstrate the temporal sequence of branch remodeling in the lamellipodia.