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PERSPECTIVE

Science communication: a career where PhDs can make a difference
R. Irion

ARTICLES

Biosynthesis and Biodegradation

Identification of protein disulfide isomerase 1 as a key isomerase for disulfide bond formation in apolipoprotein B100
Shiyu Wang, S. Park, V. K. Kodali, J. Han, T. Yip, Zhouji Chen, N. O. Davidson, and R. J. Kaufman

Pdi1 knockdown decreases apoB100 synthesis, reduces MTP activity and apoB100 lipidation, and impairs the oxidative folding of apoB100, which causes defective VLDL secretion. PDI1 promotes formation of disulfide bonds in apoB100 and serves as its disulfide isomerase.

Cell Cycle

Nup2 requires a highly divergent partner, NupA, to fulfill functions at nuclear pore complexes and the mitotic chromatin region
S. Markossian, S. Suresh, A. H. Osmani, and S. A. Osmani

Among nuclear pore proteins, Nup2 is unique because it transfers to the mitotic chromatin region to fulfill unknown functions. Analysis of Nup2 and a novel targeting partner, NupA, shows that they are required for normal anaphase and nucleokinesis. Their functions also involve an import pathway for Mad1 but apparently not general nuclear protein import.

Cell Motility

Arrestins regulate cell spreading and motility via focal adhesion dynamics
W. M. Cleghorn, K. M. Branch, S. Kook, C. Arnette, N. Bulus, R. Zent, I. Kaverina, E. V. Gurevich, A. M. Weaver, and V. V. Gurevich

Cells lacking both nonvisual arrestins show excessive spreading, defects in focal adhesion disassembly, and sensitivity to microtubules. This phenotype is rescued by wild-type arrestins but not mutants deficient in clathrin binding, suggesting that arrestins regulate focal adhesion disassembly by linking microtubules and clathrin.

Cell Physiology

Asef controls vascular endothelial permeability and barrier recovery in the lung
Xinyong Tian, Yufeng Tian, G. Gawlak, Fanyong Meng, Y. Kawasaki, T. Akiyama, and A. A. Birukova

This is the first report of Asef involvement in the regulation of endothelial vascular permeability in vitro and in vivo. Asef activation in endothelial cells by hepatocyte growth factor suppressed the Rho-dependent pathway of agonist-induced endothelial permeability and promoted Rac1-dependent endothelial barrier recovery.

c-di-GMP induction of Dictyostelium cell death requires the polyketide DIF-1
Yu Song, M.-F. Luciani, C. Giusti, and P. Golstein

Two inducers, DIF-1 and c-di-GMP, each separately shown to play a major role in Dictyostelium cell death induction in vitro, in fact cooperate. A similar cooperation with polyketides might occur for c-di-GMP effects in other situations and organisms, in particular in innate immunity and cell death in animal cells.
ADAM10 controls collagen signaling and cell migration on collagen by shedding the ectodomain of discoidin domain receptor 1 (DDR1)
Collagen receptor DDR1 is shed upon collagen binding by ADAM10 metalloproteinase. This shedding controls the half-life of DDR1 signaling and cell migration on the collagen matrix. This event may be a part of a regulatory mechanism of microenvironment signaling.

A Highlights from MBoC Selection

Genetic mosaic analysis of a deleterious mitochondrial DNA mutation in Drosophila reveals novel aspects of mitochondrial regulation and function
Zhe Chen, Yun Qi, S. French, Guofeng Zhang, R. C. Garcia, R. Balaban, and Hong Xu 674–684
A lethal mtDNA mutation affecting COX is fully rescued by AOX. The mutant genome level remains constant in the somatic tissues along the aging process in heteroplasmic flies. A genetic scheme creates tissue-specific homoplasy in otherwise heteroplasmic background and reveals that Ca²⁺ mishandling contributes to the neurodegeneration.

Cytoskeleton

Cytoskeletal forces during signaling activation in Jurkat T-cells
King Lam Hui, L. Balagopalan, L. E. Samelson, and A. Upadhyaya 685–695
Cytoskeletal forces are implicated in T-cell–receptor activation, but their determinants are not known. Traction force microscopy was used to measure forces generated during T-cell activation. Whereas actin dynamics were essential for force generation, myosin contractility played a limited role. T-cells were also found to be mechanosensitive.

FAP206 is a microtubule-docking adapter for ciliary radial spoke 2 and dynein c
Radial spokes are conserved macromolecular complexes that are essential for ciliary motility. Little is known about the assembly and functions of the three individual radial spokes, RS1, RS2, and RS3. In Tetrahymena, a conserved ciliary protein, FAP206, docks RS2 and dynein c to the doublet microtubule.

Stepping stone: a cytohesin adaptor for membrane cytoskeleton restraint in the syncytial Drosophila embryo
Jiangshu Liu, D. M. Lee, Cao Guo Yu, S. Angers, and T. J. C. Harris 711–725
A major cytohesin Arf-GEF binding partner is identified in Drosophila. Named Stepping stone (Sstn), it seems to be a divergent homologue of FRMD4A, a mammalian cytohesin adaptor. In vitro and in vivo work argues that Sstn is an adaptor for the Drosophila cytohesin Steppke and that Sstn aids Steppke for cytoskeleton restraint in the early embryo.

Membrane Trafficking

Seipin performs dissectible functions in promoting lipid droplet biogenesis and regulating droplet morphology
B. R. Cartwright, D. D. Binns, C. L. Hilton, Sungwon Han, Qiang Gao, and J. M. Goodman 726–739
Loss-of-function mutations in seipin cause severe lipodystrophy, yet seipin’s function in incompletely understood. Seipin is shown here to be important specifically for initiation of droplet formation, and a deletion mutant allows dissection of this function from maintenance of droplet morphology and vectorial droplet budding.

Clathrin-dependent entry and vesicle-mediated exocytosis define insulin transcytosis across microvascular endothelial cells
P. M. Azizi, R. E. Zyla, Sha Guan, Changsen Wang, Jun Liu, S.-S. Bolz, B. Heit, A. Klip, and W. L. Lee 740–750
How insulin traverses the continuous endothelium of the microvasculature has been poorly studied. Development of a novel assay to measure insulin transcytosis reveals an unexpected role for clathrin in insulin transendothelial transport. Insulin transcytosis is dynamin and clathrin dependent but does not require cholesterol or caveolin-1.

PAR3 and aPKC regulate Golgi organization through CLASP2 phosphorylation to generate cell polarity
A PAR complex (PAR3, PAR6, and aPKC) plays a central role in the establishment of cell polarity. Another polarity protein, CLASP2, binds directly with PAR3 and is phosphorylated by aPKC. Through CLASP2 phosphorylation, aPKC and PAR3 regulate the localization of CLASP2 to the trans-Golgi network, thereby controlling the Golgi organization.
Methods

Fast protein-depletion system utilizing tetracycline repressible promoter and N-end rule in yeast
S. V. Gnanasundram and M. Koš 762–768

An improvement to the yeast protein-depletion systems using a promoter shutoff is presented. The described combination of tetracycline promoter with N-terminal ubiquitin fusion allows very fast depletion of the target protein in less than an hour. The depleted protein does not require fusion of any large degradation tag.

Signaling

Calcineurin regulates the yeast synaptojanin Inp53/Sjl3 during membrane stress
E. L. Guiney, A. R. Goldman, J. E. Elias, and M. S. Cyert 769–785

Hyperosmotic shock drives a reorganization of calcineurin and Inp53/synaptojanin. Calcineurin accumulates at sites of polarized growth, dephosphorylates Inp53 to maintain normal membrane and actin cytoskeleton morphology, and causes it to dissociate from clathrin and bind to endocytic proteins Bsp1, Bzz1, and Sla1.

Emergence and subsequent functional specialization of kindlins during evolution of cell adhesiveness

Kindlins are essential for integrin-mediated cell adhesion. This study focuses on the evolutionary origin and subsequent functional specialization of kindlins and their role in evolutionary adaptation of cell adhesiveness in multicellular organisms.

Systems Biology

The volumes and transcript counts of single cells reveal concentration homeostasis and capture biological noise
H. Kempe, A. Schwabe, F. Crémazy, P. J. Verschure, and F. J. Bruggeman 797–804

We present data on cell-to-cell variability (“noise”) of gene expression in human cells, obtained through a combination of single-molecule mRNA FISH and single-cell volume measurements. We find that noise in terms of mRNA numbers exceeds the noise in terms of mRNA concentration. This study provides an improved method to determine gene expression noise.

A Highlights from MBoC Selection

The Dictyostelium prestalk inducer differentiation-inducing factor-1 (DIF-1) triggers unexpectedly complex global phosphorylation changes
C. Sugden, M. D. Urbaniak, T. Araki, and J. G. Williams 805–820

DIF-1, a polyketide, has been primarily characterized as a transcriptional regulator, but proteome-wide identification of peptides that change phosphorylation level in DIF-treated cell reveals many novel targets. Thus a small-molecule regulator of gene transcription plays additional roles as a multifunctional regulator of protein modification.