# Contents

## EDITORIAL

Want 20,000 eyes focused on your next publication?

D. G. Drubin 3263

## ASCB AWARD ESSAYS

A chemist building paths to cell biology

D. B. Weibel 3264–3266

Teaming up: from motors to people

S. L. Reck-Peterson 3267–3269

A sustained passion for intracellular trafficking

E. A. Miller 3270–3272

Scientific approaches to science policy

J. M. Berg 3273–3274

E. E. Just Award Lecture

J. V. Garcia 3275–3277

A question of taste

T. J. Mitchison 3278–3280

An enduring enthusiasm for academic science, but with concerns

J. R. Pringle 3281–3284

## PERSPECTIVES

Life as a professor at a small liberal arts college

J. Sandquist, L. Romberg, and P. Yancey 3285–3291

Creating opportunities for science PhDs to pursue careers in high school education

K. M. H. Doyle and R. D. Vale 3292–3296

From bench to museum—an unlikely journey

K. Yu 3297–3299

## ARTICLES

### Biosynthesis and Biodegradation

Sterol-induced dislocation of 3-hydroxy-3-methylglutaryl coenzyme A reductase from membranes of permeabilized cells

R. Elsabrouty, Youngah Jo, T. T. Dinh, and R. A. DeBose-Boyd 3300–3308

This study establishes permeabilized cells as a viable system in which to elucidate mechanisms for Insig-mediated, sterol-induced ubiquitination and subsequent dislocation of HMG CoA reductase from endoplasmic reticulum membranes into the cytosol for degradation by 26S proteasomes.

### Cell Biology of Disease

Adenovirus RIDx uncovers a novel pathway requiring ORP1L for lipid droplet formation independent of NPC1

N. L. Cianciola, D. J. Greene, R. E. Morton, and C. R. Carlin 3309–3325

Expression of the adenovirus protein RIDx rescues the cholesterol storage phenotype in NPC1-deficient cells by inducing formation of lipid droplets. The function of RIDx is independent of NPC1 but dependent on NPC2 and the oxysterol-binding protein ORP1L. This study provides the first evidence that ORP1L plays a role in sterol transport and LD formation.
Differential topical susceptibility to TGFβ in intact and injured regions of the epithelium: key role in myofibroblast transition

P. Speight, H. Nakano, T. J. Kelley, B. Hinz, and A. Kapus

Intact and cell contact–deprived regions of an epithelial monolayer are differentially sensitive to the transforming effect of TGFβ. This topical susceptibility is mediated by the interplay between TGFβ- and cell contact–dependent transcription factors and might play a key role in the cell biology of wound healing and fibrosis.

Cell Cycle

Mzt1/Tam4, a fission yeast MOZART1 homologue, is an essential component of the γ-tubulin complex and directly interacts with GCP3Alp6


Fission yeast MOZART1 homologue Mzt1 associates with γ-tubulin and is found at MTOCs. It plays an essential role in microtubule regulation, as well as in septum formation and cytokinesis. Recombinant Mzt1 interacts directly with GCP3Alp6. This interaction may assist MTOC activity of the γ-tubulin complex.

The DNA damage and the DNA replication checkpoints converge at the MBF transcription factor


DNA damage and DNA replication checkpoints regulate differently the G1-to-S phase transcriptional program, resulting in the repression or induction, respectively, of the same set of genes. When this signaling is disrupted, cells are unable to cope with DNA-damaging agents, leading to increased cell lethality.

Cell Interactions

CD47 plays a critical role in T-cell recruitment by regulation of LFA-1 and VLA-4 integrin adhesive functions


CD47 plays an important but incompletely understood role in innate and adaptive immune responses. CD47 associates in cis with T-cell LFA-1 integrins and regulates expression of high-affinity conformations of both LFA-1 and VLA-4.

Cell Motility

Mammalian target of rapamycin and Rictor control neutrophil chemotaxis by regulating Rac/Cdc42 activity and the actin cytoskeleton

Yuan He, Dong Li, S. L. Cook, Mee-Sup Yoon, A. Kapoor, C. V. Rao, P. J. A. Kenis, Jie Chen, and Fei Wang

Rictor, a component of mammalian target of rapamycin complex 2 (mTORC2), controls neutrophil chemotaxis by regulating the dynamics of the actin cytoskeleton via Rac and Cdc42. This function of Rictor is independent of mTORC2 and the kinase activity of mTOR.

Cell Physiology

The tails of apical scaffolding proteins EBP50 and E3KARP regulate their localization and dynamics

D. Garbett, C. Sauvanet, R. Viswanatha, and A. Bretscher

ERM-binding protein of 50 kDa (EBP50) and NHE3 kinase A regulatory protein (E3KARP) are closely related but show dramatically different dynamics in microvilli. The high dynamics of EBP50 is determined by a region in its tail and is inhibited by its PDZ domains, but is activated upon PDZ ligand binding. Proteomic analysis of the effects of EBP50 dynamics identifies a novel PDZ binding partner, IRSp53.

Cytoskeleton

srGAP1 regulates lamellipodial dynamics and cell migratory behavior by modulating Rac1 activity

D. Yamazaki, T. Itoh, H. Miki, and T. Takenawa

srGAP1 limits Rac1 activity at lamellipodia in a negative feedback manner, allowing concomitant activation of Rac1 and Rhoa at lamellipodia. Rho signaling causes membrane ruffling through actomyosin contractility and removes the protrusive structures. Such coordination of Rac and Rho determines migratory behavior through lamellipodial dynamics.
Membrane Trafficking

Sec16 influences transitional ER sites by regulating rather than organizing COPII
N. Bharucha, Yang Liu, E. Papanikou, C. McMahon, M. Esaki, P. D. Jeffrey, F. M. Hughson, and B. S. Glick

It has been proposed that during the budding of COPII vesicles from transitional ER (tER) sites, Sec16 plays two distinct roles: negatively regulating COPII turnover and organizing COPII assembly. New data suggest that Sec16 does not in fact organize COPII and that regulation of COPII turnover can explain the influence of Sec16 on tER sites.

A Highlights from MBoC Selection

Identification and characterization of multiple novel Rab–myosin Va interactions
A. J. Lindsay, F. Jollivet, C. P. Horgan, A. R. Khan, G. Raposo, M. W. McCaffrey, and B. Goud

A systematic screen of the entire human Rab GTPase family for interactions with myosin Va identified 10 novel Rab partners for myosin Va, all of which belong to the endocytic recycling and post-Golgi secretory membrane network. However, Rab10 and Rab11 appear to be the major determinants of its recruitment to intracellular membranes.

Signaling

Endosomal acidification by Na+/H+ exchanger NHE5 regulates TrkA cell-surface targeting and NGF-induced PI3K signaling
G. H. Diering, Y. Numata, S. Fan, J. Church, and M. Numata

The role of endosomal pH in neurite formation, one of the principal processes of neuronal differentiation, is unknown. This study shows that the neuron-enriched Na+/H+ exchanger NHE5 potently acidifies recycling endosomes and regulates TrkA trafficking, NGF-TrkA signaling, and neurite outgrowth.

Targeted inactivation of β1 integrin induces β3 integrin switching, which drives breast cancer metastasis by TGF-β

Chemotherapeutic targeting of β1 integrin has been proposed as a way to alleviate breast cancer metastasis. It is shown here that inactivation of β1 integrin elicits compensatory expression of β3 integrin, which rescues mammary tumor growth and metastasis, as well as promoting oncogenic TGF-β signaling in late-stage breast cancer.

A Highlights from MBoC Selection

Drosophila Ric-8 interacts with the Gα12/13 subunit, Concertina, during activation of the Folded gastrulation pathway
K. A. Peters and S. L. Rogers

A novel tissue culture model for studying cellular constriction is introduced and used to show that activation of the Fog signaling pathway depends on Ric-8 and that Ric-8 preferentially binds and localizes inactive Cta. Conserved residues are identified within Ric-8 that are important for the binding and function of Cta.

Integrins on eggs: focal adhesion kinase is activated at fertilization, forms a complex with integrins, and is necessary for cortex formation and cell cycle initiation
D. Chan, C. J. Thomas, V. J. Taylor, and R. D. Burke

FAK is phosphorylated at fertilization and recruited to the cortex as integrins are expressed and the cortex develops. The integrin–FAK complex functions in the formation of actin arrays in the egg cortex and provides signaling inputs for cell cycle initiation.