Contents

PERSPECTIVE

A view from the NIH bridge: perspectives of a program officer
M. Zatz 2661–2663

ARTICLES

Cell Biology of Disease

Interaction of the human prostacyclin receptor with the PDZ adapter protein PDZK1: role in endothelial cell migration and angiogenesis
Prostacyclin is widely implicated in re-endothelialization and angiogenesis but through unknown mechanisms. Herein the HDL scavenger receptor class B, type 1 adapter PDZK1 was identified as a direct, functional interactor of the human prostacyclin receptor and was found to influence prostacyclin-mediated endothelial migration and in vitro angiogenesis.

Cell Cycle

Overlapping kinetochore targets of CK2 and Aurora B kinases in mitotic regulation
CK2 associates with kinetochore protein Mif2/CENP-C. Loss of CK2 results in defects in chromosome segregation, short mitotic spindle, and activation of the spindle assembly checkpoint. CK2 phosphorylates Mif2 and Ndc10. CK2 phosphorylation plays antagonistic and synergistic roles with Aurora B phosphorylation of Mif2 and Ndc10, respectively.

Cytoskeleton

Functional interaction between dynein light chain and intermediate chain is required for mitotic spindle positioning
M. D. Stuchell-Brereton, A. Siglin, J. Li, J. K. Moore, S. Ahmed, J. C. Williams, and J. A. Cooper 2690–2701
The role dynein light chain subunits play in cytoplasmic dynein function remains an open question. We demonstrate that incorporation of Dyn2, the LC8 homologue in Saccharomyces cerevisiae, into the dynein complex is important for overall function and recruitment of dynactin to cytoplasmic microtubule plus-ends.

Membrane Trafficking

The yeast kinase Yck2 has a tripartite palmitoylation signal
A. F. Roth, I. Papanayotou, and N. G. Davis 2702–2715
Yck2, like many palmitoylation substrate proteins, lacks hydrophobicity for targeting to membranes and thus to its Golgi-localized palmitoyl-transferase. Perhaps accommodating this targeting need, the Yck2 palmitoylation signal is found to be large and complex, consisting of domains local to, and distant from, the modification site cysteines.
A laminopathic mutation disrupting lamin filament assembly causes disease-like phenotypes in *Caenorhabditis elegans*

E. M. Bank, K. Ben-Harush, N. Wiesel-Motiuk, R. Barkan, N. Feinsteina, O. Lotan, O. Medalia, and Y. Gruenbaum

Mutations in human LMNA cause Emery-Dreifuss muscular dystrophy; however, a mechanistic link between the effect of mutations on lamin filament assembly and disease phenotype has not been established. Here we show that changes in lamin filament structure translate into disease phenotypes in *Caenorhabditis elegans* by altering the character of the nuclear lamina.

Nab2 functions in the metabolism of RNA driven by polymerases II and III

C. González-Aguilera, C. Tous, R. Babiano, J. de la Cruz, R. Luna, and A. Aguilera

The hnRNP Nab2 is associated with actively transcribed RNAPII and RNAPIII genes. Nab2 has a function in RNAPII transcription and participates in rRNA metabolism and ribosomal subunit export, and, as a consequence, nab2 mutations confer translation defects. Results support Nab2 as a key regulator of gene expression.

Histone H2B ubiquitylation and H3 lysine 4 methylation prevent ectopic silencing of euchromatic loci important for the cellular response to heat


Evidence is presented that the linked histone modifications H2B ubiquitylation and H3 methylation play an important role in preventing the ectopic association of silencing proteins with telomere-distant euchromatic genes important for the cellular response to heat.

Signaling

A phosphodegron controls nutrient-induced proteasomal activation of the signaling protease Ssy5

D. J. Omnus, T. Pfirrmann, C. Andréasson, and P. O. Ljungdahl

The Ssy1-Ptr3-Ssy5 (SPS) sensor of extracellular amino acids coordinates the sequential activity of general signaling factors and the 26S proteasome in a novel proteolytic activation cascade to activate the intracellular signaling protease Ssy5, which endoproteolytically activates two latent transcription factors.

VEGF binding to NRP1 is essential for VEGF stimulation of endothelial cell migration, complex formation between NRP1 and VEGFR2, and signaling via FAK Tyr407 phosphorylation

B. Herzog, C. Pellet-Many, G. Britton, B. Hartzoulakis, and I. C. Zachary

We show for the first time, to our knowledge, that binding of vascular endothelial growth factor (VEGF) to the neuropilin-1 b1 domain is essential for VEGF complex formation with VEGFR2/KDR (kinase insert domain-containing receptor) and is important for endothelial cell migration and tubulogenesis.

c-Met recruits ICAM-1 as a coreceptor to compensate for the loss of CD44 in *Cd44* null mice

V. Olaku, A. Matzke, C. Mitchell, S. Hasenauer, A. Sakkaravarthi, G. Pace, H. Ponta, and V. Orian-Rousseau

CD44v6 acts as a coreceptor for the receptor tyrosine kinases c-Met and VEGFR-2. It is shown that ICAM-1 can act as a new coreceptor in CD44v6-negative tumor cells. Furthermore, ICAM-1 can substitute for CD44v6 as a coreceptor for c-Met in primary hepatocytes and in liver regeneration in Cd44 null mice.

Systems Biology

Dynamic profiling of mRNA turnover reveals gene-specific and system-wide regulation of mRNA decay

S. E. Munchel, R. K. Shultzaberger, N. Takizawa, and K. Weis

A pulse-chase approach is outlined for measuring mRNA turnover rates under changing growth conditions.