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Articles of Significant Interest Selected from This Issue by the Editors

Distinct Roles for α-Arrestins in Desensitization and Clearance of G-Protein-Coupled Receptors

Alvaro et al. (p. 2660–2681) show that three members of the α-arrestin family of endocytic adaptors contribute in distinct ways to constitutive and agonist-induced downregulation of the α-factor pheromone receptor Ste2 in the yeast *Saccharomyces cerevisiae.* The actions of these α-arrestins are also regulated differentially. Since this yeast lacks homologs of mammalian β-arrestins, this analysis suggests that α-arrestins (at least eight identified members in animal cells) are likely to be the proteins primarily responsible for GPCR downregulation and internalization in all eukaryotes.

The WASP-Interacting Protein WIP Is a Transcriptional Regulator

A dynamic actin cytoskeleton is essential for many cell functions. The N-WASP/WASP binding protein WIP stabilizes F-actin. Ramesh et al. (p. 2600–2610) demonstrate that $Wip^{-/-}$ cells exhibit defective focal adhesions (FA), stress fiber assembly, and substrate adherence. These phenotypes were restored by transduction of wild-type WIP. Protein and mRNA levels of several FA constituents regulated by the myocardin-related transcription factor (MRTF)–serum response factor (SRF) transcription factor complex were reduced, while G-actin, which sequesters MRTF in the cytoplasm, was increased in $Wip^{-/-}$ fibroblasts. By regulating G-actin↔F-actin equilibrium, WIP modulates the nuclear translocation of MRTF and the activity of the MRTF-SRF complex and thereby regulates FA and stress fiber assembly.

Caveolin-1 Is a Novel Regulator of Genomic Glucocorticoid Signaling in Embryonic Neural Stem/Progenitor Cells

Antenatal glucocorticoids (GCs) reduce respiratory distress in premature infants but are associated with altered neurodevelopment. The glucocorticoid receptor (GR) activates both rapid and genomic signaling pathways to reduce proliferation of embryonic neural stem/progenitor cells (NSPCs). Peffer et al. (p. 2611–2623) demonstrate that the GR transcriptome is altered in caveolin-1 (Cav-1)-deficient NSPCs. Moreover, Cav-1 is required for GC-dependent site-specific phosphorylation of GR, chromatin recruitment of GR to select target genes, and the antiproliferative response of NSPCs to GCs. The insights provided by Peffer et al. identify Cav-1 as a putative pharmacologic target for minimizing neurodevelopmental deficits triggered by antenatal GC treatment.

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