IN BRIEF

CELL SIGNALLING

Control of local Rho GTPase crosstalk by Abr

Vaughan, E. M. *et al. Curr. Biol.* **21**, 270–277 (2011)

During single-cell wound healing in *Xenopus laevis*, the rho family GTPases rhoa and cdc42 are activated in non-overlapping concentric circles to organize the appropriate formation of actin and myosin II filaments at the wound site. By wounding *X. laevis* oocytes with a laser, Vaughan *et al.* identified abr, a GTPase regulator that can act as both a GTPase-activating protein (GAP) and a guanine nucleotide exchange factor (GEF), as a crucial mediator of rho GTPase crosstalk during wound healing. They show that abr is recruited by activated rhoA to wound sites, where it amplifies rhoa activation using its GEF domain and inactivates cdc42 with its GAP domain. This leads to the spatial segregation of rhoa and cdc42 activity. This new method of controlling local rho GTPase crosstalk may be applicable to other GTPases.

CELL GROWTH

Activation of mTORC2 by association with the ribosome

Zinzalla, V. *et al. Cell* **144**, 757–768 (2011)

Mammalian target of rapamycin complex 2 (mTORC2) had been found to associate with the ribosome and to modify AKT co-translationally. This study now shows that the association of mTORC2 with the ribosome is required for its activation and for its ability to post-translationally phosphorylate proteins such as AKT. A genetic screen in yeast indicated that nuclear import protein 7 (Nip7), which is required for ribosomal maturation, is essential for TORC2 signalling. The authors then showed that ribosomes also activate mTORC2 and that this occurs independently of protein synthesis. Furthermore, ribosome-bound mTORC2 was active and could phosphorylate AKT *in vitro*. The association of mTORC2 with the ribosome was regulated by insulin, which is known to activate mTORC2 through phosphoinositide 3-kinase signalling. Indeed, mTORC2 co-immunoprecipitated with 60S ribosomal protein L6 in serum-starved cells that had been treated with insulin, and this interaction correlated with AKT phosphorylation.

PROTEIN FOLDING

Selective inhibition of a regulatory subunit of protein phosphatase 1 restores proteostasis

Tsaytler, P. *et al. Science* 3 Mar 2011 (doi:10.1126/science.1201396)

During endoplasmic reticulum (ER) stress, transcription and translation are modulated to restore proteostasis. This is partly mediated by PRKR-like ER kinase (PERK), which phosphorylates the α-subunit of eukaryotic translation initiation factor 2 (eIF2α) to halt protein synthesis while indirectly inducing the expression of PPP1R15A, a regulatory subunit of protein phosphatase 1 (PP1). PPP1R15A then recruits the catalytic subunit of PP1C, which dephosphorylates eIF2α to restore protein synthesis. Tsaytler *et al.* show that guanabenz, an α2-adrenergic receptor agonist, reduces protein misfolding in cells subject to ER stress by delaying the recovery from the block in translation. Guanabenz prevents the PPP1R15A–PP1C interaction, which results in the persistent phosphorylation of eIF2α. However, it does not inhibit the related PPP1R15B–PP1C complex, which regulates constitutive protein synthesis. The authors propose that "Sustained translation attenuation caused by guanabenz during ER stress is likely to increase the ratio of chaperones to substrates and favor protein folding."