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IN BRIEF

AGEING

Cdc42 GTPase-activating protein deficiency promotes genomic instability and premature aging-like phenotypes.

Wang, L. *et al. Proc. Natl Acad. Sci. USA* **104**, 1248–1253 (2007)

The Rho GTPase CDC42 regulates reorganization of the actin cytoskeleton, polarity and cell growth. Wang *et al.* now shed light on a new CDC42 function by showing that increased CDC42 activity correlates with the course of natural ageing in mice. CDC42 GTPase-activating protein (CDC42GAP) is a negative regulator of CDC42, and knocking out CDC42GAP results in increased levels of CDC42, shortened lifespan of the mutant mice and premature ageing phenotypes in various tissues. CDC42GAP-deficient cells also show increased genomic instability and undergo early senescence, which is p53 dependent.

RNA

bicoid RNA localization requires specific binding of an endosomal sorting complex.

Irion, U. & St Johnston, D. *Nature* **445**, 554–558 (2007)

The localization of *bicoid* mRNA to the anterior of the *Drosophila melanogaster* oocyte is important for embryonic patterning. However, how *bicoid* mRNA is targeted to the anterior is not clear, although the Staufen protein is known to be important. The authors show that mutants of all subunits of the ESCRT-II complex, which functions in endosomal sorting, abolish the Staufen-dependent step in *bicoid* mRNA localization. Their findings indicate that *bicoid* mRNA localization is independent of endosomal sorting, and that the ESCRT-II component VPS36 is recruited to the anterior of the oocyte by *bicoid* mRNA, where it binds to *bicoid* mRNA in a sequence-specific manner.

SIGNAL TRANSDUCTION

Kinesin-mediated transport of Smad2 is required for signalling in response to TGF-β ligands.

Batut, J. *et al. Dev. Cell* **12**, 261–274 (2007)

During early vertebrate development, Nodal and Activin of the transforming growth factor-β (TGFβ) family of ligands signal through SMAD2, which is phosphorylated and accumulates in the nucleus. Batut *et al.* now show that SMAD2 continuously shuttles between the nucleus and the cytoplasm, both in the presence and absence of Nodal or Activin signalling, as a way of monitoring receptor activity. Phosphorylation and nuclear localization of SMAD2 in early vertebrate embryos and in mammalian tissue-culture cells requires a kinesin-1-dependent transport system.

STEM CELLS

FoxOs are critical mediators of hematopoietic stem cell resistance to physiologic oxidative stress.

Tothova, Z. *et al. Cell* **128**, 325–339 (2007)

Conditional deletion of *FoxO1*, *FoxO3* and *FoxO4* of the forkhead O subfamily of transcription factors causes a dramatic reduction in the number of haematopoietic stem cells (HSCs). FoxO-deficient HSCs also show an increase in reactive oxygen species, and the cells respond to oxidative stress by increased cell cycling and apoptosis, which leads to terminal differentiation and thereby the loss of long-term repopulating ability.