IN BRIEF

● CELL GROWTH

A new target for TOR

Target of rapamycin (TOR) has a key role in regulating cell growth, in part through its effects on protein synthesis. Here the authors identify RNA polymerase III (Pol III) as a new TOR target in Drosophila melanogaster. A link between TOR signalling and Pol III was first established when the authors observed that the Pol III factor BRF induced the growth effects of TOR signalling in both endoreduplicating and mitotically dividing cells. Moreover, loss of BRF led to growth defects at both the cellular and the organismal level, and depletion specifically in the fat body reduced larval growth rates owing to decreased systemic insulin signalling. TOR promotes Pol III transcription by blocking the effects of the transcriptional repressor MAF1 and also partly through the transcription factor MYC. As Pol III promotes the synthesis of non-coding RNAs, this regulation of Pol III-mediated transcription represents another mechanism by which TOR controls protein synthesis.

ORIGINAL RESEARCH PAPER Marshall, L., Rideout, E. J. & Grewal, S. S. Nutrient/TORdependent regulation of RNA polymerase III controls tissue and organismal growth in Drosophila. EMBO J. 24 Feb 2012 (doi:10.1038/emboj.2012.33)

SIGNALLING

Insulin at work without AKT

The metabolic transition that accompanies feeding depends on insulin, which promotes the phosphorylation and activation of AKT protein kinases. AKT kinases modulate metabolism through several downstream pathways, one of which involves phosphorylation and inactivation of forkhead box O (FOXO) transcription factors. In the liver, FOXO1 induces the transcription of genes encoding gluconeogenic enzymes, and this activity is suppressed by the insulin-AKT pathway after feeding. In the current model of hepatic metabolism, AKT is an obligate insulin signalling intermediate. However, Lu et al. now show that mice livers can respond to nutrients and insulin signalling even in the absence of AKT when Foxo1 is also deleted. Rather than mimicking a state of continual insulin presence, liver-specific deletion of Foxo1. or Akt and Foxo1. did not suppress the expression of gluconeogenic genes from fasting to feeding, which suggests that another pathway, that is independent of AKT, can mediate the response to insulin.

ORIGINAL RESEARCH PAPER Lu, M. et al. Insulin regulates liver metabolism in vivo in the absence of hepatic Akt and Foxo1. Nature Med. 18, 388–395 (2012)

AUTOPHAGY

Dietary lipids hinder quality control

Cellular homeostasis is maintained by targeting cytosolic proteins to lysosomes for degradation through chaperone-mediated autophagy (CMA). CMA is activated in response to stress and is impaired with age. A recent study in mice has revealed that dietary lipids inhibit lysosomal uptake of proteins through lysosome-associated membrane glycoprotein 2A (LAMP2A), thereby limiting CMA. The lipid composition of lysosomal membranes was altered following a high-fat diet, resulting in the formation of lipid microdomains, where LAMP2A is proteolytically degraded. Interestingly, similar changes in the composition of lysosomal membranes were observed in ageing mice, indicating that a common mechanism underlies impaired CMA activity. The authors suggest that the emerging regulatory role of lipid metabolism in CMA could be targeted in ageing and age-related diseases.

ORIGINAL RESEARCH PAPER Rodriguez-Navarro, J. A. *et al.* Inhibitory effect of dietary lipids on chaperone-mediated autophagy. *Proc. Natl Acad. Sci. USA* 13 Feb 2012 (doi:10.1073/pnas.1110306109)