# IN BRIEF

## AUTOPHAGY

### A genome-wide siRNA screen reveals multiple mTORC1 independent signaling pathways regulating autophagy under normal nutritional conditions

Lipinski, M. M. *et al. Dev. Cell* **18**, 1041–1052 (2010)

Although the signalling pathways activating autophagy during starvation are well characterized, those regulating it under normal nutrient conditions were unclear. A genome-wide small interfering RNA screen identified 236 genes encoding growth factors and cytokines, the depletion of which affected autophagy when nutrients were not limiting. Knockdown of most of these genes increased autophagy. This could be achieved independently of mammalian target of rapamycin complex 1 (mTORC1), the inhibition of which increases autophagy under starvation. Instead, the encoded proteins block autophagy by inhibiting the type III phosphoinositide 3-kinase (PI3K) through the activation of signalling pathways involved in promoting cell proliferation and growth. So, under normal nutrient conditions, autophagy is regulated by extracellular factors that act through many pathways that converge at the type III PI3K.

## MOLECULAR MOTORS

### Kinesin-1 heavy chain mediates microtubule sliding to drive changes in cell shape

Jolly, A. L. *et al. Proc. Natl Acad. Sci. USA* **107**, 12151–12156 (2010)

Microtubules in cultured cells buckle and loop during interphase. The authors reveal that in *Drosophila melanogaster* S2 cells this is caused by microtubules sliding against each other. RNA interference against the heavy chain of kinesin 1 (a molecular motor comprising heavy and light chains that is known to drive organelle transport), but not against the kinesin 1 light chain or other molecular motors, eliminates microtubule sliding during interphase. It also reduces the formation of long cellular processes made up of parallel microtubule bundles, which suggests that the kinesin 1 heavy chain mediates microtubule sliding to drive the formation of such processes. The kinesin 1 heavy chain is also required for microtubule sliding in *Xenopus laevis* and mammalian cells. Thus, the authors propose that in addition to functioning in organelle transport, kinesin 1 mediates cytoplasmic microtubule sliding.

## GENE EXPRESSION

### Conserved role of intragenic DNA methylation in regulating alternative promoters

Maunakea, A. K. *et al. Nature* **466**, 253–257 (2010)

DNA methylation of 5′ promoters is known to suppress gene expression, but the function of intragenic DNA methylation is controversial. Using next-generation sequencing, Maunakea *et al.* generated a DNA methylation map of the human brain, which they used to analyse the methylation status of CpG islands (CGIs) that are often found in regulatory sequences. Whereas 34% of intragenic CGIs were methylated, most 5′ promoter regions were unmethylated. Furthermore, intragenic methylation is tissue-specific, suggesting it might regulate gene expression. Consistently, intragenic CGIs correlated with alternative transcriptional start sites used in specific tissues. Low methylation levels at intragenic CGIs also correlated with histone H3 Lys4 trimethylation, a modification enriched at promoters, suggesting intragenic CGIs function as alternative promoters. This study highlights the role of intragenic DNA methylation in the regulation of tissue-specific promoters.