AUTOPHAGY

Putting on the brakes

Autophagy is an evolutionarily conserved catabolic process that is ubiquitous among eukaryotic cells. It involves the sequestration of cytoplasmic components for lysosomal degradation, and its role is to maintain the balance between the production of cell structures, their degradation and their turnover. There seems to be a connection between autophagy and apoptosis — the autophagy protein beclin-1 has been shown to interact with the anti-apoptotic protein BCL2 — although the significance of this interaction has remained unknown. Pattingre *et al*. now report in *Cell* that BCL2 also functions as an anti-autophagy protein.

Disruption of the beclin-1 orthologue in yeast prevents starvation-induced autophagy. Would the interaction between beclin-1 and BCL2 affect the autophagy process? Pattingre and colleagues showed that the beclin-1–BCL2 interaction contributed to inhibiting beclin-1-induced autophagy in yeast and mammalian cells, as well as in murine cardiac muscle.

Next, the authors examined the effects of BCL2 expression on the formation and activity of the complex through which beclin-1 functions in autophagy with class III phosphatidylinositol 3-kinase (PI3K). They found that complex formation was inhibited by BCL2, and that BCL2 decreased the activity of beclin-1-associated class III PI3K activity. In addition, they showed that cellular nutrient status regulated the interaction between beclin-1 and BCL2, suggesting that the dissociation of BCL2 from beclin-1 might be important in stimulating autophagy in response to starvation or other physiological stimuli.

Pattingre *et al*. noted that beclin-1 mutants that were unable to bind BCL2 induced higher levels of autophagy associated with the induction of autophagy-mediated cell death. The authors proposed a model in which the beclin-1–BCL2 complex functions as a rheostat to ensure that autophagy levels remain within a physiological range — the consequence for straying outside this range being autophagy-dependent cellular demise.

The BCL2 family of proteins are pivotal intermediates in cell-death signalling. The new findings of Pattingre and colleagues indicate that BCL2 has a dual role in cell death: in addition to its well-known anti-apoptotic properties, BCL2 also functions as a brake on autophagy-induced cell death. Because autophagy genes have different physiolgical roles, including differentiation, development, tumour suppression and promoting survival under stress conditions, these results might represent a novel mechanism by which BCL2 contributes to the modulation of these processes.

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References and links

ORIGINAL RESEARCH PAPER Pattingre, S. *et al.* Bcl-2 antiapoptotic proteins inhibit Beclin 1-dependent autophagy. *Cell* **122**, 927–939 (2005)

IN BRIEF

CYTOSKELETON

Integrin-dependent actomyosin contraction regulates epithelial cell scattering.

De Rooij, J. *et al. J. Cell Biol.* 10 Oct 2005 (doi:10.1083/jcb.200506152)

This study reveals that different extracellular-matrix conditions influence epithelial-cell scattering by modulating cytoskeletal organization and the contractility of actomyosin. De Rooij and colleagues show that integrin-dependent actomyosin tension mediates the disruption of cell–cell adhesion during epithelial-cell scattering, and propose that actomyosin promotes the cross talk between integrins and cadherins in epithelial cells.

MICROSCOPY

Correlated light and electron microscopic imaging of multiple endogenous proteins using quantum dots.

Giepmans, B.N.G. *et al. Nature Methods* **2**, 743–749 (2005)

Light microscopy has been extensively used for mapping protein localization, but many studies require the extra resolution of electron microscopy. Giepmans *et al.* now report the use of small semiconductor nanocrystals (Quantum dots) to perform pre-embedding multiprotein labelling for correlated light and electron microscopy. They demonstrate successful staining using several different antigens in cultured cells and tissues. This is a valuable addition to existing tools for specific and easy-to-use determination of multiple-protein localization.

DEVELOPMENT

Wnt11 functions in gastrulation by controlling cell cohesion through Rab5c and E-cadherin.

Ulrich, F. *et al. Dev. Cell* **4**, 555–564 (2005)

Wnt11 has a crucial role in zebrafish gastrulation, but the molecular mechanisms that affect this process are still unclear. Ulrich and colleagues now shed light on these mechanisms by showing that Wnt11 regulates the cohesion of mesodermal and endodermal progenitor cells. The authors found that Wnt11 and the GTPase Rab5c control the endocytosis — and therefore the localization — of E-cadherin, and are both required for E-cadherin-mediated cohesion of mesendodermal cells. Whether this mechanism for tissue morphogenesis is evolutionarily conserved remains to be seen.

CELL CYCLE

A novel motif governs APC-dependent degradation of *Drosophila* ORC1 *in vivo*.

Araki, M. *et al. Genes Dev.* 29 Sept 2005 (doi:10.1101/gad.1361905)

The anaphase-promoting complex (APC) regulates cell-cycle progression by targeting proteins for degradation. Four different APC-targeting motifs in substrates have been identified, and Araki *et al.* now report a fifth one. The origin recognition complex protein-1 (ORC1) — which is degraded at the end of M phase — has a novel motif, the O-box, which is necessary and sufficient to direct APC-dependent polyubiquitylation *in vitro* and degradation *in vivo*. Further analysis indicated that this motif might be responsible for the degradation of several cell-cycle proteins.