IN BRIEF

RNA DECAY

The where and when of NMD

Nonsense-mediated decay (NMD) is a cellular process that targets mRNAs carrying a premature termination codon (PTC) for degradation. The kinetics and cellular location (nucleus versus cytoplasm) of NMD had remained under debate. To answer this question, the authors used fluorescence *in situ* hybridization (FISH) to locate individual β-globin mRNAs within individual cellular compartments, thus obtaining temporal and spatial information on mRNA abundance in intact cells. They identified two mRNA populations within single cells. Most PTC-carrying β-globin mRNAs were degraded soon after nuclear export (<1 minute) close to the nuclear envelope. The remaining second population had a half-life of >12 hours, which is similar to that of PTC-free mRNAs, indicating that it had evaded NMD and was degraded in the cytoplasm by other mechanisms. The authors conclude that there is a spatially and temporally defined checkpoint for NMD that some mRNAs can bypass to escape further NMD surveillance.

ORIGINAL RESEARCH PAPER Trcek, T. *et al.* Temporal and spatial characterization of nonsense-mediated mRNA decay. *Genes Dev.* 21 Feb 2013 (doi:10.1101/gad.209635.112)

AUTOPHAGY

Pinpointing the mysterious membrane donors

Whether the autophagosomal membrane is derived from the endoplasmic reticulum (ER), mitochondria or the plasma membrane has been controversial. Here, Hamasaki *et al.* find that, in mammalian cells, autophagosomes originate at ER–mitochondrion contact sites. During starvation the pre-autophagosome marker ATG14 accumulated at ER–mitochondrion contact sites, and, similarly, co-fractionated with mitochondrion-associated ER membranes (which contain the contact sites). Moreover, ATG5, which is involved in autophagosome elongation and closure, also localized at ER–mitochondrion contact sites. Interestingly, knockdown of the ER SNARE protein STX17 during starvation hindered the localization of ATG14 specifically at these contact sites and decreased autophagy, indicating a crucial role for STX17-dependent ATG14 recruitment in autophagosome formation. The finding that ER–mitochondrion contact sites act as autophagosome membrane donors explains why previous studies had obtained evidence for both the ER and mitochondria in this process.

ORIGINAL RESEARCH PAPER Hamasaki, M. *et al.* Autophagosomes form at ER–mitochondria contact sites. *Nature* 03 Mar 2013 (doi:10.1038/nature11910)

DEVELOPMENT

SMURF2 targets ephrin B1 for degradation

Ephrin–EPH signalling, which requires cell–cell interaction as ephrin ligands and EPH receptors are both membrane bound, regulates tissue separation in embryogenesis. Hwang *et al.* show that ephrin B1 interacts with the E3 ligases SMAD ubiquitylation regulatory factor 1 (SMURF1) and SMURF2, and that SMURF2 promotes ephrin B1 degradation. Ephrin B1 was stable when SMURF1 and SMURF2 were co-expressed in *Xenopus laevis* embryos, suggesting that SMURF1 inhibits SMURF2-mediated ephrin B1 degradation. To assess ephrin B1-dependent separation of mesoderm from ectoderm, the authors introduced morpholinos against SMURF1 or ephrin B1 into mesoderm and found that tissue separation was inhibited. The co-introduction of morpholinos against SMURF1 and SMURF2 stabilized ephrin B1 and rescued this phenotype. Thus, SMURF2 regulates ephrin B1–EPH signalling during development by promoting ephrin B1 degradation; SMURF1 antagonizes SMURF2 in this setting.

ORIGINAL RESEARCH PAPER Hwang, Y.-S. *et al.* The Smurf ubiquitin ligases regulate tissue separation via antagonistic interactions with ephrinB1. *Genes Dev.* **27**, 491–503 (2013)