Nature Reviews Molecular Cell Biology | AOP, published online 16 October 2013; doi:10.1038/nrm3686

PhotoDisc/Getty Images

Primary cilia, which function as sensory and signalling organelles, are generated at basal bodies and require intraflagellar transport (IFT) for elongation and function. Autophagy is a process by which cells break down cytoplasmic material, including organelles, to maintain cellular energy levels. Two studies now show that autophagy and ciliogenesis are intricately linked. Tang *et al.* describe how autophagy promotes ciliogenesis by degrading OFD1 (oral facial digital syndrome 1) at centriolar satellites (particles surrounding centrosomes and basal bodies). By contrast, Pampliega *et al.* reveal that autophagy negatively regulates ciliogenesis by degrading the essential ciliary protein IFT20; they also show that Hedgehog (HH) signalling from primary cilia promotes autophagy, in support of a bidirectional interplay between these processes.

Tang *et al.* discovered that OFD1, a protein that localizes to centrioles and centriolar satellites, interacts with the autophagosome marker LC3. OFD1 was degraded by autophagy; its levels were decreased upon serum starvation and this depended on both the autophagy-related (ATG) protein ATG5 and lysosome function. Interestingly, OFD1 degradation was specific to the centriolar satellite pool of this protein as OFD1 levels at centrioles remained unchanged following serum starvation.

OFD1 at the distal end of centrioles is known to be necessary for primary cilia formation and the recruitment of IFT88, but its role at centriolar satellites is unclear. Thus, Tang *et al.* asked whether OFD1 levels at centriolar satellites, and thus autophagy, influence ciliogenesis. The percentage of ATG5-null cells that formed a primary cilium and the length of this organelle were reduced compared with wild-type cells. Strikingly, depleting ATG5-null cells of OFD1 using short hairpin RNA (shRNA) restored primary cilia formation, suggesting that OFD1 at centriolar satellites suppresses ciliogenesis and that starvation-induced autophagy removes OFD1 from centriolar satellites to promote it.

Pampliega e*t al.* also asked whether autophagy influences ciliogenesis, observing that ATG5-null cells formed cilia at a faster rate, and of a longer length, than wild-type cells under basal conditions and following prolonged serum starvation; this correlated with increased IFT20 levels. As the inhibition of lysosome function also increased IFT20 levels in cells, basal autophagy seems to negatively regulate ciliogenesis by degrading IFT20.

In addition, Pampliega *et al.* explored the effect of ciliogenesis on autophagy. They used cells in which IFT proteins, and thus ciliogenesis, were compromised to determine whether primary cilia influence autophagy. Starvation-induced autophagy and autophagosome biogenesis were defective in cell lines in which IFT20 or IFT88 were knocked down or mutated, respectively, suggesting that primary cilia promote autophagosome formation. Further experiments revealed that signalling by the HH pathway, components of which are recruited to cilia by IFT, is required for cilia-induced autophagy. For example, activating or reducing HH signalling induced or hindered autophagic flux, respectively, in wild-type but not IFT-compromised cells.

> “These studies show context-specific roles for autophagy in the regulation of ciliogenesis and for ciliogenesis in the regulation of autophagy.”

As well as functioning in ciliogenesis, IFT helps to deliver non-ciliary proteins to the plasma membrane, where autophagosomes may be formed. Thus, Pampliega *et al.* determined whether components required for autophagosome biogenesis are trafficked by anterograde IFT. Five key ATG proteins localized along the ciliary axoneme in serum-starved cells, and nine ATG proteins associated with the basal body under specific conditions; ATG16L localized to both places. A closer look at ATG16L revealed that it is trafficked to the basal body in response to starvation in a manner dependent on IFT20, with which it interacts.

These studies show context-specific roles for autophagy in the regulation of ciliogenesis and for ciliogenesis in the regulation of autophagy. Future work may reveal how autophagy levels are balanced to ensure the degradation of proteins (such as OFD1) that inhibit ciliogenesis, while preserving the levels of proteins (such as IFT20) that promote it.

Katharine H. Wrighton

ORIGINAL RESEARCH PAPERS Tang, Z. *et al.* Autophagy promotes primary ciliogenesis by removing OFD1 from centriolar satellites. *Nature* http://dx.doi.org/10.1038/nature12606 (2013) | Pampliega, O. *et al.* Functional interaction between autophagy and ciliogenesis. *Nature* http://dx.doi.org/10.1038/nature12639 (2013)