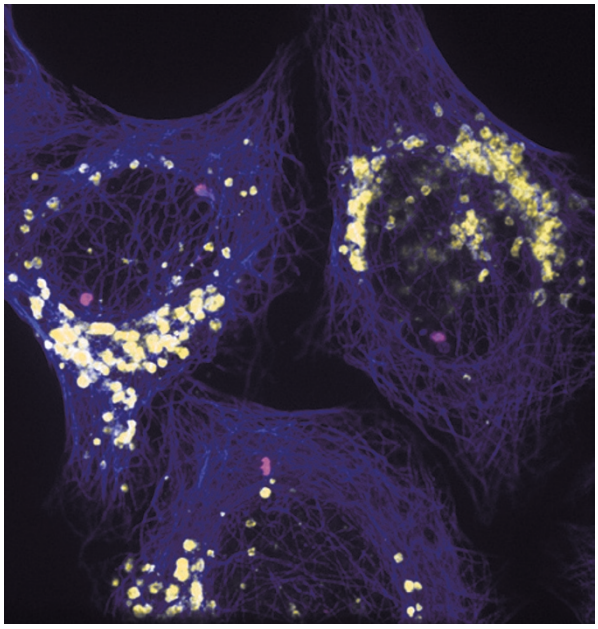
Nature Reviews Molecular Cell Biology | AOP, published online 12 October 2011; doi:10.1038/nrm3612

ORGANELLE DYNAMICS

Inheritance for pluripotency

> MBds increased the efficiency of iPS cell formation.

Midbodies — which form during cytokinesis in the intercellular bridge between two daughter cells and are required for their separation — can remain in daughter cells as midbody derivatives (MBds), the fate and function of which are unclear. Kuo, Chen and colleagues now report that MBds are selectively degraded by autophagy in specific cell types and are linked to pluripotency and tumorigenesis.



MCF7 breast cancer cells treated with lysosomal inhibitors accumulate post-mitotic midbodies (pink) in the cytoplasm but not in lysosomes (yellow). Microtubules are shown in blue. Image courtesy of S. Doxsey, University of Massachusetts Medical School, USA.

Using a fluorescent midbody marker, the authors first observed the fate of MBds in different cultured cell types and found that they accumulated in some cells but not others. By also visualizing centrosomes, they showed that the inherited MBds associated with the daughter cell containing the older centrosome.

Next, they determined the localization of MBds in human and mouse tissues. They found that MBds accumulated within stem cell niches, such as the basal compartment of seminiferous tubules of testes and the subventricular zone of mouse embryo brains. This indicates that MBds are retained and accumulate in stem cells *in vivo*. To further test this theory, the authors examined the fate of MBds during somatic cell reprogramming and stem cell differentiation *in vitro*. As expected, MBds were lost on differentiation of human embryonic stem cells to fibroblasts and, consistently, MBds accumulated in induced pluripotent stem (iPS) cells generated from fibroblasts.

But what is the mechanism that leads to MBd accumulation in specific cell types? Interestingly, the authors found that MBds are degraded through autophagy in a cell-specific manner; cells that normally contained few MBds accumulated them to a greater extent if autophagy and subsequent lysosomal degradation were inhibited. Furthermore, Kuo, Chen and colleagues showed that MBd degradation involves receptor-mediated autophagy pathways. They found that NBR1 is the main mammalian autophagy receptor involved in MBd degradation, as *NBR1* silencing increased MBd levels, whereas depletion of p62 (which had been previously reported to have a role in MBd clearance) did not.

Finally, the authors questioned the functional relevance of MBd accumulation. By silencing *NBR1* and thus increasing MBd levels in embryonic fibroblasts, they found that high levels of MBds increased the efficiency of iPS cell formation. Furthermore, they observed that cancer cell populations accumulate greater amounts of MBds than their normal counterparts and have higher rates of anchorage- independent growth *in vitro*, suggesting that MBds might increase their tumorigenic potential.

This work shows that MBds accumulate in specific cell types and are selectively degraded by autophagy. It also suggests roles for MBds in stem cell pluripotency and in tumorigenicity, but further work should elucidate the mechanisms underlying these functions.

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ORIGINAL RESEARCH PAPER Kuo, T.-C. *et al.* Midbody accumulation through evasion of autophagy contributes to cellular reprogramming and tumorigenicity. *Nature Cell Biol.* **13**, 1214–1223 (2011)