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Journal club

ACCIDENTALLY ENUCLEATING AUTOPHAGY

In an afternoon coffee break at Nobel Symposium No 144 (23–26 May, 2010), in the foyer of the Nobel Forum, I had a cordial discussion with an overseas guest, Daniel J. Klionsky (University of Michigan, MI, USA). I asked Dan, an expert in the field of autophagy — a catabolic process that results in the autophagosome-dependent lysosomal degradation of bulk cytoplasmic components — whether he thought that the post-translational modification of histones had a role in autophagy. In unison, we agreed that this was probably not the case, as autophagosome formation can be observed in enucleated cells according to Tasdemir *et al*. In order to elegantly illustrate that p53 can influence autophagy independently of its nuclear transcriptional function, they demonstrated that cytoplasts (cells that have had the nucleus removed) still accumulate puncta that include the autophagy marker MAP1LC3 in response to autophagic stimuli.

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One sentence and, in the context of autophagy, the nucleus had vanished! However, how could we, based on these observations, preclude a role for nuclei in autophagy regulation? I should have paid more attention to the simultaneous discovery a decade earlier, by Beck and Hall, Hardwick *et al*. and Cardenas *et al*., that the signalling pathway under the control of target of rapamycin (TOR), a central regulator of autophagy, prominently regulates transcription in response to autophagic stimuli. Despite my preconceived idea, I asked Dan if we should look into the role of histone modifications in autophagy anyway. As a result, together we found that autophagy induction is coupled with the downregulation of the histone H4 lysine 16 acetyltransferase hMOF and a reduction in acetylation at this mark, and that this histone modification regulates the outcome of autophagy (Füllgrabe *et al*.). This brought renewed attention to the nuclear regulation of autophagy.

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FURTHER READING Füllgrabe, J., Klionsky, D. J., & Joseph, B. The return of the nucleus: transcriptional and epigenetic control of autophagy. *Nature Rev. Mol. Cell Biol.* **15**, 65–74 (2014)