

Journal club



SHINING LIGHT ON AUTOPHAGY

Thirty years after Christian de Duve coined the term 'autophagy' to describe the lysosomal-mediated degradation of intracellular material after sequestration in the autophagosome, I discovered a fascinating aspect of the cell biology of autophagy by reading the review that Seglen and Bohley published in 1992. This review described the cutting edge of our knowledge in this field at the time. The phagophore, a name given by Seglen to a specialized membrane involved in the very early stage of autophagy, seemed to provide the functional connection between endocytosis and autophagy.

Subsequent 'quantum leaps' in our understanding of autophagy were the discoveries of autophagy-related (ATG) proteins in 1993 by Yoshinori Ohsumi and by Mizushima and colleagues in 1998 of the role of

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a protein conjugation system that is essential for the formation of autophagosomes. Today, we know that the phagophore elongates and seals to form autophagosomes by recruiting ATG proteins, and that the endocytic compartments contribute both to the early stage of autophagosome formation and to its maturation before fusion with lysosomes.

In 1999, work in Beth Levine's laboratory, published in a paper by Liang *et al.*, revealed that the protein Beclin 1 (ATG6 in yeast) is encoded by a tumour suppressor gene and that it is a partner of the anti-apoptotic protein BCL-2. This was the first direct evidence that autophagy contributes to malignancies. This article paved the way for research into the function of autophagy and ATG proteins in physiology and human disease. Furthermore, the discovery that Beclin 1 interacts with proteins of the BCL-2 family initiated studies on the complex crosstalk between autophagy and apoptosis.

Although we have gained many insights into autophagy since Christian de Duve coined the term, we clearly still have much more to learn. In this regard, I would like to end with a quote from the review by Seglen and Bohley: "To obtain reliable information about the biochemistry of autophagy more specific assay methods would therefore be desirable." It is obvious that ATG-based methods have moved autophagy studies into new territories and that they will continue to do so in the future.

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ORIGINAL RESEARCH PAPERS Mizushima, N. *et al.* A protein conjugation system essential for autophagy. *Nature* **395**, 395–398 (1998) | Liang, X. H. *et al.* Induction of autophagy and inhibition of tumorigenesis by beclin 1. *Nature* **402**, 672–676 (1999)

FURTHER READING Seglen, P. O. & Bohley, P. Autophagy and other vacuolar protein degradation mechanisms. *Experientia* **48**, 158–172 (1992)