

Structural Study of Atg5 and Atg16 Essential for Autophagy

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Atg5 is a 34 kDa protein which is covalently modified by a ubiquitin-like protein, Atg12 by a ubiquitin-like conjugation system [1]. The Atg12-Atg5 conjugate then forms a multimeric complex with Atg16 [2]. Atg12-Atg5/Atg16 complex is essential for autophagy, the main pathway for the degradation of cytoplasmic components such as proteins and organelles in all eukaryotic cells. In autophagy, cytoplasmic components are enclosed by double-membrane structures termed autophagosomes, which subsequently fuse with the vacuole / lysosome. Atg12-Atg5/Atg16 complex is localized to autophagosome precursors (isolation membrane). The localization implies that the complex plays major roles in the development of autophagic isolation membranes into autophagosomes.

We determined the crystal structure of Atg5 in complex with the N-terminal region of Atg16 using methods of multiple isomorphous replacement with anomalous scattering (MIRAS) and multiwavelength anomalous dispersion (MAD). Atg5 consists of two ubiquitin-like domains and a helical domain. The N-terminal region of Atg16 has a long helical structure, which binds to the helical domain of Atg5 via salt bridges and hydrophobic interactions. Biological analyses of Atg5/Atg16 complex are now in progress.

[1] Mizushima N., Noda T., Yoshimori T., Tanaka Y., Ishii T., George M.D., Klionsky D.J., Ohsumi M., Ohsumi Y., *Nature*, 1998, **395**, 395. [2] Mizushima N., Noda T., Ohsumi Y., *EMBO J.*, 1999, **18**, 3888.

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