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Structural basis of Atg conjugation systems essential for autophagy

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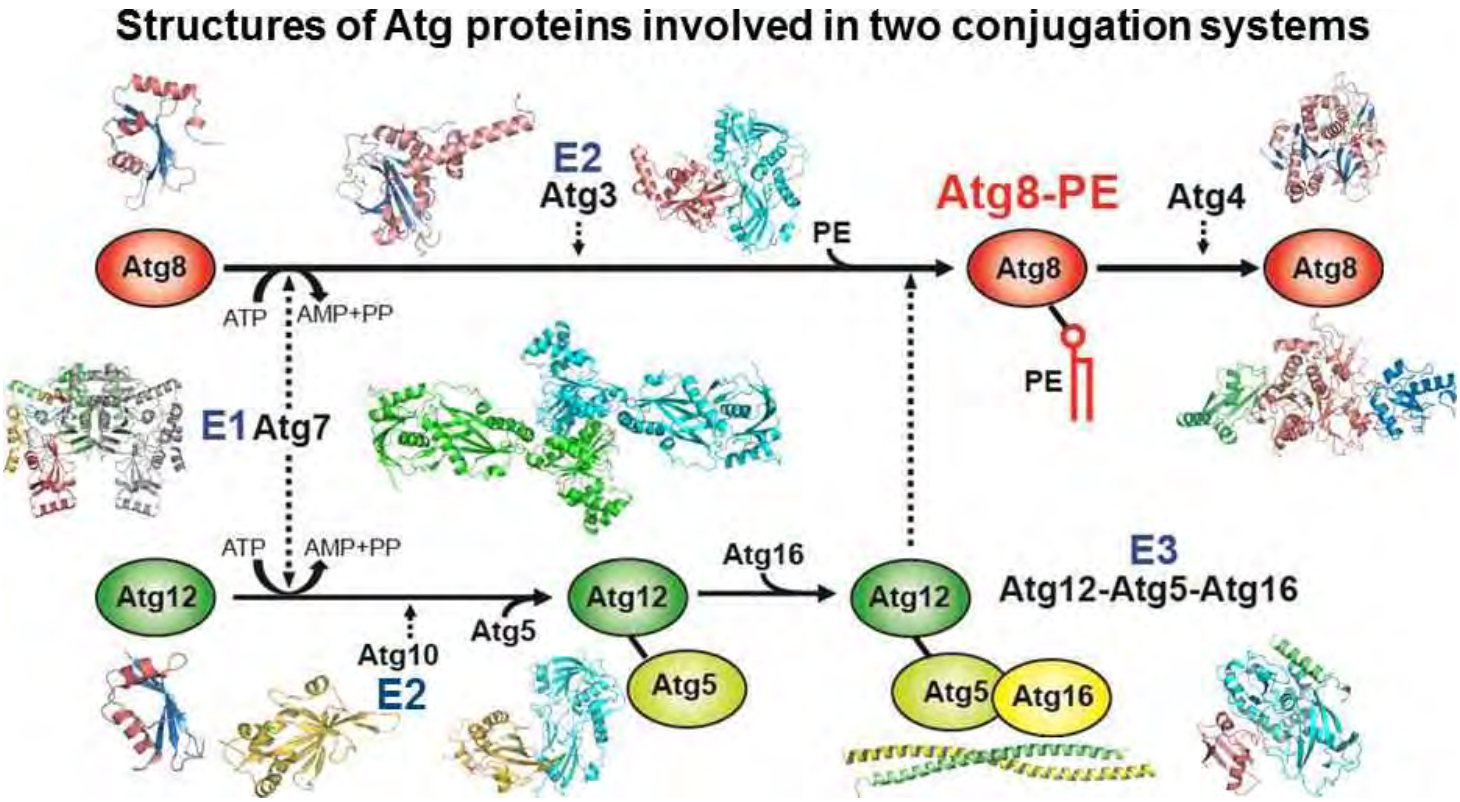
Autophagy is an evolutionarily-conserved, intracellular degradation system for which two ubiquitin-like modifiers, Atg8 and Atg12, play essential roles. After processed by Atg4, the exposed C-terminal glycine of Atg8 is activated by Atg7 (E1) and is then transferred to Atg3 (E2), and is finally conjugated with a phospholipid, phosphatidylethanolamine (PE) through an amide bond. Whereas, Atg12 is activated by the same E1, Atg7, without processing, and is then transferred to Atg10 (E2), and is finally conjugated with Atg5 through an isopeptide bond. Atg12-Atg5 conjugates, together with Atg16, function as an E3-like enzyme to facilitate the conjugation reaction between Atg8 and PE. During autophagy, Atg8-PE conjugates play a critical role in selective cargo recognition in addition to autophagosome formation. We determined the structures of all these Atg proteins and their complexes mainly by X-ray crystallography, and performed structure-based biochemical analyses on them [1,2]. These studies established the molecular mechanisms of Atg8 and Atg12 modification reactions that have many unique features compared with canonical ubiquitin-like systems. Furthermore, we found a conserved motif named the Atg8-family interacting motif (AIM), through which Atg8 recognizes specific cargoes and selectively incorporates them into autophagosomes for degradation [3].

[1] *N. N. Noda, Y. Ohsumi, F. Inagaki, Chemical Reviews, 2009, 109, 1587-1598,* ***[2]*** *N. N. Noda, Y. Fujioka, T. Hanada et al, EMBO Reports, 2013, 14, 206-211,* ***[3]*** *N. N. Noda, Y. Ohsumi, F. Inagaki, FEBS Letters, 2010, 584, 1379-1385*



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