Cellular Recycling in Health and Disease – Molecular Principles of Autophagy

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Autophagy is a cellular recycling pathway that degrades damaged or unwanted cytoplasmic material. The process starts with the formation of a cup-shaped membrane, termed phagophore, which captures cargo. Expansion and sealing of phagophores give rise to autophagosomes that transport their cargo to lysosomes for degradation. Under physiological conditions, phagophores capture cargo in a highly selective manner, while stress or starvation induces the formation of phagophores that sequester bulk cytoplasm. A particularly interesting step during autophagy involves the conjugation of ubiquitin-like ATG8 proteins to lipids of the phagophore. ATG8 proteins are involved in many steps during the biogenesis of autophagosomes. They tether cargo to phagophores, promote expansion and closure of phagophores and regulate recruitment of autophagosomes to lysosomes and fusion of both organelles. How ATG8 proteins fulfil these different functions remain less well understood. In my talk, I will present our most recent studies in which we reconstituted phagophore formation in the test tube using purified components. We discovered an unexpected novel function of ATG8 during this process, providing insights into the molecular mechanism of phagophore formation.