



Research Group “Molecular Membrane and Organelle Biology“ (Dr. Thomas Wollert)

Cellular Waste in Molecular “Recycling Bags”

Recycling is an essential process for cells and of course occurs without the use of a yellow sack, blue bin or glass container. Cellular waste is not separated first, but is packaged right from the start individually and precisely by a membrane and delivered to the lysosomes for recycling. In a current study, Thomas Wollert and his research group “Molecular Membrane and Organelle Biology“ showed how this autophagic process takes place in detail.

The components of the cell are constantly exposed to adverse environmental influences. If they are damaged in the process they must be degraded via autophagy, a term that roughly means “self-digestion”. A reduced activity of this process leads to an accumulation of unwanted or damaged material. These protein aggregates are particularly threatening for neurons and their accumulation contributes to the development of neurodegenerative diseases such as Parkinson’s and Alzheimer’s disease. Cancer and aging processes can also be attributed in part to a disruption of autophagy.

Autophagy is a highly complex process, and Wollert’s team was particularly interested in one question: Why is the membrane curved? Without a proper curvature no membrane vesicles can be formed to enclose the waste. The shape of the membrane therefore plays an important role, especially in the early phase of autophagosome biogenesis. Membranes consist of floating lipid bilayers that are interspersed with proteins. Special stabilizers are needed to bring membranes into a defined shape. In the study, the researchers were able to unravel how autophagosomes are formed out of a cup-shaped membrane sack that initially captures cellular material. Key to this process is a rigid protein scaffold that covers the membrane like a flat mesh, keeping the membrane in shape during its expansion.

The team recapitulated this process in the test tube employing purified proteins and synthetic membranes. Using this innovative but challenging approach, the team was able to monitor the assembly and disassembly of this delicate structure in real time. First, small molecules of the protein Atg8 are anchored as nodes of the scaffold in the autophagosomal membrane and then linked. The Atg8 molecules are not cut off from the membrane until the molecular “recycling bag” completely encloses the waste. The net is then no longer needed. In a next step, these structures called autophagosomes transport their cargo to the lysosomes. These cellular waste disposal stations are likewise enclosed by a membrane and can fuse with the autophagosomes, absorb the waste and break it down into its basic building blocks for recycling.

Wollert’s team is now seeking to elucidate how autophagy is initiated. It is unclear which proteins stimulate the formation of the cup-shaped membrane and how the assembly and disassembly of the stabilizing scaffold is coordinated. The researchers hope that a detailed understanding of autophagy and its functioning will lead to new therapeutic approaches for neurodegenerative diseases and cancer.

