The lysosome in health and disease

Lysosomes are organelles that are critically involved in the degradation of macromolecules mainly delivered by endocytosis and autophagy. Degradation is achieved by more than 60 hydrolases sequestered by a single phospholipid bilayer. The lysosomal membrane facilitates interaction and fusion with other compartments and harbours transport proteins catalysing the export of catabolites, thereby allowing their recycling. The importance of lysosomal pathways including autophagy is emphasized by recent findings that reveal new roles for lysosomal proteins in cellular physiology and in an increasing number of diseases that are characterized by defects in lysosome biology. Lysosomal storage diseases (LSDs) are characterized by disturbances in the interplay between hydrolases, membrane proteins and the cytosolic world. They are characterized by intralysosomal accumulation of substrates, often only in certain cell types. It will be discussed how lysosomal storage affects downstream functions linked to lysosomes, such as membrane repair, autophagy, exocytosis, lipid homeostasis, signaling cascades and cell viability. Therapies must aim to correct lysosomal storage not only morphologically, but reverse its (patho)biochemical consequences. It is currently explored in how far more common diseases such as cancer, cardiovascular and neurodegenerative diseases such as Parkinson Disease and Alzheimer Disease may profit from a correction of an impaired lysosomal function.