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Saraya, Ruchi; Veenhuis, Marten; van der Klei, Ida

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Peroxisomes as dynamic organelles

Ida J. van der Klei

Molecular Cell Biology, Groningen Biomolecular Sciences and Biotechnology Institute, Kluyver Centre of Industrial Genomics, University of Groningen, The Netherlands

Peroxisomes are cell organelles that are present in almost all eukaryotic cells. Their enzyme content – and hence their function – is highly variable and depends on the organism, cell type and developmental stage, and (in 'yeast and filamentous fungi) on the growth conditions. Peroxisomes are highly dynamic organelles: both their function and their abundance (number per cell, size) may rapidly change in response to external stimuli.

The first minireview by the Erdmann group (Wolf *et al.*) describes recent progress in understanding the dynamics and regulation of peroxisomal matrix protein import. Most peroxisomal matrix proteins contain either of the two known peroxisomal targeting signals, PTS1 or PTS2, which are recognized by the soluble receptor proteins Pex5 or Pex7. Upon cargo binding these receptors associate with the peroxisomal translocon, of which Pex14 is a major component. Peroxisomes can import folded and oligomeric proteins. How this is achieved has been an enigma for a long time. Recently, however, the Erdmann group showed that a reconstituted complex isolated from yeast peroxisomes can form a highly flexible large pore, of which Pex5 and Pex14 are the most abundant components. This complex can form a pore larger than 9 nm, which indeed may accommodate folded and oligomeric proteins. This pore must be tightly regulated as peroxisomal membranes are not permeable for small compounds such as ATP or acetyl CoA.

In the second review, by Saraya *et al.,* different aspects of the regulation of peroxisome abundance are discussed. Peroxisomes can multiply by the fission of pre-existing peroxisomes. Importantly, in yeast fission appears to be the most important mechanism of peroxisome proliferation. Surprisingly, in most organisms, peroxisomes and mitochondria share the same molecular machinery for organelle fission. Conserved components of this machinery are the tail anchor protein (Fis1) and a soluble dynamin-related protein.

In mutant cells that lack pre-existing peroxisomes, new peroxisomes can be formed from the endoplasmic reticulum (ER). Although this process is firmly established in both higher and lower eukaryotes, it is still unclear what the significance of this process is during normal conditions in wild-type yeast cells. It is evident that physical and functional links exist between peroxisomes and the ER. For instance, important lipids of the peroxisomal membrane are synthesized at the ER. The process of lipid transfer from the ER to peroxisomes – for which molecular details are still missing – may explain the transient localization of certain peroxisomal membrane proteins at the ER and do not necessarily represent intermediate stages of new peroxisome formation from the ER.

Saraya *et al.* also present the latest findings on peroxisome inheritance in yeast. This tightly regulated process involves the actin cytoskeleton and the Myo2 motor protein. Recently, residues in Myo2 that are essential for binding to the peroxisomal receptor protein, Inp2, have been identified. Interestingly, Pex3, a peroxin important for peroxisomal membrane biogenesis, was shown to be the docking protein for Inp1, the protein essential for peroxisome retention in mother cells.

In the third minireview, Oku and Sakai discuss the process of autophagy and selective autophagic degradation of peroxisomes (pexophagy). In addition to its role in reducing organelle numbers, pexophagy is also implicated in remodeling during cell differentiation.

The authors also present an overview on core factors for forming pexophagic membrane structures [the pexophagosomes and the micropexophagy specific membrane apparatus (MIPA)] and the interface molecules between peroxisomes and autophagic membrane structures that determine the selectivity towards peroxisomes. In addition to Atg30, unexpectedly also Pex14 (which is important in protein import) and Pex3 (crucial for peroxisomal membrane biogenesis and organelle retention) are involved in the recognition of peroxisomes by the autophagic machinery.

Ida van der Klei is Professor in Molecular Cell Biology at the University of Groningen, the Netherlands. She received her PhD at the same university and was a postdoctoral fellow at the Ludwig Maximilians-Universität Munich, Germany. She was a recipient of an EMBO Long Term Fellowship and a PIONIER grant of the Netherlands Organisation for Scientific Research (NWO). Her research in yeast focuses on unraveling the principles of peroxisome inheritance, fission and formation from the ER as well as on the role of peroxisomes in ageing. Using the filamentous fungus *Penicillium chrysogenum* she studies the role of peroxisomes in penicillin production.

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