Yeast Pex11 is involved in the regulation of expression of carbohydrate metabolism genes through chromatin modification by re-routing the acetyl-CoA transport from peroxisomes to mitochondria

Mojca Mattiazzi Ušaj, Petra Kaferle, Mojca Brložnik, Janez Kokošar, Jernej Šribar, Harald Hofbauer, Christoph Kurat, Heimo Wolinski, Sepp D. Kohlwein, Igor Stagljar, Klaus Natter, Uroš Petrovič

β-oxidation of fatty acids in *S. cerevisiae* takes place exclusively in the peroxisomes. Acetyl-CoA, the product of this pathway, is a central molecule of cellular metabolism both as a substrate for anabolic or catabolic pathways, as well as for gene expression regulation via histone acetylation and metabolism regulation through non-histone proteins, e.g. enzymes acetylation. We found a set of peroxisomal proteins – most notably Pex11, a putative homolog of mammalian nuclear receptors – whose change in activity affected expression of a set of genes which are among the most highly expressed genes in yeast cells. With a combination of transcriptomics, interactomics and high content imaging approaches we established that the underlying mechanism behind the observed changes in gene expression is increased histone acetylation, and we found evidence of a novel route for acetyl-CoA transport from peroxisomes to mitochondria. Our results have implications also for yeast-based biotechnological processes, since they provide molecular targets for redirecting the cellular flux of acetyl-CoA, an important substrate for a number of economically interesting bioproducts.