Seminar/Talk

Selective membrane sensing via an amphipathic helix in Opi1 to control lipid metabolism in yeast

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A key decision in cellular physiology is the decision between membrane biogenesis and lipid storage. The regulatory pathways underlying these cellular processes must be carefully coordinated and tightly controlled. The lipid metabolite phosphatidic acid (PA) represents the branch point between glycerophospholipid production for cell proliferation and triacylglycerol synthesis for fat storage1. PA molecules have a high metabolic turnover and also serve as critical signaling lipids. In the bakers yeast Saccharomyces cerevisiae, the PA level of the ER is constantly monitored by the soluble repressor Opi1 via its polybasic PA binding domain to control the transcriptional program of glycerophospholipid biosynthesis2. However, mechanistic details on the binding mode of Opi1 remain yet elusive.We here identified and characterized an amphipathic helix (AH) in Opi1s PA binding domain that is additionally capable for acyl chain sensing of the lipid bilayer after initial electrostatic membrane recruitment. Using a combined in vivo, in vitro and in silico approach, we provide evidence that directed tuning of the helix affects its membrane binding selectivity as well as binding strength. Thus, the AH enables specific membrane recognition that goes beyond sensing of total PA levels and allows Opi1 to rapidly respond on various derailments of membrane lipid homeostasis by directly adjusting glycerophospholipid metabolism.Taken together, our data reveal novel insights into fundamental aspects of membrane sensing by using the AH of Opi1 as show box for highly selective target membrane recognition. These findings potentially help to generate fine-tuned membrane sensors as well as synthetically optimized antimicrobial peptides in future projects.References:1.Henry, S. A., Kohlwein, S. D. & Carman, G. M. Metabolism and Regulation of Glycerolipids in the Yeast Saccharomyces cerevisiae. Genetics 190, 317349 (2012).2.Loewen, C. J. R. et al. Phospholipid metabolism regulated by a transcription factor sensing phosphatidic acid. Science 304, 16447 (2004).

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Mondi Seminar Room 2, Central Building

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