Lipid Metabolism Regulation By Sit4p Is Mediated By Sap190p.

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The Ser-Thr phosphatase Sit4 plays a central role in multiple cellular processes by participating in the TOR kinase pathway. Sit4p forms a complex with four regulatory proteins called SAP (Sit4 associated proteins) which share significant homology and compete among themselves for binding to Sit4p. One of the remarkable role of Sit4p is the regulation of energetic metabolism, since ?*sit4* strains show glycogen accumulation and a shift of metabolism from fermentation to respiration. Our group has observed that ?*sit4* mutant presents low levels of lipid particles, organelles responsible for neutral lipids storage in cells, thus, elicitating a new role of *sit4* regulation in lipid metabolism. In this work, we investigated the involvement of Sit4p in neutral lipid metabolism. We hypothesized that Sit4p might positively regulate lipid synthesis by acting on Acetyl-CoA (ACCase) carboxylase, an essential enzyme and a key step of fatty acid synthesis. We tested sensitivity soraphen A of different mutant strains, an ACCase specific inhibitor, as an indicator of ACCase activity. We observed that *sit4* deletion increases soraphen A sensitivity. In order to evaluate whether this sensitivity is mediated by SAPs, we checked the phenotype of the four individual SAPs deletions. Increased sensitivity was only observed for ?*sap190* mutant. Further investigation revealed that ?*sap190* mutant presents lipid particles levels comparable to ?*sit4* mutant. Thus, our results suggest that Sit4p participates in lipid metabolism in a Sap190p dependent manner. We are currently investigating ACCase activity and its phosphorylation levels in these strains.

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