Ach1 is involved in shuttling mitochondrial acetyl units for cytosolic C2 provision in Saccharomyces cerevisiae lacking pyruvate decarboxylase

Acetyl-coenzyme A (acetyl-CoA) is not only an essential intermediate in central carbon metabolism, but also an important precursor metabolite for native or engineered pathways that can produce many products of commercial interest such as pharmaceuticals, chemicals or biofuels. In the yeast Saccharomyces cerevisiae, acetyl-CoA is compartmentalized in the cytosol, mitochondrion, peroxisome and nucleus, and cannot be directly transported between these compartments. With the acetyl-carnitine or glyoxylate shuttle, acetyl-CoA produced in peroxisomes or the cytoplasm can be transported into the cytoplasm or the mitochondria. However, whether acetyl-CoA generated in the mitochondria can be exported to the cytoplasm is still unclear. Here, we investigated whether the transfer of acetyl-CoA from the mitochondria to the cytoplasm can occur using a pyruvate decarboxylase negative, non-fermentative yeast strain. We found that mitochondrial Ach1 can convert acetyl-CoA in this compartment into acetate, which crosses the mitochondrial membrane before being converted into acetyl-CoA in the cytosol. Based on our finding we propose a model in which acetate can be used to exchange acetyl units between mitochondria and the cytosol. These results will increase our fundamental understanding of intracellular transport of acetyl units, and also help to develop microbial cell factories for many kinds of acetyl-CoA derived products.
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