

Supplementary figure 2.6

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  "PRJNA102287": {
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    "title": "Prolonged Maltose-Limited Cultivation of Saccharomyces cerevisiae",
    "description": "Prolonged cultivation (>25 generations) of Saccharomyces cerevisiae in aerobic, maltose-limited chemostat cultures led to profound physiological changes. Maltose hypersensitivity was observed when cells from prolonged cultivations were suddenly exposed to excess maltose. This substrate hypersensitivity was evident from massive cell lysis and loss of viability. During prolonged cultivation at a fixed specific growth rate, the affinity for the growth-limiting nutrient (i.e., maltose) increased, as evident from a decreasing residual maltose concentration. Furthermore, the capacity of maltose-dependent proton uptake increased up to 2.5-fold during prolonged cultivation. Genome-wide transcriptome analysis showed that the increased maltose transport capacity was not primarily due to increased transcript levels of maltose-permease genes upon prolonged cultivation. We propose that selection for improved substrate affinity (ratio of maximum substrate consumption rate and substrate saturation constant) in maltose-limited cultures leads to selection for cells with an increased capacity for maltose uptake. At the same time, the accumulative nature of maltose-proton symport in S. cerevisiae leads to unrestricted uptake when maltose-adapted cells are exposed to a substrate excess. These changes were retained after isolation of individual cell lines from the chemostat cultures and nonselective cultivation, indicating that mutations were involved. The observed trade-off between substrate affinity and substrate tolerance may be relevant for metabolic engineering and strain selection for utilization of substrates that are taken up by proton symport. Keywords: Evolution Overall design: In a recent study (25) we analyzed glucose efflux upon exposure of S. cerevisiae to excess maltose, with yeast cells originating from "young" chemostat cultures (<20 generations). In these experiments no cell lysis was observed upon exposure to excess maltose. However, in further work on this subject, we observed an apparent effect of chemostat culture age on transport capacity. The aim of the present study was to further investigate the effect of prolonged maltose-limited chemostat cultivation on the physiology of S. cerevisiae. To this end we monitored the affinity for maltose, genome-wide transcript levels, activities of key enzymes, and physiological responses to maltose excess during long-term cultivation in maltose-limited chemostat cultures. Jansen, M. L. A., J. H. de Winde, and J. T. Pronk. 2002. Hxt-carrier-mediated glucose efflux upon exposure of Saccharomyces cerevisiae to excess maltose. Appl. Environ. Microbiol. 68:4259-4265.",
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