

## Supplementary figure 2.5

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$ ffq -l 2 CRX102293 -o metadata.json
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{
  "PRJNA102293": {
    "accession": "PRJNA102293",
    "title": "Formaldehyde as source of free-energy during growth of engineered Saccharomyces cerevisiae on glucose",
    "description": "Previously, it has been demonstrated that formate can be utilized by Saccharomyces cerevisiae as additional energy source using cells grown in a glucose-limited chemostat. Here, we investigated utilization of formaldehyde as co-substrate. Since endogenous formaldehyde dehydrogenase activities were insufficient to allow co-feeding of formaldehyde, the H. polymorpha FLD1, encoding formaldehyde dehydrogenase, was introduced in S. cerevisiae. Chemostat cultivations revealed that formaldehyde was co-utilized with glucose, but the yield was lower than predicted. Moreover, formate was secreted by the cells. Upon co-expression of the H. polymorpha gene encoding formate dehydrogenase, FMD, the levels of secreted formate decreased, but the biomass yield was still lower than anticipated. Transcriptome comparisons of cells of the engineered FLD1/FMD-expressing S. cerevisiae strain grown with or without formaldehyde feed, suggested that the cells experienced biotin limitation, possibly due to inactivation of biotin by formaldehyde in the feed. When separate feeds were used for formaldehyde and biotin, the engineered S. cerevisiae strain was able to efficiently utilize formaldehyde as additional energy source. Keywords: response to additional compound Overall design: In industrial biotechnology, the cost of feedstocks (often sugars) are crucial for production of both biomass related products, such as proteins, or for the production of commodity chemicals. In many such processes a large fraction of the sugars is dissimilated to either provide free-energy (in the form of ATP) or to provide electrons (in the form of NADH). Co-consumption of methanol, which can be derived from fossil sources (via natural gas) or from biomass (via syngas) , via the above mentioned route can provide NADH and/or ATP, thereby creating the possibility to utilise the sugars more efficiently. It would therefore be advantageous to co-feed S. cerevisiae with methanol during fermentations since it is a cheap alternative to sugars as energy source. Efficient dissimilation of the intermediate formaldehyde is a crucial first step for utilisation of methanol by S. cerevisiae. Therefore, this study analyses the effect of co-expression of H. polymorpha FLD1 encoding NAD+-dependent formaldehyde and FMD encoding formate dehydrogenases, on tolerance to formaldehyde and co-consumption of formaldehyde by S. cerevisiae.",
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