Fatty alcohols in the C12-C18 range are used in personal care products, lubricants, and potentially biofuels. These compounds can be produced from the fatty acid pathway by a fatty acid reductase (FAR), yet yields from the preferred industrial host Saccharomyces cerevisiae remain under 2% of the theoretical maximum from glucose. Here we improved titer and yield of fatty alcohols using an approach involving quantitative analysis of protein levels and metabolic flux, engineering enzyme level and localization, pull-push-block engineering of carbon flux, and cofactor balancing. We compared four heterologous FARs, finding highest activity and endoplasmic reticulum localization from a Mus musculus FAR. After screening an additional twenty-one single-gene edits, we identified increasing FAR expression; deleting competing reactions encoded by DGA1, HFD1, and ADH6; overexpressing a mutant acetyl-CoA carboxylase; limiting NADPH and carbon usage by the glutamate dehydrogenase encoded by GDH1; and overexpressing the 9-desaturase encoded by OLE1 as successful strategies to improve titer. Our final strain produced 1.2 g/L fatty alcohols in shake flasks, and 6.0 g/L in fed-batch fermentation, corresponding to similar to 20% of the maximum theoretical yield from glucose, the highest titers and yields reported to date in S. cerevisiae. We further demonstrate high-level production from lignocellulosic feedstocks derived from ionic-liquid treated switchgrass and sorghum, reaching 0.7 g/L in shake flasks. Altogether, our work represents progress towards efficient and renewable microbial production of fatty acid derived products.

General information
State: Published
Organisations: Novo Nordisk Foundation Center for Biosustainability, Synthetic Biology Tools for Yeast, Lawrence Berkeley National Laboratory
Pages: 115-125
Publication date: 2017
Peer-reviewed: Yes

Publication information
Journal: Metabolic Engineering
Volume: 42
ISSN (Print): 1096-7176
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 7.95 SJR 3.337 SNIP 1.787
Web of Science (2017): Impact factor 7.674
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 8.33 SJR 3.626 SNIP 1.865
Web of Science (2016): Impact factor 8.142
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 8.2 SJR 3.6 SNIP 1.809
Web of Science (2015): Impact factor 8.201
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 7.23 SJR 3.395 SNIP 2.009
Web of Science (2014): Impact factor 6.767
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 8.43 SJR 4.036 SNIP 2.164
Web of Science (2013): Impact factor 8.258
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): CiteScore 6.72 SJR 2.989 SNIP 1.847
Web of Science (2012): Impact factor 6.859