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Engineering of *Saccharomyces cerevisiae* toward n-butanol production

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Biobutanol represents a second generation biofuel, which can be produced naturally by a number of microorganisms. This alcohol has a number of significant advantages over bioethanol in terms of its physical properties as a fuel, but production systems suffer from various drawbacks. Therefore, we sought to transplant an entire butanol production pathway (the ABE pathway) into a *Saccharomyces cerevisiae* strain. However, this pathway was incapable of generating reasonable yields of butanol without further metabolic alteration to channel carbon towards the substrate of butanol production, acetyl CoA. For instance, the major alcohol dehydrogenase, *ADH1*, was deleted and two enzymes involved in acetyl-CoA biosynthesis were overexpressed to give strains capable of producing 300 mg/L butanol. Surprisingly, deletion of the *ADH1* gene alone is sufficient to produce 40 mg/L butanol from an endogenous pathway. Previously, this endogenous butanol production pathway was characterized and proposed to derive from the mitochondrial catabolism of threonine via multiple leucine biosynthetic genes and the conversion of 2-ketovalerate to butanol. Therefore, in the studies described here, we aimed to understand the relative contribution of exogenous and the endogenous pathways of butanol synthesis to overall butanol yields. Work will be presented to suggest that both pathways are active in yeast *adh1*Δ mutants, but that the endogenous route for butanol synthesis is weaker and does not use the pathway previously proposed via Leucine metabolic enzymes. This work therefore makes use of synthetic biology and metabolic engineering to effectively set the scene for an initiative towards higher yields of butanol in yeast via concerted interventions in both the endogenous and exogenous pathways.

Biography

Reem Swidah has completed her PhD from Manchester University in 2016 and she has been working with her supervisors Mark Ashe and Chris Grant on biofuel production from yeast. She has published her first paper in *Biotechnology for Biofuels.*

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