

Rerouted PKA Signaling Coordinates Sugar And Hypoxia Responses For Anaerobic Xylose Fermentation In Yeast

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Project Goals:

We aim to better understand the metabolism of strains engineered and evolved for anaerobic xylose fermentation using multi-omics and network analysis. Using these data, we also set out to improve anaerobic xylose fermentation and to decouple metabolism from growth in order to promote flux of carbon toward ethanol production rather than cell biomass. The knowledge gained from this study can potentially be applied to other strains for production of other desired chemicals using cellulosic biomass and yeast.

Microbes can be engineered for novel metabolism to produce biofuels and chemicals, but rerouting metabolic flux toward products remains a major hurdle. We used multi-omics and network analysis to explore cellular rewiring across a panel of yeast strains engineered for anaerobic xylose fermentation, important for sustainable biofuel production from plant cellulosic biomass. We show that rerouted Protein Kinase A (PKA) signaling regulates both hypoxia and sugar responses, in part via the transcription factor Azf1, catalyzing a cascade of effects correlated with anaerobic xylose growth. By deleting the PKA regulatory subunit we successfully decoupled growth and metabolism, enabling us to distinguish phosphorylation changes related to xylose-dependent growth *versus* metabolism. Using this information, we generated an industrially relevant strain with high rates of anaerobic xylose conversion.

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