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Lipid Accumulation in Nitrogen and Phosphorus-Limited Yeast is Caused by Less Growth-Related Dilution

Background/Objective

Oleaginous yeasts commercially produce oleochemicals and have strong potential for biodiesel production. Under nitrogen (N) or phosphorous (P) limitation, they accumulate lipids, primarily as triacylglycerols. Previous work investigated potential mechanisms how these limitations induce lipid biosynthesis without verifying whether lipid biosynthesis flux is actually enhanced. Here, we investigated lipid biosynthesis of two divergent oleaginous yeasts, *Rhodotorula toruloides* and *Yarrowia lipolytica*, to find the main driver of lipid accumulation.

Approach

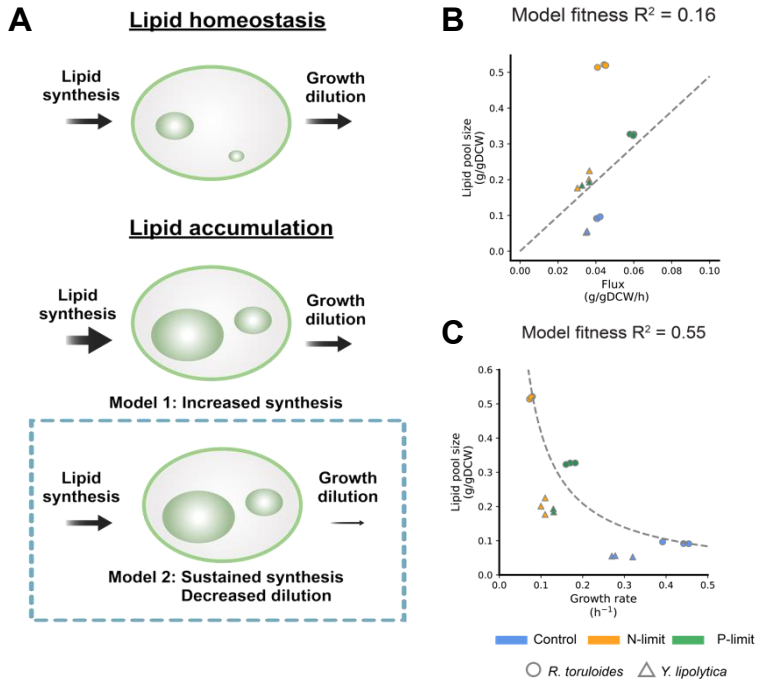
Each yeast was grown under N-limited, P-limited and non-limiting (control) conditions, and biosynthetic fluxes to lipid and protein biomass were quantified using ^{13}C-glucose isotope tracing. Quantitative proteomics measured protein abundances across nutrient conditions to assess pathway-level proteome allocation. The data were integrated into a simple model to assess whether biosynthetic flux or growth-related dilution is the primary driver of changes in lipid pool size.

Results

Under N- or P- limitation, lipid accumulation occurs without consistent increases in lipid biosynthetic flux. At the proteome level, lipid biosynthetic enzymes are largely preserved, while ribosomal proteins are strongly downregulated. Accordingly, nutrient limitation, rather than triggering greatly enhanced lipid synthesis, results in sustained lipid enzyme levels and biosynthetic flux. Due to slower lipid dilution by cell division, this suffices to drive marked lipid accumulation.

Significance/Impacts

This work highlights a central role for cellular growth rate in controlling bioproduct titers.



(A) Two models for lipid accumulation in response to nutrient limitation. (B) Lipid pool sizes with variable biosynthetic flux and fixed growth rate, and conversely, (C) fixed flux and variable growth rate.

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