

# Nitrogen Starvation Causes Lipid Remodeling in Rhodotorula toruloides

## **Background/Objective**

Oleaginous yeast *Rhodotorula toruloides* is a promising yeast for biomanufacturing oleochemicals because it can accumulate lipids at a high biomass fraction. Metabolic engineering efforts in this organism have progressed slower than in the more extensively studied model yeasts, and few studies have investigated its lipid accumulation phenotype exhibited under nitrogen limitation conditions. Consequently, few studies exploited its lipid metabolism for higher product titers. We performed a multi-omic investigation of *R. toruloides* under nitrogen limitation to understand the mechanism of lipid accumulation.

#### **Approach**

A baseline phenotype and a lipid accumulation phenotype of *R. toruloides* IFO0880 were cultured in nitrogen-sufficient and nitrogen-limited conditions. The dynamics of lipid accumulation as a function of growth were investigated by studying the cultures in different phases of growth. Cells from both conditions underwent a comprehensive study that integrated transcriptomic and lipidomic analyses — the first of its kind for lipid accumulation in this organism.

#### Results

*R. toruloides* underwent lipid remodeling during nitrogen limitation, transferring carbon from phospholipids to storage lipids. The multi-omic analysis suggested that selective regulation within lipid biosynthesis controls for the specific increase of storage lipids.

### Significance/Impacts

These new insights in the mechanisms of lipid accumulation can lend to the success of future metabolic engineering strategies for the overproduction of oleochemicals.

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Variation in the fraction of total lipid pool in *R. toruloides* IFO0880 at each time point and for each growth condition. The solid line represents the phospholipid fraction, and the dash-dot line represents the storage lipid fraction.



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