CABBI
CENTER FOR ADVANCED BIOENERGY AND BIOPRODUCTS INNOVATION

High Yield Production of 3-Hydroxypropionic Acid using *Issatchenkia orientalis*

Background/Objective

Currently, 3-hydroxypropionic acid (3-HP) is produced almost exclusively via chemical synthesis. Both bacteria and yeasts have been extensively explored for biological production, but the inhibitory effects of the low pH fermentation on bacterial growth necessitates complex and costly downstream processing. We sought to develop a cost-effective biological process by utilizing the low-pH tolerant yeast *I. orientalis*.

Approach

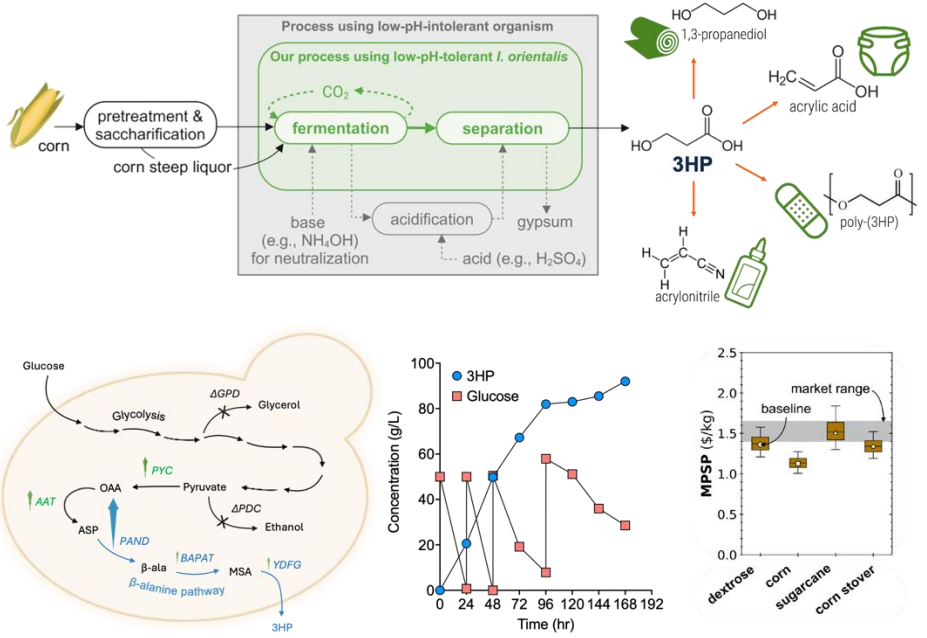
- Identified the β-alanine pathway as the most favorable route to produce 3-HP using genome-scale modeling and thermodynamic analysis.
- Discovered highly active variants of key pathway enzymes (*PAND*, *BAPAT*, and *YDFG*) to enhance efficiency using sequence similarity network analysis and enzyme screening.
- Optimized the pathway through multi-copy *PAND* integration, byproduct elimination, and reinforcement of aspartate flux by overexpression of *PDC* and *AAT* enzymes.
- Optimized fed-batch fermentation under low-pH conditions using corn steep liquor and performed techno-economic and life cycle analyses (TEA/LCA) to evaluate industrial feasibility.

Results

The engineered strain produced 3-HP at 92 g/L with 0.7 g/g yield and 0.55 g/L/h productivity at pH 4. TEA/LCA indicates that such performance could potentially enable a financially viable process for bio-based acrylic acid production.

Significance/Impacts

Engineering the acid-tolerant yeast *I. orientalis* as a robust host for low-pH 3-HP biosynthesis paves the way toward industrial translation.



Overview of engineering the low-pH-tolerant yeast *I. orientalis* for financially viable, bio-based 3-HP production

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