**Engineering *Yarrowia lipolytica* for high-yield lipid production   
from lignocellulosic biomass**

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**Highlights**

* *Yarrowia lipolytica* was engineered to efficiently convert xylose into lipids
* Isomerase-base pathway enabled *Y. lipolytica* high-yield lipid production from xylose
* Isomerase-based pathway supported simultaneous co-fermentation of glucose and xylose

**1. Introduction**

Lignocellulosic biomass is one of the most attractive renewable resources for fuels and chemicals production. *Yarrowia lipolytica*, non-conventional oleaginous yeast, is a promising host for biodiesel and oleochemical production from lignocellulosic biomass. With advances in metabolic engineering, *Y. lipolytica* efficiently converts glucose into lipids up to 90% of its cell mass [1]. Yet, *Y. lipolytica* hardly utilize xylose, the second most sugar component of lignocellulosic biomass, limiting high-yield lipid production from lignocellulosic biomass.

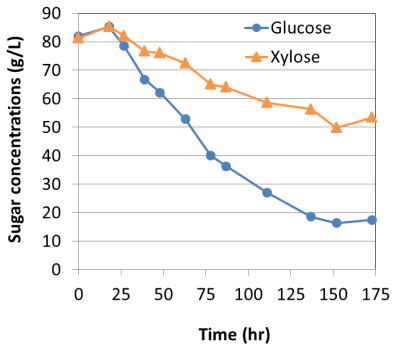
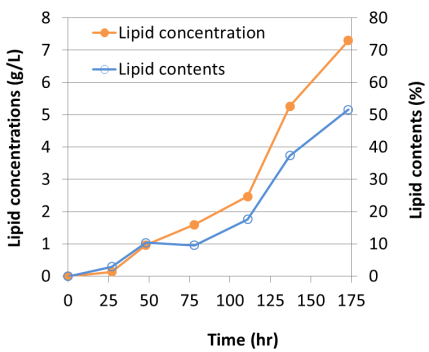
**2. Methods**

To efficiently produce lipids from lignocellulosic biomass, we developed an efficient xylose utilizing *Y. lipolytica* harboring isomerase-based pathway. To do so, we first introduced xylose isomerase pathway, and then evolved the rationally engineered strain to better support xylose metabolism. The xylose utilizing performance of the engineered strain was evaluated during xylose fermentation as a sole carbon source, and during the fermentation of lignocellulosic hydrolysates.

**3. Results and discussion**

The newly developed xylose utilizing *Y. lipolytica* (YSXAK) showed high-yield lipid production from xylose as a sole carbon source. The lipid yield of isomerase-based xylose utilizing strain of YSXAK was five times higher than that of an oxidoreductase-based strain with cofactor imbalance issue [2]. Moreover, YSXAK simultaneously utilized both glucose and xylose to produce lipids suggesting efficient co-fermentation of lignocellulosic biomass. To understand the different genetic background contributed to efficient xylose utilization, comparative whole-genome sequence analysis was conducted identifying beneficial mutations occurred during evolutionary engineering.

**A B**

**Figure 1.** Sugar consumption and lipid production of xylose utilizing *Y. lipolytica* during glucose/xylose co-fermentation

**4. Conclusions**

Through combinatorial engineering, we developed an efficient isomerase-based xylose utilizing strain of *Y. lipolytica*, and demonstrated high-yield lipid production from xylose and simultaneous co-fermentation of glucose and xylose. This study shows the potential of xylose utilizing *Y. lipolytica* harboring an isomerase pathway for more economical and sustainable biodiesel and oleochemical production from lignocellulosic biomass.

**References**

1. J. K. Ko, S. Lee, Curr. Opin. Biotech. 50(2018) 72-80
2. H. Li, H. Alper, Biotechnol. J. 11 (2016) 1230-1240