

Leveraging Comparative Population Genomics to Dissect the Mechanisms of *Issatchenkia orientalis* Fluconazole Resistance

Ping-Hung Hsieh^{1,2}, Yusuke Sasaki^{1,2}, Jing Ke², Zhiying Zhao², and Yasuo Yoshikuni^{1,2*}
(yyoshikuni@lbl.gov)

¹DOE Center for Advanced Bioenergy and Bioproducts Innovation, ²Lawrence Berkeley National Laboratory, Berkeley, CA

<https://cabbi.bio/>

Project Goals: Short statement of goals. (Limit to 1000 characters)

Issatchenkia orientalis is an emerging non-model ascomycetes yeast with unparalleled ability to tolerate multiple stresses, including extremely low pH, high temperature, and high concentrations of lignocellulosic inhibitors, salts, alcohols, and organic acids. These unique characteristics may make *I. orientalis* an attractive chassis for producing biofuels and bioproducts directly from lignocellulosic hydrolysates. Understanding how *I. orientalis* evolved to tolerate multiple stresses may allow engineering of a strain more suitable for industrial use than natural isolates are. We performed a population genomics study of 162 strains collected from various habitats and identified 305,435 single nucleotide polymorphism (SNPs), 16,177 insertions and deletions (indels), and other genetic variations, including ploidy, gene copy number, and pan-genome variations. We are currently working on genome-wide association study (GWAS) to understand genetic variations underlying various phenotypes. Here we discuss the results for fluconazole resistance, an unfavorable characteristic for industrial utilization of microbes.

References

1. Mesquita, Vanessa A., et al. (2015) Impact of Multi-Metals (Cd, Pb and Zn) Exposure on the Physiology of the Yeast *Pichia kudriavzevii*. *Environmental Science and Pollution Research*. 22(14): 11127–11136.
2. Isono, Naoto, et al. (2012) A Comparative Study of Ethanol Production by *Issatchenkia orientalis* Strains under Stress Conditions. *Journal of Bioscience and Bioengineering*. 113(1): 76–78.
3. Peter, Jackson, et al. (2018) Genome Evolution across 1,011 *Saccharomyces cerevisiae* Isolates. *Nature*. 556(7701): 339–344.

Funding statement.

This work was funded by the DOE Center for Advanced Bioenergy and Bioproducts Innovation (U.S. Department of Energy, Office of Science, Office of Biological and Environmental Research under Award Number DE-SC0018420). The work conducted by the U.S. Department of Energy Joint Genome Institute, a DOE Office of Science User Facility, is supported under Contract No. DE-AC02-05CH11231. Any opinions, findings, and conclusions or recommendations expressed in this publication are those of the authors and do not necessarily reflect the views of the U.S. Department of Energy.