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UNIVERSITY OF WISCONSIN–MADISON

FRESH Seminar: "*Saccharomyces* Diversity and the Tools to Tap It"
Presented by Chris Hittinger, PhD, Dept. of Genetics, UW–Madison
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MADISON, Wis. (FRI) – Chris Todd Hittinger, PhD, Assistant Professor of Genetics at UW-Madison, provided an illuminating discussion of the evolutionary history of *Saccharomyces*, the applicability of this yeast genus as a model system, and how the diversity now apparent within the genus might be "tapped" at the second FRI-sponsored FRESH seminar on Sept. 30.

Bread, wine, and beer production all have depended upon yeast for thousands of years, and yeast continues to be important to humans, both as an opportunistic pathogen and in new commercial areas such as biofuel production. Until recently, however, little has been known about where *Saccharomyces* originated or its evolutionary history.

In addition to its commercial utility, *Saccharomyces* also is valued highly as a model organism in genetic research. Among its strengths: it can exist as a single-celled eukaryote and replicates quickly. It can undergo sexual reproduction, making it useful in evolutionary studies. Its genome is 300-fold smaller than the human genome, which makes genomic analyses cheap. And finally and importantly, it is possible to have complete genetic and environmental control of the organism.

There are, however, some reasons why yeasts are not ideal model organisms. First, yeast strain collections are missing large swaths of biodiversity as they are biased heavily towards those used for commercial applications. General tools for genetic manipulation across yeast species have not been available. Hittinger's lab has worked to remove some of these obstacles to the more widespread and generalizable use of *Saccharomyces* in research and industry.

In 1999, the taxonomy of *Saccharomyces* was relatively "boring," with only three known species. Now there are 7 known species, with at least 4 used commercially as interspecies hybrids to produce fermented beverages. Lager yeast is an interspecies hybrid between *S. cerevisiae* and *S. eubayanus*, while many Belgian-style brews (including some products from local brewery New Glarus Brewing Company) utilize a different interspecies hybrid (between *S. cerevisiae* and *S. kudriavzevii*. These interspecies hybrids arise when two haploid spores from different species form a diploid strain (or by slightly more complicated mechanisms) that cannot then generate spores due to the large amount of genetic diversity between the original haploid strains. The hybrids can reproduce clonally, but not sexually.

Finding the wild progenitors of the interspecies hybrid strains used in brewing has been an important challenge in understanding the evolution of *Saccharomyces*. Hittinger was part of the group that found the first parent *S. eubayanus* strain in Patagonia, and now more than 200 wild isolates of *S. eubayanus*

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have been identified there. A citizen-science program initiated by Hittinger's lab to collect yeast isolates from soil and trees around the United States recently discovered the first isolate of *S. eubayanus* in North America (in Sheboygan, Wis.); other isolates in the U.S. have been found since by the team.

Sequencing Patagonian *S. eubayanus* strains led to the realization that there are two distinct *S. eubayanus* populations in South America, and that *S. eubayanus* is native, but not endemic to Patagonia. The related cold-tolerant species, *S. uvarum*, which is the progenitor of many Champagne yeasts, also has two distinct populations in Patagonia, one of which is related to the North American/European/Asian isolates, which exhibit little diversity.

In addition to improving the understanding of the evolution of and diversity in *Saccharomyces* strains, Hittinger's group also has engineered general tools that can be used to manipulate yeast across fungal species. Such a system requires a selectable (+) marker, a counterselectable (-) marker, and a double-stranded break generator. The lab took advantage of the fact that fungi lack the enzyme thymidine kinase; thymidine kinase (TK) is, therefore, used as the selectable marker, while antifolate substrates of TK can be used to kill cells that are TK(+). The Hittinger group also has engineered a novel method using a 3.2 kB DNA cassette to generate double-stranded DNA breaks at the same place in both chromosomes, greatly improving the probability that diploid cells would pick up exogenous linear DNA rather than simply repairing the double-strand break.

Using Hittinger's system, even wild diploid yeast strains, such as those his group continues to isolate, can now be engineered, opening the door for manipulation of many different yeast strains, not just highly similar laboratory strains, for commercial use.

Summary by Wendy Bedale, Science Writer, Food Research Institute

About the Food Research Institute

The Food Research Institute (FRI), a part of the College of Agricultural and Life Sciences at the University of Wisconsin–Madison, operates its own laboratories and administers its own research and service programs. The mission of FRI is to catalyze multidisciplinary and collaborative research on microbial foodborne pathogens and toxins and to provide training, outreach and service to enhance the safety of the food supply. To fulfill this mission, FRI conducts fundamental and applied research, provides accurate and useful information and expertise, delivers quality education and training, and provides leadership in identifying and resolving food safety issues to meet community, government, and industry needs.

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