

# Heads up: New DNA study reveals evolution of beer yeasts

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Lager lovers convinced that their beer of choice stands alone should prepare to drink their words this Oktoberfest. New research by geneticists at the Stanford University School of Medicine indicates that the brew, which accounts for the majority of commercial beer production worldwide, owes its existence to an unlikely pairing between two species of yeast - one of which has been used for thousands of years to make ale.

The research offers a fascinating glimpse into the early history of beer brewing, as well as an unheralded sneak peek at the early days of the evolution of a new yeast species. Then, as now, brewers reused yeast in several successive fermentation batches, unconsciously selecting for the traits that made the most desirable beer.

"These long-ago brewers were practicing genetics without even knowing it," said geneticist Gavin Sherlock, PhD. "They've given us a very interesting opportunity to look at a relatively young, rapidly changing species, as well as some very good beer." The research will be published online Sept. 11 in *Genome Research*.

It all started with some unhappy Bavarians. Dissatisfied with the quality of beer brewed in the summer months, they forbade brewing the beverage when the weather was warm. However, colder winter temperatures inhibited fermentation by the ale yeast that had been used for hundreds of years and fostered an unlikely pairing with a second, heartier species-producing an unusual crisp, clear brew that became

today's lager.

Sherlock, an assistant professor of genetics, and Barbara Dunn, PhD, a senior research associate at the medical school, studied the genetic sequences of 17 unique lager yeast strains from breweries in Europe and the United States. They used customized DNA microarrays capable of analyzing the relative contribution of each parent, combined with limited DNA sequencing, to determine that the hybridization event actually occurred not once, as previously speculated, but twice. This genetic encore suggests that each partner brought specific, unique advantages to the match.

"It's possible that the ale strain provides a certain flavor profile, while the second strain conferred the ability to ferment at cooler temperatures," said Dunn. "Mixing them together is a nice way for the yeast to double its genetic options."

Traditionally, ales are fruity-flavored and likely to be cloudy. Although they may have a more complex flavor profile than lagers, they are best consumed at warmer temperatures and are less stable. In fact, the word "lager" is a derivative of a German word that means "storage."

Most yeast reproduce primarily by asexual budding - pinching off one identical daughter cell after first duplicating the parent's genetic material. Occasionally they go through sexual reproduction and form spores that can mate with another spore of the same species and then continue to bud asexually. The parental strains of the lager yeast chose yet another path. They looked outside their own kind, hybridizing (or fusing) to form a blend of both species better suited to the new, colder conditions.

The participants in this microscopic alliance were members of a larger genus known as *Saccharomyces*. One species in the group,

*Saccharomyces cerevisiae*, commonly known as "bakers' yeast," has been used for thousands of years to make both bread and ale. *S. cerevisiae* grows best at temperatures between about 85 and 90 degrees Fahrenheit. The other, *S. bayanus*, grows best at about 70 to 75 degrees and can tolerate even colder temperatures. Together they formed a lineage known as *S. pastorianus*. Sherlock and Dunn compared the *S. cerevisiae* parent of *pastorianus* to a variety of strains, including those involved in fermenting wine and sake, before pegging it as an ale-specific strain.

"We were excited to find this connection, because it makes so much sense," said Sherlock. "The same breweries were used for both ale and lager, so it was really gratifying."

As often happens, the offspring of such an unconventional union exhibited abnormal amounts of genetic material. Sherlock and Dunn believe that one lineage began with approximately equal amounts of each yeast's genome, whereas the other has between two to three more times *S. cerevisiae* than *S. bayanus* DNA. Studying the spread of the two groups provides a genetic snapshot of lager brewing in Europe during the past 600 years: one lineage is associated primarily with Carlsberg breweries in Denmark and others in what is now Czechoslovakia, while the other group localizes to breweries in the Netherlands, including Heineken.

Furthermore, it's normal after such a hybridization event for the progeny to slowly lose excess DNA. Parsing out what has been lost and when in the relatively young hybrids is one way researchers can shed light on the process of evolution and the specific genes responsible for pleasing the palates of beer drinkers worldwide.

"When we look at the genes that have either been lost or amplified in copy number, we can make the case that some of them could be related to brewing," said Sherlock. Specifically, the researchers identified

differences in genes involved in sugar metabolism and the clumping of the yeast after fermentation.

Why was beer so important in the Middle Ages?

"Beer, or ale, was the standard drink at the table," said Dunn. "Alcohol was considered healthy, in part because water at that time was often contaminated. And if you're drinking beer every day, you might want something that tasted pretty good."

Source: Stanford University

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