# Japanese sake: The new pick-me-up? Yeast strain makes fatigue-fighting amino acid

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Fans of sake, the traditional Japanese alcoholic beverage, may have even more reason to enjoy it now: Japanese scientists have discovered that a mutant strain of sake yeast produces high levels of the amino acid

ornithine.

In a study published this month in *Metabolic Engineering*, researchers from the Nara Institute of Science and Technology and the Nara Prefecture Institute of Industrial Development have revealed that a mutant strain of sake yeast produces 10 times the amount of the amino acid ornithine compared with the parent yeast strain.

Ornithine is a non-protein-making amino acid and a precursor to two amino acids—arginine and proline. It has been found to perform several physiological functions, such as reducing fatigue and improving sleep quality.

"We wanted to obtain sake yeast strains with improved ethanol tolerance," says a first author of this article, Masataka Ohashi. "During sake fermentation, the yeast is exposed to high concentrations of ethanol, which impedes yeast cell growth, viability and fermentation. Increased ethanol tolerance in sake yeast strains could improve ethanol production and reduce fermentation time."

To find ethanol-tolerant yeast strains, the researchers isolated mutants that accumulated proline, which can alleviate ethanol toxicity, using a conventional mutagenesis (i.e., one that doesn't involve genetic modification). They also conducted whole genome sequencing analysis, and performed brewing tests with sake yeast strains. Then they identified and analyzed a new mutation in a gene that encodes a variant of N-acetyl glutamate kinase that increases intracellular ornithine level.

"We previously constructed self-cloning industrial yeast strains that accumulate proline to increase ethanol tolerance and productivity of yeast," explains Prof. Hiroshi Takagi, a corresponding author. "But those yeasts have not been yet acceptable to consumers because they're considered to be genetically modified, even though a self-cloning yeast

has no foreign genes or DNA sequences—they only have yeast DNA."

The researchers successfully isolated non-genetically modified yeasts that produced 10 times the amount of ornithine compared with the parent strain, which is widely used in Japanese sake breweries, and the sake brewed with them contained 4-5 times more ornithine.

The results of this study will contribute to the development of improved yeast strains for production of high levels of ornithine, and the strain obtained in this study could be readily applied to sake, wine, and beer brewing. Ornithine-accumulating yeast strains could also be used in the production of ornithine-rich dietary supplements made from these yeasts and their products.

Prof. Takagi also describes "There are two major purposes for breeding of industrial yeast: improvement of fermentation ability with enhanced tolerance to environmental stresses during fermentation processes and diversity of product taste and flavor with modified metabolic pathways. In yeast, amino acid metabolisms vary under different growth environments and the metabolic styles form a complicated but robust network. The elucidation of metabolic regulatory mechanisms and physiological roles for amino acids is important fundamental research for understanding life phenomenon. The yeast is reliable and safe in food production, and thus the development of novel strains that overproduce 'functional amino acids' such as ornithine, proline and branched-amino acids, would greatly contribute to food-related industries."

**More information:** Masataka Ohashi et al. High-level production of ornithine by expression of the feedback inhibition-insensitive N-acetyl glutamate kinase in the sake yeast Saccharomyces cerevisiae, *Metabolic Engineering* (2020). DOI: 10.1016/j.ymben.2020.08.005

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