NAIST® Research Highlights

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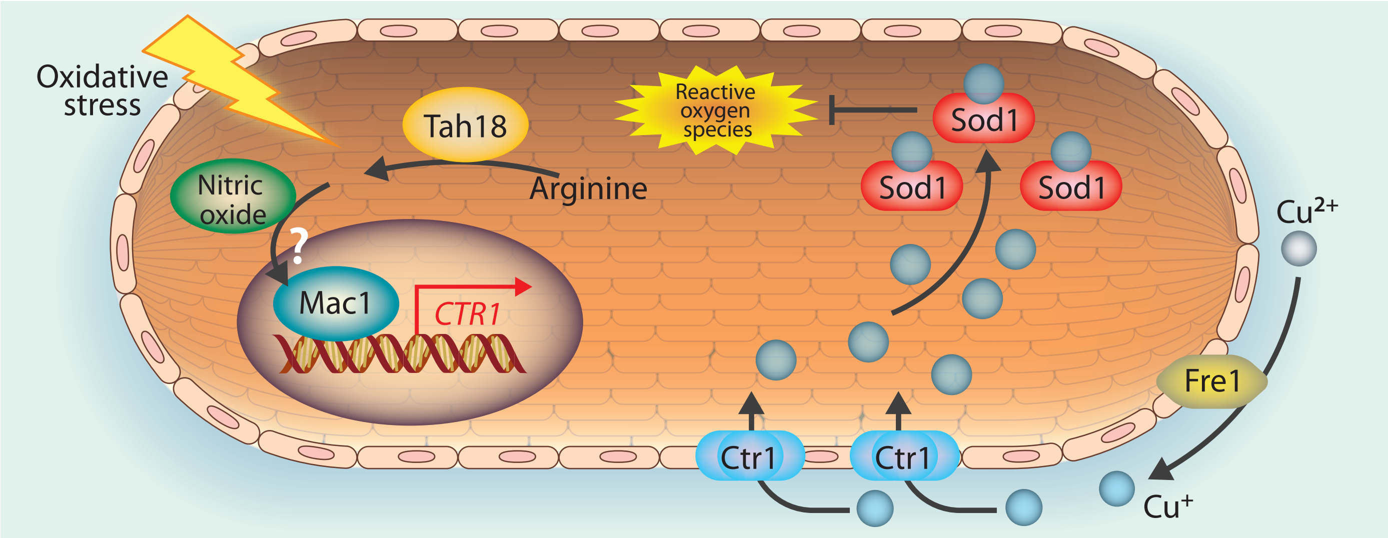

Nitric oxide (NO) produced by yeast cells in response to oxidative stress triggers an influx of copper (Cu) through the activity of the regulatory protein Mac1.

Microbiology

Yeasts with better stress tolerance

Copper helps yeast deal with temperature extremes, pointing to gains in fermentation and biofuels

Yeast responds to the stress of high temperatures by activating a genetic pathway involved in copper uptake and metabolism, researchers at Japan's NAIST have found[1]. The discovery could help bioengineers develop heartier yeast varieties for use in the food and biotechnology industries.

"Environmental stresses induce growth inhibition or cell death, which limits the fermentation ability of yeast," says Hiroshi Takagi, a molecular microbiologist at NAIST who led the study. "Our findings could contribute to the construction of new yeast strains with higher stress tolerance, leading to the effective production of breads, alcoholic beverages and bioethanol."

In 2013, Takagi and his colleagues discovered a novel mechanism by which the budding yeast *Saccharomyces cerevisiae* — widely used in winemaking, baking and brewing — deals with the potential damage wrought by outside pressures such as elevated temperatures. They found that the microorganism produces nitric oxide (NO), a molecule that confers protection against the damaging reactive oxygen species created in the wake of extreme heat[2]. Takagi's team showed that a protein called Tah18 was involved in NO production, but the mechanism underlying how NO aids in stress tolerance remained unclear.

The researchers therefore analyzed the gene expression profile of yeast cells exposed to NO in the laboratory. They have now discovered that genes involved in the transport of heavy metal ions, such as copper, are activated by the NO treatment. These genes are under the control of a regulatory protein called Mac1. Since Mac1 is important for tolerance to other types of stress, Takagi's team suspected that it might play a role in NO-mediated stress responses as well.

Indeed, the researchers found that NO produced under stressful conditions of high temperatures activated Mac1 in the yeast. This set in motion a molecular cascade that increased the amount of copper inside the cell; and the influx of copper in turn triggered an enzyme called Sod1, a type of 'superoxide dismutase' that destroys toxic free radicals and thus helps to boost cell viability (see figure).

Putting all the pieces together, Takagi says: "Our main conclusion of this work is that NO enhances the activity of Sod1, which is one of the most important antioxidative enzymes." This knowledge could pave the way for synthetic biologists to craft stress-resistant yeast strains for the fermented breads, beverages and biofuel sectors[3]. These designer yeast strains could be a huge economic boost for the fermentation industries.

References

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2. Nishimura, A., Kawahara, N. & Takagi, H. The flavoprotein Tah18-dependent NO synthesis confers high-temperature stress tolerance on yeast cells. *Biochemical and Biophysical Research Communications* **430,** 137–143 (2013).
3. Sasano, Y., Haitani, Y., Hashida, K., Ohtsu, I., Shima, J. & Takagi, H. Enhancement of the proline and nitric oxide synthetic pathway improves fermentation ability under multiple baking-associated stress conditions in industrial baker's yeast. *Microbial Cell Factories* **11,** 40 (2012).

More information about the group's research can be found at the Laboratory of Applied Stress Microbiology webpage: http://bsw3.naist.jp/eng/courses/courses305.html