Kimura Kazuyoshi et al., Bioenergetics 2017, 6:2(Suppl)
DOI: 10.4172/2167-7662-C1-003

Improvement in sustainable production of valuable lipids by lipid-accumulating yeast

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We have obtained oleaginous yeast transformants culture using genetic engineering and fermentation technology using *Saccharomyces cerevisiae* which is originally poor in lipid. We showed the attractive production system of the alternative resource of lipids using the oleaginous transformants. Natural *S. cerevisiae* accumulates storage lipids only around 5% in the cell. From this yeast, we have constructed transformants with high lipid content. A transformant overexpressing DGA1 and LEU2 in the nitrogen-limited medium showed lipid content of 27%. Furthermore, the dga1 disruptant overexpressing DGA1 and LEU2 in the medium containing 10% glucose showed lipid content of 38% and the disruptant overexpressing modified DGA1 and LEU2 showed 45%. Using this dga1 disruptant, we establish a new palmitoleic acid (POA, 16:1n-7) production system. POA has been reported to prevent lifestyle diseases such as diabetes and cardiovascular disease. POA is relatively rare in common plant oils and its supply is not currently sufficient. Using the above transformant, POA production was increased at the high concentration of methionine (2 g/l). Finally, we achieved the yeast cells of 45% lipid content with POA content up to 55%. We have constructed the PUFA (polyunsaturated fatty acids)-producing *S. cerevisiae* system using the transformants overexpressing DGA1, LEU2 and desaturase genes in the snf2 disruptant. Delta-6 desaturation, known as the rate-limiting step in PUFA biosynthesis, was investigated in detail to improve its productivity. The above transformant with Δ6 desaturase gene converted only 5% of added α-linolenic acid (ALA; 18:3n-3) to stearidonic acid (STA; 18:4n-3) under the usual culture condition. Addition of histidine more than 0.2 g/l increased the STA production nearly twice. Furthermore, the simultaneous addition of some alkylphenol ethoxylate surfactants at high concentrations improved the STA production. Finally, more than 0.35 g/l STA were produced in the broth with more than 35% STA yield against the source ALA.

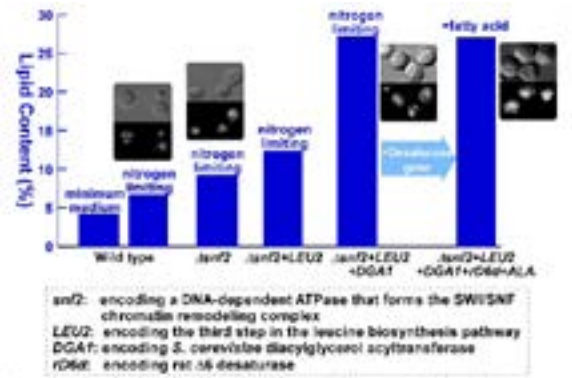

Figure 1: Lipid content was improved by the *snf2* disruption, *LEU2* overexpression, and *DGA1* oversexpression to produce PUFA

Recent Publications:

1. Kamisaka Y, Tomita N, Kimura K, Kainou K and Uemura H (2007) DGA1 (diacylglycerol acyltransferase gene) overexpression and leucine biosynthesis significantly increase lipid accumulation in the Δsnf2 disruptant of *Saccharomyces cerevisiae*. Biochemistry Journal 408:61-68.
2. Kamisaka Y, Kimura K, Uemura H and Yamaoka M (2013) Overexpression of the active diacylglycerol acyltransferase variant transforms *Saccharomyces cerevisiae* into an oleaginous yeast. Applied Microbiology and Biotechnology 97:7345–7355.
3. Kamisaka Y, Kimura K, Uemura H and Yamaoka M (2015) Addition of methionine and low cultivation temperatures increase palmitoleic acid production by engineered *Saccharomyces cerevisiae*. Applied Microbiology and Biotechnology 99:201–210.
4. Kimura K, Tomita N, Uemura H, Aki T, Ono K and Kamisaka Y (2009) Improvement of stearidonic acid production in oleaginous *Saccharomyces cerevisiae*. Bioscience, Biotechnology and Biochemistry 73(6):1447-1449.
5. Kimura K, Kamisaka Y, Uemura H and Yamaoka M (2013) Increase in stearidonic acid by increasing the supply of histidine to oleaginous *Saccharomyces cerevisiae*. Journal of Bioscience and Bioengineering 117:53–56.

Biography

Kimura Kazuyoshi is a Senior Researcher in Bioproduction Research Institute, National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba, Japan. His research interest includes lipid metabolism and fermentation technology for the lipid production using microbes.

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