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Editorial overview: Food biotechnology: Critical gap filler in the nexus of food, energy, and waste for a prosperous future

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Introduction

The rapidly increasing world population is expected to reach 8.5 billion by 2030. Improving yields and rates of traditional food production based on classical chemical and physical principles will not be able to meet the leaping demands. As such, food biotechnology will play an important role in the nexus of food, energy, and waste for maintaining quality of human life. In particular, economic, sustainable, and safe production of food through biotechnological innovations will be critically necessary. The research directions of food biotechnology are thus categorized into three areas. First, we will need to produce food materials and ingredients more and better using less energy with less production of waste. Second, we will need to maintain quality and ensure safety of foods during the production, distribution, and consumption periods. Third, we will need to expand the functions of food for promoting health and preventing diseases beyond the supply of energy and nutrition. While these are daunting tasks, recent advances in biological research tools, such as systems and synthetic biological methods, have enabled impressive progress in the area of food biotechnology.

The idea of employing biotechnological approaches to produce crops with desired traits but requiring less agricultural management has not been well-received by consumers due to perceived environmental and health uncertainties. However, the production of food materials and ingredients through genetically engineered microorganisms (GMOs) in contained bioreactors and their applications into various foods after purification can improve consumer acceptability as associated uncertainties and risks become managed. Indeed, numerous cases of engineered microorganisms and their fermentation products have been submitted to the U.S. Food and Drug Administration (FDA) in order to obtain Generally Recognized As Safe (GRAS) status. Many of the approved cases by the FDA are currently at the stage of commercial production. For instance, the engineered *Saccharomyces cerevisiae* ML01 strain expressing malolactic enzyme from *Oenococcus oeni* and malate permease from *Schizosaccharomyces pombe* has obtained a GRAS notice (GRN 120) for the intended use in wine making. The engineered yeast can perform malo-lactic fermentation by itself so that lengthy and spoilage-prone secondary bacterial fermentations are not necessary for converting malic acid into lactic acid in red wine. Another recent example is the production of eicosapentaenoic acid (EPA)-rich triglyceride oil using engineered *Yarrowia lipolytica*. The engineered *Yarrowia* contained well-characterized genetic perturbations eliciting the enhanced production of omega-3-fatty acids. The EPA-rich oil is now under GRAS status (GRN 355) for intended uses as food ingredients. While

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detailed disclosures of strain construction, fermentation, and purification processes along with toxicological testing results are required to register, more and more engineered microorganisms and their products have been added into the FDA GRAS notice inventory.

Despite the potential benefits of genetically engineered organisms, there are at least two concerns of growing and using GMOs. The most obvious concern is regarding the incorporation of unnecessary and uncharacterized genetic elements, such as antibiotics markers, origin of replication, and multi-cloning sites, which are necessary for genetic manipulations, into GMOs. Second, the uncharacterized impacts of the introduced genetic perturbations on cellular physiology of GMOs and subsequent influences to various ecosystems have been debated for decades. Recently developed systems and synthetic biological research methods can be exploited for resolving these two concerns. Omics technologies, such as next-generation genome sequencing, RNA sequencing, and metabolite profiling, can be used to capture unknown impacts of the introduced genetic perturbations and to prove the equivalences of genetically engineered strains as compared to their parental strains. Breathtaking developments of *in vivo* genome editing methods based on Cas9 nucleases will enable precise and sophisticated genetic perturbations for constructing engineered strains using non-model microorganisms as well as model microorganisms. Omics technologies capable of reading cellular information and genome editing technologies capable of writing a code for re-programming cellular physiology as designed became two pillars of food biotechnology research. In this issue, 13 review papers addressing the key issues and breakthroughs in the following three major research directions are selected.

Sustainable and economic production of food materials and ingredients

Numerous food materials and ingredients have been produced by microbial fermentation. Mostly, naturally existing or superior mutant strains obtained by random mutagenesis have been exploited for the microbial conversion of inexpensive sugars into various food materials and ingredients. Examples include amino acids, organic acids, lipids, and sugar alcohols. Nielsen and Chen update the current status of citric acid and lactic acid *via* microbial fermentation and introduce metabolic engineering strategies for producing 3-hydroxypropionic acid and succinic acid that can be used as industrial chemicals and building blocks of various polymers. Oleaginous yeast strains accumulate substantial amounts (more than 60%) of lipids under nitrogen-limited conditions. Moreover, as improved genetic tools are available, yeast can be engineered to produce specific polyunsaturated fatty acids (PUFAs). Aggelis *et al.* discuss the microbial production of targeted PUFAs and triacylglycerols with altered structures. Not only rational engineering strategies, but also adaptive experimental evolution methods for altering the production levels, chain lengths, and degrees of desaturation of PUFAs are introduced. Sugar alcohols, such as xylitol, sorbitol, and erythritol, have been used as non-calorigenic sweeteners in the food industry. Until recently, the scale of sugar alcohol production was relatively small and the production methods were based on chemical reduction rather than microbial conversion. As sugar alcohols can be used as substrates of chemical catalysis for the production of various commodity chemicals, such as ethylene glycol and propylene glycol, the large-scale production of sugar alcohols *via* microbial fermentation of inexpensive feedstock sugars is anticipated. Seo *et al.* introduce metabolic engineering strategies that might enable economic production of sugar alcohols from lignocellulosic hydrolysates. As sugar alcohol-producing reactions require NADH or NADPH as a cofactor, cellular redox balancing strategies are discussed as well.