Strategies for producing natural and non-natural chemicals by microorganisms

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In our everyday life, we use gasoline, diesel, plastics, rubbers, and numerous chemicals that are derived from fossil oil through petrochemical refinery processes. Fossil resources are limited and not sustainable. Our world is facing problems associated with climate change and other environmental problems resulted from lavish consumption of fossil fuels. One solution to address these problems is to use renewable, non-food biomass for the production of chemicals, fuels, and materials through biorefineries.

In their paper published online in *Nature Chemical Biology* on May 17th, Professor Sang Yup Lee and his colleagues at the Department of Chemical and Biomolecular Engineering, Korea Advanced Institute of Science and Technology (KAIST), newly present general strategies for systems metabolic engineering to develop microorganisms for the production of natural and non-natural chemicals from renewable biomass.

Microorganisms are used as biocatalysts to convert biomass into the products of interest. When microorganisms are isolated from nature, however, their efficiency of producing desired chemicals and materials is rather low. Metabolic engineering is performed to improve cellular characteristics to desired levels.

Over the last decade, great advances have been made in systems biology that allows system-wide characterization of cellular networks, both qualitatively and quantitatively, followed by whole-cell level engineering

based on these findings. Furthermore, rapid advances in synthetic biology allow design and synthesis of fine controlled metabolic and gene regulatory circuits. The strategies and methods of systems biology and synthetic biology are rapidly integrated with metabolic engineering, thus resulting in "systems metabolic engineering."

According to the paper, the researchers classified the chemicals to be produced into four categories based on whether they have been identified thus far to exist in nature (natural vs. non-natural) and they can be produced by inherent pathways of microorganisms (inherent, noninherent, or created): natural-inherent, natural-noninherent, non-natural-noninherent, and non-natural-created ones.

General strategies for systems metabolic engineering of microorganisms for the production of these chemicals using various tools and methods based on omics, genome-scale metabolic modeling and simulation, evolutionary engineering, and synthetic biology are suggested with relevant examples. For the production of non-natural chemicals, strategies for the construction of synthetic metabolic pathways are also suggested. Having collected diverse tools and methods for systems metabolic engineering, the authors also suggest how to use them and their possible limitations.

Professor Sang Yup Lee said, "It is expected that increasing number of chemicals and materials will be produced through biorefineries. We are now equipped with new strategies for developing microbial strains that can produce our desired products at very high efficiencies, thus allowing cost competitiveness to those produced by petrochemical refineries."

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