



Optimize Production through Metabolic Engineering

Metabolic engineering is an emerging research field that focuses on optimizing genetic and regulatory processes within cells to increase the cells' production of a particular substance. Metabolic engineering techniques can be used to redirect cellular metabolisms to produce chemicals, fuels, novel materials, and pharmaceuticals. Researchers can use metabolic engineering tools to better understand and diagnose metabolic defects, as well as study environmental and ecological issues such as microbiome metabolism and bioremediation.

The field was originally comprised of just a few individuals attempting to combine metabolic pathways from multiple organisms into a single organism. But it has grown to include thousands of scientists and engineers across a broad range of industries and from organizations that range in size from small startups to some of the largest companies in the world.

The Society for Biological Engineering (SBE) held the Metabolic Engineering 11 Conference (ME11) in June 2016 in Awaji, Japan, with the theme of design, synthesis, and system integration for metabolic engineering. Recent advances in DNA synthesis and sequencing technologies have been geared toward applications for the design of complex biological systems. The metabolic engineering community has been a leader in designing these complex systems. Thus, ME11 served as a venue for discussing these advances, as well as how they are enabling new approaches to metabolic engineering. One area of research is in increasing the length of synthetic DNA constructs to enable not only the complete synthesis of entire pathways, but also the synthesis of entire genomes.

CRISPR/Cas9 has enabled DNA editing technologies such as targeted gene-disruption (gene knockout) and precise in-frame integration of exogenous DNA. It is vital that the metabolic engineering community rapidly adopt

these advances in DNA editing technology, which will help to facilitate genetic alteration and optimization. The synthetic biology community will benefit from employing the broad expertise and knowledge base provided by metabolic engineering to create applications that involve redirecting complex cellular chemistries to produce fuels, chemicals, pharmaceuticals, and other products.

Organisms have been engineered to produce biodegradable polymers, which are used to create compostable packaging materials and resorbable materials for medical applications. Metabolic-engineered organisms are also expected to play a role in the production of persistent polymers, which are used in automobile and construction industries.

Metabolic engineering may help to aid sustainability efforts. Innovative BioProduction Kobe (iBioK) is a collaborative project that aims to realize the bioproduction of various chemicals, such as rare inositols (a six-fold alcohol of cyclohexane used for diverse applications) from renewable biological resources like agricultural plant residues. Metabolic engineering has also helped increase the yield of biofuels produced in yeast and bacteria. Global Bioenergies, Inc., has developed innovative metabolic pathways for the production of light olefins (ethylene, propylene, linear butylene, isobutylene, and butadiene). And recently, the company successfully developed artificial metabolic pathways that are capable of generating isobutene from glucose and sucrose without any chemical treatment.

Metabolic engineering of yeast, bacteria, and mammalian cell lines to produce pharmaceuticals, chemicals, fuels, and novel materials has been used for over a decade. Advances in DNA synthesis, genome engineering, and the omics sciences (*e.g.*, genomics, proteomics, etc.), as well as the accumulation of comprehensive knowledge of living systems and species, has helped to accelerate the development and optimization of organisms used for the production of some chemicals. Economic support for the metabolic engineering community and steady technological advances will likely expand the range of products that can be synthesized using metabolic engineering, which should reduce the production cost of useful molecules and products.

To learn more about this topic, participate in the International Conference on Plant Synthetic Biology and Bioengineering (ICPSBB) in Miami, FL, Dec. 16–18, 2016, and the 7th International Conference on Biomolecular Engineering (ICBE) in San Diego, CA, Jan. 8–11, 2016. Visit www.aiche.org/sbe for more details.

► Microorganisms can be engineered to produce biofuels from cellulose-derived sugars.

