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In This Issue

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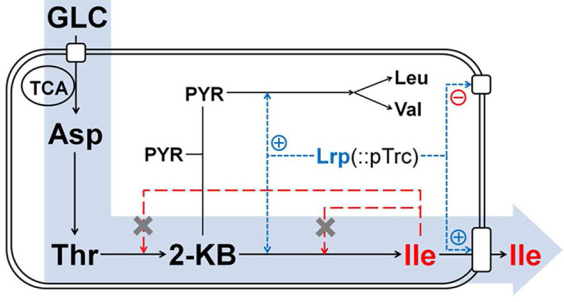
E. COLI FOR L-ISOLEUCINE PRODUCTION

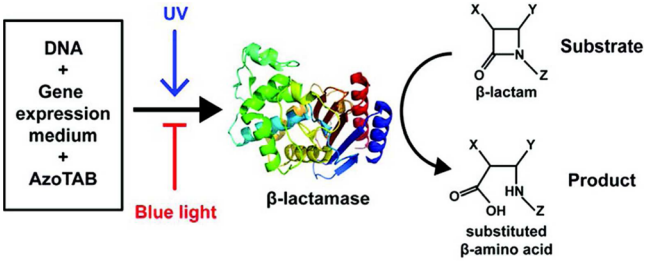
Traditionally, amino acid producers have been developed by repeated random mutation and selection processes. However, random mutations in regions not directly related to amino acid biosynthesis can cause growth retardation and other unwanted physiological changes. Thus, the development of genetically well-defined strains has become an important task. L-Isoleucine is a constituent of infusions and functional products, such as dietary products and beverages, and also plays an important role in the synthesis of hormones and enzymes. Here, Park et al. (DOI: 10.1021/sb300071a) provide the first report detailing the development of a completely genetically defined *E. coli* strain efficiently producing L-isoleucine.



Using rational metabolic engineering, the authors obtained a final L-isoleucine titer of 9.46 g/L, comparable to that obtained with the strain constructed by classical random mutagenesis. The approach described in this paper can further be applied, in general, for developing strains for the efficient production of other metabolites.

MODIFICATION-FREE PHOTOCONTROL OF ENZYME SYNTHESIS

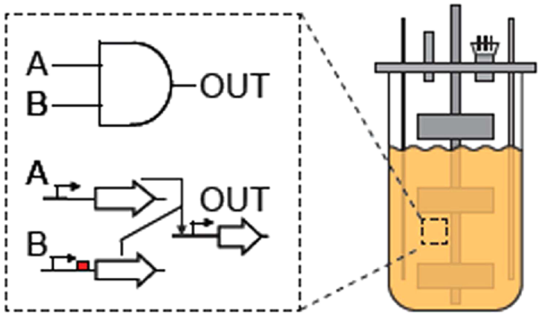
The ability to photocontrol chemical reactions holds promise for several chemical and biological applications. Methods to date have involved the chemical modification of enzymes based on a protein-specific approach. Now, Venancio-Marques et al. (DOI: 10.1021/sb300010a) describe the first method for *in vitro* photocontrol of enzyme synthesis resulting in light-controllable substrate conversion, without gene or protein modification.



Using a custom-built photosensitive nucleic acid binder, a commercially available gene expression system, and β-lactams as target enzyme substrates, the authors show that a short UV illumination triggers β-lactamase synthesis and the subsequent conversion of different kinds of β-lactam substrates. This approach is sequence-dependent and does not involve modification of gene expression machinery or the enzyme itself. Additionally, since extensive knowledge of the protein structure is not required, this method has the potential to be applied to several kinds of enzymes that can be synthesized *in vitro* in a functional form.

GENETIC CIRCUIT PERFORMANCE UNDER INDUSTRIAL BIOREACTOR CONDITIONS

While synthetic genetic programs have several applications in biotechnology and industrial processes, programs used in these processes need to maintain their functionality in varying and complex environments. However, the conditions that cells in bioreactors are exposed to often vary greatly from those used to characterize gene circuits in the laboratory. Here, Moser et al. (DOI: 10.1021/sb3000832) detail the performance of two synthetic circuits in *E. coli* under industrially relevant conditions, such as the selection of media, strain, and growth rate.



The authors use two previously characterized genetic circuits, the AND gate and a NOR gate, to compare performance under industrial conditions. These two gates were chosen to enable comparison between two circuit architectures that impart different loads on the cell. The results from these studies highlight the challenges faced while implementing complex genetic circuits in an industrial setting and suggest strategies to circumvent them.

ENGINEERING THE β-OXIDATION CYCLE

The β-oxidation cycle is one of biology's most fundamental processes, used by species that range from bacteria to humans to break down fatty acids and generate energy. The authors recently reversed this cycle and showed that it can be used as a promising platform for the production of a variety of advanced fuels and chemicals. However, the previous work relied on engineering global regulators, a system-level approach that makes it difficult to determine which of the many deregulated enzymes are responsible for product synthesis and limits both our ability to fine-tune the synthesis of specific products and the transfer of the engineered pathway to other organisms.

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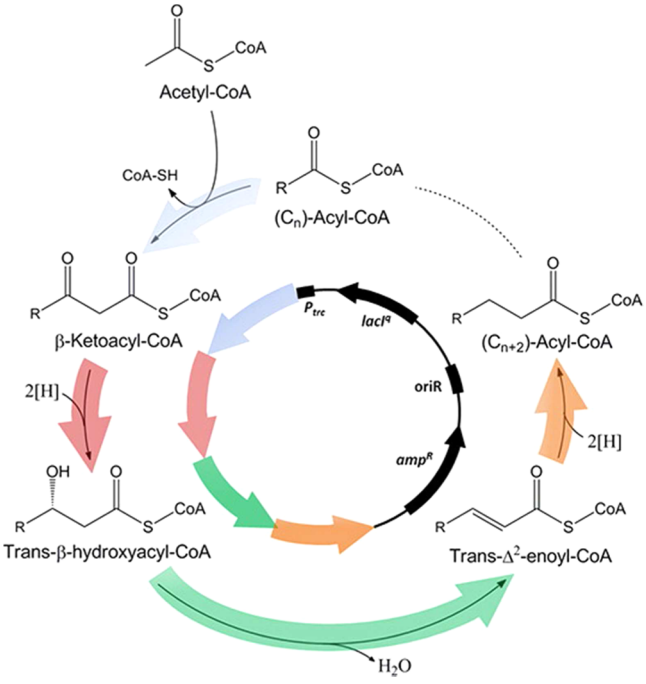
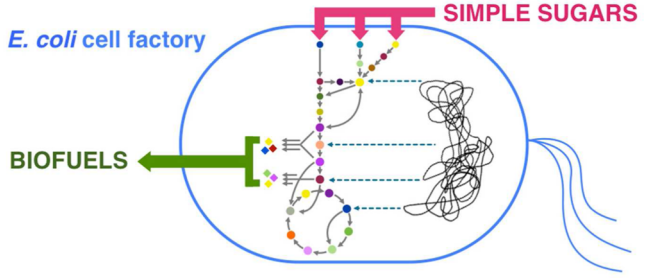
Now, Clomburg et al. (DOI: 10.1021/sb3000782) use a synthetic/bottom-up approach based on the *in vitro* kinetic characterization of individual functional units and their *in vivo* assembly to construct a functional reversal of the β-oxidation cycle.



This modular framework for the synthesis of 4-C and higher compounds provides a "clean" platform that can be transferred to other industrial hosts allowing the advantageous nature of a reversal of the β-oxidation cycle to be fully exploited for the synthesis of a wide array of drop-in biofuels and biochemicals.

■ ADVANCES IN BIOFUEL PRODUCTION

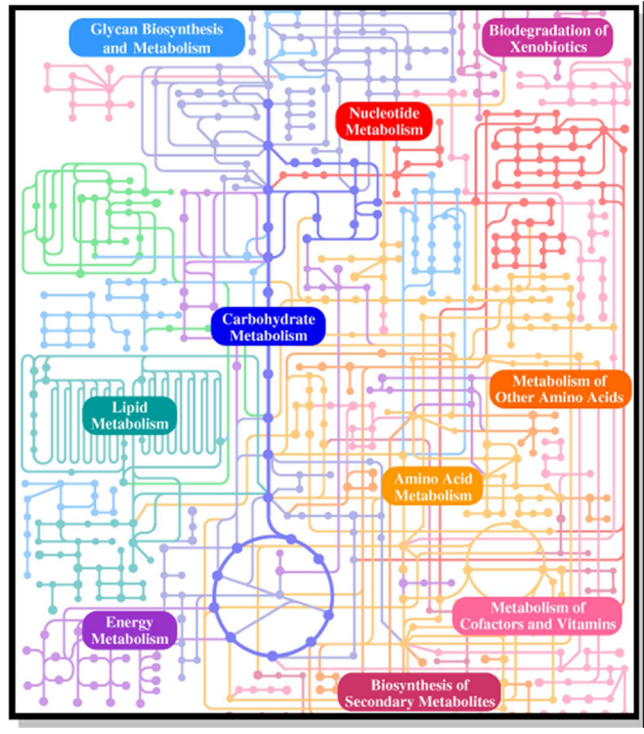
As the serious effects of global climate change become apparent, synthetic biologists and metabolic engineers are looking toward greener sources for transportation fuels. The design and optimization of microorganisms to produce gasoline, diesel, and jet fuel compounds from renewable feedstocks can significantly reduce our dependence on fossil fuels. Over the past few years, a tremendous volume of research has been performed toward the development of host microbial strains to produce advanced fuel compounds derived from alcohol, fatty acid, and isoprenoid biosynthesis. Novel engineering strategies have also been conceived that streamline these biological processes for enhanced biofuel production.



In this review, Kung et al. (DOI: 10.1021/sb300074k) present an overview of the fuel targets that are currently being pursued, with specific attention to the pathway design approaches that have been devised. In addition, a description of the engineering strategies that have been successfully deployed in microbial biofuel production has also been provided.

■ SYNTHETIC BIOLOGY AND METABOLIC ENGINEERING

Metabolic engineering involves the modification of microbial metabolic pathways to facilitate overproduction of various products. It employs the engineering of native and non-native pathways of product biosynthesis, which is made easier by the availability of synthetic DNA, the primary enabling technology in the field of synthetic biology.



Here, Stephanopoulos (DOI: 10.1021/sb300094q) reviews the origins of the fields of synthetic biology and metabolic engineering, their areas of overlap and the challenges they face in their quest to increase scientific and public awareness of their technological capabilities.

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