Engineering Microbes for Chemicals and Fuels

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Synthetic biology is the design and construction of new biological entities such as enzymes, genetic circuits, and cells or the redesign of existing biological systems. Synthetic biology builds on the advances in molecular, cell, and systems biology and seeks to transform biology in the same way that synthesis transformed chemistry and integrated circuit design transformed computing. The element that distinguishes synthetic biology from traditional molecular and cellular biology is the focus on the design and construction of core components (parts of enzymes, genetic circuits, metabolic pathways, etc.) that can be modeled, understood, and tuned to meet specific performance criteria, and the assembly of these smaller parts and devices into larger integrated systems that solve specific problems. Just as engineers now design integrated circuits based on the known physical properties of materials and then fabricate functioning circuits and entire processors (with relatively high reliability), synthetic biologists will soon design and build engineered biological systems.

We have used synthetic biology to create inexpensive, effective, anti-malarial drugs. Currently, malaria infects 300–500 million people and causes 1-2 million deaths each year, primarily children in Africa and Asia. One of the principal obstacles to addressing this global health threat is a lack of effective, affordable drugs. The chloroquine-based drugs that were used widely in the past have lost effectiveness because the Plasmodium parasite which causes malaria has become resistant to them. The faster-acting, more effective artemisinin-based drugs — as currently produced from plant sources — are too expensive for large-scale use in the countries where they are needed most. The development of this technology will eventually reduce the cost of artemisinin-based combination therapies significantly below their current price. To reduce the cost of these drugs and make them more widely available, we have used synthetic biology to engineer microorganisms to produce artemisinin from renewable resources.

Having successfully completed the artemisinin work, we are now engineering the metabolism of the same microorganisms (*Escherichia coli* and *Saccharomyces cerevisiae*) for production of advanced biofuels and chemicals that might otherwise be produced from petroleum. Unlike ethanol, the advanced biofuels have the full fuel value of petroleum-based biofuels, will be transportable using existing infrastructure, and can be used in existing automobiles and airplanes. Similarly, the microbially sourced chemicals can be dropped into existing processes used to produce existing materials. These chemicals will be produced from natural biosynthetic pathways that exist in plants and a variety of microorganisms as well as from pathways that have no representation in the natural world. Large-scale production of these chemicals and fuels will reduce our dependence on petroleum and reduce the amount of carbon dioxide released into the atmosphere, while allowing us to take advantage of our current transportation infrastructure and products supply chains.