Hearing on Developments in Synthetic Genomics and Implications for Health and Energy

Committee on Energy and Commerce
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Chairman Waxman, Ranking Member Barton, Chairman Emeritus Dingell and distinguished members of the Committee, thank you for inviting me to testify at this important hearing. Research and scientific innovation is the key to America's long-term health and economic vitality. My scientific colleagues and I appreciate your shining a light on this new and exciting field of research and its great potential to benefit the world.

My name is Jay Keasling. I am a Professor in the Departments of Chemical Engineering and Bioengineering at the University of California at Berkeley; Acting Deputy Director of Lawrence Berkeley National Laboratory, a U.S. Department of Energy (DOE) multipurpose national laboratory operated by the University of California; Chief Executive Officer of the DOE-funded Joint BioEnergy Institute; and Director of the Synthetic Biology Engineering Research Center.

Synthetic biology is the engineering of biology to solve important problems. It is basic science with a focus on application. This emerging field of fundamental science has great potential for developing solutions to large-scale societal challenges.

Although most people are familiar with "genetic engineering" or "molecular biology," synthetic biology uses an approach and tools that differ significantly from both. The differences are in the approach and the tools utilized. For example, early molecular biologists cobbled together natural biological components and hoped that the engineered system would work. Assembling the components was challenging, and as a result, engineered organisms rarely functioned as desired. Today, synthetic biologists have improved the reliability and safety of engineered organisms by assembling standardized well-characterized components from existing well-studied organisms much like how one might assemble a computer from standard components such as a hard drive, sound card, motherboard, and power supply.

My research focuses on engineering microorganisms to produce pharmaceuticals and biofuels. In my lab, we use well-known microorganisms such as *E. coli* and yeast that

have been widely used for many years by the biotechnology industry. We introduce into these microorganisms DNA that encodes biological components such as metabolic pathways that enable the organism to transform inexpensive sugars into valuable, useful products. These products include drugs for diseases that afflict people in the developing world and carbon-neutral biofuels to reduce our dependence on foreign oil.

When I started my career in 1992 as an assistant professor at the University of California at Berkeley, biological components were relatively crude, making the engineering of microorganisms time-consuming and costly. But my colleagues and I had the idea that one could engineer microorganisms into chemical factories that produce nearly any important chemical from sugar. Unfortunately, there were few tools available to us at the time. So we began by developing tools to accurately produce a chemical of interest by controlling the expression of genes that had been transferred into cells. At that time, there was no name for what we were doing, but now it is known as synthetic biology.

Thanks to the National Science Foundation's investments in the Synthetic Biology Engineering Research Center (SynBERC), my colleagues and I are now establishing standards for the engineering of biology and creating and characterizing biological components that can be readily assembled to solve important problems. SynBERC brings together many of the pioneers (biologists and engineers from world-class institutions) of synthetic biology who are laying the foundation for the new field of synthetic biology. We are working together to construct standard, reliable, and safe building blocks that can be used in a myriad of applications. We are also studying safety, security, preparedness, and ethics issues around these powerful technologies to ensure they are used safely and wisely.

One of the most important and well-known applications of synthetic biology has been our work on engineering microorganisms to produce the anti-malarial drug artemisinin. There are 300 to 500 million cases of malaria at any one time. One to three million people die from the disease each year, and 90 percent of those are children under the age of five. While conventional quinine-based drugs are no longer effective, plant-derived artemisinin combination therapies are highly effective but cost prohibitive for much of the world.

To decrease the cost of artemisinin, we engineered a microorganism to produce a precursor chemical to the drug by transferring the genes responsible for making the drug from the plant to the microorganism. Through funding from the Bill and Melinda Gates Foundation, we completed the science in three years, largely due to ready access to well-characterized biological components. The microbial production process

has been licensed by Sanofi-Aventis, which will scale the process and produce the drug within the next two years; selling it at cost in the developing world.

The process for producing artemisinin is akin to brewing beer. The microorganism takes in a sugar and secretes a precursor to artemisinin rather than alcohol, which the yeast would produce naturally from sugar. We predict that when this process is fully implemented, the drug produced by this engineered organism could save a large fraction of the two million or so children who die every year from malaria. Launching this process in 2011 or 2012 is crucial, as the plant-derived version of the drug will soon be in short supply.

Because the engineering of biology is time-consuming and unpredictable, the artemisinin project required $25 million in funding and roughly 50 people working on the project for the past three years. Through synthetic biology, we hope to make the engineering of biology more predictable and reliable, thereby reducing the cost to develop medicines and other useful products ranging from chemicals and fuels to consumer and commercial products.

Speaking of fuels, ethanol, which has been widely used as an oxygenate in gasoline and is the majority component of E-85, is not an ideal gasoline replacement. A gallon of ethanol packs only two-thirds of the energy of a gallon of gasoline. Ethanol is corrosive to engines and pipelines and requires energy-intensive distillation to purify. As such, its use would require significant changes to our transportation infrastructure, including replacing pipelines and automobiles at a significant cost.

Fortuitously, artemisinin is a hydrocarbon, a fundamental building block for fuel. We are now re-engineering the artemisinin-producing microbes to produce drop-in biofuels. That is, through advances in synthetic biology, we can engineer these same safe, reliable, industrial microorganisms to produce biofuels that will work within our existing transportation infrastructure.

The Joint BioEnergy Institute (JBEI), a Lawrence Berkeley National Laboratory–led scientific partnership between Sandia National Laboratories, the University of California campuses at Berkeley and Davis, the Carnegie Institution for Science, and the Lawrence Livermore National Laboratory, is exploring the potential of synthetic biology to advance the development of the next generation of biofuels—liquid fuels derived from the solar energy stored in plant biomass. JBEI is one of three DOE Bioenergy Research Centers funded by the Office of Biological and Environmental Research with the Department’s Office of Science.

The approach of JBEI is to use the advances in synthetic biology to engineer microorganisms to transform sugars derived from cellulosic biomass and starch into hydrocarbon-based biofuels that have the same qualities as the fuels that are currently

derived from petroleum. These new, advanced biofuels reduce the production of greenhouse gases, as they are derived from plants that use sunlight and atmospheric carbon dioxide to grow. These biofuels will reduce our dependence on foreign oil and could rejuvenate the U.S. agriculture economy, potentially making the American Midwest the new Middle East. My research is the foundation for two California-based advanced biofuel companies that are currently employing hundreds of people.

JBEI researchers have used synthetic biology and metabolic engineering techniques in *E. coli* and yeast to produce these advanced "drop-in" fuels that perform better than ethanol. The scientists are redirecting central metabolic, fatty acid, and cholesterol biosynthetic pathways to produce candidate gasoline, diesel, and jet fuel molecules. In work performed collaboratively with a Bay Area–based advanced biofuel company, my laboratory recently reported the engineering of *E. coli* to produce a biodiesel from the sugar polymer hemicellulose, a major component of plant biomass. The engineered microorganism secreted enzymes that digested hemicellulose, imported the sugar, transformed the sugar into diesel fuel, and secreted the diesel into the fermentation broth. The diesel floats to the top of the tank where the engineered *E. coli* are grown and can be skimmed off and used with very little purification. This engineering feat would not have been possible just a few years ago and certainly not without the recent advances in synthetic biology.

JBEI also has developed a new metabolic pathway that potentially could produce both advanced fuels and other molecules that might otherwise be produced from petroleum, paving the way to replace a significant portion of petroleum-based products with sugar-based products.

Very similar technologies are being used at JBEI to engineer plants to become efficient producers of cellulose with minimal input of water and fertilizer. Indeed, the advances in synthetic biology will allow us to have plentiful food to feed the population of the U.S. and the world as well as biomass for biofuels.

JBEI is also looking at the development of new and better enzymes. To break down the rugged lignocelluloses of biomass material, JBEI researchers have analyzed microbial communities in Puerto Rican rainforest soils that boast some of the planet's highest rates of biomass degradation. To perform the analysis, scientists used the Phylochip, a credit card–sized microarray developed at Lawrence Berkeley National Laboratory that can quickly detect the presence of up to 9,000 microbial species in samples. Using bags of switchgrass as "microbe traps," the researchers conducted a census of these soil microbes to identify the most efficient biomass-degrading bacteria and fungi. Understanding how these microbes work may provide synthetic biology solutions to more efficient and affordable deconstruction of biomass for advanced biofuels production.

Many other applications could benefit from advances in synthetic biology, including nitrogen-fixing crops that do not need ammonia-based fertilizers, microorganisms engineered to produce all of the chemicals currently produced from petroleum, and entirely new classes of drugs to fight cancer, infections of multidrug-resistant bacteria such as those that cause tuberculosis, and a host of other diseases.

I hope that my testimony has illustrated for you the remarkable potential of synthetic biology and the important role that it has to play in our nation's research and innovation enterprise. Your actions and the support of Congress will determine whether the efforts described today are ultimately successful. This is a marathon, not a sprint, and requires consistent and continuous nourishing and care.

We are very encouraged by the language adopted by the House Committee on Science and Technology regarding synthetic biology in the America COMPETES Act, and stand ready to assist Congress in any way we can as you explore and learn more about this exciting research area.

Finally, thank you, again, for holding this important hearing and for inviting me to participate. Please let me know if I may ever be of any assistance. I will be happy to answer any questions.

Jay D. Keasling Biography

Jay Keasling was named as Lawrence Berkeley National Laboratory's Acting Deputy Director in March 2009. While serving in this interim position, he has continued his duties as the Chief Executive Officer of the U.S. Department of Energy's Joint BioEnergy Institute and as a professor of chemical and bioengineering at the University of California at Berkeley. From April 2005 to June 2009, he served as Director of Lawrence Berkeley National Laboratory's Physical Biosciences Division. He joined that division in 1992, and in 2002 became the first head of its Synthetic Biology Department. In addition, he directs UC Berkeley's Synthetic Biology Engineering Research Center and is also a founder of Amyris Biotechnologies, a leading firm in the development of renewable fuels and chemicals.

Keasling is one of the foremost authorities in the field of synthetic biology research. His work has focused on engineering microorganisms for the environmentally friendly synthesis of small molecules or degradation of environmental contaminants. He led the breakthrough research in which bacteria and yeast were engineered to perform most of the chemistry needed to make artemisinin, the most powerful anti-malaria drug in use today. In 2004, the Bill and Melinda Gates Foundation awarded a $42.6 million grant to further develop the technology, which is now nearing commercialization. For this research, Keasling received the 2009 Biotech Humanitarian Award from the Biotechnology Industry Organization. Keasling is now applying his synthetic biology techniques towards the production of advanced carbon-neutral biofuels that can replace gasoline on a gallon-for-gallon basis.

Keasling grew up on his family's corn and soybean farm in Harvard, Nebraska, then earned his bachelor's degree from the University of Nebraska, and his graduate degrees in chemical engineering from the University of Michigan. He is the recipient of the American Institute of Chemical Engineers Professional Progress Award (2007) and Scientist of the Year, *Discovery Magazine* (2006). He is a Fellow of the American Academy for Microbiology (2007) and the American Institute of Medical and Biological Engineering (2000). In 2006, he was also cited by *Newsweek* as one of the country's 10 most esteemed biologists.