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Synthetic Biology Makes Scary Headlines, but Universities Promote It as a Lifesaver

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ABSTRACT

The discipline is a tactical upgrade in the search for better medicines, making computerized machines out of living cells.

FULL TEXT

The renowned scientist J. Craig Venter got top-shelf attention last spring when his lab implanted modified DNA into growing bacteria and he pronounced it "the first synthetic species" of life.

On Capitol Hill, lawmakers convened a hearing to study the implications. Down Pennsylvania Avenue, President Obama asked his bioethics commission to investigate, saying the event raised "genuine concerns."

But there is a far more compelling story about how this field, known as synthetic biology, is taking shape, largely on university campuses. It is not primarily about making new life forms. It is, rather, a major tactical upgrade in the long-running search for better medicines, fuels, and renewable materials. The idea involves sophisticated new gene-altering techniques that essentially make computerized machines out of tiny living cells.

These biological devices may be able to detect and kill cancer cells and treat malaria. "The power to do this kind of stuff is getting better pretty quickly," said Sean R. Eddy, leader of a computational-genomics group at the Virginia-based Janelia Farm Research Campus of the Howard Hughes Medical Institute, which finances research at more than 50 U.S. universities.

The technology is also highly complex, and successes will be incremental, stretching across years and decades, experts say. Experimentation with genetic structures, after all, goes back centuries, to breeding animals and plants for specific traits. In the 1970s, scientists learned how to insert foreign genes into organisms, and we began to see things like genetically modified corn. In the late 1990s, they discovered how to rework multiple genes to give organisms completely new functions. "That is," said James J. Collins, a professor of biomedical engineering at Boston University, "to make them programmable."

That means that synthetic biology practitioners such as Mr. Collins have been able to coax cells to take a complicated series of actions when confronted with specific circumstances, such as making a group of proteins in a specific amount upon receiving a chemical signal.

As with computers, the applications are widespread and profound. At the Massachusetts Institute of Technology, Ron

Weiss hopes for nothing less than curing cancer. Mr. Weiss, an associate professor of biological engineering, is designing detector cells that can read the complex chemical signatures of a cancer cell. The detectors would give a signal that triggers a chemical process in the body that kills the malignant cell.

The detectors consist of a network of cells, with elements genetically programmed to react in different ways to each of six different chemical characteristics of an analyzed cell. Just as the police combine measurements such as height, weight, and fingerprints to narrow their choice of a crime suspect, the combination of six chemical outputs from Mr. Weiss's detector cells would greatly improve the accuracy of identifying a suspected cancer cell.

His innovation is to create a linked network of the six chemical outputs that, in a cascading chain of genetically programmed responses, combines them into a final signal. That final chemical signal, for each cell being analyzed in the patient's body, either triggers or cancels a chemical reaction that would kill the analyzed cell.

That kind of treatment may be years from reaching patients. But a malaria drug developed with synthetic-biology techniques may be a lot closer. Malaria sickens more than 200 million people a year and kills nearly 800,000, according to the World Health Organization. A drug made from artemisinin, derived from the sweet wormwood plant, is known to be highly effective. Sweet wormwood, however, produces artemisinin only in highly limited locations and conditions.

So over the past several years, a team led by Jay D. Keasling, a professor of chemical and biomolecular engineering at the University of California at Berkeley, has been taking the necessary genes from the wormwood, implanting them into a strain of E. coli bacteria, and growing large quantities of artemisinin. "This has the potential for revolutionizing the treatment of a very deadly and prevalent disease," said the head of President Obama's bioethics commission, Amy Gutmann, president of the University of Pennsylvania.

The basic method of using genetic manipulation to make a drug, by growing an important protein inside bacteria, is well developed. But cases such as artemisinin are trickier, requiring a complex interplay among several genes. Mr. Keasling solved that by figuring out how to cobble together a network of such processes, in which one gene leads to a protein that then needs to be processed by other proteins.

With the malaria drug now going through its final safety approvals and expected to reach mass production late this year, Mr. Keasling is busy applying synthetic-biology techniques in his new role as head of the Joint BioEnergy Institute, four miles from the Berkeley campus, one of three federally financed research centers established nationwide to develop renewable fuels.

As with artemisinin, Mr. Keasling is trying to solve a shortage of a natural compound-in this case, the yeasts that ferment sugars into biofuels-by altering the genes of micro-organisms so that those micro-organisms can pump out needed compounds.

"Doing chemistry inside microbes is very powerful," Mr. Keasling said. "We can produce drugs or fuels that we might not get through other routes."

It can also be drawn out and tedious, far less likely to attract the headlines garnered by Mr. Venter. Already a celebrity from racing against the government to sequence the human genome, Mr. Venter-president of the 400-scientist-strong J. Craig Venter Institute-spent 15 years and $40-million to take more than 1,000 sections of DNA from one type of bacteria and insert that DNA package, without making any meaningful changes in its function, into a different type of bacteria.

That achievement, while impressive and attention-grabbing, didn't necessarily advance the immediate practical goals of the field, several university scientists said. George M. Church, a professor of genetics at Harvard University, used the analogy of designing a new car: Researchers such as Mr. Keasling have been trying to modify and improve the parts and processes, such as the engine and the transmission, while Mr. Venter essentially showed how to carve a new car out of a single chunk of metal.

The Venter lab's replacement of an entire genome might eventually prove itself a useful technique, Mr. Church said. But for now, he said, it seems an unnecessary diversion given the more immediate value of identifying the specific genes that cause a specific function in a micro-organism, and then learning how to alter those genes and functions. "Almost nobody else wanted to do that," Mr. Church said of Mr. Venter's work.

Private industry appears to share Mr. Church's sentiment. Several companies, large and small, are already heavily invested in exploiting some of the same basic techniques used by Mr. Keasling to fight malaria and pursued by Mr. Weiss to fight cancer.

The DuPont chemical company, after 10 years of research, has opened a facility in Tennessee that uses advanced genetic technology to convert corn sugar into a chemical that replaces a compound previously obtained from oil. The chemical is essential to making a variety of common consumer products, including clothing, cosmetics, lotions, and carpets.

Basic research such as that pursued by Mr. Church and Mr. Collins is key to enabling that kind of discovery, whether in corporate or university labs. Mr. Collins is working to mold micro-organisms into generic "switches" that, like the common transistor, can be used in a limitless variety of applications. Mr. Church helped initiate the Human Genome Project, and now he's leading the push for next-generation methods of quickly and comprehensively identifying the genetic makeup of various organisms. That would give synthetic biologists a robust tool kit for their field.

In some cases, the work is taking university scientists themselves into the corporate world. Kevin A. Jarrell, a former professor of biochemistry at Harvard, is now chief executive of Modular Genetics Inc., which has developed micro-organisms to convert agricultural waste into the chemicals needed to make personal-care products. Researchers from the University of Colorado founded OPX Biotechnologies Inc., which makes substitutes for petroleum-based acrylic. Mr. Keasling founded Amyris Biotechnologies Inc. to further his work with biofuels.

As is often the case with basic research, big-money payoffs aren't certain, or even central. In the case of the malaria drug, Mr. Keasling and Berkeley researchers were supported by the Bill & Melinda Gates Foundation, and they are licensing the technology at no cost to Sanofi-Aventis S.A. so that the French drug maker can mass-produce the life-saving medicine at the lowest possible cost.

And the political climate, despite the concern generated by Mr. Venter's announcement last May, looks favorable. Mr. Keasling and his colleagues have largely escaped the kind of public opposition that's entangled researchers working with human embryonic stem cells and many genetically modified foods.

The ethics commission led by Ms. Gutmann reported back to President Obama last month, suggesting that government agencies scrutinize synthetic biology more carefully but saying that no new federal laws seemed necessary for the time being. Major religious groups largely agreed.

Many people, it seems, are treating synthetic biology as meaningfully different from genetic experimentations with their embryos and their food, said Gregory E. Kaebnick, a research scholar at the Hastings Center, a nonprofit group that studies the ethics of biotechnology.

The reflexive alarm over Mr. Venter's claim to have created a new species of life does suggest some eventual limit to how much the public will tolerate synthetic biology, Mr. Kaebnick said. For now, however, the most sophisticated work in the field largely involves mere micro-organisms, on the scale of bacteria and yeast cells.

"It just hasn't led to a lot of opposition," he said, "and I don't expect it to."

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GRAPHIC: Jay D. Keasling, a professor at the U. of California at Berkeley and head of the Joint BioEnergy Institute in Emeryville, Calif., uses the gene-altering techniques of synthetic biology in efforts to develop biofuels and a plant-related drug for fighting malaria.
Alison Yin for The Chronicle
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