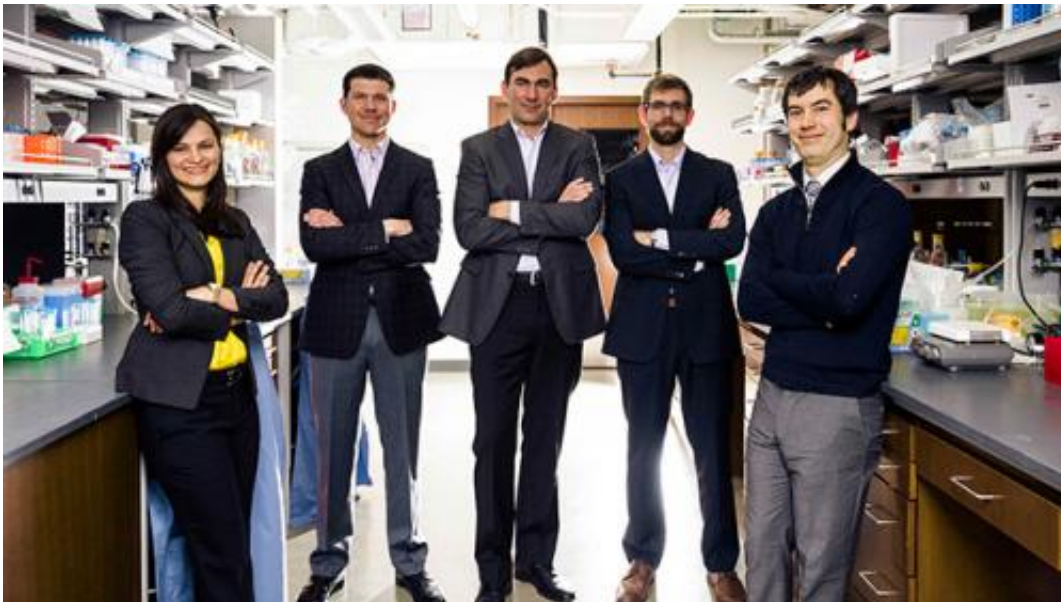


# Synthetic biologists break new ground in medicine, energy

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Five Northwestern scientists have joined together to pursue advances in the cutting-edge field of synthetic biology. Scroll your mouse over the individual researchers pictured above to see what each has to say. Credit: Jim Prisching

With such ambitious goals as helping cure cancer and eradicating pervasive disease, some of the most talented scientists in the country from the emerging field of synthetic biology are breaking new ground at Northwestern University.

The hot field of [synthetic biology](#) uses tools and concepts from physics, engineering and computer science to build new biological systems.

Newly understood genomic sequencing and advances in molecular biology, as well as the ability to work at much smaller scales, have accelerated the work.

A group of five young researchers in this field includes Northwestern scientists from a range of disciplines—chemistry, biology and engineering—working with an interdisciplinary approach to solve pressing challenges in global public health and environmental stewardship.

The scholars, at the McCormick School of Engineering and Applied Science, Weinberg College of Arts and Sciences and Feinberg School of Medicine, put Northwestern on the map as a national leader in this growing area of study, joining early pioneers such as Massachusetts Institute of Technology, Harvard University, Stanford University and the University of California at Berkeley.

Much of the research focuses on reprogramming cells by changing their DNA. In this way, researchers are working to engineer biology much as they engineer high-tech machines, creating new and environmentally friendly fuels and less expensive and more potent drugs and biological therapies. Some such approaches utilize successful solutions found in nature as inspiration for designing artificial systems. These scholars also reflect on the ethical issues of the technology they employ.

The field has gained a lot of attention over the past several years for its potential to be a game changer for scientific breakthroughs in public health and the environment. A recent PBS feature on the field put it simply: "[Why Synthetic Biology Is the Field of the Future.](#)"

Philanthropists such as Bill and Melinda Gates are funding some of the research and have already helped bring about a recent breakthrough—achieving low-cost production of a drug for treating

malaria in developing countries. By producing this drug in engineered cells rather than in plants, where crop yields fluctuate dramatically from year to year, this technology is stabilizing both supplies and prices of this drug.

"We have a newfound ability to read, write and edit DNA, the code of life," said Michael Jewett, among the leading [synthetic biologists](#) on campus. "What synthetic biology enables us to do is analyze biological systems faster and more cheaply than ever before. In turn, engineering living systems can now benefit society in new and powerful ways. The key idea is to use our newfound abilities to make something useful, such as a new sustainable chemical or fuel or to fight disease or improve agriculture."

Joshua Leonard, a member of this Northwestern group who focuses on integrating synthetic biology into medicine—for example, by programming immune cells to build customized cancer therapies—argues that synthetic biology will have major economic impacts, too.

"There are many signs that synthetic biology will usher in the next big technological wave, driving innovation and economic activity just as we saw at the dawn of the information age," Leonard said. "The ability to engineer living technology is simply not a capability we have had in the past, and this is a tantalizing prospect with broad-reaching potential impact."

The work of the synthetic biologists is directly in line with at least two of the pillars of Northwestern's 2011 Strategic Plan. It underscores the University's mission to "discover creative solutions" by working together through research and innovation to find answers to problems "that will improve lives, communities and the world." It also evokes Northwestern's priority to "engage with the world" through strategic

partnerships in order "to heighten our global impact for the greater good."

Despite its lofty goals and promising advances, synthetic biology has generated controversy, too, prompting President Barack Obama to order investigations into the ethical and global implications of the work. Some researchers have urged caution, fearing that scientists manipulating the DNA of living organisms are essentially "playing God" and have the ability to cause great harm to biological and ecological systems. References to "Jurassic Park" permeate some of the more critical literature on the field.

Regardless, synthetic biology has emerged relatively unscathed from much of the scrutiny, with the government commissions concluding that the appropriate safety nets are in place and the potential for positive health impacts are too great to halt progress.

Laurie Zoloth, a professor of both religious studies and of bioethics at Northwestern, is aware of both the potential of synthetic biology for extraordinary medical research that could address terribly intractable problems and of the potential for the powerful technology to be used in destructive ways. "This is a feature of all powerful new and transformative technologies," she said. "Using synthetic biology is like smelting iron. You can make sewing needles, and you can make spears. There is always the possibility of dual use."

What makes Zoloth interested in synthetic biology is the potential for the field to apply engineering principles to solve so many pressing human problems, such as global environmental concerns and [public health](#) crises in impoverished countries with limited access to food and medicine. At the same time, she said many skeptics are concerned that the tools of the technology could get into the wrong hands.

The main fear is rooted in one of the field's most powerful ideas—that science should be available for all. "Synthetic biology is being widely taught," Zoloth said. "And therefore, that makes it doable in very simple conditions, and unlike, for example, nuclear power, it does not need a state apparatus or complex materials, and that makes it harder to regulate. The idea is: What happens if the very thing that makes synthetic biology so exciting gets in the wrong hands or the hands of someone who simply makes a mistake?"

Zoloth argues that, so far, the leading synthetic biology researchers—especially those at Northwestern—are already embracing the ethical questions, looking for the proper safeguards and policies to regulate the field and teaching the essential values needed to thoughtfully shape research. A recent research grant from the Keck Futures Foundation included funding for ethics research and for a seminar series that featured not only the scientists but also Northwestern historians, scholars of [religious studies](#), philosophers and medievalists debating the ethics of emerging technology in the field.

Julio M. Ottino, dean of the McCormick School, sees great potential for Northwestern to continue building on its worldwide reputation in this field.

"At McCormick, we encourage interdisciplinary thinking, and when we put our resources behind synthetic biology, we saw a team of young researchers who are catapulting us into the highest levels of the field," he said. "Since this field is so young, we do not yet know which ideas will become game changers, but we do know this is a long-term investment, and the possibilities are enormous."

Clearly, the Northwestern scientists already are gaining traction on much of their promising research, attracting investments from such highly regarded philanthropies as the David and Lucile Packard Foundation,

which awarded Jewett with its prestigious Packard Fellowship for Science and Engineering, as well as the Bill & Melinda Gates Foundation, which has awarded three separate research grants to Northwestern synthetic biologists. The goal of the Gates foundation grants, part of the "Grand Challenges Explorations" program, is for scientists to address some of the world's most immediate health needs, such as HIV, malaria, cancer and tuberculosis.

Keith Tyo, among the synthetic biologists recruited to Northwestern, is a researcher on all three of the \$100,000 Gates grants, one of which is a collaboration with Leonard to engineer yeast-based biosensors to serve as cost-effective, easily deployed diagnostics. In addition, Tyo is submitting an application for a \$1 million Gates grant to further the yeast-based biosensors research.

"One of the primary things I care about in the world is alleviating suffering associated with poverty," Tyo said. "I'm specifically interested in solving technical problems, so I chose synthetic biology as a research field because of the unique and profound ways that the field can affect the resource-poor in our world."

Tyo's research tries to resolve the high cost of existing drugs for HIV and tuberculosis by using cells to synthesize these drugs more cheaply to attack those diseases. His work, with that of all the synthetic biology researchers, is generating a lot of interest from undergraduates who see the field as one of the most promising and exciting new areas of scientific research.

Early this year, Tyo taught a new project-based class called Global Health and Biotechnology that attracted undergraduate and graduate students from a variety of disciplines, including chemical engineers, biology majors, computer scientists and civil engineers.

Tyo also is leading an initiative to train synthetic biologists on global health through internships in Nigeria and South Africa. He is challenging students to think about diseases and potential synthetic biology solutions, such as a banana that contains vaccine proteins, therefore allowing people to be vaccinated simply by eating a banana. "We also considered protein engineering and looking at how you would make therapeutic proteins that help with cancer or different blood diseases," Tyo said.

Another sign of the growing interest in the synthetic biology field from undergraduates is the International Genetically Engineered Machine competition, or iGEM, which now attracts more than 200 teams of students worldwide, including a Northwestern team co-mentored by Leonard, Jewett and Tyo. For the competition, student researchers use a kit of biological parts to conceive, design and build new biological systems that operate in living cells and may perform useful functions. Students also explore the ethical, legal and social aspects of their research. In 2012, Northwestern's iGEM team received top honors by winning the Best Model at the Americas competition for their work developing an E. coli-based biosensor that could help detect the presence of a pathogen in hospital settings.

Northwestern's work to advance the synthetic biology field got a big boost after former University of Chicago scientist Milan Mrksich joined the Northwestern researchers in 2011. Mrksich is a nationally renowned biomedical engineer and chemical biologist. He's worked for years to develop a technology that measures biochemical reactions on sophisticatedly engineered metal plates, each the size of a large notecard, in an extremely fast, low-cost way.

The technology, which he dubbed SAMDI, or self-assembled monolayers desorption ionization, has been more than 10 years in the making and is generating a lot of excitement from pharmaceutical companies. Among its applications, it can allow scientists to study how

proteins function and how their activities are different in a diseased organ. In that way, scientists might pinpoint whether a person is at risk for certain diseases.

At the same time, SAMDI can help identify drugs that might be effective in fighting disease much more quickly than has ever been possible. Researchers can perform 100,000 tests per day of interactions using just two people to run them. Without SAMDI, researchers would have been lucky to conduct 1,000 tests in a day.

While the drug development process can take years before winning FDA approval, Mrksich expects that his technology will lead to pharmaceutical breakthroughs in the very near future. At the same time, he hopes SAMDI also can help scientists around the world replicate his work.

"It's really exciting," Mrksich said. "We're producing tens of thousands of protein patterns so you can really look inside a diseased cell and figure out what's gone wrong. ... Every biologist is going to want to use these arrays to see how protein functions vary."

The most recent addition to the synthetic biology effort at Northwestern is Neda Bagheri, an expert in computational biology. She develops algorithms that uncover the dynamic communication blueprints of cellular systems. These algorithms are designed to predict how changes to gene or protein activity manifest into unique cellular function. In this way, her models can identify new interventions, for instance, as well as therapeutic strategies to personalize patient care on an individual basis. To her one of the most exciting aspects of the work is its collaborative and global nature, with scientists reaching out to other like-minded researchers on campus and around the world. Together, they integrate different disciplines and work to address pressing public challenges.



"Current scientific challenges are multifaceted and complex," Bagheri said. "In order to push science forward and discover enduring solutions, we must be creative and think outside the box. The easiest way to do that is to do what we're doing here—transforming our approach by bringing people with different expertise together to work as a team."

Dean Ottino agrees that the group of researchers brought together at Northwestern—and led by the work of Mrksich—clearly have the potential to make powerful contributions to the field.

"The best and most radical ideas often happen at the intersections of disciplines. James Watson and Francis Crick used their training in physics to look at biology in a new way and discover DNA," Ottino said. "Synthetic biologists work at such an intersection of disciplines, using engineering thinking to reframe biology. It is this pursuit that could change the face of medicine and energy."

Provided by Northwestern University

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