Scientists have announced a milestone in the emerging field of cellular and genetic research known as synthetic biology. While scientists have used DNA to develop genetically modified cells for many years, for the first time, all of the natural genetic material in a bacterial cell has been replaced with a synthetic set of genes. This development raises the prospect of important benefits, such as the ability to accelerate vaccine development. At the same time, it raises genuine concerns, and so we must consider carefully the implications of this research.

President Barack Obama

*In a letter to Presidential Commission on Bioethical Issues*

Will synthetic biology be the solution to Earth’s biggest problems or an intolerable abomination against nature? In 2010, the Presidential Commission for the Study of Bioethical Issues, in light of the recent accomplishment of synthesizing an entire bacterium’s genome from scratch, came together to identify the future implications of this hotly controversial and growing field of synthetic biology. With opponents citing the dangers of changing the natural environment with alternatively designed organisms and proponents citing the potential unprecedented advantages of the field, the commission compiled the information at the intersection of progress in science, policy, ethics, and religion. They produced the final decision that “synthetic biology offers extraordinary promise to create new products for clean energy, pollution control, and medicine, to revolutionize chemical production and manufacturing, and to create new economic opportunities,” with which comes “a duty to attend carefully to potential risks, be responsible stewards, and consider thoughtfully the implications for humans, other species, nature, and the environment” (2). Therefore, the commission suggested that the field be allowed to continue to grow in the coming years without restrictive federal oversight.

Synthetic biology refers to the world of designing and creating organisms for a particular function, like genetically modified plants which can produce a much higher yield, or microbes which can produce sugars.
However, this still-emerging field has faced criticism and opposition, both in fear of the technology’s potential to alter the structures of the natural environment and natural organisms and in fear of the potential global socio-economic disadvantages this field poses for those who may produce “natural” products, like farmers. In this exciting time of unprecedented advances in synthetic biology, Dr. Pamela Silver, professor of Systems Biology at the Harvard Medical School, is on the forefront of progress, currently working on the design and construction of organisms that can not only change the human condition, but also hopefully change the world for the better.

Silver’s journey in synthetic biology began with a cross-country move from the University of California to Harvard, where she worked with genetic engineering and the construction of novel types of proteins. However, in recent years together with MIT bioengineers and computer scientists she has become part of a team focused on making biology faster and cheaper to engineer – a team which became the Synthetic Biology Group at MIT. To get students involved, Silver and her colleagues began offering intersession, optional courses at MIT, and eventually created the iGEM competition, which offers students the opportunity to create forms of synthetic biology they design. Currently in its 10th year, the iGEM competition has grown to include more and more participating university teams, and Silver has been the mentor of the Harvard Team throughout a number of the past years (3).

Located in the Warren Alpert Building of the Harvard Medical School, the Silver Lab is constantly busy, running a multitude of complex projects at once. These projects are as varied as they are complex, including experimentation to develop new cancer therapeutics, culturing cyanobacteria which can synthesize sucrose as fast as sugarcane can, and designing synthetic probiotic bacteria to help with stomach health. The implications of these experiments may change the way medical treatments and agricultural industries are structured, and with the fast pace of the lab’s work, Silver finds her greatest academic accomplishments changing from decade to decade.

“Back when I was more of a cell and molecular biologist,” Silver said. “My big discovery was how proteins are targeted into the nucleus of the cell, and that’s a very generalizable phenomenon. In the next decade, I think the thing that was super exciting was making some of the first movies watching the Green Fluorescent Protein in the cells. And fast forwarding, I think about 12 years ago [2001], we started using principles of cell biology for drug discovery. We discovered some molecules that act as cancer therapeutics, and they’ve actually gone into a Phase 1 [clinical] trial, so we’re excited about that. Most recently, we have come up with a novel way to engineer cells whereby we [can apply] the principles of DNA nanotechnology to [make] RNA fold in certain ways in cells and compartmentalize certain processes in the cells. So by doing this, we were able to make cells that make a decent amount of hydrogen [which can possibly be used as energy sources].”

With this sort of interesting biochemistry, others like Dr. Emily Balskus, Professor of Chemistry and Chemical Biology at Harvard, have been working to harness the released hydrogen from the cells and use them to make catalysts for chemical reactions, creating a chemistry that is as dynamic and responsive as living systems. For Silver, however, the world of synthetic biology has so many more facets left to explore, especially in understanding human biological systems and possibly being able to create targeted biological treatments.
“Engineering the immune system is something I think is very important and can happen,” Silver said. “And a favorite of mine is understanding if there is a genetic basis for behavior, and really nailing that down one way or another. And I think there are some behavioral things that are impacting our society that are stigmatized, like pain and sleep. There’s a stigma in our society surrounding pain and sleep medication. I think these are two things that impact human health and should be studied more.”

As for the world of public policy and the regulations placed on the exploration of this new and budding field, Silver has served on advisory panels for the National Academy of Sciences, the National Institutes of Health, and for the Office of the Security of Defense/Office of Net Assessment Biodefense Workshop. She has also recently written a white paper for the Office of Science and Technology for the President of the United States on integrating biology and computer science. Drawing upon her experience working as a scientific advisor in the political sphere, Silver pointed to funding constraints as the major cause of strain between public policy and synthetic biology exploration. In fact, Silver asserted that Washington policy makers were actually hungry for more such research work in newer fields and were actually reaching out to make such work possible. In her opinion, the largest obstacles in bringing the worlds of public policy, synthetic biology, and science in general together are a lack of effective communication and funding constraints more than anything else.

“I think some of the people are doing a great job already,” Silver commented. “There was a presidential commission on synthetic biology which basically found that we should forge ahead. There is a tendency to issue reports, some which are fantastically written [and discuss a lot of policy]. Then the question [becomes] how do you get those out, and who reads them, and who understands them. And that’s the [biggest] disconnect. I don’t know what happens with those reports with regard to the public. Washington searches for information, tries to assimilate it, but then what happens to it?”

And while Silver is a believer in the powerful benefits of working with synthetic biology, the potential negatives questioned by some are important to address as well.

“There are a number of ethical issues,” Silver explained. “Say you want to wipe out malaria. People did that in the sixties using DDT and that didn’t work out so well. It actually did work for getting rid of malaria, but [the DDT] ended up poisoning the ecosystem. Now, people are trying to genetically engineer mosquitoes [such that the] malaria-bearing [strain] will essentially breed itself out of existence. But there are some who ask what that will do the ecological niche and what [will happen] if those genes [for breeding out existence] spread within the population [including those mosquitoes not affected by malaria]. These are a lot of the same arguments that have been used against GMOs - genetically modified crops. So I think we have a social responsibility to be aware of what the downsides are of what [researchers] are doing. I am not conflicted about engineering aspects of the environment or life. I think it’s worth a try in many cases. I think it should be done in controlled and smart ways. I think that the engineering of biology is the future, we shouldn’t turn our backs on it in fear, and we should think about how to do it in a safe sort of way.”

But for Silver, the world of synthetic biology only has an even brighter future. With some of the world’s biggest problems yet to be solved, the engineering of biology may potentially hold some of those solutions.

“So there are some really big issues facing the planet - there’s food, fuel, water,” Silver described. “And biology’s going to have a role in solving those problems. So I would like to see people going into research to at least think about some of these bigger issues and frame their research in terms of that. I personally like the idea of big research projects with a focus. It’s like [the moment when the hundreds of] people in the [JPL] who worked on the Mars [rover] project, stood up and cheered when wheels were down on Mars. I want biology to be the same way. I want people to achieve big things and then stand up and cheer.”

And for Silver, there’s no better time for young scientists to start doing big things in synthetic biology.

“I want to see excited young scientists,” Silver said. “I’m a big proponent of women in science, and I want to see other continents more involved. Third world countries have the possibility of benefiting even more from synthetic biology than we do, and so I would love to see more engagement at the education level for the Third World. I think there’s a huge exciting future here for young people and I want to make it look that way, so they’ll know it.”

Shree Bose ’16 is a prospective Molecular and Cellular Biology concentrator in Straus Hall.

References