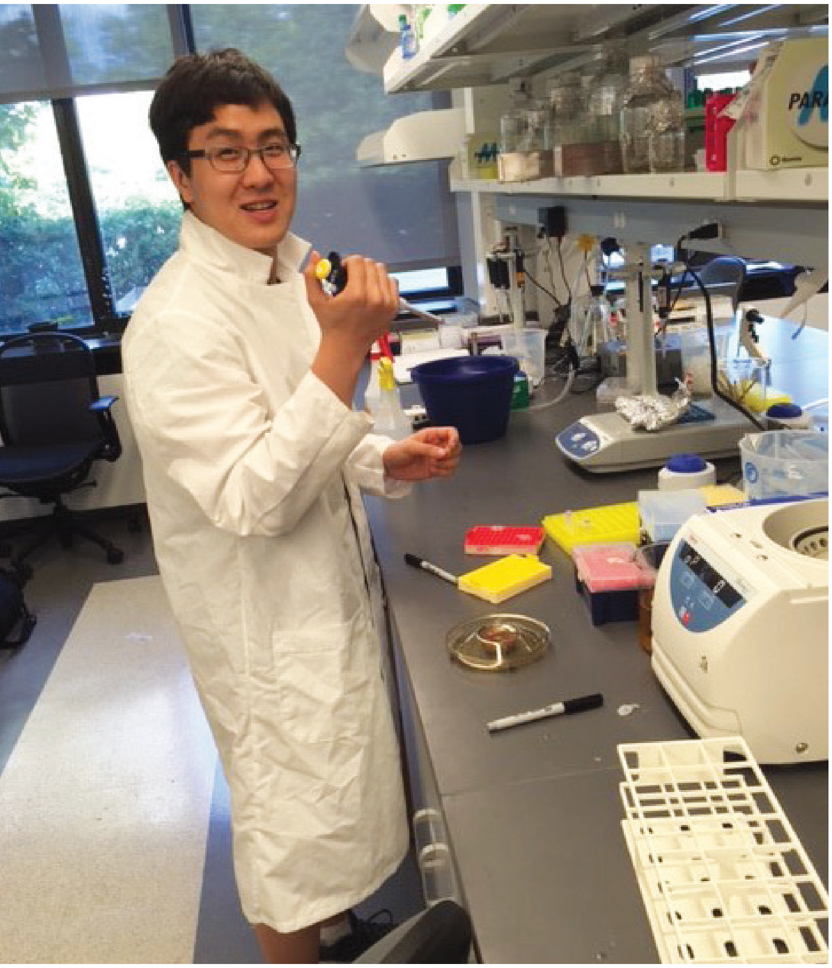
Under Constr

Forging a Path in Synthetic Biology

by Jeremy Wang

I've always been excited about DNA. In elementary school, as I learned about biology through websites like BrainBop and magazines like *Zoobooks*, I was especially fascinated by DNA and how it served as a blueprint for every action a cell would take. I wanted to know how and why it functioned the way it did, and wondered if it could be changed or controlled.

I took my first formal biology course in ninth grade. Of all the topics we discussed in class, the one I found most interesting was gene regulation, a process by which modifications to DNA change how or whether certain genes are expressed. In particular, our teacher discussed the lac operon system, a mechanism in *E. coli* that switches on a gene that allows the bacteria to digest lactose when glucose, its typical energy source, is not available.



This surprised me at first: Was this system really turned on and off like a circuit? We went on to learn that this system, one of the first examples of prokaryotic gene regulation to be understood, is often modified in genetic research. I was excited once again by the idea that the blueprint for how a cell functions could be changed.

Genetics by Design

I decided to spend part of the following summer learning more about genetics at the Boston Leadership Institute in Biological Research, an intensive three-week research course held at Dana Hall School in Wellesley, Massachusetts. The course was taught by biologist Jim Dixon, one of the developers of the synthetic biology curriculum called BioBuilder.

Each day started with a lesson taught by Mr. Dixon on topics ranging from a general overview of synthetic biology to epigenetics to bioinformatics. After lunch, we gathered in a state-of-the art lab to learn techniques relevant to the field of synthetic biology, such as inserting genes into bacteria. Through this experience, I began to grasp the extraordinary potential of synthetic biology to design entirely new genetic parts (called biobricks), genetic circuits, or even whole genomes from scratch.

When the program ended, I continued learning by independently studying the AP Biology curriculum and taking edX courses in molecular biology, including Proteins: Biology's Workforce, offered by Rice University, and Principles of Synthetic Biology, offered by MIT. Although they were extremely difficult to complete on my own, I at least gained an understanding of the general concepts covered in each lesson.

To continue developing my lab skills, I applied for an internship at a local biotechnology organization called Genspace. There, I practiced many of the techniques I'd learned at Boston Leadership Institute, such as DNA minipreps and gel electrophoresis, until they

uction

ISTOCK.COM/JK1991

were completely routine to me. I also learned a technique called replica plating, in which bacteria from a master plate are transferred to several other plates containing different growth media. This allowed me to select bacteria colonies with a desired trait, such as resistance to a particular antibiotic in one of the cultures.

When I started looking for research opportunities for the next summer, I learned about the Princeton Laboratory Learning Program, which places students in science or engineering labs of Princeton researchers. My eyes widened as I read about "Yeast Genetic Engineering for the Production of Biofuels and Chemicals," a project conducted by Dr. José Avalos. The descriptions of both that project and Dr. Avalos's research interests mentioned synthetic biology several times, and I knew immediately that I wanted to work with him. After an extensive application process that included responses to several essay questions and an interview, I was ecstatic to be accepted as one of 30 high school students who were placed in various labs as part of the program.

Taking the Bench

During the first weeks of the program, Dr. Avalos taught me about his ongoing research in metabolic engineering (and gave me more than 10 papers to read!). We then practiced and reviewed biological techniques that, fortunately, I was familiar with from my experience at Genspace and the Boston Leadership program. In the lab, I performed those techniques alongside some of Dr. Avalos's undergraduate and grad students.

The main difference from the work I'd done before was that I was working for the first time with *S. cerevisiae*, a species of yeast that is widely used in synthetic biology, which we were modifying to be able to produce lactic acid. To do this, we performed gene knockouts, a technique in which certain genes are made inoperative, and added genes responsible for the direct production of lactic acid.

I soon reached a point where I needed to conduct a DNA ligation, a procedure used to combine two pieces of DNA into one long strand. This is a common procedure, but it was a new one for me. I completed the ligation with two pieces of DNA, one a lactic acid-producing gene and the other a larger sequence which serves as a "backbone," both from *E. coli*. After the ligation, I performed a test called a colony PCR to see if the insert was successful, but the results revealed that the pieces did not combine. I decided to repeat the same procedure more carefully another day, but the ligation failed again—and several more times. Even after I cut the DNA pieces again using precise scissor-like proteins called restriction enzymes, taking extra care to ensure that the two pieces of DNA were correct, the ligation still failed. Despite my continued ligation failures, I was encouraged to keep working by the sweet aroma of yeast growing in the lab incubator. That was the yeast I would modify once the ligation was successful.

As I spent more and more hours in the lab working on this ligation, the end of August drew closer and closer. Finally, the ligation was successful. The next step was to introduce the DNA into yeast and then measure its lactate production, but someone else in the lab would have to do that part: It was the end of summer and school was starting, marking the end of my time in the lab.

Although I was disappointed not to have completed my project, Dr. Avalos reassured me that this was how research is done and that researchers sometimes repeat the same procedures for months and never gain the expected results. In the end, I realized that I had made a contribution to Dr. Avalos's research, and I was grateful to have had the opportunity.

The Laboratory Learning Program intensified my passion for synthetic biology and affirmed my desire to become a professional scientist. In the meantime, I continue to volunteer and gain laboratory experience at Genspace. And as I researched colleges to apply to, I looked at the strength of their biochemistry departments as well as the availability of internships and fellowships that would allow me to conduct original research. I hope to eventually earn a Ph.D. so I can design and conduct research.

Synthetic biology, the field I imagined as a third-grader, even before I knew it existed, is now a realistic research and career path. My experiences at Princeton, and those that led to it, have shown me that it is definitely the path I want to follow. ■

Jeremy Wang lives on Long Island, NY, and is a senior at Syosset High School, where he holds leadership positions in science-related activities such as Science Olympiad and in music-related clubs such as the Tri-M Honor Society and Chamber Music Club. Jeremy enjoys playing the piano and reading about life, especially in *Campbell Biology*.

Learn more about the Princeton Lab Learning Program at research.princeton.edu/students/research-opportunities.