For years scientists strived to understand the body at a small scale.

**To understand the foundation for life: cells, proteins, then DNA.**

When engineers look at these building blocks, they see them in a new way:

*Now that we know how they work,*

**how can we make them work for us?**

One answer is to redesign cells and organisms into little factories that perform new duties or to build biological systems to provide new kinds of therapeutics.

It’s a new way of looking at the building blocks that make up our bodies and refashioning them for the greater good. This emerging field is called synthetic biology, and its implications are far-reaching. For instance, in one of the field’s first successes, researchers at the University of California, Berkeley, recently created a cell factory that converts sugar (a cheap commodity) into artemisinic acid, an antimalarial drug that was previously too expensive to provide to the areas of the world that need it most. This synthetic biology approach reduced the cost of the treatment to less than a dollar per person, making it possible to widely distribute this medicine and save millions of lives each year.

Now two new McCormick faculty members — Josh Leonard (opposite, left) and Mike Jewett (opposite, right), both assistant professors of chemical and biological engineering — are building their labs at McCormick in hopes of creating synthetic biology successes of their own.

**PROGRAMMING CELLS TO TARGET TUMORS**

A major challenge in the treatment of cancer is that tumors evade and co-opt the body’s immune response to further their own survival. But what if scientists and engineers could reprogram immune cells to go directly to the site of the tumor and repair the immune dysfunction that the tumor causes? “This could allow the natural immune response, which would otherwise be impaired, to take over and clear the cause,” says Leonard.

That is what his research group is trying to do. Arriving from a postdoctoral fellowship in the immunology branch of the National Cancer Institute, Leonard is building a research program that applies his expertise in immunology, gene therapy, and protein engineering to pressing medical needs. “We’re using genetic engineering to custom design immune responses,” he says. As a graduate student at Berkeley, Leonard developed a way to genetically engineer T cells to suppress HIV infections. Now Leonard is working to modify dendritic cells and macrophages — cells that can regulate a body’s overall immune response. By introducing new genetic “programs” into these cells, researchers can change the way cells gather information and respond to their environment.

For example, Leonard can engineer protein-based sensors that allow a cell to detect molecules produced by tumors. These sensors can be coupled through signaling networks to genes encoding immune-stimulating proteins called cytokines. Thus, when the engineered cell encounters a tumor, it responds by producing cytokines that recruit and activate the body’s immune defenses against the tumor.

This example shows how Leonard uses cells as devices that can process information and perform useful functions and that eventually can be programmed and designed. By changing the way a cell interprets inputs and regulates outputs, Leonard hopes to build synthetic cells that function in ways that natural cells do not.

“Each immune response consists of the coordinated actions of a network of many different cells exchanging many different types of information,” he says. “In the case of cancer, these networks become dysfunctional. We need to better understand not only how individual cells function in these environments, but also how all these pieces fit together in order to initiate and maintain those pathological states.”

Then we will better understand how to alter or repair the network, which should be useful for treating a wide variety of diseases.”

**REMOVING THE “OVERHEAD” OF A CELL**

Jewett takes a different approach to synthetic biology, using cell-free systems to create protein therapeutics and unnatural polymers for materials, medicine, and nanotechnology. To do this, Jewett removes both the wall and the DNA of a cell — in his case, an E. coli cell — to get at the systems inside. In doing this, he removes the “overhead” of a cell and is more easily able to manipulate it.

“A cell has its own operating system,” he says. “Its objective is to live, replicate, and multiply. We’re trying to get it to carry out a new user-defined function that’s often at odds with the cell’s main function. By removing the cell wall, we’re able to directly activate and control the catalysts we’re most interested in.”

Jewett takes a bottom-up approach to the biology-by-design problem by trying to create new, more reliable biological systems rather than reengineer existing ones. At Stanford University, Jewett invented a cost-effective crude cell lysate system that is now being used for the production of personalized medicines to fight cancer.

Coming to Northwestern after receiving a National Institutes of Health Pathway to Independence Award while at Harvard Medical School, Jewett is now focused on building and evolving ribosomes, the cell’s factory for protein synthesis. He is making synthetic ribosomes to better understand life and to make custom-designed biological machines that can discover and produce new drugs. Collaborating with scientists at universities across the country, Jewett hopes that learning to build ribosomes will contribute toward our ability to construct a biological system that can self-replicate in vitro.

Both Jewett and Leonard are working with Laurie Zoltob, professor of medical humanities and bioethics and of religion and director of the Center for Bioethics, Science, and Society at Northwestern, to explore the ethical implications of synthetic biology. For example, Jewett’s self-replicating system would require compounds that aren’t found in nature (i.e., they couldn’t survive outside of a test tube), and Leonard’s customized immune system approach pushes the boundaries of how we engineer our own biology while creating therapeutic options that are both safer and more effective than current alternatives.

“There are certainly important questions that we as scientists need to be asking ethically,” Jewett says. “We have some very good practices in place, and at the end of the day, the research that’s coming out of synthetic biology will help people. I think that’s important.”

Emily Ayers