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Three Caltech Profs Get More Than $5 Million in Grants from the NSF

Three Caltech professors have received grants from the National Science Foundation (NSF) totaling more than $5 million. Their work aims to create an inexpensive process for manufacturing devices on the smallest scale using DNA, to develop "microbiome-in-a-pill" particles, and to better understand how problems in cell signaling and molecular circuits can lead to cancer.

Using DNA to Manufacture Nanoscale Devices

William Goddard III, the Charles and Mary Ferkel Professor of Chemistry, Materials Science, and Applied Physics, has received $1.25 million from the NSF to develop a process that will take advantage of DNA's talent for self-assembly in order to arrange nanomaterials such as carbon nanotubes and proteins into configurations designed for use in devices such as sensors, transistors, and optical components.

(from left) Michael Elowitz, William Goddard III, and Rustem Ismagilov

"Our long-term vision is a bench-top factory in which functional nanomaterials, such as carbon nanotubes and proteins, are assembled with the help of DNA into high-quality nanostructures arranged according to a carefully designed layout," says Goddard. "Unlike previous efforts, where DNA-linked components have been left in solution to assemble on their own, here we want to both monitor and electronically control the assembly, in real time, on a surface."

Imagine, for instance, that engineers want to mass-produce biosensors capable of monitoring protein interactions at the nanoscale and optically communicating their findings. That would involve integrating several different nanodevices, determining whether they're working properly, and fixing any problems with the assembly. "This sort of component integration and quality assurance is routine for the world of everyday, or macroscopic manufacturing, but we don't yet have anything like it for DNA assembly at the nanoscale," says Si-ping Han, a postdoctoral scholar in Goddard's lab and a coinvestigator on the new grant. "We'd like to combine the best features of macroscopic and nanoscale assembly to crank out high-quality devices and widgets in a scalable and economical way."

Goddard's coinvestigators on the new three-year grant include Han; Marc Bockrath of the University of California, Riverside; and Ned Seeman and Jim Canary, both of New York University.

Developing "Microbiome-in-a-Pill" Particles

Rustem Ismagilov, the John W. and Herberta M. Miles Professor of Chemistry and Chemical Engineering,

has received a $2 million NSF award from the Office of Emerging Frontiers in Research and Innovation (EFRI) to develop a method of creating and studying communities of bacteria that are precisely spaced with relation to one another. His group hopes to lay the groundwork for "microbiome-in-a-pill" particles, which could one day deliver spatially structured mixes of needed microbes to prevent or treat conditions associated with microbial imbalance.

"Scientists are discovering that the microbes in us and on us play an important role in many aspects of our health and well-being," says Ismagilov. Indeed, one of his coprincipal investigators, Sarkis Mazmanian, assistant professor of biology at Caltech, studies the relationship between gut bacteria and health conditions such as inflammatory bowel disease, colitis, and multiple sclerosis. Ismagilov's group has found that the spatial distribution of bacteria, which determines how easily they can exchange metabolites and signaling molecules with one another, can make a big difference in terms of microbial growth as well as in the production or consumption of molecules. And all of that can affect the host.

"In preliminary experiments we've shown that you can make small microcolonies on chips and control how the microbes communicate chemically with one another," Ismagilov says. "But you can't ask people to be swallowing chips, so we'd like to take what we're discovering on a chip and actually mass produce it in the quantities that are sufficient to start testing these communities *in vivo*."

It's estimated that the project will last for four years. Additional coprincipal investigators include Alexander Chervonsky, Christopher Henry, and Folker Meyer of the University of Chicago. Henry and Folker are also affiliated with the Argonne National Laboratory.

Understanding the Role of Signaling and Cell Fate Decision Circuits in Cancer

Michael Elowitz, professor of biology and bioengineering, is principal investigator on a second $2 million EFRI grant. This project aims to understand what happens to cell-to-cell communication and the circuits of interacting biomolecules that control differentiation and other normal cellular processes when cancer takes hold. Using colon-cancer stem cells as its model system, the group will produce devices for tracking colon stem-cell behavior, create mathematical models of what they observe, and then engineer synthetic genetic circuits to test how cell organization and signaling can cause normal stem cells to become cancerous.

Elowitz is working with Steven Lipkin of Weill Cornell Medical College, Xiling Shen of Cornell University, and Ron Weiss of the Massachusetts Institute of Technology on this four-year project.

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