A Call for Collaboration

PILOT PROGRAM FROM HHMI AWARDS $40 MILLION TO EIGHT MULTIDISCIPLINARY TEAMS.

UNTIL FOUR YEARS AGO, DANNY REINBERG'S RESEARCH COMFORTABLY revolved around molecules and cells, just what Reinberg—a biochemist and HHMI investigator at New York University—had been trained to study. But then, at a scientific meeting, colleague Shelley Berger of the Wistar Institute mentioned her recent fascination with ant behavior, after observing leafcutter ants in Costa Rica. She suggested that ants might be a perfect organism for studying gene expression and behavior.

That encounter led to a unique, multidisciplinary collaboration that calls on the expertise of everyone involved. It's one of eight such collaborative projects that HHMI is funding as part of a $40 million pilot program.

The Collaborative Innovation Awards represent the first time the Institute will provide funding for specific research projects rather than funds for investigators to take their science in any number of directions. The new funds are intended to encourage HHMI investigators to join with scientists outside HHMI to undertake projects that are new and so large in scope that they require a team covering a range of fields. In Reinberg's case, that means collaborating with Berger as well as Juergen Liebig of Arizona State University, a leader in studying the complicated social dynamics of insect societies. The team hopes to explain how gene expression—rather than gene sequence—is passed to generations of ants, affecting their behavior, social roles, and aging.

Left to right: *Catherine Dulac, Harvard University; Susan Lindquist, Whitehead Institute for Biomedical Research; Douglas Rees, California Institute of Technology; Danny Reinberg, New York University School of Medicine; Simon John, Jackson Laboratory; Peter Walter, University of California, San Francisco; Xiaowei Zhuang, Harvard University; Huda Zoghbi, Baylor College of Medicine.*

HHMI's vice-president and chief scientific officer, Jack Dixon, says the newly funded projects represent an important step for the Institute. "This award permits our investigators to assemble the team of experts they need to attack these complex scientific problems," he says. "We were looking for projects that could represent breakthroughs—those that could really change the way we think."

At the Jackson Laboratory, in Bar Harbor, Maine, HHMI investigator Simon John has spent more than a decade using mouse models to study glaucoma—a major cause of vision loss and blindness. Glaucoma researchers desperately need new tools for measuring intraocular pressure, according to John. High intraocular pressure, which damages nerve cells in the eye, is a common cause of glaucoma.

With the help of a Collaborative Innovation Award, John will work with two Purdue University engineers to develop the world's

Dulac: Matt Kalinowski Lindquist: Cheryl Senter / AP, ©HHMI Rees: Rene Macura / AP, ©HHMI Reinberg: Bizuayehu Tesfaye / AP, ©HHMI
John: Michael C. York / AP, ©HHMI Walter: George Nikitin / AP, ©HHMI Zhuang: Cheryl Senter / AP, ©HHMI Zoghbi: Bob Levey / AP, ©HHMI

first ultraminiature pressure-sensing device that can be implanted in the eyes of mice that have—or are at risk of developing—glaucoma.

"This program requires the investigators to step outside their normal comfort zone and expertise," says John. "We thought our plan was a good match."

Only slightly thicker than a human hair, and capable of transmitting the data it collects to the researchers via a tiny wireless antenna, the sensor could have other applications, says John—monitoring blood pressure or cerebrospinal fluid, for example.

HHMI investigator Catherine Dulac, of Harvard University, will use the new funding to lead a team of neuroscience experts in studying the impact of gene imprinting—a phenomenon in which only a single gene copy is expressed rather than both chromosomal copies—on behavior and brain development. She's collaborating with three other Harvard researchers who specialize in how neurons make decisions, the role of genetics in neurological disorders, and the evolutionary role of imprinting in the embryo. By some estimates, the team could find 600 or more genes controlled by imprinting, but Dulac doesn't really know what they'll find.

"I have been thinking for many years about the mechanisms of gene regulation—such as imprinting—and the coevolution of neuronal function and behavior," she says. "This has triggered the interest of several colleagues with very different fields of expertise, who can now brainstorm and test key hypotheses together."

HHMI plans to evaluate the progress of the eight collaborative projects selected for this pilot phase and expects to expand the program in coming years. Philip Perlman, a senior scientific officer at HHMI who oversees the program, stresses that such funding is valuable because scientists often hesitate to undertake large collaborations, which can be seen as detracting from a lab's primary focus. "Many research groups find it difficult to allocate resources to allow one or more members to devote years to a project that could yield important results but may never directly further the lab's own mission," says Perlman.

Reinberg, who now has to make room in his lab for boxes of ants frozen in liquid nitrogen and shipped from Arizona, loves his new collaboration because it allows him to study new areas—like neuroscience. "I have been working in cells for more than 20 years," he says. "And now I have the opportunity to work on whole organisms and move into neurobiology. This project has opened the door for my next 20 years of science." ■

—SARAH C.P. WILLIAMS

OTHER COLLABORATIVE INNOVATION AWARD PROJECTS

DOUGLAS REES, of the California Institute of Technology, is leading a team of three experts in structural biology and protein chemistry to develop a novel way to solve the three-dimensional structures of proteins embedded in membranes. Such proteins are vital to cells—they act as gatekeepers between compartments and between the cell and its surroundings—but they are notoriously hard to work with.

PETER WALTER, at the University of California, San Francisco, an expert in protein folding, will enlist five collaborators in San Francisco and Chile to probe whether it's possible to target drugs to different steps of the pathway that guards cells against misfolded proteins.

SUSAN LINDQUIST, at the Whitehead Institute for Biomedical Research, wants to find strategies to target the biological mechanisms that break down in Parkinson's disease and other neurodegenerative disorders. Her long-term goal is to develop personalized treatments for patients. Partners include stem cell expert Rudolf Jaenisch and colleagues at the University of Alabama, Boston University, and Purdue University.

HUDA ZOGHBI has a plan for speeding up drug discovery. Her team, at Baylor College of Medicine and the University of Minnesota, is working on a rapid way to identify hundreds of genes involved in clearing disabled proteins from the brain—a process that goes awry in Parkinson's disease. "If we can figure out the neurobiology for one of these diseases, it can then be applied to many of the other neurodegenerative disorders," says Zoghbi.

XIAOWEI ZHUANG, whose Harvard University lab develops imaging techniques, is taking a closer look at the brain. By collaborating with creators of some of the most powerful and innovative methods for imaging, data analysis, and sample preparation, Zhuang seeks to map out all the neural connections in mammalian brains.