



Solving Big Questions

BY KATHRYN BROWN

POISED TO ENGAGE IN SOME OF SCIENCE'S LARGEST RIDDLES, SEVEN RESEARCHERS ARE APPOINTED TO BE THE FIRST GROUP LEADERS AT HHMI'S JANELIA FARM RESEARCH CAMPUS.

> Some scientific problems get solved at 3:00 a.m., with a jolt of insight in the dark. Some need 5 years of solid, steady work. And then there are the Big Ones—looming, bewitching scientific riddles that could take 100 years to crack. *How does the human brain work? What is consciousness?* > It takes a rare researcher to pursue big questions with creativity and focus. But HHMI recently found seven such scientists. In June, HHMI announced the selection of seven group leaders for its Janelia Farm Research Campus. Slated to open next year in Ashburn, Virginia, Janelia Farm is HHMI's first freestanding research community. The \$500 million campus will bring together small research groups in a highly collaborative environment to tackle fundamental biomedical problems that linger unsolved in traditional research settings. > “HHMI always has sought to support the most original, creative science,” says Janelia Farm Director Gerald M. Rubin, also a vice president at HHMI. “Janelia Farm extends this effort, opening a new frontier for the Institute.” Rubin calls the campus a “once-in-a-generation opportunity” for science to build something new. > Janelia Farm's first set of group leaders have diverse backgrounds, from mathematics and physics to computational biology and genetics. Their wide-ranging

interests include mathematical theories of brain design, gene and genome function and structure, the neural circuits behind specific behavior, and image analysis.

TOGETHER, THESE GROUP LEADERS WILL LAUNCH AN AMBITIOUS AGENDA. Janelia Farm will pursue two basic, and intertwined, goals: identifying the general principles that allow neural circuits to process information and developing imaging technologies and computational methods for image analysis. > Put simply, Janelia Farm scientists will develop new ways to peer inside a working brain, revealing brain anatomy and function in unprecedented detail.

To do that, each group leader will head a small team of up to six scientists. These interdisciplinary teams will work side by side, breaking down big scientific questions into smaller steps. When new tools—from specialized microscopes to specific computer programs—are needed, they (and support staff) will simply build them.

GREAT ADVENTURE: > Group leader Nikolaus Grigorieff, currently an HHMI investigator at Brandeis University, calls Janelia Farm “a great adventure.” Grigorieff develops cellular image-processing techniques based on electron microscopy. “To win grant funding in academics, you generally have to propose research that’s practically guaranteed to be successful, and that can be boring,” says Grigorieff. > “But at Janelia, we’re going to be given resources and time, with the trust that we’ll have good ideas. That’s very different.” While at Janelia Farm, Grigorieff plans to collaborate with neurobiologists, perfecting imaging techniques to spotlight activity at brain synapses.

Group leaders are roughly equivalent to academic professors in that they’re intellectually independent and direct a research team of postdoctoral fellows, graduate students, and technicians. But that’s where the similarities end. Unlike their academic peers, Janelia Farm group leaders will not teach, write grant proposals, or do administrative tasks. > Instead, they will devote their full attention to research, with minimal distractions.

In return, Janelia Farm group leaders agree to spend 75 percent of their professional time focused on research at the campus. In their remaining time, leaders can attend conferences, review for journals, give outside seminars, and pursue other scientific activities. Group leaders also may use part of this time to consult for industry, in accordance with HHMI policies.

That schedule suits group leader Sean Eddy, currently an HHMI investigator at Washington University in St. Louis. Eddy knew he wanted to join Janelia Farm 5 years ago, when he first heard Rubin describe the campus. “I’m the kind of guy who prefers to work with my own hands,” says Eddy, a computational biologist who builds mathematical tools to probe genomes. “I enjoy being a professor, but I’m constantly training, training, training. At Janelia Farm, I will get to do the science.” While at the campus, Eddy plans to adapt his computational techniques to the study of neural circuits.

> RUBIN ENVISIONS JANELIA FARM AS A COMBINATION THINK TANK AND RESEARCH LAB, with an unstructured, open environment that invites brainstorming and long, meaningful debate. The plan for the campus emerged as HHMI leadership realized that some biomedical research problems cannot be adequately addressed in a university environment. Developing new tools for biological discovery, for instance, requires diverse expertise. But university scientists often work in distant departments, with little opportunity to collaborate extensively.

HHMI modeled Janelia Farm after the best features of two widely respected institutions: the Medical Research Council Laboratory of Molecular Biology (MRC LMB) in Cambridge, United Kingdom, and AT&T’s Bell Laboratories in the United States. Although these organizations have had different missions, both incorporated small research groups, generous funding, and top support services.

In addition to the incoming group leaders, HHMI has appointed two senior fellows to Janelia Farm: Nobel laureate Sydney Brenner of the Salk Institute for Biological Studies in La Jolla, California, who is the former director of MRC LMB, and Charles V. Shank, former director of Lawrence Berkeley National Laboratory, who also worked at Bell Labs. The senior fellows will advise Rubin, spend several weeks a year in residence at Janelia Farm, and help shape its research program.

The incoming group leaders and their current affiliations



DMITRI B. CHKLOVSKII
COLD SPRING HARBOR LABORATORY,
NEW YORK



SEAN R. EDDY
HHMI INVESTIGATOR AT WASHINGTON
UNIVERSITY SCHOOL OF MEDICINE
IN ST. LOUIS



NIKOLAUS GRIGORIEFF
HHMI INVESTIGATOR AT BRANDEIS
UNIVERSITY, MASSACHUSETTS

YES, THERE IS SOME RISK THE EXPERIMENT WILL FAIL, AND WE'LL HAVE TO READJUST. BUT IF WE'RE SUCCESSFUL, WE'LL CREATE A DIFFERENT WAY OF DOING BIOMEDICAL RESEARCH. ■

> “There are three critical ingredients for a leading lab: stable funding, top scientific leadership, and scientific focus,” says Shank. “Janelia Farm has all three. This HHMI effort is poised to make fundamental contributions to the understanding of neural networks, laying the foundation for a new understanding of the human brain.”

The research programs at Janelia Farm naturally extend HHMI’s commitment to offering creative scientists freedom from research constraints. Janelia Farm’s campus and scientific program will complement HHMI’s long-standing investigator program, which currently consists of more than 300 researchers at 64 universities throughout the United States who have the freedom and flexibility to push the bounds of biomedical research. > HHMI recently announced the selection of 43 of the nation’s most promising biomedical scientists as new HHMI investigators.

LIKE HHMI’S INVESTIGATOR POSITIONS, JANELIA FARM APPOINTMENTS ARE TEMPORARY. Group leaders will be appointed for an initial 6-year term. At that point, outside experts and HHMI leadership will review each group leader’s contribution, including research progress, collaboration, and mentoring. Successful group leaders will be offered a 5-year renewal, with an invitation to stay at Janelia Farm. (The review process will be repeated every 5 years.) Those leaders also can choose to move on, as HHMI investigators, to another U.S. research institution.

If successful group leaders develop interests that stray from Janelia Farm’s mission, they may be offered renewal, without an invitation to stay. Those leaders, too, will be offered HHMI investigator appointments at other research institutions. Finally, group leaders who are not renewed will be given 2 years of research support.

PURE SCIENCE: > As a postdoctoral fellow at the University of Wisconsin–Madison, incoming group leader Julie Simpson says this is the perfect time in her career to experience Janelia Farm. “This is a unique opportunity, and I’m fortunate that the timing works so well,” Simpson says. “I’m delighted to be going because Janelia is a chance to do pure science.” Simpson investigates the neural basis of particular behaviors, such as motor control, in the fruit fly *Drosophila*.

To recruit the first wave of Janelia Farm group leaders, HHMI looked for scientific researchers in the fields of biology, chemistry, computer science, engineering, mathematics, and physics who were interested in neuronal circuits and imaging. “We also considered applications from exceptionally talented individuals working outside these defined areas,” adds Rubin. > HHMI used both targeted recruitment and an open international competition, which yielded more than 300 applications. Those applications were reviewed by groups of HHMI researchers, supplemented as needed with physicists, engineers, and computer scientists.

This fall, HHMI plans to announce a second open application process. This round will include a December application deadline, resulting in offers to perhaps five additional group leaders by the spring of 2006. **LATER NEXT YEAR, WHEN JANELIA FARM OPENS ITS DOORS, HHMI WILL BEGIN CONTINUALLY RECRUITING FOR ADDITIONAL STAFF.** By 2009, when the campus is fully operational, it will include 24 group leaders and a permanent research staff of about 300 scientists.

Known for his entrepreneurial verve, Rubin acknowledges that Janelia Farm is a risky endeavor. > “We’re doing an experiment here,” he says. “Yes, there’s some risk the experiment will fail, and we’ll have to readjust. But if we’re successful, we’ll create a different way of doing biomedical research.” ■



EUGENE W. MYERS
UNIVERSITY OF CALIFORNIA,
BERKELEY

JULIE H. SIMPSON
UNIVERSITY OF WISCONSIN–MADISON

ROLAND STRAUß
UNIVERSITY OF WÜRZBURG,
GERMANY

KAREL SVOBODA
HHMI INVESTIGATOR AT COLD SPRING
HARBOR LABORATORY, NEW YORK

©PAUL FETTERS