them to quickly change their proteins to bind to different cell receptors. The researchers, who encountered this genetic property while working on an unrelated project, believe that this discovery could lead to the use of genetically engineered phages to treat bacterial infections that have become resistant to antibiotics.

The discovery was made by researchers at the University of California, Los Angeles led by Jeffery F. Miller, PhD, professor and chair of microbiology, immunology, and molecular genetics. Dr. Miller's team found that the genome of the phage that infects *Bordetella bronchiseptica*, a relative of the bacterium that causes whooping cough, contains a series of genes that change the part of the virus that binds to the bacterial cell. These genes allow the phage to rapidly evolve new variants that can recognize and attack bacteria that may have become resistant to the previous phage.

Dr. Miller's team is continuing to study this genetic mechanism to learn more about its biochemical properties and to determine whether higher forms of life have similar classes of genes. He believes that, in time, they will be able to use the knowledge gleaned from this discovery to generate proteins in the laboratory that will bind to almost any molecule of interest.

# HHMI, NIBIB/NIH to Invest up to $35 Million in Interdisciplinary PhD Programs

As biomedical science becomes more interdisciplinary, research progress will depend on contributions from life scientists who are familiar with the tools and ideas of the physical and computational sciences and engineering. The Howard Hughes Medical Institute (HHMI) and the National Institute of Biomedical Imaging and Bioengineering (NIBIB) of the National Institutes of Health (NIH) are joining forces to provide both start-up funds and sustaining support for graduate training programs that integrate the biomedical sciences with the physical sciences and engineering. HHMI will award up to 10 3-year grants of as much as $1 million each to support the development and early phases of the interdisciplinary programs. NIBIB, a new NIH institute with broad, interdisciplinary goals, will provide 5 additional years of support to the HHMI grantees through peer-reviewed institutional training grants.

Building on work begun by the Whitaker Foundation, the National Science Foundation, and the Burroughs Wellcome Fund, HHMI and NIBIB together have created a new model to support the initiation, development, and maintenance of new graduate programs to provide upcoming biomedical scientists with the cross-disciplinary knowledge and skills they will need.

In October 2004, HHMI will open a competition for up to 10 grants to educational institutions, totaling as much as $1 million each. The grants will be awarded in November 2005. All US institutions that grant PhD degrees in the biologic sciences will be eligible for the 3-year awards.

The HHMI-NIBIB partnership will capitalize on the different strengths of each organization. The new NIH Roadmap and recent reports from the National Academies Convocation on Facilitating Interdisciplinary Research and the Association of American Medical Colleges' Graduate Research, Education and Training Group emphasize the need for a new kind of graduate education that will prepare scientists to work across disciplinary lines to solve complex biomedical problems.

The new graduate training program parallels HHMI's commitment to bring together biologists, computer scientists, engineers, physicists, chemists, and mathematicians to conduct collaborative research at Janelia Farm, HHMI's new research campus now under construction in Loudoun County, Virginia.



# First NIH Director's Pioneer Award Recipients Named

The National Institutes of Health (NIH) has selected the first recipients of the NIH Director's Pioneer Award, a program designed to support individual scientists and thinkers with highly innovative ideas and approaches to contemporary challenges in biomedical research. A central component of the NIH Roadmap for Medical Research, the Director's Pioneer Award was established in January 2004 to encourage exceptional researchers and thinkers from multiple disciplines to conduct high-risk, high-impact research related to the improvement of human health.

To inaugurate this new program, the NIH will provide $500,000 in direct costs per year for 5 years to each Pioneer Award recipient, allowing them the time and resources to test far-ranging ideas with the potential to make extraordinary contributions to medical research:

- Laurence F. Abbott, PhD, Brandeis University, Waltham, Massachusetts. Dr. Abbott is the Brandeis Professor

of Neuroscience at Brandeis University. He received his PhD in physics at Brandeis in 1977. After a 10-year career in theoretical particle physics, Abbott switched his research interests to the mathematical modeling and analysis of neurons and neural networks. His research involves using analytic techniques and computer simulation to study the electrical characteristics of single neurons, to determine how neurons interact to produce functioning neural circuits, and to investigate how large populations of neurons represent, store, and process information. He is the author of numerous research articles in particle physics and neuroscience, as well as a widely used textbook on theoretical neuroscience.

- George Daley, MD, PhD, Children's Hospital Boston, Boston, Massachusetts. Dr. Daley is associate professor of biologic chemistry and pediatrics at Harvard Medical School in Boston, Massachusetts. He earned his doctorate in biology in 1989 from the Massachusetts Institute of Technology and his medical degree in 1991 from Harvard Medical School. Dr. Daley studies stem cells of the blood to define the molecular basis of human leukemia and to gain insights into normal blood development. He has won several awards and has published 85 journal articles. In 2003, his germ cell research was cited as a top 10 breakthrough by *Science* magazine.
- Homme Hellinga, PhD, Duke University Medical Center, Durham, North Carolina. Dr. Hellinga is professor of biochemistry at Duke University Medical Center. He received a doctorate in molecular biology in 1986 from the University of Cambridge. His research interests include combined theoretical and experimental approaches to protein and drug design, molecular simulation, and protein engineering. Dr. Hellinga has published more than 44 journal articles. He holds three patents, with three more pending approval.
- Joseph McCune, MD, PhD, University of California, San Francisco (UCSF). Dr. McCune is a senior investigator at the Gladstone Institute of Virology and Immunology, a professor of medicine and of microbiology and immunology at UCSF, and an associate director of the General Clinical Research Center at San Francisco General Hospital/UCSF. He earned his medical degree from Cornell University Medical College and his doctorate in immunology and cell biology from The Rockefeller University and then completed a residency in internal medicine at UCSF. Dr. McCune's laboratory focuses on the pathogenic mechanisms of the human immunodeficiency virus (HIV). He won the Elizabeth Glaser Pediatric AIDS Foundation Scientist Award in 1996 and the Burroughs Wellcome Fund Clinical Scientist Award in Translational Research in 2000. He holds 20 patents and inventions and has published 120 journal articles.
- Steven McKnight, PhD, University of Texas Southwestern Medical Center, Dallas. Dr. McKnight is professor and chairman of the biochemistry department at University of Texas Southwestern Medical Center. He earned his doctorate in biology in 1977 from the University of Virginia. The McKnight laboratory seeks to understand the regulation of transcription factors, the regulatory proteins that switch genes on and off, at a biochemical level with keen attention to biologic relevance. He is a member of the National Academy of Sciences and serves on the Scientific Advisory Board of the Howard Hughes Medical Institute and the Board of Trustees of the Carnegie Institution of Washington.
- Chad Mirkin, PhD, Northwestern University, Evanston, Illinois. Dr. Mirkin is the George B. Rathmann Professor of Chemistry and director of the Institute for Nanotechnology at Northwestern University. Mirkin is pioneering the development of nanoscale chemical and biologic sensors. He also invented and developed Dip-Pen Nanolithography, a groundbreaking nanoscale analytical tool. Some of his many honors include the Raymond and Beverly Sackler Prize in the Physical Sciences, the ACS Nobel Laureate Signature Award, the ACS Award in Pure Chemistry, the Feynman Prize in Nanotechnology, and the Leo Hendrick Baekeland Award. Mirkin has authored over 200 publications and 75 patents, serves on the editorial advisory board of 12 chemistry journals, and is the founding editor of the international journal of nanotechnology, *Small*. He is also the founder of two companies, Nanosphere and NanoInk.
- Rob Phillips, PhD, California Institute of Technology, Pasadena, California. Dr. Phillips is professor of engineering and applied science at the California Institute of Technology in Pasadena. He received his doctorate in physics in 1989 from Washington University in St. Louis, Missouri. His laboratory's research projects are aimed at exploring nanoscale mechanics in biologic systems. Several recent case studies include mechanical processes such as deoxyribonucleic acid (DNA) ejection and DNA packing that occur during the life cycle of bacterial viruses and the study of how certain classes of ion channels are gated by mechanical forces. His extensive work in modeling materials culminated in a book entitled *Crystals, Defects and Microstructures*.
- Stephen Quake, PhD, Stanford University, Palo Alto, California. Dr. Quake, formerly of the California Institute of Technology, is currently a professor of bioengineering at Stanford University. He earned his doctor of philosophy in 1994 from Oxford University. After a postdoctoral fellowship at Stanford, he began his independent career at the California Institute of Technology in 1996, where he rose through the ranks to become the Thomas E. and Doris Everhart Professor of Applied Physics and Physics. Dr. Quake's laboratory is broadly interested in biophysics and bioengineering and uses techniques such as single-molecule spectroscopy and microfluidics to address a variety of fundamental and technological questions.
- Sunney Xie, PhD, Harvard University, Cambridge, Massachusetts. Dr. Xie is professor of chemistry in the Department of Chemistry and Chemical Biology at Harvard University. He earned his doctorate in chemistry in 1990 from the University of California, San Diego. His research objectives are to understand conformational and chemical dynamics of biomolecules such as enzymes through single-molecule spectroscopic studies; to study the biochemical activities of macromole-

cules in living cells, gene expression in particular, at the single-molecule level; and to develop new microscopy techniques for cellular imaging. Dr. Xie holds three patents and has published more than 70 journal articles. In 2003, he won the Raymond and Beverly Sackler Prize in the Physical Sciences

The nine recipients represent a broad spectrum of scientific disciplines, including quantitative and mathematical biology, pathogenesis, epidemiology and translational clinical research, molecular and cellular biology, integrative physiology, instrumentation, and bioengineering.

Applicants underwent a rigorous nomination and selection process to establish who among them appeared to hold the greatest potential for addressing critical scientific questions that would greatly impact biomedical science and health care. Nominees and applicants were expected to demonstrate a commitment to accepting considerable risk in addressing critically important scientific questions relevant to the mission of the NIH.

External evaluators representing a broad range of scientific disciplines screened approximately 1,000 nominations and recommended that a subset of 240 nominees be invited to submit award applications. Further review by external evaluators resulted in the selection of 21 candidates, who were invited to the NIH for interviews and to present their ideas. The recommendations of the panel of external evaluators who interviewed the 21 candidates were considered by the Advisory Committee to the Director, NIH, and the NIH director.

The applicants were evaluated based on the following criteria: evidence of scientific innovation and creativity; testimony of intrinsic motivation, enthusiasm, and intellectual energy; and potential for scientific leadership and evidence of, or potential for, effective communication skills.

# Hopkins Scientists Use Blood Proteins to Detect Ovarian Cancer

Johns Hopkins Kimmel Cancer Center researchers have designed a blood test to detect ovarian cancer using three proteins found in common in the blood of women with the disease. Their preliminary studies with the new test suggest a molecular signature exclusive to this deadly cancer, known for its ability to remain undetected and spread quickly.

The Hopkins test, described in the August 15, 2004, issue of *Cancer Research*, identifies the proteins as a truncated form of transthyretin, a fragment of ITIH4 and apolipoprotein A1, teased out with a rigorous evaluation of protein patterns present in blood samples from ovarian cancer patients at several US and international hospitals. Other research groups are evaluating ovarian cancer blood tests that use protein profiles consisting of tens of thousands of unidentified molecules.

This research was funded by the National Cancer Institute and Ciphergen Biosystems of Fremont, California, which licensed the test.

The study, led by Daniel W. Chan, PhD, professor and director of the Biomarker Discovery Center, emphasizes that the test will not be commercially available for screening the population at large until completion of further validation studies in larger groups of patients. Even then, Chan notes, it is never going to be possible for a blood test to correctly diagnose 100% of cancerous tumors 100% of the time. They believe, however, that with some refinements, it may already have use for helping determine whether a pelvic mass is ovarian cancer.

In a systematic search to find the most promising blood proteins for their test, the Hopkins scientists conducted a multicenter study and used protein chip technology to screen 195 blood samples from two groups of ovarian cancer patients, healthy people, and patients with benign ovarian tumors. A sophisticated bioinformatics program was used to select proteins present at unusually high or low levels in ovarian cancer samples compared with normal patients or benign tumors. Samples in the two groups were analyzed separately to account for differences in patient populations and sample collection techniques. Then the researchers compared protein profile results in these two groups and ultimately narrowed the search for potential marker candidates to the three proteins, one of which (ITIH4) is commonly found at high levels in ovarian cancer and the other two at lower levels.

The new proteins were screened against a separate collection of blood samples from patients with normal and cancerous tissues. Of 23 patients with early-stage ovarian cancer, the three protein markers plus cancer antigen (CA) 125 correctly identified cancer 74% of the time (17 of 23) compared with 65% (15 of 23) with CA 125 alone. Although the sample size was too small for this difference to be statistically significant, the scientists conducted further studies, lowering the cutoff value for CA 125 to below current standards. The new test plus CA 125 and CA 125 alone detected 83% (19 of 23) of the cancers. In addition, the new test plus CA 125 correctly identified healthy samples 94% of the time (59 of 63) compared with 52% (33 of 63) for CA 125 alone.

To verify that the candidate markers were specific to ovarian cancer, the scientists also compared the results of the protein profiles with a separate group of blood samples from 142 Johns Hopkins ovarian, breast, colon, and prostate cancer patients and healthy people. Protein markers from these ovarian cancer samples matched those from the other two groups of blood samples. Breast, colon, and prostate cancer samples exhibited levels of the three proteins closer to those of normal patients, indicating that the markers may be exclusive to ovarian cancer.

The scientists will conduct further studies to map all three proteins to the genetic pathways linked to ovarian cancer development and combine the blood test with radiologic tools, such as ultrasonography. They also will search for more proteins to add to the current panel of markers.