NIH BACKGROUNDER

National Institutes of Health September 2005

NIH Roadmap for Medical Research

Celebrating Two Years of Progress

New Pathways to Discovery

- **Building Blocks, Biological Pathways, and Networks**
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- **Patient-Reported Outcomes Measurement Information System (PROMIS) Network**

For more information about the NIH Roadmap for Medical Research, please go to: http://nihroadmap.nih.gov/.

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New Pathways to Discovery

The human body is dauntingly complex. To truly revolutionize medicine and improve human health, we need a more detailed understanding of the vast networks of molecules that comprise our cells and tissues, their interactions, and their regulation. We also must have a more precise knowledge of the combination of molecular events that lead to disease. New Pathways to Discovery is the NIH Roadmap theme that sets out to advance our understanding of biological systems and to build a better "toolbox" for medical research in the 21st century.

Building Blocks, Biological Pathways, and Networks
Better Tools and Technologies for a Better Tomorrow

In the human body, all biological components – from individual genes to entire organs – work together to promote normal development and to sustain health. This amazing feat of biological teamwork is made possible by an array of intricate and interconnected pathways that facilitate communication among genes, molecules, and cells.

While some of these biological pathways have already been discovered, many more remain to be found. Further research is also needed to understand how these pathways are integrated in humans and other complex organisms, as well as to determine how disturbances in these pathways may lead to disease and what might be done to restore disturbed pathways to their normal functions.

Through the Building Blocks, Biological Pathways, and Networks (BBPN) initiatives, part of the New Pathways of Discovery theme of the NIH Roadmap for Medical Research, researchers are focusing on the development of new technologies to accelerate discovery and to facilitate comprehensive study of biological pathways and networks. One of the central components of such networks is the set of proteins encoded by an organism's genome, commonly referred to as the "proteome." Another critical focus is providing researchers with novel analytical tools to better understand the metabolic components and networks within the cell, commonly referred to as the "metabolome."

To better understand the proteome, innovative tools are being developed to enable researchers to determine in real time the amounts, locations, and interactions of large numbers of individual proteins within a single cell. NIH has established a series of National Technology Centers for Networks and Pathways (TCNPs) to promote the development of new proteomic technologies.

Such capability is crucial to expanding the identification of biological pathways and developing treatments for diseases involving these pathways.

In the field of metabolomics, researchers are eager for technologies that will enable them to measure local concentrations of carbohydrates, lipids, amino acids, and other metabolites within a single cell or even within a specific part of a single cell. Current areas of research emphasis include approaches that will address the widely fluctuating range of metabolite concentrations and complexity of metabolite mixtures, the vast number of unidentified compounds present within single samples, and the dynamic nature of the cell's entire set of metabolites. This type of comprehensive information may pave the way for the development of better methods to detect metabolic differences between normal and diseased cells.

In addition to projects that explore technology and knowledge development, BBPN initiatives also support workshops that allow experts from all over the world to come together to discuss ideas for advancing the state of the science in the fields of proteomics and metabolomics research. In January 2005, the BBPN sponsored a workshop in Bethesda, Maryland, entitled, "Standards in Proteomics." The purpose of this workshop was to develop a community-based plan, as well as mechanisms for implementation, for the consistent analysis, representation, dissemination, and publication of proteomic data. In addition, the BBPN sponsored an August 2005 workshop entitled, "Standards in Metabolomics." This internationally attended workshop was held to help investigators in the field of metabolomics develop the necessary informatics standards to improve exchange of information and its analysis in metabolomics.

Ultimately, the NIH hopes that the information generated through BBPN initiatives will be used in biomedical research to discover earlier and more precise diagnosis, prevention, and treatment strategies for a wide variety of diseases.

Molecular Libraries and Molecular Imaging

Screening Centers Operational, Expanding; Results Released in Public Database

A short two years after conceiving the idea, the first public, high throughput-screening centers for small molecules have begun releasing results in a new, freely available database, including efforts aimed at identifying potential treatments for AIDS, cancer and rare genetic disorders.

The new results are coming from the Molecular Libraries and Imaging initiatives of the New Pathways to Discovery portion of the NIH Roadmap. Molecular libraries are collections of chemical compounds – often called small molecules by researchers – that can probe the functions of genes, cells and biochemical pathways in health and disease. NIH researchers designed the project to produce a better toolbox for revealing the workings of complex biological systems.

The first component of this initiative, the NIH Chemical Genomics Center (NCGC), began operations in June 2004. Since then, nine more centers in the Molecular Libraries Screening Center Network began work in June 2005 at a cost of $88.9 million over three years. The other centers in the network are located in Pennsylvania, California, New York, Florida, Georgia, Tennessee, Alabama, and New Mexico.

To feed the network with small molecules for testing, NIH created the Molecular Libraries Small Molecule Repository, located at the San Francisco facilities of Discovery Partners International. Once fully operational, the network will be able to screen more than ten thousand small molecules against a minimum of 10 distinct bioassays at each center this year. In the future, a collection of 500,000 small molecules will be registered and housed at the molecular repository for screening against as many bioassays as possible.

All of the data produced by the screening network is immediately made freely available to public and private researchers in the PubChem database, http://pubchem.ncbi.nlm.nih.gov/, which was built by the National Center for Biotechnology Information, part of the National Library of Medicine, and launched in September 2004. PubChem provides information on chemical structures and links the structural information to biological activities and the biomedical literature.

In addition to the screening network data, PubChem contains data from NIH-funded programs such as the National Cancer Institute's Developmental Therapeutics Program, the National Institute of General Medical Sciences' LIPID Metabolites And Pathways Strategy, and the ZINC database at the University of California at San Francisco. PubChem also includes data donated from many other public and private sector sources, and there is even a requirement by the new journal *Nature Chemical Biology* that all published chemical structures be deposited in PubChem, which receives data from 25 organizations.

A specialized database was launched in September 2005 called the Molecular Imaging and Contrast Agent database, http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=micad.TOC. This database catalogs imaging probe information from the peer-reviewed literature, describing the specificities, activities and applications of imaging probes for a wide range of diseases and biological functions.

Other efforts funded by the NIH Roadmap project to support the Molecular Libraries and Molecular Imaging initiatives include:

- **Exploratory Centers for Cheminformatics Research (ECCR)** – Six ECCR's have been funded at a total of $2.2 million to develop computer algorithms and software tools for computational chemistry.

- **New Chemical Libraries** – Over each of the next three years, eight investigators will receive grants totaling approximately $3.3 million per year to generate chemical libraries for the NIH Small Molecule Repository. The compounds in these libraries will have unique molecular structures that cannot be obtained commercially.

- **New Methodologies for Natural Products Chemistry** – Six investigators have received three-year grants worth approximately $2.2 million a year to develop new methods for the discovery and production of natural products from sources such as microorganisms, marine organisms and plants.

• **Assay Diversity** – This initiative funded 30 investigators last year to develop a continuously evolving stream of scientifically novel and technologically outstanding bioassays that can be automated and used by the screening centers. This year, an additional 38 investigators have received more than $5.3 million in grants to develop bioassays aimed at cancer, AIDS, neurodegenerative diseases, malaria, and antibacterial and antiviral therapeutics.

• **Instrumentation** – Eight grants totaling $4 million per year are being made to substantially improve the speed, sensitivity, and accuracy of the high-throughput instrumentation to screen the synthetic and natural product libraries.

• **Predictive Absorption, Distribution, Metabolism, Excretion (ADME)/Toxicology** – This effort supports novel approaches to obtain comprehensive ADME and toxicological profiles of chemical probes. Funded by five grants totaling $1.7 million, it will help eliminate the trial-and-error approach to testing.

• **High-Specificity/High-Sensitivity Molecular Imaging Probes** – During the next four years, 11 researchers will use approximately $15 million in grants to support innovative leaps in the creation of molecular probes and imaging systems that are sensitive enough to detect and image individual molecules within living cells while limiting probe toxicity.

Structural Biology

Focus on Membrane Protein Structures Promises Future Medical and Scientific Applications

Scientists seeking to understand the function of molecules often turn to structural biology, which is the determination of the molecule's detailed, three-dimensional structures. But this approach, which has been wildly successful with some proteins, doesn't work well with membrane proteins. Out of the 15,000 or so unique proteins whose structures have been solved, fewer than 100 are membrane proteins. Only two or three of these are from humans. Membrane protein structures are difficult to determine because the molecules, which normally reside within oily cell membranes, don't dissolve easily in water, an essential first step in most structural biology studies.

Why do scientists care about membrane proteins? They are vital to health, comprising about one-third of all human proteins. They control the trafficking of information and materials between cells and mediate critical activities like nerve impulses and hormone action. Defects in membrane proteins cause a host of diseases. In addition, most medications work by exerting their effects on membrane proteins. Clearly, improving the understanding of membrane proteins could shed light on myriad biological processes and dramatically advance the ability of doctors to detect, treat, and prevent disease.

To improve and accelerate structural biological studies of membrane proteins, the NIH Roadmap is awarding 18 new grants in September 2005. These grants are expected to total approximately $19 million over 5 years and include one 5-year program project grant, nine 5-year regular research grants, and eight 2-year exploratory, "high risk, high impact" projects.

The grants encompass a number of structural biology techniques, including X-ray crystallography, magnetic resonance spectroscopy, and cryo-electron microscopy. Some of the projects focus on streamlining the determination of specific membrane proteins, including those targeted by drugs that treat heart disease, cancer, diabetes, depression, tuberculosis, AIDS, and many other ailments. Other projects focus on enhancing one or more critical steps in the structural biology pipeline: expressing the proteins in bacteria, then isolating, purifying, crystallizing, and determining the structures of the molecules. The overall goal of the initiative is to reduce the risk, difficulty, and cost of solving membrane protein structures.

"Membrane proteins are the most challenging – but arguably the most important – proteins for structural biologists to tackle. By lowering the barriers to solving their structures, these projects could lead to new scientific and medical insights that hinge on understanding membrane proteins," said Peter Preusch, Ph.D., the program director at the National Institute of General Medical Sciences, who spearheaded the NIH Roadmap membrane protein effort.

Bioinformatics and Computational Biology

National Centers for Biomedical Computing Create Tools to Use Diverse Datasets

For decades, scientists have developed databases and computational tools to analyze data collected in their laboratories or clinics or to help address specific biological questions. Because each tool was designed independently and functions differently, in most cases they are not compatible with each other. Recent advances in technology make it possible to bring together these resources synergistically to benefit all biomedical scientists.

Toward that end, the NIH Roadmap is funding three new National Centers for Biomedical Computing. Together with four additional centers that NIH funded last year, these centers will serve as the core of a universal computing infrastructure, allowing the biomedical community – including researchers and physicians – to seamlessly integrate, analyze, model, and share data on human health and disease. The new centers, supported by grants projected to total more than $56 million over 5 years, are listed below.

- National Center for Integrative Biomedical Informatics, Brian D. Athey, Ph.D., University of Michigan in Ann Arbor

- National Center for Multi-Scale Analysis of Genetic and Cellular Networks (MAGNet), Andrea Califano, Ph.D., Columbia University in the City of New York

- National Center for Biomedical Ontology, Mark A. Musen, M.D., Ph.D., Stanford University in Palo Alto, CA

"This is a major commitment by the NIH Roadmap to provide powerful – and much needed – computational tools for the biomedical community. These centers will provide user-friendly software and computational infrastructure that will help scientists identify factors critical for improving the health of everyone," said C. John Whitmarsh, Ph.D. Acting Director, Center for

Bioinformatics and Computational Biology at the National Institute of General Medical Sciences, which is leading this Roadmap initiative.

The centers will also play a major role in educating and training researchers to engage in biomedical computing. For example, one of the centers funded in 2004 launched a quarterly magazine called Biomedical Computation Review that offers easy-to-read news and feature articles aimed at researchers who want to use mathematical and computational methods to answer biological questions.

For a free subscription to this publication, go to www.biomedicalcomputationreview.org or e-mail subscriptions@biomedicalcomputationreview.org. For more information about the four existing centers, go to http://www.nigms.nih.gov/news/ncbc.html.

Nanomedicine

Today's Research for Tomorrow's Health Care Solutions

Nanomedicine is an emerging research field with the goal of developing new technologies on a molecular scale to cure disease or repair damaged tissues such as bone, muscle or nerve. It is precisely at this size scale that structures and processes inside living cells operate throughout all the tissues of the body.

It is expected that nanotechnologies can be developed to search out and destroy new cancer cells before they form tumors, to replace broken parts of cells, and to pump life-saving medicines precisely into diseased tissue where and when needed.

The Nanomedicine Initiative, part of the NIH Roadmap, is led by Paul A. Sieving, M.D., Ph.D., Director of the National Eye Institute, and Jeffery Schloss, Ph.D., Program Director, Technology Development, National Human Genome Research Institute, in partnership with the other 25 NIH institutes and centers.

The initiative brings an engineering approach to the study of subcellular and cellular systems. Possibilities include fixing broken subcellular machines and modifying subcellular structures or cells to perform different functions to mitigate disease or tissue damage.

Nanomedicine Development Centers will be established across the country and will be staffed by multidisciplinary scientific teams, including biologists, physicians, chemists, physicists, mathematicians, engineers, and computer scientists. Four new Nanomedicine Development Centers will be awarded in fiscal year 2005 and are projected to receive $43 million over the five year award period. These teams will conduct research and will train the next generation of students in this new research area of medical science.

For the first few years, researchers at the Nanomedicine Centers will gather extensive information about the physical properties of structures inside cells to determine how biology's molecular machines are built. This will require development of a common language to integrate engineering and biological terms and definitions.

As the catalogue of the interactions between molecules and larger structures develops, researchers will be able to map with great precision the processes and networks inside living cells. Understanding how these networks change over time and during disease processes will enable researchers to detect and correct a wide range of biological defects in unhealthy cells.

Dr. Paul Sieving said, “Future progress in medicine will depend on our understanding the complexity of biological systems. The NIH Roadmap, including the Nanomedicine Initiative, will advance our knowledge of biological systems. This will provide the scientific foundation for new strategies to diagnose, treat, and prevent disease.”

It is estimated that nanomedicine will begin to yield practical benefits within 10 years.

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Research Teams of the Future

The scale and complexity of today's biomedical research problems demand that scientists move beyond the confines of their individual disciplines and explore new organizational models for team science. Advances in molecular imaging, for example, require collaborations among diverse groups – radiologists, cell biologists, physicists, and computer programmers. NIH wants to stimulate new ways of combining skills and disciplines in the physical, biological, and social sciences to realize the great promise of 21st century medical research.

Interdisciplinary Research
Merging Scientific Disciplines to Improve Public Health

A generation ago, scientists still spent their careers searching for "the magic bullet," the single drug or therapy with the ability to cure a specific disease, such as diabetes or cancer. Today, as researchers have become more adept at studying the inner workings of cells, tissues, and even human behavior, they have a greater appreciation of the enormous complexity that underlies most human disease. This recognition has raised the stakes for 21st century biology: How does one cut through this sometimes staggering complexity to gain a greater understanding of human health and disease?

One of the best approaches is interdisciplinary research, which integrates the analytical strengths of two or more often disparate scientific disciplines to create a new hybrid discipline. By engaging these seemingly unrelated disciplines, traditional gaps in terminology, approach, and methodology might be gradually eliminated. With potential roadblocks removed, a true collaboration can take place: one that broadens the scope of investigation into biomedical problems, yields fresh and possibly unexpected insights, and gives rise to new interdisciplines that are more analytically sophisticated.

Since its launch two years ago, the NIH Roadmap Initiative is well on its way to establishing interdisciplinary research as an essential component of the biomedical sciences. "We started at square one a few years ago, envisioning the infrastructure that would be required to catalyze interdisciplinary research at grantee institutions across the country," said Lawrence A. Tabak, D.D.S., Ph.D., a co-chair of the interdisciplinary research working group and the director of the NIH's National Institute of Dental and Craniofacial Research (NIDCR). "Since the public launch of the NIH Roadmap, the initiative has progressed at a phenomenal rate. The response from the research community has been overwhelming."

In advancing interdisciplinary research, the NIH Roadmap has:

- Launched 21 3-year Exploratory Centers for Interdisciplinary Research in fiscal year 2004 throughout the country with awards of more than $36 million through fiscal year 2006. These centers allow grantee institutions to build their first interdisciplinary teams, bringing together researchers from the life, physical, material, and computational sciences. Thereafter, the institutions will be prepared to apply for 8 to 10 large NIH research consortia grants, which will enable grantees to apply interdisciplinary approaches directly to complex biological issues.

- Supported a series of long- and short-term training awards. Collectively know as the "Training for a New Interdisciplinary Research Workforce" initiative, these awards have trained a cadre of investigators in fiscal year 2004 and 2005 in interdisciplinary approaches to complex biomedical problems. The training encompasses multiple scientific disciplines, empowering trainees to meld the various disciplines and develop novel experimental approaches to research problems.

- Established supplemental funding to existing NIH research grants in fiscal year 2004 and 2005 that are allowing scientists to fuse behavioral or social science approaches with other biomedical research disciplines. Because the supplements were available to all NIH institutes and centers, they will have an impact across the research spectrum.

- Helped to examine NIH research grant policy regarding the feasibility of recognizing multiple principal investigators on an individual grant. Traditionally, NIH research grants have been awarded to one, rather than multiple, principal investigators. This single-investigator focus has served as a disincentive in building interdisciplinary teams because team members receive unequal credit for their participation.

For more information on the Research Teams of the Future Interdisciplinary Research initiatives, contact Elizabeth Wilder, National Institute of Diabetes and Digestive and Kidney Diseases, (301) 594-1409, wildere@mail.nih.gov.

High-Risk Research: NIH Director's Pioneer Award Program

Supporting Visionary Scientists at the Medical Frontier

The NIH Director's Pioneer Award supports a highly select group of exceptionally creative scientists who take innovative approaches to major challenges in biomedical research. By focusing on people, the Pioneer Award is unlike other NIH grants, which fund research projects. The program enables awardees to address a range of disciplines from new perspectives.

The first nine Pioneer Award recipients were selected in September 2004. They are presenting their advances – in areas ranging from stem cell biology to protein engineering – at the first annual NIH Director's Pioneer Award Symposium on September 29, 2005.

"Each Pioneer awardee is forging new ground in an important scientific field," said NIH Director Elias A. Zerhouni, M.D. "It is obvious just from their first year of work that these scientists are making good on their promise to pursue far-ranging ideas that merit exploration."

Also on September 29, NIH is announcing the second group of 13 Pioneer awardees. A same-day news release lists their names and affiliations and provides details on the selection process. Bio sketches of the awardees are at http://nihroadmap.nih.gov/pioneer/Recipients05.aspx.

2004 Pioneer Awardee Research

Larry Abbott, Ph.D., Columbia University, is using mathematical modeling to study the neural networks responsible for our actions and behaviors. He has devised a new model of synaptic signaling for memory storage and retrieval. Abbott is testing the model and exploring its implications for learning and for designing optimal training strategies.

George Q. Daley, M.D., Ph.D., Children's Hospital Boston/Harvard Stem Cell Institute, aims to define the code that directs an embryonic stem cell to specialize, then use that information to regenerate function lost to disease. His goal is to reprogram body cells by means other than nuclear transfer, which he describes as essentially erasing everything and starting from scratch, and which he believes may be more drastic than necessary.

Homme W. Hellinga, Ph.D., Duke University Medical Center, uses molecular simulation and protein engineering to build components of biological systems and manipulate their interactions. Hellinga has developed a highly automated system to fabricate designed proteins, eliminating a major bottleneck in the process.

Mike McCune, M.D., Ph.D., Gladstone Institute of Virology and Immunology/ University of California, San Francisco, is exploring host immune responses that can suppress HIV infection and disease progression. He is testing the hypothesis that effective immunity against HIV disease progression relies on a balance between immune responses that can clear virus and those that favor viral replication and spread.

Steven L. McKnight, Ph.D., University of Texas Southwestern Medical Center, is studying yeast metabolism to shed light on circadian rhythm, the built-in clock that controls wakefulness, sleep, feeding, and hunger in humans and many other organisms. He has found that the yeast metabolic cycle is controlled by genes that are expressed in an oscillatory manner that is in perfect alignment with the shift between respiration and glycolysis, the two ways that yeast generate energy.

Chad Mirkin, Ph.D., Northwestern University, is using nanobiology to examine how viruses recognize and infect cells as well as to probe complex cellular processes such as adhesion, motility, growth, differentiation, and death. He has developed several nanotechnology tools to advance this research. He has also begun to develop gold nanoparticles that can carry antisense DNA into a cell to alter gene expression.

Rob Phillips, Ph.D., California Institute of Technology, is using the principles of mathematics and physics to describe the machines within cells, their mechanical responses to various stimuli, and how cells and viruses interact. He has determined how bacterial viruses manage their genomes during viral assembly and infection. Phillips is also building artificial membranes and testing models that describe the interactions between ion channels and the lipids they encounter in their membrane environments.

Stephen R. Quake, D.Phil., Stanford University, designs microchips to analyze DNA and single cells and to grow crystallized proteins. For example, using a chip that partitions microliters of fluid into thousands of independent chambers that hold only one molecule per chamber, Quake is measuring gene expression of transcription factors at levels as low as six gene copies.

Sunney Xie, Ph.D., Harvard University, is developing tools to visualize the actions of a single enzyme or protein inside a living cell. His aim is to understand how molecular machines function in real time, individually and together. Xie has recently become the first to observe individual protein molecules being generated in live *E. coli* cells.

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Re-Engineering the Clinical Research Enterprise

The 21st century is witnessing an increasing need to move research results more quickly to clinical settings. NIH recognizes that the current system of clinical research must change if it is to respond to these changing scientific and health care needs. Meeting these demands will require new and more efficient approaches to discovery and clinical validation of research results. But while clinical research helps assure that new treatments are safe and effective, it is a lengthy and sometimes inefficient process. The current system of clinical research must be re-engineered if it is to respond to these changing scientific and health care needs. Meeting these demands will require new and more efficient approaches to discovery and clinical validation of research results. One example, the Patient-Reported Outcomes Measurement Information System (PROMIS) Network, is highlighted below.

PROMIS (Patient-Reported Outcomes Measurement Information System) Network
PROMISing Developments in Patient Assessment

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) is managing a trans-NIH initiative that will use new technologies to develop a way to assess patient-reported outcomes broadly relevant to a wide range of chronic diseases. The initiative, called "PROMIS" (Patient-Reported Outcomes Measurement Information System), is part of the NIH Roadmap's charge to re-engineer the clinical research enterprise.

PROMIS will utilize advances in computer technology and modern measurement theory to assess outcomes important to patients, including symptoms (such as pain and fatigue) and other aspects of health-related quality of life, in a standardized manner. The initiative should result in assessment instruments that significantly reduce the number of questions asked of patients, thus requiring less time and effort from patients while maintaining high validity and reliability.

Following a call for grant applications, a collaborative network of seven universities – a statistical coordinating center and six primary research sites – has been established to collect self-reported data from a diverse population of patients with chronic diseases, including those from racial and ethnic minority groups. The network, which will support a comprehensive, integrated approach to data collection, storage, and management, includes Northwestern University (coordinating center), the University of Washington, Stanford University, the University of North Carolina, the University of Pittsburgh, the State University of New York at Stonybrook and Duke University.

Network teams will develop a large bank of “items,” key questions to assess the degree of patient functioning for such specific health dimensions as mobility or pain. Computerized adaptive testing methods will result in less cumbersome health questionnaires that are tailored specifically to individual patients. Testing and validation of these PROMIS components should result in a publicly available, adaptable and sustainable system for assessing self-reported symptoms and health-related quality-of-life issues across a wide range of chronic diseases. Ultimately, the system should prove useful in medical practice to measure treatment response and to guide therapy.

Network scientists are already moving forward to analyze archival patient questionnaire data and to decide which items to include in initial assessment for possible use in the final item banks. Representatives of the Food and Drug Administration and the Centers for Medicare and Medicaid Services will be liaisons to the initiative’s scientific advisory board. Interest in PROMIS has also been expressed by national and international agencies and professional societies.

“In PROMIS,” said Stephen I. Katz, M.D., Ph.D., director of NIAMS, “we can envision a tool that will allow doctors to accurately assess, in a standardized fashion, people’s symptoms and functioning, and how these important aspects of quality of life are affected by various treatments.”

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Working Groups and Co-Chairs

New Pathways to Discovery

Molecular Libraries and Imaging

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Director, National Human Genome Research Institute (NHGRI)

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Building Blocks, Biological Pathways and Networks

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Structural Biology

Jeremy M. Berg, Ph.D.
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Paul A. Sieving, M.D., Ph.D.
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Bioinformatics and Computational Biology

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Nanomedine

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Research Teams of the Future

Interdisciplinary Research

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Director, National Institute of Nursing Research (NINR)

David A. Schwartz, M.D.
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Larry A. Tabak, Ph.D.
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High Risk Research

Jeremy M. Berg, Ph.D.
Director, National Institute of General Medical Sciences (NIGMS)

Nora D. Volkow, M.D.
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Re-Engineering the Clinical Research Enterprise

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