NIGMS Funds Center for Quantitative Biology

To probe the complexities of living systems, the National Institute of General Medical Sciences (NIGMS), part of the National Institutes of Health (NIH), has established its fifth Center of Excellence in Complex Biomedical Systems Research. The new center, headed by David Botstein, PhD, at Princeton University in Princeton, New Jersey, will explore how biologic molecules interact with each other and their environment to create dynamic systems.

NIGMS will award $3 million to the center this year and expects the project to total $14.8 million over 5 years. Central to the effort is the integration of multidisciplinary research and teaching. In addition to bringing together 40 scientists from physical, computational, and biologic science fields, the center will establish a new undergraduate and graduate curriculum at Princeton that focuses on quantitative biology and collaborative research.

Called the Center for Quantitative Biology, the effort will focus on three key biologic questions: how body patterns are established during an organism's early development, how cells control their internal functions and communicate with each other, and how viruses interact with host cells. The researchers will use state-of-the-art microscopes and imaging tools to examine molecules in living cells and tissues. They will also create gene chips to study the activities of genes from viruses, bacteria, yeast, mice, rats, and humans.

A key feature of the project is the use of advanced computational methods to model complex biologic systems based on large quantities of experimental data, a systems biology approach. To help spur further biomedical discoveries, the center will make all of its data and analysis tools freely available to the scientific community.

The goals and approaches of the center fit squarely with the NIGMS mission, according to Jeremy M. Berg, PhD, NIGMS director. The Princeton center joins other Centers of Excellence in Complex Biomedical Systems Research at the University of Washington Friday Harbor Laboratories, Case Western Reserve University, Harvard University, and the Massachusetts Institute of Technology.

Genome Research Initiative Establishes Four University Centers for Excellence

The National Institutes of Health (NIH) National Human Genome Research Institute (NHGRI) has selected four universities to serve as interdisciplinary centers for a new initiative that will address some of the most pressing ethical, legal, and social questions raised by recent advances in genetic and genomic research. The NHGRI initiative, The Centers for Excellence in Ethical, Legal and Social Implications Research, will receive significant contributions from the US Department of Energy and the NIH National Institute of Child Health and Human Development. The first four interdisciplinary centers to be awarded funding for this initiative are Case Western Reserve University's Center for Genetic Research Ethics and Law, Duke University's Center for the Study of Public Genomics, Stanford University School of Medicine's Center for Integration of Research in Genetics and Ethics, and University of Washington's Center for Genomic Health Care and the Medically Underserved.

NIH Funds Centers to Study Islet Transplant

The National Institutes of Health (NIH) announced that it plans to award about $75 million over 5 years to five clinical centers and a data coordinating center to conduct studies of islet transplant in patients with type 1 diabetes. The network includes centers located in Iowa City, Miami, Minneapolis, and Philadelphia, as well as in Edmonton, Alberta, Canada, and Uppsala, Sweden.

The studies will focus on improving the safety and long-term success of methods for transplanting islets, the insulin-producing cells of the pancreas, in people whose own islets have been destroyed by the autoimmune process that characterizes type 1 diabetes. Some studies will focus on improving combined islet and kidney transplants in patients with type 1 diabetes and kidney failure, a common complication of diabetes.

Type 1 diabetes accounts for up to 10% of diagnosed cases of diabetes in

the United States (up to 1 million people). This form of diabetes usually strikes children and young adults, who need several insulin injections a day or an insulin pump to survive. Insulin, although critical for controlling blood glucose, is no cure. Most people with type 1 diabetes eventually develop one or more complications, including damage to the heart and blood vessels, eyes, nerves, and kidneys.

In islet transplant, islets are extracted from the pancreas of a deceased donor and infused into a person with difficult-to-control type 1 diabetes through the portal vein of the liver. In successful transplants, the cells lodge in the liver's small blood vessels and begin producing insulin.

In the 1990s, islet transplant rarely succeeded in freeing patients from insulin injections for more than a year. In June 2000, however, a research team led by Dr. James Shapiro at the University of Alberta in Edmonton, Canada, reported sustained insulin independence in seven patients transplanted with islets from two to four donor pancreases. The patients received an immunosuppressive regimen that omitted glucocorticoids, also known as corticosteroids, which were often used to prevent rejection but are now thought to be toxic to islets. In the next few years, researchers participating in the Immune Tolerance Network, a collaboration of clinical and basic researchers sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and the Juvenile Diabetes Research Foundation International, replicated what became known as the Edmonton protocol.

Despite these gains, scientists continue to grapple with several impediments to the wider testing of islet transplant. One is the scarcity of islets. Only about 6,000 donor pancreases become available each year, and many are used for whole-organ transplant. Posing another obstacle are the potentially serious side effects, such as anemia, nerve damage, meningitis, and vulnerability to infection from immunosuppressives. Finally, in some transplanted patients, donor islets function well initially, but, in time, diabetes recurs. Why the islets die is not well understood.

Researchers in the newly funded centers will be designing studies to improve the isolation and viability of islets, reduce the complications of the transplant procedure (eg, bleeding and clotting), reduce the side effects of immunosuppression, trace the fate of islets after transplant and determine why donor islets sometimes fail, and evaluate new ways to safely prevent immune rejection of donor tissues.

Newly designed studies will be submitted for review by the US Food and Drug Administration, the NIDDK/NIAID Islet Transplantation Data and Safety Monitoring Board, and local institutional review boards before being offered to patients. Patient enrolment is scheduled to begin in 2005.

The consortium consists of the following principal investigators and centers: Dr. William Clarke, University of Iowa (Data Coordinating Center), Iowa City, Iowa; Dr. Camillo Ricordi, University of Miami, Miami, Florida; Dr. Bernhard Hering, University of Minnesota, Minneapolis, Minnesota; Dr. Ali Naji, University of Pennsylvania, Philadelphia, Pennsylvania; Dr. James Shapiro, University of Alberta, Edmonton; and Dr. Olle Korsgren, Uppsala University, Uppsala.

The consortium is supported by a special funding program for type 1 diabetes research, which provides a total of $1.14 billion from fiscal year 1998 through fiscal year 2008 to supplement other funds for type 1 diabetes research made available through the regular NIH appropriations process.

Other NIH-funded initiatives are also fostering progress in islet transplant. The Collaborative Islet Transplant Registry (<http://www.nih.gov/news/pr/sep2004/niddk-07.htm>), which recently published its first annual report, collects, analyzes, and disseminates data on islet transplants performed in the United States and Canada. Ten Islet Cell Resource Centers (<http://www.ncrr.nih.gov/clinical/cr_icr.asp>) harvest, purify, and ship islets for transplant and research. The Immune Tolerance Network (<www.immunetolerance.org>) is an international consortium dedicated to evaluating new treatments for autoimmune diseases, asthma, and allergic diseases and to preventing the rejection of transplanted organs and islets. The Beta Cell Biology Consortium (<www.betacell.org>) facilitates interdisciplinary efforts to understand islet development and function. The Non-Human Primate Islet Transplantation Consortium develops and tests new protocols for immune suppression in transplant recipients before these protocols are tested in patients.

NIAID Forms Clinical Consortium to Improve Success of Organ Transplants

The National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health (NIH), launched a three-site consortium spanning Boston, Cleveland, and Philadelphia that will work to improve the outcomes of organ transplant. Although organ replacement prolongs survival for people suffering from end-stage organ failure, it rarely restores normal life expectancy and can sometimes lead to health problems associated with long-term use of immunosuppressive drugs, which reduce the risk of transplant rejection but also weaken the immune system against disease.

The consortium will also receive support from two other NIH components, the National Institute of Diabetes and Digestive and Kidney Diseases and the National Heart, Lung, and Blood Institute. Funding for the three 5-year grants totals an estimated $43 million.