

A Message from the NorthShore University HealthSystem Research Institute President

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Since the last issue of *Continuum*, ENH has changed its name to NorthShore University HealthSystem (NorthShore) and has a new teaching affiliation with The University of Chicago Pritzker School of Medicine. With these changes, the Research Institute remains strong. In this issue of *Continuum*, the newsletter for the NorthShore Research Institute, scientists studying areas as diverse as medical genetics, cancer, diabetes and viral infections describe their work. The need for their contributions is becoming ever more critical as we enter our second decade renowned as one of the top hospital-based research programs in the nation.

Why does an integrated healthcare system need to provide facilities and resources to support these researchers, and the many other physicians and scientists at the NorthShore University HealthSystem Research Institute? Quite simply, intense environments of discovery enable today's investigators to become tomorrow's opinion leaders in their respective disciplines, as their findings affect the discovery of new ways to practice medicine and change patient care—for the better.

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Gregor Mendel knew little of the actual mechanisms that govern heredity—genes and chromosomes—when he began his experiments with the common garden pea plant ...

But his contributions have led directly to the work of modern genetic scientists at NorthShore University HealthSystem Research Institute. **Turn to page 2** and read more about how the Centers for Medical Genetics and Psychiatric Genetics are studying the human genome and conducting large-scale DNA sequencing to understand molecular medicine in nearly every clinical specialty.

Offering a comprehensive research program also allows us to recruit and retain top talent across specialties—and ultimately to provide our patients with access to the newest and most innovative drugs, devices, diagnostic procedures and treatments.

In its first decade, the Research Institute doubled in size five times in terms of funding from external sources. Like every other research program in the country, it is a net negative financial operation. As we grow, our deficit also grows because research typically consumes more resources than it creates.

Private support enables the NorthShore Research Institute to continue to survive—and to thrive—as it pursues clinical trials to study new treatments for care, outcomes research to improve quality of care and translational research to directly change the content of care. In fact, the growth rate of philanthropic support determines our rate of research growth in the future.

Our legacy of private sources to support research dates to the early 20th century, when Louis Sauer, M.D., whose work relied heavily on philanthropy, developed a vaccine for whooping cough on an annual budget of \$1,300.

The Dr. Sauers of today include Pablo Gejman, M.D., and Wendy Rubinstein, M.D., Ph.D.—who are finding ways to understand how subtle variations in genes predispose each of us to major medical disorders. Other physicians and scientists, many of whom you will read about in this issue of *Continuum*, are using viruses to attack cancer, developing new types of magnetic resonance imaging (MRI) to see things never seen before and using light-scattering technology that is 50 times more sensitive than current screening methods to detect tumors. With your interest and commitment, these 21st century Dr. Sauers can continue our contribution to ease human suffering and improve the options our patients have.

Thank you for your consideration.

Leopold G. Selker, Ph.D.

President, NorthShore University HealthSystem Research Institute

Medical Genetics: Knowledge is Power When the Family is the Patient



Gregor Mendel knew little of the actual mechanisms that govern heredity—genes and chromosomes—when he began his experiments with the common garden pea plant. But by selectively crossbreeding, he observed that basic traits passed from parent to offspring according to particular patterns, or laws of inheritance.

The contributions of this obscure 19th century monk, whose research was forgotten for nearly a century, have led directly to the work of modern genetic scientists at the NorthShore University HealthSystem (NorthShore) Research Institute. Today as practicing physicians take the well-established family medical history to assess a patient's risk for inherited disorders, our researchers in medical genetics are studying the structure of the human genome and conducting large-scale genotyping and DNA sequencing to better understand molecular medicine in nearly every clinical specialty. They do this so that someday soon physicians will be able to predict, prevent and treat disease with unprecedented accuracy.

The Trajectory of Genetic Medicine

Subtle variations in our genes predispose us to certain medical diseases. In fact, since researchers completed sequencing the entire human genome in 2003, they have developed genetic tests to diagnose or predict risk for nearly 1,400 diseases, a 700 percent increase since 1997. Knowing risk is important because the effects of many genetic diseases can be prevented or reduced through early diagnosis and management.

"The trajectory of genetic medicine includes learning how to detect genetic disease, calculate genetic risk and treat common diseases based on genetic factors," said Wendy S. Rubinstein, M.D., Ph.D., Director of the Center for Medical Genetics, which

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**Wendy S. Rubinstein
M.D., Ph.D., Director
of the Center for
Medical Genetics**

The Center for Medical Genetics is staffed with specially trained physicians and certified genetic counselors and provides counseling, testing, information and referrals for a variety of illnesses, including cancer, neurological conditions, heart disease and metabolic diseases.

was launched with a \$1 million grant from The Auxiliary of NorthShore University HealthSystem and receives ongoing support from the Daniel F. and Ada L. Rice Foundation. "Our collective strengths uniquely position us as one of only a few institutions with the necessary multidisciplinary skill sets and resources already in place to capitalize on genetic medicine's pathway allowing genetic research in cancer and other serious diseases."

Genetic susceptibility for a few disorders, such as cystic fibrosis and mutations in BRCA1 and BRCA2 that cause a higher risk of breast-ovarian cancer, are relatively straightforward. But some of the most common major disorders, such as heart disease, diabetes, many cancers and certain psychiatric illnesses, arise from an array of genetic interactions. "Our mission is to close the gap between what we know and what we need to know in order to reduce the incidence of serious medical conditions and prevent them for generations to come," Dr. Rubinstein said.

"Genetic components of illness affect every family," said Pablo V. Gejman, M.D., Director of the Center for Psychiatric Genetics, who has built an internationally prominent research program on the genetics of schizophrenia. "The goal of our generation of researchers is to understand the complex genetics of common medical disorders and the interaction of genes and environmental factors that contribute to illness."

Studying the Full Spectrum of Medical Genetics

The Center for Medical Genetics is one of the largest adult genetic centers and gene testing sites in the country. As Director, Dr. Rubinstein's clinical and research efforts span the spectrum—from discovering genes that cause a high risk of cancer and finding their "Achilles heel" so effective, targeted treatments based on the cancer's genetic signature can destroy them—to providing screening tests and genetic counseling for individuals and entire families—to leading national public health initiatives that create and evaluate family history software in order to assess the genetic risk of disease.

"The larger, public health aspect of medical genetics is fascinating," Dr. Rubinstein said. "Genome studies provide enormous amounts of information, but how we link what we know with getting people to change certain health behaviors or undergo screening tests based on their family history and genetic risk for serious illnesses will show us the true value of this information."

Dr. Rubinstein is renowned for helping patients understand how medical disorders are passed from one generation to the next and how to manage their risk of developing an inherited disease. For instance, her team, led by Suzanne O'Neill, Ph.D., clinical researcher and genetic counselor, developed the *MyGenerations* family health history screening tool through generous support from the Susan Willis Heiberger Memorial Fund.

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MyGenerations is a unique, user-friendly program that allows patients to use touch-screen technology at computerized kiosks located at several locations at NorthShore and online at www.northshore.org/mygenerations.

With support from philanthropic and public funding sources, Dr. Rubinstein's work includes several areas of cutting-edge interest, among them:

- Establishing the Center for Functional Genomics, where physician-scientists develop and use new techniques to study tens of thousands of genes at once using sophisticated bioinformatics techniques: This new method of genome-wide cancer analysis enhances cancer detection and improves the effectiveness of treatments. The Center is led by San Ming Wang, Ph.D., and supported with a grant from the Daniel F. and Ada L. Rice Foundation. Particular areas of focus are leukemia, lymphoma and breast cancer.
- Using DNA genomic technologies to identify genes that cause familial breast cancer with a grant from the Susan G. Komen Breast Cancer Foundation and funding from the Falk Medical Research Trust: The focus of this work is to use gene expression profiling to identify breast cancer susceptibility genes.
- Spearheading an initiative with the Centers for Disease Control and Prevention (CDC) to evaluate its computerized family history tool called Family Healthware™ in primary care practices: This project involves automated calculation of a person's risk of cancer, heart disease, stroke and diabetes. It will determine if this information results in favorable outcomes by changing an individual's lifestyle or motivating them to get appropriate screening tests. More than half of the over 3,700 study participants are from NorthShore.
- Participating in several large international studies, including evaluating screening and prevention techniques and quality of life for patients with ovarian cancer, analyzing the psychological impact of false positive results using magnetic resonance imaging (MRI) to detect breast cancer, and enrolling individuals for genetic association studies: With generous funding from Jack and Judy Baker, the Center has joined the international IMPACT trial, which will determine the usefulness of prostate specific antigen (PSA) screening beginning at age 40 for men with BRCA1 and BRCA2 mutations who are at high risk for prostate cancer.
- Establishment of the Pancreatic Cancer Family Registry, a biorepository of families, DNA, tissue samples and dietary/exposure information to use as a resource for pancreatic cancer research: The Pancreatic Cancer Family Registry is a valuable resource to learn about the biological basis of this cancer in order to guide early detection, prevention and treatment.

"Philanthropic support will allow us to develop several new areas of investigation," Dr. Rubinstein said. "These include an

initiative to understand how individuals use information about their inherited risk of disease, studies in pharmacogenomics to test how individuals respond to certain medications so drug treatments can be tailored to a person's unique genetic makeup, the development of technologies to analyze the entire human genome, and programs to create access for individuals who are uninsured or underinsured and can not afford genetic testing."

Hunting for the Genetics of Schizophrenia

As one of the world's top investigators studying susceptibility genes, or inherited risk factors, for major psychiatric disorders, Dr. Gejman directs some of the largest and most comprehensive genetic experiments in the field of schizophrenia research. He leads a team of NorthShore University HealthSystem researchers and oversees a network of research centers and international scientists to understand the complex, interactive chain of genetic and environmental events that cause schizophrenia.

"Our primary goal is to understand the biology of schizophrenia and then integrate other factors that contribute to the disease, particularly environmental risks such as stress, poverty, perinatal infections and older parents at birth," said Dr. Gejman, who holds the Dr. Louis W. Sauer Chair of Research and received one of the largest National Institutes of Mental Health (NIMH) research grants ever awarded to a psychiatrist in the United States.

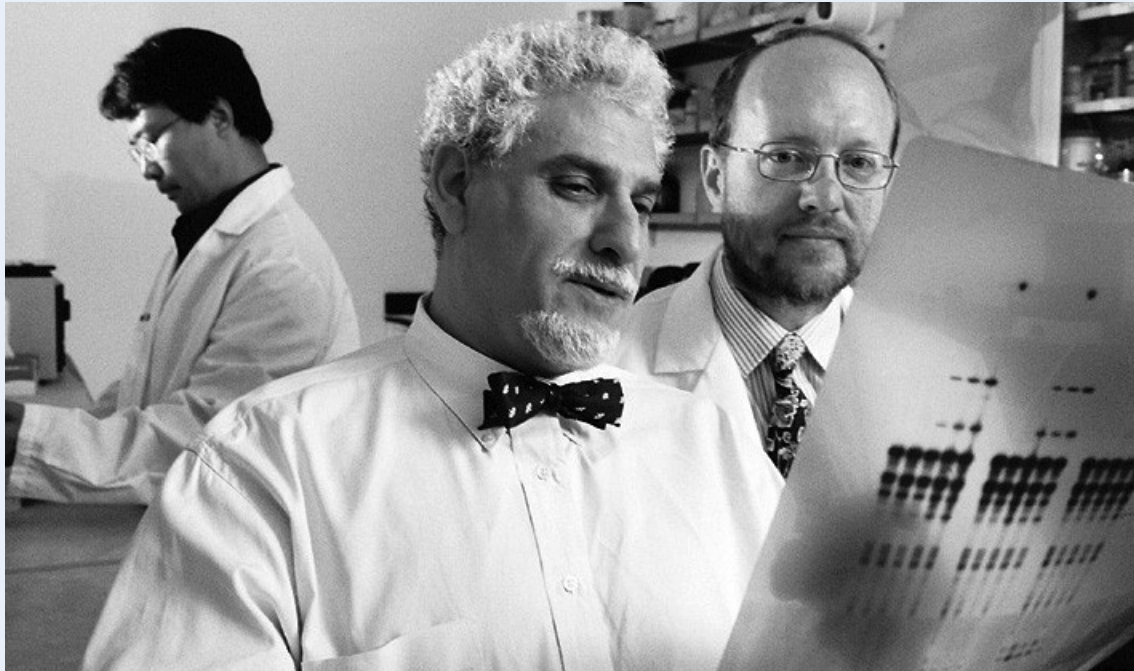
Already credited with identifying an important gene for schizophrenia and manic-depressive bipolar disorder, Dr. Gejman and his team of gene-hunting researchers are

"NorthShore University HealthSystem is at the center of the largest DNA clinical study to date. Our collaborators are among the most reputable diagnosticians ..."

—Pablo V. Gejman, M.D.,
Director of the Center for Psychiatric Genetics

collecting an unprecedented amount of genetic information on families affected by schizophrenia. Their database will be used to find molecular genetic evidence for schizophrenia, discover ways to prevent environmental risk factors and diagnose this psychiatric disorder at an early stage, and improve psychopharmaceutical therapies.

"NorthShore University HealthSystem is at the center of the largest DNA clinical study to date. Our collaborators are among the most reputable diagnosticians who study schizophrenia. We collaborate with an international group of statisticians who specialize in large-scale experiments, and we



**Pablo V. Gejman, M.D.,
Director of the
Center for
Psychiatric Genetics**

Dr. Gejman (left) and Alan Sanders, M.D., Director of the Behavior Genetics Unit, Center for Psychiatric Genetics, conduct gene-hunting studies at the NorthShore Research Institute.

lead the field of psychiatric genetics for experimental quality control," Dr. Gejman said.

For more than a century, researchers have observed that schizophrenia clusters in families. But in the last 20 years, advances in molecular genetics research and biotechnology, as well as more sophisticated statistical methods that enable scientists to analyze vast amounts of data, will provide invaluable clues to understand schizophrenia and offer hope to families affected by this illness.

In studies of complex genetics, it is imperative to have extremely large sample sizes and uniform methodologies to support the experimental design. Because of this, Dr. Gejman is leading an international team that recruited the largest clinical sample yet of 4,500 control subjects and 4,500 persons with schizophrenia in order to collect blood samples to study DNA and biological mechanisms that lead to schizophrenia. This study, the Molecular Genetics of Schizophrenia Collaboration, has a database that is unmatched in size and with superior statistical power to address genetic research questions posed by Dr. Gejman's team and the future scientific community.

Using this data, and with support from the Genetic Association Information Network (GAIN) of the National Institutes of Health, Dr. Gejman's team also is conducting one of the largest and most definitive genome-wide experiments to identify multiple gene mutations for schizophrenia and bipolar disorder. They are leading research to support subsequent experiments based on findings from the GAIN

study and conducting a genome-wide association study to identify and characterize genetic variation that contributes to schizophrenia susceptibility, based on genotypes from individuals with European or African-American ancestry.

Government funding remains insufficient to continue these and other research efforts. "With philanthropic support, the Center for Psychiatric Genetics could further its work by recruiting new researchers and expert lab technicians, purchasing sophisticated technology to perform DNA sequencing and high-speed quantitative analyses, and expanding our work space and lab facilities," Dr. Gejman said.

As scientists at the Research Institute, like Dr. Gejman and Dr. Rubinstein, expand our knowledge of the molecular basis of disease, medical genetics will have the potential to revolutionize the future of medicine. "Physicians and scientists will be able to prevent and diagnose disease with new levels of accuracy and individualize care based on each patient's unique genetic traits," Dr. Rubinstein said.

For more information about these programs, please visit www.northshore.org/research/centers.

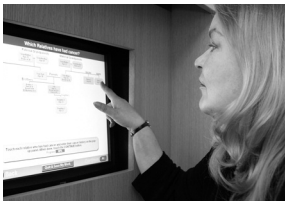
If you are interested in supporting these programs, please contact John Hanson, Director of Philanthropy, NorthShore University HealthSystem Foundation, (224) 364-7208 or jhanson@northshore.org.

Meet Leading NorthShore University HealthSystem Medical Genetics Researchers



Jubao Duan, Ph.D., Director of Genotyping Core at the Center for Psychiatric Genetics, has published seminal work in *Human Molecular Genetics* and the *American Journal of Human Genetics*. Using genotyping technology and powerful genome-wide association studies (GWAS), Dr. Duan is analyzing the entire

human genome to find and map genes or mutations that contribute to susceptibility to schizophrenia and other psychiatric disorders.



Suzanne O'Neill, Ph.D., clinical researcher and genetic counselor at the Center for Medical Genetics, created *MyGenerations*, which enables individuals to document their family medical history and

receive a risk analysis of hereditary diseases. Currently, this tool creates individual risk assessments for hereditary cancers, such as breast, ovarian and prostate cancer. Future plans include expanding the program to other inherited disorders like heart diseases, diabetes and mental health conditions.



Alan R. Sanders, M.D., is Director of the Behavior Genetics Unit at the Center for Psychiatric Genetics. He is principal investigator for an international gene-hunting study entitled the Molecular Genetic Study of Sexual Orientation. Earlier studies suggest that sexual orientation runs in families, and

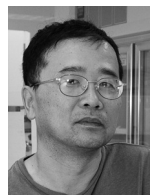
Sanders and his team of researchers are analyzing

questionnaires and DNA samples from more than 750 pairs of homosexual brothers to search for genes influencing male sexual orientation, both homosexuality and heterosexuality.



Prem Seth, Ph.D., Director of the Gene Therapy Program, is conducting cancer gene therapy research to develop a breakthrough therapeutic approach using viral “smart bombs” that infect and destroy

primary tumor cells in patients with breast cancer and inhibit bone metastases, a complication in approximately 70 percent of patients with advanced breast cancer. He also is applying this gene therapy to treat bone metastasis of prostate cancer. Dr. Seth is an international expert in the study of cancer-killing viruses and targeted gene therapies. His breast cancer research is supported by grants from the National Institutes of Health and the U.S. Department of Defense. His prostate cancer research is funded by philanthropic support from Jonathan and Sally Kovler and Jimmie Alford and Maree Bullock.



San Ming Wang, Ph.D., Director of the Center for Functional Genomics, is developing next-generation DNA sequencing techniques to analyze the genome structure, identify genetic mutations and diagnostic markers, and develop therapeutic targets for cancer and other genetic diseases. His focus is to

create technology that has the capability to comprehensively identify genetic mutations that contribute to disease—and that is less expensive, easier to use and more accurate than conventional technology.

NAMES IN THE NEWS



Joseph T. Bass, M.D., Ph.D.—Head of the Division of Endocrinology and Metabolism, received a \$495,000 grant from the Juvenile Diabetes Research Foundation entitled the “Role of Circadian Clock Transcription Network in Beta Cell Failure.” Type 1 diabetes is a leading cause of childhood metabolic disease. This study will apply the powerful tools of genetic analysis to pinpoint the link between the body’s internal biological clock, pancreas development and insulin production in order to improve therapies for people with type 1 diabetes.

Dr. Bass’ internationally renowned diabetes-related research focuses on diet and circadian rhythms and demonstrates that overeating alters the core mechanism of the body clock, throwing off the timing of internal signals, including appetite control.

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A Message from NorthShore University HealthSystem Foundation President

As we begin a new fiscal year, we celebrate the Foundation achieving a historic milestone—reaching and surpassing its five-year \$150 million fundraising goal for The Campaign. Thank you for your philanthropic support and generosity!

Your philanthropic support enables us to develop new research programs, direct unrestricted gifts to research and add newly endowed chairs in areas as diverse as neuroscience research, breast cancer research, outcomes research and perinatal research.

The NorthShore University HealthSystem (NorthShore) Research Institute, along with priority clinical areas, were the focus of The Campaign. As it concludes, the Board of Directors has set for 2009 an annual goal of \$20 million in philanthropic support.

Philanthropy is important to the Research Institute for several reasons. It is a critical component of the Research Institute's strategy and growth initiatives—and support will bring continued distinction to the Research Institute as a national and international opinion leader, allowing new findings to move directly from the laboratory into clinical care.

The NorthShore University HealthSystem Foundation raises private resources to support the delivery of clinical care, academic medical education, innovative research and community engagement. In the months ahead, the

Foundation will continue to pursue the power of philanthropy, partnering with friends to raise much-needed funds critical to find new treatments and discoveries. In the year ahead, we will explore the feasibility of a new campaign of philanthropic support with the Research Institute well-positioned as a funding priority.

As the No. 1 ranked Comprehensive Independent Research Hospital in Illinois and ninth in the nation based on National Institutes of Health (NIH) funding, NorthShore joins other leading teaching hospitals and medical centers in the top tier. Philanthropy will ensure this continued leadership distinction well into the future.

We thank you, most kindly, for your continued engagement and community leadership as we pursue our transformational strategy of philanthropic support. We invite your ideas for partnering to help catalyze a remarkable, donor-driven culture of philanthropy.

Colleen D. Mitchell,
President, NorthShore University HealthSystem Foundation



Curt M. Horvath, Ph.D.—Senior Scientist, who recently was invested with the Jean Ruggles Romoser Chair of Cancer Research, has received the following grants from the National Institutes of Allergy and Infectious Disease:

- “Molecular Basis of Paramyxovirus-Induced STAT Degradation”—The major goals of this grant for \$1,689,375 are to identify cellular mediators and understand viral immune suppression.
- “Crosstalk in RNA Mediated Innate Antiviral Responses”—This is an exploratory project, with a grant for \$419,375, that focuses on the interaction between antiviral responses to

infection and the cell functions that regulate gene expression and immune response.

- “Helicase Regulation of dsRNA Signaling and Innate Antiviral Immune Responses”—This five-year grant for \$1,909,115 will further the study of antiviral signaling proteins that represent the first line of defense against viral infections.

Dr. Horvath's internationally renowned research focuses on the fundamental mechanics of genetic control of the immune system, which will lead to improved therapies and strategies for managing cancer, as well as viral infections and the body's immune system response.

The NorthShore University HealthSystem Research Institute

The Research Institute is the research entity of NorthShore University HealthSystem (NorthShore), a fully integrated, multihospital healthcare delivery system serving northern metropolitan Chicago.

It provides the venue for talented clinicians and scientists to pursue ideas, make discoveries and translate findings into new therapies and treatments that improve patient care. More than 200 nationally and internationally renowned researchers lead nearly 1,000 active research projects through the Research Institute, with the intent of fostering new options for patients and families in their struggles to overcome devastating diseases and illnesses.

The NorthShore Research Institute comprises the *Research Park Building*, providing clinical and translational research space in



Evanston Research Park; the *Owen L. Coon Research Center*, located on the Evanston Hospital campus and a hub for clinical research efforts; and the *Charles R. Walgreen, Jr. Building* on the Evanston Hospital campus (above), a research and administrative building with office and laboratory space for clinical researchers and faculty members.



Research Institute

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www.northshore.org/foundation

The NorthShore University HealthSystem Research Institute and NorthShore University HealthSystem Foundation publish *Continuum* two times a year to provide informative articles about research and to raise awareness in the communities NorthShore University HealthSystem serves. To make a gift, please contact Jeff Pickering, Assistant Vice President, Fund Development, NorthShore University HealthSystem Foundation, (224) 364-7205, or jpickering@northshore.org.

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