A Message from the Chief Scientific Officer

NorthShore University HealthSystem (NorthShore) Research Institute has long been recognized for pioneering research aimed at advancing our mission “to preserve and improve human life.” Our dedicated, growing team of physician-scientists leads vital initiatives designed to help us provide the finest care to patients today and tomorrow and to generate new knowledge and life-saving treatment options.

In recent years, we at the Research Institute have refocused our efforts, leveraging our strengths in three major areas: personalized medicine, excellence in informatics and a broad range of clinical trials.

Personalized medicine is ushering in an incredibly exciting time in medicine and medical research, and NorthShore Research Institute is poised to be a leader in this arena with our Genomic Health Initiative (GHI). A comprehensive genomic research program designed to investigate genetic variation contributing to diseases, the GHI is collecting a large number of patient blood samples for DNA extraction and subsequent genetic research, which will ultimately help predict and prevent disease. In addition, our Program for Personalized Cancer Care is a comprehensive clinical and research program designed to identify new approaches to prevent and treat cancer. Its new genetic risk score is currently being tested in patients to identify those most at risk who would benefit from early and intensive screening.

NorthShore has established state-of-the-art research laboratories to conduct this groundbreaking research. Our work has already led to discoveries about various diseases, including cancer, Parkinson’s disease, schizophrenia and others—and more importantly, these studies help provide personalized treatment plans for our patients.

Our well-demonstrated strength in informatics continues to build, leveraging NorthShore’s award-winning electronic health records. Collaborative experts work across a range of clinical areas and computational methods to foster scientific discovery and, over time, change the way medicine is practiced.

Approximately 1,000 active clinical trials across multiple disciplines—including oncology, neurology, orthopaedics and cardiovascular care—are offered at NorthShore, providing patients sophisticated treatment options and in many cases renewed hope. A growing number of trials with a personalized medicine focus are also part of our robust trial portfolio, which includes studies initiated at NorthShore and many in collaboration with other leading medical institutions across the country.

With more than 250 principal investigators and $80 million in total external funding, NorthShore Research Institute is poised for continued success and growth. While many of our investigators are supported with competitive grants from the National Institutes of Health and other federal and industry sponsors, the need for philanthropic support is critical to our ability to pursue innovative research. We are grateful to the many visionary individuals and foundations whose donations enable this vital work.

As we look forward to a future full of promise, we are pleased to present this report highlighting some of our current research endeavors. Thank you for your interest.

Michael Caplan, MD
Chief Scientific Officer
Chairman, Department of Pediatrics
NorthShore University HealthSystem

2015 Financial Summary

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<th>Vital Signs</th>
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<td>Number of Proposals</td>
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NorthShore University HealthSystem (NorthShore) Research Institute is the research arm of NorthShore that supports the organization’s core mission “to preserve and improve human life” through superior clinical care, academic excellence and innovative research.

The research enterprise at NorthShore encompasses a wide range of research activities, including lab-based translational research, advanced imaging, biomedical research informatics and clinical trials. The Research Institute supports these research activities for all NorthShore clinical departments by providing both administrative and regulatory oversight of research as well as research space at both NorthShore Evanston Hospital and the Evanston-Northwestern Research Park.

Although the research program at NorthShore reflects the comprehensive nature of the clinical program, the Research Institute has achieved a national and international reputation in a focused set of research areas, including oncology, cardiovascular care, medical imaging, neuroscience, perinatal medicine, personalized medicine, cancer biology, primary care and biomedical informatics.

Over the past several years, the continued efforts to build excellence in patient care at NorthShore have leveraged key areas of research prowess and driven NorthShore to focus its research efforts toward an even more contemporary set of initiatives that reflect the truly integrated nature of research and clinical care at NorthShore.

This report highlights particular achievements in the following programs and centers:

- Genomic Health Initiative
- Center for Psychiatric Genetics
- Program for Personalized Cancer Care
- NorthShore Neurological Institute/Center for Brain Health
- Center for Advanced Imaging
- Center for Basic Magnetic Resonance Research
- Gynecological Pain and Minimally Invasive Surgery

By focusing on these key institutional initiatives, the Research Institute channels its resources in support of areas where there is the greatest opportunity to improve the lives of patients and families served by NorthShore.

In addition to directing resources to enhanced patient treatment options, NorthShore is also increasing efforts to improve the ability of healthcare professionals, and patients themselves, to assess and manage their risk for disease.

NorthShore’s teaching affiliation with The University of Chicago Pritzker School of Medicine offers a dynamic environment for medical research. In particular, NorthShore’s the participation as an affiliate of the Institute of Translational Medicine (ITM) at the University of Chicago acts as an anchor for research collaboration with not only the University of Chicago, but also the other University of Chicago ITM affiliates, including Rush University, Illinois Institute of Technology and now Loyola University.
The Genomic Health Initiative (GHI) is a NorthShore-wide effort to collect tens of thousands of DNA samples and transform medicine through genomic research. The large sample size will enable study of the widest range of genetic variants in DNA. This comprehensive genomic research program is designed to investigate genetic variation contributing to diseases. The GHI team will conduct research aimed at identifying genetic risk factors for common disorders with a goal of developing early diagnosis, prevention strategies and personalized treatment options to ensure optimal health for individual patients.

State-of-the-art technique is used in GHI data collection, and the team stays abreast of rapidly evolving biomedical technology. Disorders currently being studied include cancer, diabetes, high blood pressure, asthma, obesity, abnormal heart rhythms, glaucoma, psoriasis and others.

Community participation is critical to the GHI—to participate, individuals donate a very small amount of blood and grant access to their Electronic Medical Record (EMR). Individual patients, as well as their family members and others, may benefit as findings will guide advances in personalized medicine now and for future generations.

The GHI in some cases may expose individual genetic findings that are directly relevant to the health of participants, such as high risk for some cancers or for certain cardiovascular disorders that are associated with sudden death. Genetic characteristics that confer risk to severe toxic reactions to some medications may also be uncovered. In these cases, the GHI team will reach out to individual patients (if the patient chooses to learn this information) and their physicians to share the important findings.

The GHI maintains explicit patient confidentiality, and all samples are de-identified with names replaced by random research numbers for study-related data.

GHI scientists continue to engage the community at various open events and public forums. Additionally, the GHI serves as a resource for many other key initiatives at NorthShore related to genomic aspects of diagnosing, preventing and treating disease.

For more information or to participate in the Genomic Health Initiative, visit northshore.org/ghi.

Pablo V. Gejman, MD, Vice President for Genomic Research, Dr. Louis W. Sauer Chair of Research, leads the Center for Psychiatric Genetics (CPG) in its study of genetic factors that contribute to mental health. The CPG conducts a variety of highly analytical and innovative research projects, including transcriptomics of schizophrenia, induction of pluripotent stems cells as models of neuropsychiatric disorders and genome-wide linkage studies of sexual orientation.

Selected Presentations

Jubao Duan, PhD, Oral Platform Presentation: “Open chromatin dynamics and genetic perturbation by CRISPR editing in iPSC-derived neurons at the MIR137 schizophrenia risk locus” at the Cold Spring Harbor Laboratory (CSHL) 2015 meeting on Genome Engineering: The CRISPR/Cas Revolution. Cold Spring Harbor, NY.

Led by Charles Brendler, MD, Executive Research Director, the Program for Personalized Cancer Care (PPCC) brings together a team of cancer genomicsists, biologists, pathologists, biomedical engineers and biostatisticians to create research innovation in personalized cancer care. The program’s focus on translating genomic discoveries into highly effective, tailored cancer care relies on both analyzing genetic changes in an individual patient’s cancer (somatic) DNA to help determine the most effective chemo-therapy, and analyzing genomic DNA alterations to develop individualized preventive and screening strategies for those at higher risk of developing cancer.

Jianfeng Xu, MD, DrPH, Vice President, Translational Research, Ellrodt-Schweighauser Family Chair of Cancer Genomic Research, leads a team of epidemiologists, genomicsists and biostatisticians to develop and validate risk assessment tools known as the genetic risk score (GRS) for specific cancer types. The GRS, which assesses a panel of genomic DNA alterations specific to a disease or particular cancer type, can then be used in combination with family history, often unknown or incomplete, to improve assessment and planning for potential inherited disease, particularly prostate, breast, pancreatic, colorectal and thyroid cancer. Dr. Xu’s team also developed and optimized genetic testing for DNA copy number alterations found in prostate biopsy samples to predict disease progression in patients who may choose an active surveillance of their disease as an alternative to immediate surgical intervention.

**Key Cancer Initiatives of the PPCC**

**Addressing Prostate Cancer Screening Controversy:** Recent controversy over prostate-specific antigen (PSA) screening has resulted in fewer men undergoing PSA screening. While decreased PSA screening has undoubtedly spared many men unnecessary treatment and adverse side effects, some men with lethal prostate cancer may not be diagnosed. Therefore, a smarter screening approach based on inherited prostate cancer risk to identify which men are likely to develop aggressive prostate cancer, and benefit from PSA screening was developed.

**Distinguishing Indolent from Aggressive Prostate Cancer:** In collaboration with Johns Hopkins University School of Medicine, the PPCC Cancer Genomics Core analyzed genomic DNA from 96 men who died of prostate cancer to find that 20 percent shared a panel of inherited genetic alterations only rarely found in other men with non-life threatening prostate cancer. This finding is currently being confirmed in 1000 additional patients. In a related study, two chromosomal abnormalities predictive of prostate cancer mortality were identified. Taken together, these findings suggest that patients with either the lethal gene panel or these chromosomal abnormalities should be treated immediately and aggressively.

**Stabilization of Prostate Cancer:** Led by Simon Hayward, PhD, Director of Cancer Biology, Jean Ruggles Romoser Chair of Cancer Research, the PPCC Cancer Biology Core is developing a novel strategy using a combination of non-toxic biological agents in low doses to stabilize early prostate cancer and prevent it from growing. If successful, patients may avoid high dose chemotherapy and its associated side effects. The Cancer Biology Core focuses on the tumor microenvironment, a complex milieu of cells including immune/inflammatory cells, nerves, muscles cells and fibroblasts because it is the communication between these cells that maintains a stable, tumor-free state.

**Precision Medicine Based on Big Data:** Under the direction of Yuan Ji, PhD, Assistant Vice President, the Center for Computational Genomics and Medicine focuses on the development of computational tools and software to facilitate precision medicine. During this past year, the Center focused its efforts on three areas. First, it developed Zodiac, a comprehensive information system of cancer genomic interactions, by analyzing approximately 200 million gene pairs to create a database and search engine that provide a resource to examine functional interactions in the whole genome. Second, the Center developed computational tools to understand the genetic landscape of tumor subclones or subtypes to better target and personalize cancer treatment. Finally, Dr. Ji’s group developed next-generation, dose-finding clinical trial designs aimed at finding subgroups of patients to more accurately and precisely assess new cancer drugs.

**New Grants**

Simon Hayward, PhD, “Mechanisms of BPH Progression.” National Institute of Diabetes and Digestive and Kidney Diseases (1U04DK104280-01A1).

Yuan Ji, PhD, “Bayesian Inference for Tumor Heterogeneity with Next-Generation Sequencing Data.” National Cancer Institute (2R01CA132897-06A1).

**Selected Presentations**


Jinfeng Xu, DrPH, Invited Seminar Speaker: “Proactive and Total Personalized Care of Prostate Cancer,” Prostate Cancer Research Forum, Duke University, Durham, NC, April 14, 2015.
NorthShore Neurological Institute (NNI) is a multispecialty system of care where the most advanced technology and clinical integration are available to treat neurological conditions. The NNI not only provides access to innovative medical and surgical interventions, but also invests resources in clinical education and leading-edge clinical research.

The NNI is co-led by Medical Director Demetrius M. Maraganore, MD, the Ruth Cain Ruggles Chair of Neurology, and Surgical Director Julian E. Bailes, MD, the Arlene and Marshall Bennett and Joseph A. Tarkington, MD, Chair of Neurosurgery.

In 2015, the NNI had several major initiatives that demonstrate the integrated nature of research at NorthShore. These include:

**The DodoNA Project** is a research initiative to develop DNA-based prognostic tests and therapies to predict, prevent and halt neurological disorders. As part of the DodoNA initiative, NNI researchers have collaborated with NorthShore’s Electronic Medical Record (EMR) team to build customized “toolkits” within the EMR that capture and store data from routine office visits. This data, along with a “biobank” of DNA and plasma collected from 11,000 patients, will be used to study brain tumors, epilepsy, memory disorders, migraine, mild traumatic brain injury, multiple sclerosis, neuropathy, Parkinson’s disease, restless legs syndrome, stroke and Alzheimer’s disease.

**The Neurology Practice-Based Research Network (NPBRN):** Through an initiative to advance quality improvement and practice-based research, NorthShore has built into Epic—NorthShore’s EMR system—state-of-the-art critical decision-support tools that meet American Academy of Neurology (AAN) guidelines, standardize care, write progress notes and capture up to 1,000 discrete data points per office visit to hardwire quality and outcomes research in neurology and individualize medicine at the point of care. With funding by a $1.2 million grant from the Agency for Healthcare Research and Quality (AHRQ), NorthShore will share these EMR tools with seven institutions nationwide, the NPBRN, that also use the Epic EMR system.

**Genetic Epidemiology of Parkinson’s Disease Consortium (GEO-PD):** The GEO-PD is an international consortium of 60 centers worldwide that share DNA and data from more than 85,000 Parkinson’s disease patients and controls to identify genetic predictors. Currently, the GEO-PD is undertaking the Longitudinal Clinical and Genetic Study of Parkinson’s Disease (LONG-PD), a study of 4,000 Parkinson’s disease patients worldwide over 15 years using a web-based REDCap platform to capture and share clinical severity, progression and outcomes data, which can be used to identify genetic and other factors that predict progression and outcomes in Parkinson’s disease.

The DodoNA project is one of the major research initiatives of NorthShore Neurological Institute. The purpose of the project is to predict, prevent and halt neurological disorders through the development of DNA-based prognostic tests and therapies.
**Traumatic Brain Injury (TBI) Research:** The NNI is currently leading multiple translational projects, including development of an innovative strategy designed to mitigate “brain slosh” and subsequent concussion in preparation for testing athletes and active-duty soldiers at high risk for TBI. This research involves the use of an in-vivo model to test the efficacy of compounds in reducing the level of brain injury following TBI and the creation of a novel, in-vitro model of TBI employing human neurons derived from induced pluripotent stem cells that will be used to perform high-throughput screening of potential TBI drugs.

**New Grants**

**John Finan, PhD,** “Slosh Mitigation and Its Effects on Blast Traumatic Brain Injury.” Q30 Sports Science.

**Demetrius M. Maraganore, MD,** “Quality Improvement and Practice-Based Research in Neurology Using the EMR,” Principal Investigator, Agency for Healthcare Research and Quality (1R01HS024057).

**Selected Presentations**


**Demetrius M. Maraganore, MD,** Neurology Grand Rounds, Dartmouth University, lecture titled: “Quality Improvement and Practice-Based Research in Neurology Using the Electronic Medical Record.” July 30, 2015.


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**The Traumatic Brain Injury laboratory at NorthShore Neurological Institute is one of a select few places in the country with the resources and expertise to advance new solutions to the TBI problem.**

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**Diffusion Tensor Imaging (DTI) of Rat Brain After Blast Injury**

DTI is an advanced MRI method that can image brain injuries at a microstructural level and is sensitive enough to detect nerve fiber injury and integrity of mild, moderate and severe TBI. In preliminary experiments; researchers at the TBI laboratory at NorthShore Neurological Institute have found that orientation and integrity of nerve fiber tracts decreased in certain areas of the brain after a single blast. With repetitive blasts, it is postulated that this injury will become more severe and additional regions of the brain would also be affected. Neuroimaging such as this can be studied to test strategies to mitigate the injury.
Robert R. Edelman, MD, William B. Graham
Chair of Radiology, heads a research team that
is recognized as a leader in utilization of magnetic
resonance (MR) angiography to image coronary
arteries. Through collaboration among radiologists,
biomedical engineers, physician-scientists, physi-
cists and computer scientists, the Center for
Advanced Imaging (CAI) takes advantage of
NorthShore’s dedicated MR research resources
to study novel cardiac therapies, manage gene
therapy patients, develop three-dimensional brain
maps for improved surgical planning, and invent
whole-body imaging and enhanced tools for diag-
nosing and treating conditions in utero.

In 2015, the CAI research initiatives included
Pottumarthi Prasad, PhD’s NIH-funded project
to evaluate multiparameter analysis of the kidney
in patients with stage 3 chronic kidney disease
(CKD), development of the quiescent-interval
slice-selective (QISS) technique for non-contrast-
enhanced MR angiography and Ioannis Koktzoglou,
PhD’s novel image acquisition methods to pro-
spectively detect gross motion due to involuntary
motion such as swallowing to improve carotid MR
angiography. The CAI also provided a key imaging
resource for a variety of research projects being
conducted by other departments, as well as imaging
studies for numerous clinical research projects
throughout NorthShore.

New Grants
Robert R. Edelman, MD, “Projection imaging of
peripheral vascular calcifications.” National Heart,
Lung, and Blood Institute (1R21HL126015-01A1).
Robert R. Edelman, MD, “Nonenhanced 3T
QISS MR angiography of the peripheral arteries.”
National Heart, Lung, and Blood Institute
(1R01HL130093-01).

Selected Presentations
Robert R. Edelman, MD, “Plenary Talk:
Disruptive Opportunities in Vascular MRI.”
Magnetic Resonance Angiography 27th Annual
International Conference, September 15–18, 2015,
Cincinnati, OH.
Robert R. Edelman, MD, “Breath-Hold Inner-
Volume Radial Quiescent-Interval Slice-Selective
(QISS) of the Heart, Aorta and Renal Arteries.”
Magnetic Resonance Angiography 27th Annual
International Conference, September 15–18, 2015,
Cincinnati, OH.
Robert R. Edelman, MD, “Advances in QISS Non-
Enhanced MR Angiography.” Magnetic Resonance
Angiography 27th Annual International Conference,
September 15–18, 2015, Cincinnati, OH.
Ioannis Koktzoglou, PhD, “Quiescent Interval
Slice-Selective MRA Using a Fast Low-Angle Shot
Readout Reduces Flow Artifact in Severe Stenosis,”
International Society for Magnetic
Resonance in Medicine Workshop
on Non-Contrast Cardiovascular MRI,
Long Beach, CA, March 2015.
Pohumarthi Prasad, PhD, “Blood
Oxygenation Level Dependent MRI
in Quantitative Biomarkers in Renal
MRI: From Morphology to Physiology”,
23rd Meeting of the International
Society of Magnetic Resonance in
Medicine; June 2015.
The Center for Basic Magnetic Resonance Research (CBMRR) conducts a wide spectrum of research using high-powered magnetic resonance imaging (MRI) and provides highly collaborative environments and critical resources to research projects throughout NorthShore Research Institute. During the past year, Alice Wyrwicz, PhD, and her team at the Center for Basic Magnetic Resonance Research pioneered an approach to measure the dynamics of tissue oxygen level in the brain cortex in parallel with functional MRI and electrophysiological recordings and used these techniques to measure how the dynamics of these signals change under various conditions, such as anesthesia and normobaric hyperoxia. Similarly, they are using a variety of measures, including MR imaging, to study the potential of brain hyperoxia induced by anesthesia to cause learning disabilities.

In collaboration with investigators in the PPCC, the Department of Surgery, and the Division of Gynecological Oncology, the CBMRR participated in a number of cancer imaging projects. Through these collaborations, the CBMRR developed an MR spectroscopic approach for the identification of more aggressive cancers, particularly in obese prostate cancer patients; used ex-vivo MR spectroscopy of adipose tissue from breast cancer patients in an effort to improve the diagnosis of aggressive breast cancer; and investigated the adipose tissue fatty acid composition in the omentum from ovarian cancer patients to develop novel diagnostics and therapeutics for ovarian cancer.

The CBMRR also collaborated with the Departments of Neurosurgery and Pathology at NorthShore to investigate the association of traumatic brain injury (TBI) and development of Alzheimer’s disease/AD-like neuropathology by employing an array of high-field MR imaging and MR spectroscopy techniques. Dr. Wyrwicz and P.N. Venkatasubramanian, PhD, from the CBMRR collaborated with investigators at Rush Alzheimer’s Disease Center to investigate age-related gait disorders, sleep and circadian dysfunction, spinal cord microvascular pathology and neuromuscular disorders through MR imaging of human brain-stem, spinal cord and muscle.

**Selected Presentations**

Alice M. Wyrwicz, PhD, “High Field MR Imaging of Mouse Models of AD,” Rush Alzheimer’s Disease Center ROS and MAP 2015 Investigators Meeting, Rush University Medical Center, Chicago, IL.

(From left) Drs. Alice Wyrwicz, Daniil P. Aksenov and P.N. Venkatasubramanian are involved in advanced collaborative studies related to traumatic brain injuries and the development of Alzheimer’s disease.
The Division of Gynecological Pain and Minimally Invasive Surgery (GPMIS) concentrated its research efforts on understanding the mechanisms of gynecological pain in an effort to improve treatment and care of patients experiencing these symptoms. Led by Frank Tu, MD, MPH, and Kevin Hellman, PhD, the GPMIS proudly recruited its 100th participant in a National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) clinical trial of dysmenorrhea mechanisms (Chronic Pain Risk Associated with Menstral Period Pain [CRAMPP]).

The GPMIS is also leading an effort to identify a novel biomarker of pelvic floor pain risk for women who experience such pain following vaginal examination. Determining a marker, which can be found in some pain-free women, will inform the debate about whether to offer routine pelvic exams to asymptomatic women and, consistent with a recent Veterans Administration report, encourage more detailed studies of the pelvic exam.

New Grants
Frank Tu, MD, MPH, (Co-Investigator). Interstitial Cystitis—Examination of the Central Autonomic Network (ICECAN), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) clinical trial of dysmenorrhea mechanisms (Chronic Pain Risk Associated with Menstral Period Pain [CRAMPP]).

Selected Presentations
Sangeeta Senapati, MD, MS, “Surgical Management of Pelvic Pain.” American Gynecological and Obstetrical Society meeting, Half Moon Bay, CA.
Frank Tu, MD, “Endometriosis: From Whole Genome Sequencing to Holistic Medicine,” American Society for Reproductive Medicine, October 2015.

Dr. Frank Tu leads residents and fellows in training for minimally invasive surgical procedures aimed at treating patients with gynecological pain and other conditions.
Recognized for excellence in translational research, physician-scientists at NorthShore are committed to enhancing care today with the latest findings from basic science and clinical trials. Our portfolio of prominent and promising research continues to advance knowledge and support our mission “to preserve and improve human life.”

But research, more than any other element of healthcare today, depends on philanthropic support.

Your support of NorthShore Research Institute is an investment in the health of our community and a bridge to improved prevention, detection and treatment of disease.

Your contribution will make a real difference for patients today and for generations to come.

To learn more about supporting excellence in research at NorthShore, please contact NorthShore Foundation at philanthropy@northshore.org or (224) 364-7200. Donate online at northshore.org/donate.