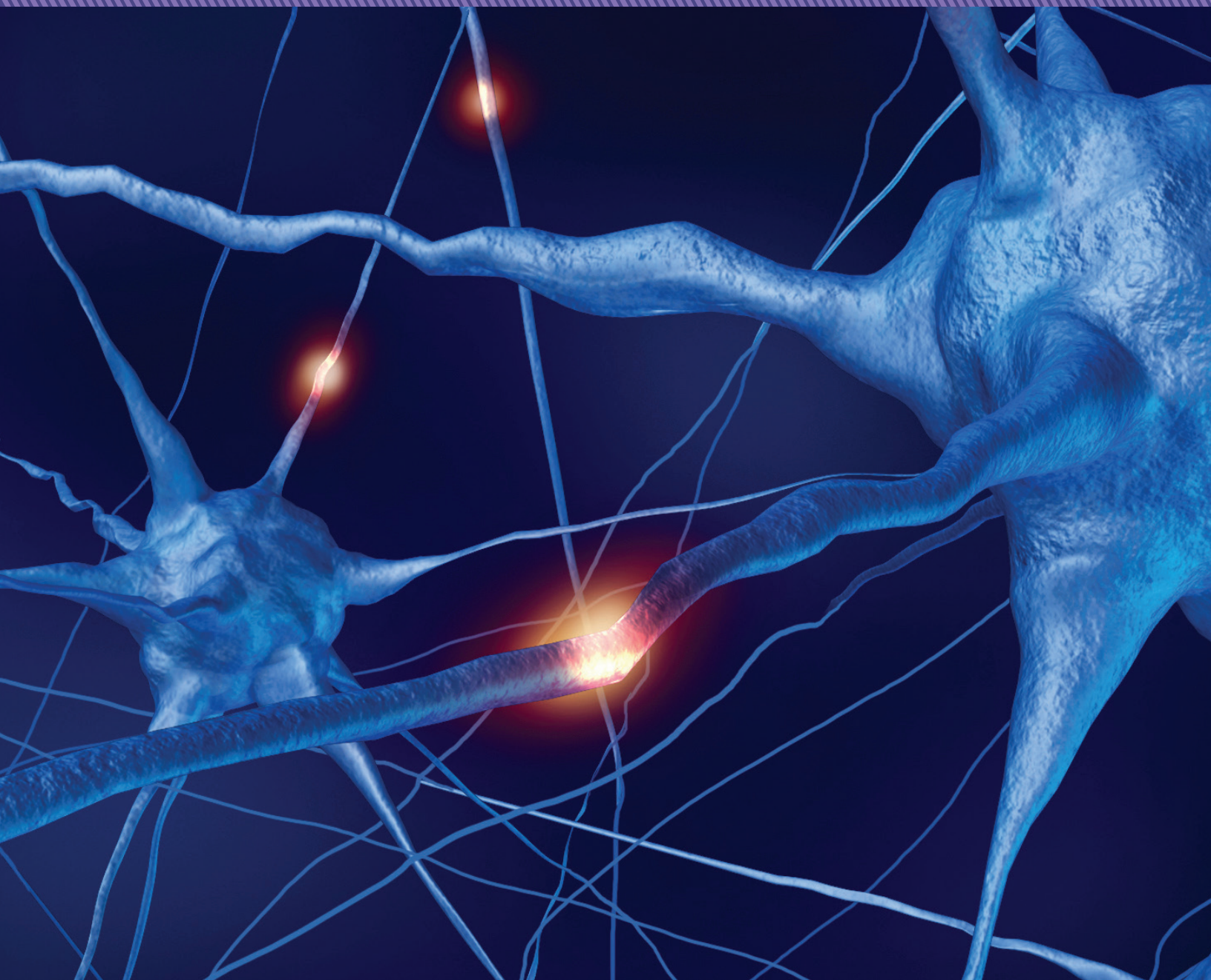# Frances Evelyn Feinberg Clinical Neuroscience Research Institute

Frances Evelyn Feinberg Clinical Neuroscience Research Institute

More than any other organ system, the brain defines who we are as human beings. Disease, traumatic injury, and even aging can impair brain function and deprive us of the ability to lead a happy and productive life. The challenge we face is to find ways of stopping and reversing the effects of disease and injury. As our population ages and becomes more vulnerable, this challenge takes on a growing sense of urgency.

The Frances Evelyn Feinberg Clinical Neuroscience Research Institute is meeting this challenge by creating a discovery incubator that will facilitate development of the next generation of therapies for disease and injury to the brain, spinal cord, sensory organs, and peripheral nervous system. A key element of this incubator will be the formation of interdisciplinary teams of leading researchers in the life, physical, engineering, rehabilitation and clinical sciences—all areas of excellence at Northwestern University—to promote cross-fertilization of ideas and innovation. To put thought into action and propel the discovery process forward, the Institute will create technical platforms where these teams can use an array of emerging, cutting-edge tools to probe disease mechanisms, progression, and treatment.

The Frances Evelyn Feinberg Clinical Neuroscience Research Institute is focusing on key areas of need and opportunity. In each of these highly interdisciplinary areas, Northwestern Medicine has assembled world leaders who are ready to accept the challenge we face and work together to meet it.

Development of Targeted Therapies for Neurodegenerative Disorders

Advances in our ability to stave off stroke, cancer, and heart disease are extending our lifespan. As a consequence, the incidence of aging-related nervous system diseases, like Alzheimer's disease, Parkinson's disease, and macular degeneration, is increasing. Alzheimer's disease and Parkinson's disease alone afflict millions of older Americans at a cost estimated to be in excess of $100 billion annually. The burden of less common, aging-related neurodegenerative disorders is steadily rising as well.

The development of new therapeutics that will slow or stop these debilitating neurological diseases has been challenging for several reasons. One reason is the brain is by far the most complex organ, making the identification of good therapeutic targets difficult. Another reason is that monitoring disease progression in an objective way—which is critical to determining whether a new therapy is working— has been difficult.

Strategies for overcoming these obstacles will only come by bringing the best scientific and clinical minds together in an environment that sparks creativity and cooperation. This kind of innovative environment is being created at Northwestern Medicine. Leading researchers in neuroscience, psychiatry, neurology, neurosurgery, and ophthalmology are using cutting-edge technologies to explore not only how disease disables neurons and networks, but also to identify the 'pressure points' that can be targeted by new therapeutics to
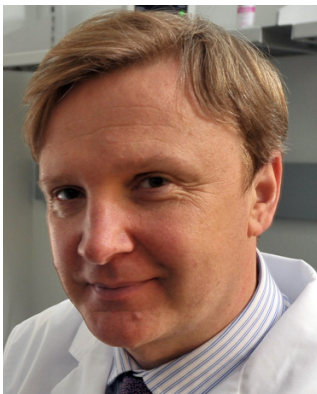
"Through the Frances Evelyn Feinberg Clinical Neuroscience Research Institute, we are applying state-of-the art technologies developed by biomedical engineers, nanotechnologists, chemists, and biologists across Northwestern to develop and deliver targeted therapies for currently untreatable brain disorders that affect children and adults."

Dimitri Krainc, MD, PhD, Aaron Montgomery Ward Professor of Neurology and Chair, Ken and Ruth Davee Department of Neurology
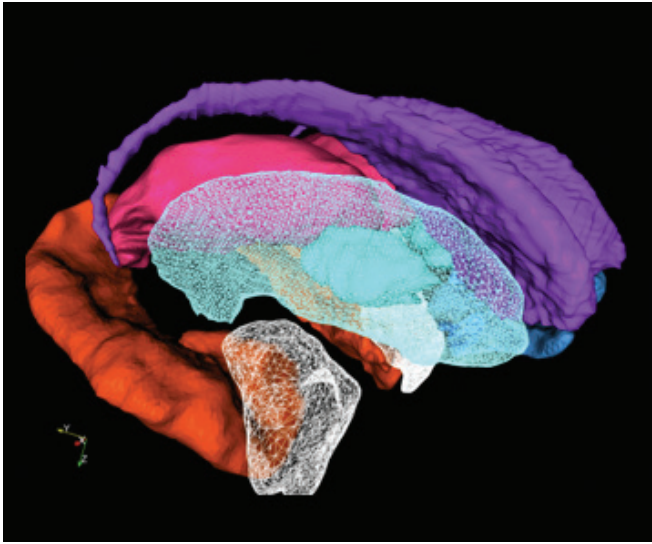
Surface renderings of structures deep within the brain derived from magnetic resonance images using atlas-based brain mapping algorithms. Age-related abnormalities of brain structure can be identified with high precision by comparing the images of individuals with and without a disorder.

slow or stop disease progression. Researchers in these core disciplines are teaming with leaders in chemistry, bioengineering, and nanotechnology to develop next-generation therapies and biomarkers for early detection and for monitoring disease progression. This interdisciplinary, bench-to-bedside approach has already led to major translational efforts in neurodegenerative disorders.

An example of this kind of cross-cutting effort has been in Parkinson's disease. The causes of Parkinson's disease have been a mystery for decades. Using an innovative array of optical, electrical, and molecular tools only available at a handful of medical centers in the world, our team discovered that the neurons at risk in Parkinson's disease are metabolically stressed. The identification of the protein responsible for this stress led to the re-purposing of a drug that is currently being tested in a Phase III clinical trial as a potential treatment for early stage Parkinson's patients.

We also are using rare diseases as a window into common neurodegenerative disorders. Our team found that Gaucher's disease, a rare lysosomal storage disease that predominately affects children, is mechanistically linked to Parkinson's disease. Specifically, we found that the enzyme linked to Gaucher's disease is also altered in Parkinson's disease. The Institute will make full use of this strategy to specify targets and mechanisms that contribute to neurodegeneration across the lifespan—facilitating the development of new therapeutics for Alzheimer's disease, Parkinson's disease, Huntington's disease, ALS, macular degeneration, and related conditions.
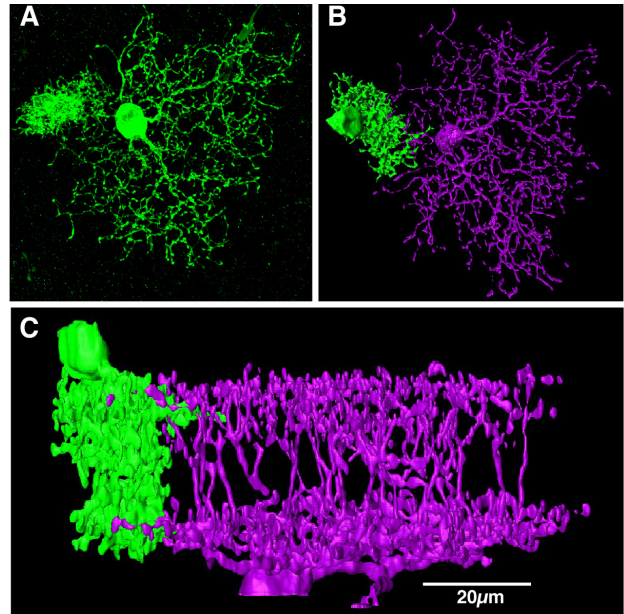
Unraveling which neurons talk to each other as they process information is one of the great challenges of brain research. In this image (1000X), we identified two neurons in the retina that talk to each other (shown in true color in A and false-colored purple and green in B, C) among thousands of neighboring neurons (not labeled) by using a rabies virus that is modified to both green-label a neuron that it enters and to cross only a single synaptic connection (laboratory of Steven DeVries, MD, PhD).

Preventing and Treating Disorders of Thought, Behavior, and Emotion

Thinking, behavior, and emotion depend upon the proper flow of information across complex networks within the brain. These neural networks are shaped in childhood and adolescence through the interplay of genetic and environmental influences and are modified by our experiences throughout life. Subtle defects in the development of these networks early in life can lead to the emergence of neuropsychiatric disorders in adolescence and adulthood, such as depression, bipolar mood disorder, Tourette's Syndrome, and schizophrenia. The accumulation of seemingly innocuous injuries also can lead to impaired network function as we age, leading to disturbances in thinking, behavior, movement, and sensation. Often, the roots of these impairments cannot be localized to any particular brain structure, but rather are distributed across network structures.

Recent imaging advances have given us a much better picture of how disturbances in the structure and function of neural networks contribute to disorders of thinking, behavior, vision, and sensation. Moreover, this work has shown that the brain and its networks have an amazing capacity to adapt when challenged by life's experiences. This capacity to adapt can be harnessed to maintain and restore the functioning of brain networks, improving the quality of our lives across the human lifespan. But to do this, we have to move beyond our current understanding of neural networks and develop new tools to normalize them. Using emerging technologies aimed at monitoring and manipulating network behavior, we will be able to identify new targets for therapy. This effort also will drive the use of new brain-machine interfaces—devices that were

once only the topics of science fiction. Used alone or in combination with drugs and psychotherapies, these new therapies hold to the promise of correcting and restoring networks that underlie human thinking and emotion, to improve the quality of our lives.

Neural Rehabilitation and Bionics

Neural injury can impair the flow of information from one part of the nervous system to another. We now have the capability to measure impairments following brain (e.g., stroke, cerebral palsy, brain tumor, retinal degeneration, head trauma) and spinal cord injuries and are using engineering technologies to correct deficits. For example, robots are being used to measure how a patient's ability to move is impaired following brain injury. They also are being used to implement novel rehabilitation therapies.

Northwestern Medicine researchers also are working to develop neural rehabilitation and bionic therapies with the goal of improving and restoring nervous system function. For example, brain-machine interfaces are being used to treat Parkinson's disease, to restore hearing, sight, and behavior, and to provide the ability to move previously paralyzed limbs. Capitalizing on computer miniaturization and our understanding of how neural networks operate, these evolving technologies have enormous potential to improve or correct the flow of information through damaged neural tissue. The use of nanotechology also is rapidly expanding at Northwestern Medicine. Engineered nanoparticles give the power to target therapies to specific populations of neurons in space and time. Nanomaterials also are giving us the ability to reconnect parts of the nervous system that have been separated by injury or disease.

These advances are being made possible by the innovative, multidisciplinary teams of scientists, engineers, and clinicians put in place at Northwestern Medicine.

Sleep and Circadian Rhythms in Neurological Disease

Sleep is fundamental to our well-being and to the health of virtually all aspects of the nervous system. Millions of Americans suffer from disrupted sleep or circadian (~24 hour) organization, resulting in impaired brain function and ultimately in a wide range of brain diseases. Combining animal models and clinical studies, researchers at Northwestern have pioneered the effort to pinpoint the molecular gears of the biological clocks that govern daily rhythms of sleep and wakefulness. Our interdisciplinary teams are now capitalizing on these groundbreaking insights to discover how these 24-hour timers regulate sleep, contribute to healthy brain function, and when they go awry, lead to disorders like autism, depression, neurodegenerative diseases like Alzheimer's and Parkinson's disease, and even obesity. Northwestern investigators are now poised to translate these fundamental discoveries and integrate 24-hour timing into the diagnosis and treatment of disease, creating a new branch of medicine – chronomedicine – that promises to transform the care delivered to patients.

THROUGH NORTHWESTERN MEDICINE, WE ARE CREATING A NATIONAL EPICENTER FOR HEALTHCARE, EDUCATION, RESEARCH, COMMUNITY SERVICE, AND ADVOCACY.

Northwestern Medicine

Northwestern Memorial HealthCare and Northwestern University Feinberg School of Medicine are seeking to impact the health of humankind through Northwestern Medicine. We aspire to be the destination of choice for people seeking quality healthcare; for those who provide, support, and advance that care through leading-edge treatments and breakthrough discoveries; and for people who share our passion for educating future clinicians and scientists. Our commitment to transform healthcare and to be among the nation's top academic medical centers will be accomplished through innovation and excellence.

We recognize that every positive contribution we have made to neuroscience care, research, and education has been made possible by donors who have entrusted us with their philanthropic support. We invite our loyal donors and interested friends to join us in advancing the Frances Evelyn Feinberg Clinical Neuroscience Research Institute and ensuring our success through gifts of outright support and endowment.