Surmeier Using NIH Blueprint to Fight Parkinson’s Disease

With no known neuroprotective treatment for Parkinson’s disease (PD), D. James Surmeier, PhD, chair of physiology, found optimism in ingenuity.

Co-PI of an innovative National Institutes of Health (NIH) grant—one of four Blueprint for Neuroscience Research awards given this year—Surmeier is part of an NIH experiment that begins with an academic parent, Northwestern, and pairs it with industry representatives to promote drug development.

The resulting partnerships build upon a recent breakthrough published by Surmeier and co-investigator Richard Silverman, PhD, John Evans Professor of Chemistry, outlining the development of a new family of compounds which might slow the progression of PD.

The new compounds target and shut a relatively rare protein channel that allows calcium to flood into dopamine neurons. This flood puts a stress on mitochondria, the power plants inside neurons that supply the energy needed to pump the calcium out. This power plant stress has been viewed as a likely cause of the disease.

“Once my lab identified the Cav1.3 calcium channel as a potential player in pathogenesis and we realized that there were no selective blockers for this channel, I knew we had a problem,” said Surmeier, Nathan Smith Davis Professor of Physiology. “That is when I reached out to Rick, knowing that he is almost the face of medicinal chemistry at Northwestern. Luckily for me, he was very interested right from the beginning.”

Together with Silverman, and the university’s High Throughput Analysis Laboratory (HTA), which provides researchers with equipment

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and expertise to screen thousands of compounds, Surmeier received funding from the RJG Foundation and the Michael J. Fox Foundation for an initial drug screening effort. The work was successful, identifying several new compounds that selectively blocked Cav1.3 channels. With these new drugs in hand, Surmeier and Silverman secured a Blueprint grant and the NIH commitment of more than $1 million per year to move the new drugs forward.

Milestone-Driven Science
Awarded in September, the Blueprint grant is milestone driven and will be reviewed by a Steering Committee each June to determine if drug development is proceeding according to plan. If adequate progress is being made, NIH funding will continue, with the goal of getting a drug into Phase I human clinical trials. The goals to be achieved in the next eight months include validating the group’s ability to meet industry standards for drug screening; improving the lead compounds identified by Silverman in terms of selectivity, potency, and pharmacokinetics (the ability of a drug to enter the brain and not be metabolized too rapidly); reducing the drug’s potential of toxicity; and determining whether lead compounds are neuroprotective in animal models of PD.

Moving the current compound closer to a drug suitable for humans is the focus of industry partner Albany Molecular Research Inc. (AMRI). The global contract research and manufacturing organization provides integrated drug discovery, development, and manufacturing services.

AMRI will take what the Silvermann lab has done in terms of medicinal chemistry and attempt to use that information to design new compounds that will be screened back at Northwestern. The company will also run tests on the most optimistic lead compounds to determine if they have the right properties for an orally-deliverable therapeutic.

“The idea of having a broadly effective neuroprotective agent against Parkinson’s disease is extremely exciting, and we’re really keen on moving ahead with this project as rapidly as possible,” Surmeier said. “If our theories about the pathogenesis of Parkinson’s disease are right, then a potent and selective antagonist for Cav1.3 channels will give us a therapeutic that will slow the progression of PD.”

Building Upon Results
The newly developed compounds work in a similar way to the drug isradipine, which is commercially available and FDA approved for the treatment of hypertension. Isradipine studies in Parkinson’s disease are moving forward led by Tanya Simuni, MD, Arthur C. Nielsen Jr. Research Professor in Parkinson’s Disease and Movement Disorders, but because the drug was developed for treatment of high blood pressure, it interacts with other channels found in the walls of blood vessels. This limits the dose the drug that can be administered to patients with PD.

Other studies by Surmeier’s group have focused on different areas of the brain. One such study is concentrated on the dopaminergic neurons in the substantia nigra, a region that plays an important role in movement. The loss of these neurons results in the core motor symptoms of PD — tremor, rigidity, and slowness.

Another study investigates the neurons in the medulla, which control the autonomic nervous system. In a recent paper in Nature Neuroscience, Surmeier’s team reported that these cells share similar features with dopaminergic neurons, engaging Cav1.3 channels and increasing mitochondrial stress. The findings suggest a common mechanism driving the development of PD.

“This elevates the feasibility that a single drug could slow or stop the progression of the disease throughout the brain,” Surmeier said.

“If isradipine works, that is terrific. But if it doesn’t or is only moderately effective, we have to be ready to take the next step and bring a more selective and potent Cav1.3 antagonist to the clinic,” he said. “There is a huge need to deliver a disease modifying therapeutic to Parkinson’s patients as soon as possible. In our view, isradipine is the best available option. That said, we cannot rest and simply wait on the outcome of that clinical trial five years from now.”

Growing the Therapeutic Window
Motivated to develop the first neuroprotective agent to fight PD, arresting the disease even for a short while would be a major breakthrough.

“And that’s important in no small measure because if you are diagnosed with PD, the symptomatic medications available are generally pretty good,” he said. “The problem is that because they don’t alter the progression of the disease, those symptomatic medications begin to wane in their efficacy.”

If new medication slowed the progression of the disease it would broaden the therapeutic window for current medications beyond the typical five years. “If we could double or triple this therapeutic window, it would be a great advance in treatment for PD.”
In NIH Funding Rankings, Feinberg Increase is Highest Among Medical Schools in Past 10 Years

In FY12, Northwestern University Feinberg School of Medicine increased its position in the National Institutes of Health (NIH) rankings to 21st among all medical schools for awards received directly from NIH.

That ranking, an all-time high for Feinberg, is up from 24 in FY11 and 41 in 1997. It represents the largest increase in ranking of the 130 schools that received funding during the last 10-year period.

“This vital NIH funding enables our investigators to make breakthrough discoveries while mentoring and training the next generation of scientists and physician-scientists,” said Eric Neilson, MD, vice president for medical affairs and Lewis Landsberg Dean. “Our new ranking is a validation of our superb Feinberg faculty and their diligent efforts to conduct important biomedical research.”

While Feinberg’s rank among medical schools increased in 2012, overall NIH dollars to medical schools did not.

“The NIH budget has been relatively flat for the last several years,” said Rex Chisholm, PhD, vice dean, scientific affairs and graduate education, Feinberg School of Medicine, and associate vice president for research, Northwestern University. “The medical school faculty hasn’t grown significantly. Feinberg faculty have been focused and effective in securing funding; we’ve been more successful than other institutions in competing for awards by increasing our market share.”

Departmental Rankings Success

In addition to rankings based on overall funding, NIH ranks individual departments of medical schools. In 2012, eight of Feinberg’s departments ranked in the top 10 of their research areas, and 11 departments ranked in the top 20:

- Departments ranked in NIH top 10 in 2012: Physiology (3); Urology (3); Obstetrics and Gynecology (4); Preventive Medicine (4); Dermatology (7); Physical Medicine and Rehabilitation (8); Cell and Molecular Biology (9); Neurology (10)
- Departments ranked 10 through 20 by NIH in 2012: Medicine (17); Otolaryngology (20); Surgery (20)
- Affiliated specialty hospitals ranked in the NIH top 10 for 2012: Rehabilitation Institute (1); Ann & Robert H. Lurie Children’s Hospital of Chicago (8)

Investing in Research, and Illinois

“Eight Feinberg departments earning rankings in the NIH top 10 for funding is really a remarkable achievement,” said Chisholm. “In 2012, Feinberg received nearly $174 million directly from the NIH.”

A 2011 AAMC report indicated that for every dollar invested in research at medical schools and teaching hospitals, $2.60 of economic activity occurs, on average. Additionally, federal and state research funding received by medical schools and teaching hospitals directly supports about 1 in every 500 jobs in the United States.

“Federal funding supports not only researchers at Northwestern University, but in the greater Chicago and Illinois economy as well,” said David Browdy, chief operating officer, Feinberg.

Grants to American medical schools accounted for approximately $11.8 billion of NIH’s $30.9 billion budget in FY12.

Research Video Debuts

National vocal talent and award-winning producer Bill Kurtis narrates a look inside Feinberg’s laboratories in a new video that debuted on YouTube recently. The video features Feinberg faculty and students talking about their research. More than 25 faculty and students on both campuses participated in the production.
Faculty Profile: Brian Mustanski, PhD
Associate Professor in Medical Social Sciences

Program in the Department of Medical Social Sciences (MSS) and the IPHAM Center for Community Health. He is currently principal investigator (PI) of a large research portfolio that includes five NIH grants (four R01s and one R21), two CDC research contracts, and a scholars award from the William T Grant Foundation.

Through his translational research he works closely with many community partners throughout Chicago that share the mission of eliminating lesbian, gay, bisexual, and transgender (LGBT) health disparities, such as the Center on Halsted, which is the most comprehensive LGBT resource center in the Midwest.

The integration of the IMPACT Program within the Center on Halsted facilitates the translation of research into practice, training of clinical researchers in LGBT health, engagement of the LGBT community with research, and provides “on the ground” expertise to inform his research agenda and methods. The IMPACT Program focuses on rapidly translating research into application by continuously conducting projects across the translational spectrum from epidemiology to intervention development to services research.

What are your research interests?

My primary research interests are in LGBT health disparities, particularly in the areas of HIV, substance use, and mental health, and in the developmental periods of adolescence through emerging adulthood. I am particularly interested in why mental, behavioral, and physical health issues cluster together in various populations. I also am very interested in how to use technology to conduct innovative research and interventions.

What is the ultimate goal of your research?

The ultimate goal of my research is to use science to identify and eliminate LGBT health disparities. For example, young gay and bisexual men represent 60 percent of HIV infections among all young people despite only being about two percent of the population. Young gay and bisexual men, particularly black young men, are the only risk group in the US showing an increasing rate of infections. This is a dramatic disparity that is being driven, in part, by lack of prevention programs tailored to the unique needs of these young men. Our longitudinal studies have helped identify risk and protective factors, and we have developed an innovative online HIV prevention program based on these factors.

My ultimate goal is to reduce the rate of infections by delivering effective prevention programs directly to these young men online, through text messaging and other communication channels.

How is your research funded?

My research is primarily funded through grants from the National Institutes of Health, although more recently we have also been funded by the CDC and the Chicago Department of Public Health. Right now I am a principal investigator of three R01 grants from the National Institute of Drug Abuse. One grant uses a natural experiment of neighborhood relocation to study the interaction between genes and neighborhood environment in predicting a cluster of health risk behaviors.

The second grant, conducted in collaboration with researchers at the Ann & Robert H. Lurie Children’s Hospital of Chicago, follows a cohort of young gay and bisexual men to understand the development of a cluster of psychosocial health issues linked to HIV.

The third grant conducts a multi-site trial of my online HIV prevention program.

I am a principal investigator of another R01 from the National Institute of Mental Health to develop and test a text messaging-based HIV prevention program and an R21 to study romantic relationship factors related to HIV risk in young couples. I am the Chicago PI of a large CDC research contract to test the reliability and behavioral effects of rapid HIV self-testing, which recently received FDA approval and dual-PI (with Michael Newcomb, PhD, research assistant professor in MSS) on a contract with the Chicago Department of Public Health to conduct a large epidemiological study of young gay and bisexual men in Chicago. Finally, I received a William T Grant Scholars

Q&A

Continued on pg. 5
Welcome New Faculty

Shi-Yuan Cheng, PhD, joins as professor of neurology.

Cheng was previously an associate professor of pathology and a member of Pittsburgh Cancer Institute at University of Pittsburgh School of Medicine in Pittsburgh, Penn. He received his doctorate degree in biochemistry from The Ohio State University in Columbus, Ohio, and his bachelor’s degree in biochemistry from Wuhan University, Wuhan, China.

He completed postdoctoral fellowships at the University of California, San Diego (UCSD) in the Laboratory of Signal Transduction (Department of Pharmacology) and the Laboratory of Tumor Biology at the Ludwig Institute for Cancer Research & UCSD.

Cheng’s research interests focus on the molecular mechanisms of human cancer tumorigenesis, progression, invasion/metastasis, and angiogenesis. He serves as PI or co-PI on four active grants, and has served as author or co-author on more than 50 articles in peer-reviewed journals. He also served as a member of various grant review study sections at National Institutes of Health, Department of Defense (Breast Cancer Research Program), and funding agencies from several other countries.

Bin Zhang, MD, PhD, joins as associate professor of medicine-hematology and oncology.

Zhang earned his Doctor of Medicine degree from the West China University of Medical Science, and his doctorate degree in cell biology from the National Laboratory of Experimental Hematology, Chinese Academy of Medical Sciences & Peking Union Medical College.

He completed his postdoctoral fellowship in pathology at the University of Chicago. He was previously assistant professor of medicine-hematology and oncology at the University of Texas Health Science Center at San Antonio.

Zhang’s research focuses on overcoming immunosuppression in the tumor microenvironment. He has served as author or co-author on more than 30 articles in peer-reviewed journals, and serves as PI on three active grants.

Mustanski Q&A, continued from pg. 4

award that supports my work on the Internet as a setting for the development of sexual health among LGBT youth.

Who makes up your research team and what role does each individual play in your research?

The IMPACT Program currently has five faculty members with training in psychology and public health. These faculty members collaborate on the projects I mentioned above, and launch their own grants to conduct translational LGBT health research. We have several master’s level data analysts and project directors with diverse training backgrounds. Across this group we have assembled a lot of expertise and experience in longitudinal and multilevel data analysis. We have an excellent group of research assistants that help collect and manage our data. The interviewers in particular are exceptional at developing rapport with our participants, and I credit them for achieving excellent retention in our longitudinal studies. Finally the Department of Medical Social Sciences has a very strong group of faculty and staff working on health information technology and it has been very productive to collaborate with them on a number of projects.

Which honors are you most proud of and why?

I am really proud of the fact that one of my studies, called Project Q2, is the longest running longitudinal study of LGBT youth ever conducted. We know surprisingly little about the healthy development of these young people, and Project Q2 has helped fill in some of these gaps. I am honored by the recognition I have received for this work, including last year receiving the Award for Distinguished Scientific Contribution to LGBT Psychology from the American Psychological Association and in 2008 being named a William T Grant Scholar. This Scholars award has been an exceptional opportunity to network with fantastic researchers around the country conducting research to improve the lives of young people. I have learned so much from these other scholars and my mentors on this award, both personally and professionally, that it has been an invaluable experience.

What do you enjoy about teaching and mentoring young scientists in the lab?

There are simply not enough scientists trained in LGBT health research to address the disparities. I feel it is critical to help train the next generation of LGBT scholars. Beyond this need in the field, I enjoy mentoring young scientists in launching their careers. I am fortunate to mentor a bright and motivated group of scholars, and I feel my main jobs are to provide them with infrastructure, connections, and training in grant writing, and then watch them launch their careers.
Student Profile: Keith Summa
Northwestern University Interdepartmental Neuroscience Program

Where is your hometown?
I’m from St. Louis, Mo.

What is your educational background?
I attended college at Georgetown University in Washington, D.C., where I majored in biology and English.

What are your research interests?
I’m interested in circadian rhythms, which are our body’s natural 24-hour cycles. In particular, I want to understand what the consequences of disrupting these rhythms are in terms of overall health and disease risk. The modern society and environment we currently live in make it incredibly difficult to properly abide by these daily cycles, and we’re just beginning to understand how disrupting these rhythms, including the sleep-wake cycle, can lead to problems and abnormalities that increase susceptibility to various diseases.

What exciting projects are you working on?
I am fortunate to be involved in several exciting projects as a member of the Fred Turek laboratory. My major focus right now concerns a long-standing and puzzling clinical question: Why do some alcoholics develop severe liver disease while others do not? We now have very exciting data from experiments in mouse models of alcoholism indicating that disruption of circadian rhythms significantly impairs the intestinal barrier, which allows leakage of proinflammatory bacterial products from the gut into the bloodstream where they can accelerate inflammation and promote liver injury. In addition, I am involved in ongoing work examining the connection between circadian rhythms and metabolism. In particular, I am conducting an experiment testing the role of feeding time in regulating body weight in mice.

What attracted you to the NUIN program?
NUIN and the Medical Scientist Training Program (MSTP) at Northwestern were very attractive to me for a number of reasons. First and foremost, the rigorous curriculum and strong academic foundation at Northwestern ensured that I would have the opportunity for excellent training, mentorship and scientific development.

Northwestern has a unique and storied role in the history of the field of circadian rhythms, with a rich tradition, exceptional reputation and a dedicated faculty of experts and leaders in the field.

Perhaps most important was the gut feeling I had during my interview and first visit to the campus that this was simply the right place for me. And finally, the appeal presented by the wonderful city of Chicago provided yet one more motivating factor for me to come here.

What has been your best experience at Feinberg?
I have had a number of great moments at Feinberg, but I’d say the best occurred on the first day of my surgery clerkship as a third year medical student. I assisted on a laparoscopic cholecystectomy (gall bladder removal) and still vividly remember (what was then) my first experience in an operating room. Although this was a relatively routine procedure completed without incident, it represented my first truly authentic experience as a member of the medical team and therefore it was a momentous step in the realization of a lifelong goal of mine to enter the field of medicine.

What do you do in your free time?
I don’t often feel that I have much free time, but I do like to explore the different neighborhoods, restaurants and opportunities of Chicago when given the chance. I play rugby for the Kellogg School of Management team, which is usually quite fun. I also enjoy cooking, hiking, and reading.

What are your plans after graduation?
I’d like to go on a nice, long trip, perhaps to New Zealand and Australia, which have long been dream destinations for me. After that, I plan on enrolling in an internal medicine residency, continuing to pursue research in circadian rhythms and hopefully contribute to the process of applying the scientific findings of the field into the realm of clinical medicine.
Staff Profile: Ann Crago
Web Content Architect, Office of Communications

Where are you originally from?
I’m from Evergreen Park, Ill.

What is your educational background?
I have a bachelor’s degree in English from the University of Illinois, Urbana-Champaign.

Please tell us about your professional background.
I have more than a decade of experience in corporate and web communications. Prior to coming to Feinberg, I worked at Northwestern Memorial Hospital, Manifest Digital (a user experience-focused agency), Blue Cross and Blue Shield Association, and LaSalle Bank.

Why did you choose to work at Northwestern?
Feinberg has such an incredible history and reputation. Coming from health insurance and finance, where people would often grumble at me when I told them where I worked, it’s a nice change of pace to see people’s eyes light up. It’s such an impressive institution, and having an opportunity to contribute to it is a real honor.

Also, the Web Communications team is comprised of talented, great people who are genuinely excited by what they do. The web content architect role is a challenging blend of responsibilities that I’ve seldom seen.

How do you contribute to the research mission at Feinberg?
Web Communications helps departments and offices at Feinberg develop user-friendly, well-organized sites with meaningful content. Through improving their presence on the web, departments at Feinberg can attract collaborators and talent, and inform the research community and public about the great work they do.

My role is to develop the narrative for a site based on the organizational goals and audience, as well as guide site owners in developing impactful, useful, web-friendly content.

What is your favorite part of the job?
I’m not a fan of clutter, and I love to tell and hear stories. Content strategy appeals to these traits.

Web content is too often developed without thought to why it needs to be there; what the audience cares about; and in what context will that content live. This leads to a lot of unhelpful, old, hard-to-read content that you can only find if you get really lucky. It’s bad storytelling.

Having a strategic approach to web content – knowing why content is there, who it’s for, what you want the audience to do with the information, how it connects to all other content, etc. – removes the clutter and organizes information into a story the reader can follow.

What do you like to do in your spare time?
I have 5-month-old daughter… so I sleep in my spare time. I also enjoy writing and reading. Prior to starting a family, I spent the last 10 years performing at local improv comedy theaters.

Call for Faculty Job Postings

Too often, faculty positions on campuses nationwide are not widely publicized, but rather circulated among limited personal networks and inboxes of senior faculty.

The Feinberg Research Office aims to create greater awareness among research students and trainees about open faculty positions by compiling a monthly list of current openings for inclusion in this newsletter. Newsletters are published monthly February through June, and August through December. These positions will be primarily research-focused and suitable for candidates who wish to pursue basic, translational, or clinical research.

If you receive information about faculty job openings that may be of interest, please forward the position description to the Research Office at fsm-research@northwestern.edu.
The process of epidermal differentiation and stratification requires biochemical and structural remodeling of intercellular adhesive junctions and associated cytoskeletal elements. These architectural components are more than just rivets and scaffolds; they also actively participate in epidermal polarization, signaling, and barrier formation. The focus of this project is on an adhesion molecule called Desmoglein 1 (Dsg1), one of a number of cadherin family members present in intercellular junctions called desmosomes that are crucial for tissues that experience mechanical stress, such as skin and heart. The importance of Dsg1 in skin is underscored by human diseases caused by mutations, autoimmune antibodies, and bacterial toxins targeting its adhesive function and leading to keratodermas and severe blistering disorders.

Desmosomal adhesion molecules are expressed in distinct, differentiation-dependent patterns within the epidermis, raising the possibility that they may do more than simply mediate adhesion (Figure 1). Dsg1 is first expressed as cells emerge from the basal proliferating layer of complex tissues and begin to differentiate, and later becomes concentrated in the superficial layer of the epidermis where it plays a key role in adhesion. We hypothesized that Dsg1 may also play a role deeper in the epidermis when it is first expressed to regulate transcriptional or morphogenetic changes that occur during the basal to suprabasal transition.

In this project we are using an in vitro model of human epidermal morphogenesis combined with analysis of human patients with Dsg1 deficiency, to test this idea. Earlier work supported by this grant showed that Dsg1 facilitates differentiation through suppression of canonical mitogen activated protein kinase (MAPK) signaling. Importantly, the adhesive ectodomain of Dsg1 is dispensable for this function, but it requires Dsg1’s unique cytoplasmic tail. To determine how the Dsg1 cytoplasmic domain regulates MAPK signaling, a DGP student in the lab, Robert Harmon, carried out an unbiased screen for Dsg1 binding partners, and several candidate mediators were identified. These include the scaffolding protein Erbin (ErbB2 Interacting protein), a member of the LAP (“LRR and PDZ” domain containing) family known to regulate MAPK signaling. Erbin co-localizes with Dsg1 at cell interfaces in suprabasal epidermis and transcriptional profiling revealed an overlapping cohort of genes controlled by Dsg1 and Erbin. Our hypothesis is that Erbin acts downstream of Dsg1 to drive suprabasal differentiation, and our goal is to determine the mechanisms by which Erbin and Dsg1 work together to perform this function. The work has led us to the discovery that Dsg1 relies on Erbin to keep the Raf-activating scaffolding protein Shoc2 away from Ras and Raf, and in this way attenuates MAPK signaling as keratinocytes emerge from the basal layer. We have been collaborating with a geneticist, Eli Sprecher at Tel Aviv University, and together have shown the involvement of this signaling nexus in patients with a skin disease called striate palmar plantar keratoderma (SPPK), caused by mutations in Dsg1.

Fig. 1: Epidermal differentiation: The epidermis, the outermost protective layer of the skin, is a stratified tissue that undergoes a continual process of self-renewal, whereby proliferating cells in the basal layer stop dividing and transit outwards towards the skin’s surface. During this process of terminal differentiation, cells undergo progressive changes in gene expression and morphology, including changes in expression of adhesion molecules and their associated cytoskeletal elements. Four desmogleins (Dsgs 1-4) are expressed in a differentiation-dependent manner. Dsg1 increases its expression as cells stratify and begin to express suprabasal keratins (K1/10) and cornified envelope proteins (loricrin) important for the epidermal barrier.

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Another goal of work funded by this grant is to determine how desmosomal cadherins control cytoarchitectural cues important for stratification and morphogenesis. In this regard we also identified Tctex, a subunit of the microtubule (MT) motor dynein, as a novel binding partner for Dsg1. Tctex is an interesting molecule because in addition to its function in dynein, it regulates cortical actin distribution important during neurite extension. We had also previously observed that Dsg1 deficiency leads to alterations in cell shape and size, accompanied by changes in the activity and distribution of key actin regulators in differentiating epidermis. A postdoctoral fellow in the lab, Oksana Nekrasova, is investigating the idea that Tctex regulates cortical actin and/or microtubule organization to promote the highly regulated process that transforms cuboidal basal proliferating cells into the flattened squames in the superficial layers of the epidermis. Her data suggest that expression of a mutant Dsg1 lacking its C-terminal Tctex binding site interferes with this process, resulting in misshapen keratinocytes and the appearance of basal-like cells high up in the epidermis. Future studies will be directed towards defining the mechanism by which Tctex regulates this process and the extent to which dynein-dependent and –independent functions play a role.

Overall these studies will reveal how Dsg1 becomes physiologically and functionally coupled to the initiation of epidermal differentiation. Elucidating how cytoarchitectural scaffolds choreograph mechanical and chemical signaling to promote differentiation will be essential for treating skin diseases where these pathways are undermined through cadherin gene defects, autoantibodies or bacterial pathogens.

**Ferdinando Mussa-Ivaldi, PhD**

**Professor in Physiology and Physical Medicine and Rehabilitation**

**Project title:** Motor Learning in a Customized Body-Machine Interface for Persons with Paralysis

**Sponsor:** National Institute of Child Health and Human Development

The goal of these studies is to enable persons paralyzed by spinal cord injury (SCI) to drive powered wheelchairs and interact with computers by acting through an interface that utilizes and adapts to their residual upper-body motor capabilities.

This is called a “body-machine interface” because it maps the motions of the upper body—detected by wearable sensors (arms and shoulders)—to the space of device control signals in an optimal way. In this way, paralyzed persons who cannot operate a joystick controller because of lack of hand mobility can effectively use their whole upper body as virtual joystick device.

An important characteristic of the proposed approach is that it incorporates an interactive learning process, in which the interface adapts to the subject’s mobility and the subject learns to act through the interface. This study aims at developing and testing the customization of this interface to a group of SCI participants with tetraplegia, resulting from high-level cervical injury. The proposed research is organized in three specific aims:

(Aim 1) To develop new functional capabilities in persons with spinal cord injury by customizing a body machine interface to their individual upper body mobility. After fitting the interface to the residual movements of each subject, participants will practice computer games aimed at training two classes of control actions: operating a virtual joystick and operating a virtual keyboard. This study will test the ability of the subjects to perform skilled maneuvers with a simulated wheelchair.

(Aim 2) To test the hypothesis that practicing the upper-body control of personalized interfaces results in significant physical and psychological benefits after spinal-cord injury. Rehabilitation of secondary complications is important in SCI. A study will evaluate and quantify the impact of practicing functional upper-body motions on the mobility of the shoulder and arms by conventional clinical methods and by measuring the subjects’ ability to generate coordinated upper-body movements and to apply isometric forces.

Other studies under this aim will evaluate the effects of operating the body-machine interface on musculoskeletal pain and on the mood and mental state of the participants.

(Aim 3) To train SCI survivors to skillfully operate a powered wheelchair using their enhanced upper body motor skills and customized interface parameters. The goal of this study is to transfer the skills learned in the virtual environment to the control of an actual powered wheelchair. After reaching stable performance in the simulated wheelchair, subjects will practice control of the physical wheelchair via the same body-machine interface within a safe testing environment.

If successful, this study will lead to effective operation of powered wheelchairs using a customized interface that adapts to the residual motor capability of its users. Physical and psychological benefits are expected to derive from the sustained and coordinated activity associated with the use of this body-machine interface.
Research in the News

Science Now November 21
Putting themselves to sleep
Phyllis Zee was quoted.

Chicago Tribune November 21
Study finds women sit around too much
Lynette Craft’s research was featured.

Wired November 20
Chemists concoct the “white noise” of smell
Jay Gottfried was quoted.

Associated Press November 20
Even among fit, heart disease a risk
John Wilkins was quoted.

CBS News (National) November 19
Multiple sclerosis study uses nanoparticles to stop immune system
Stephen Miller’s research was featured.

► Also featured in NBC News (National), Web MD, Yahoo! News UK & Ireland, Daily Mail (UK), Irish Examiner, Scotsman, and more

US News & World Report November 19
Kids with psoriasis more likely to be overweight: study
Amy Paller’s research was featured.

FOX News (National) November 16
Longer ‘exposure’ to US may raise immigrants’ obesity risk
Kiarri Kershaw was quoted.

Chicago Tribune November 13
Visible signs of aging signaled increased risk of heart disease, study finds
Jeffrey Goldberger’s research was featured.

WBEZ-FM (NPR) Chicago November 13
‘Fiscal cliff’ worries Chicago-area health care industry
Rex Chisholm was quoted.

More headlines

High Impact Factor Research October 2012


Help Feinberg Track Journals

The Feinberg Research Office regularly tracks research published by Feinberg investigators. The citations are used on web pages, in newsletters and social media, for internal reporting, and more. To more accurately track these journals, the Research Office asks that Feinberg investigators use the following institution name in the address field when publishing in peer-reviewed journals: “Northwestern University Feinberg School of Medicine.”
Funding Opportunities

**Collaborative Network for Clinical Research on Immune Tolerance (UM1)**

More information

**Sponsors:** United States Department of Health and Human Services, National Institutes of Health, National Institute of Allergy and Infectious Diseases

**Submission Deadline:** LOI: February 7 (optional); Application: March 7

**Upper Amount:** $27 million

**Synopsis:** Funding sponsors seek applications for the Collaborative Network for Clinical Research on Immune Tolerance. The Network’s goal is to develop new tolerogenic approaches for the treatment and prevention of disease in asthma and allergic diseases, autoimmune diseases, and immune-mediated rejection of transplanted solid organs, tissues and cells. The scope of research includes: the design and conduct of clinical trials at all phases to evaluate the safety and efficacy of investigational products and approaches for the induction and maintenance of immune tolerance in humans; the design and conduct of mechanistic studies and the development of tolerance assays as integral components of the clinical trials undertaken, including establishing and directing a consortium of laboratories; and the provision of bioinformatics, data collection, validation and analysis resources. In addition, the Network may support focused product development and nonclinical studies (e.g., toxicology, pharmacology, pharmacokinetics, etc.) essential for the subsequent evaluation of promising tolerance induction approaches in humans.

**NEI Translational Research Program on Therapy for Visual Disorders (R24)**

More information

**Sponsor:** United States Department of Health and Human Services, National Institutes of Health, National Eye Institute

**Submission Deadline:** January 25

**Upper Amount:** $7.5 million

**Synopsis:** The intention of this program is to make resources available to scientists from several disciplines to form research teams to address scientific and technical questions that would be beyond the capabilities of any one research group. Each project should have a well-defined end point of developing a specific treatment for a specific disease, achievable within a five-year time frame. The steps toward this end point should be clearly delineated in a series of milestones that support the development of a therapeutic approach, which can then be tested in a clinical trial.

View more funding opportunities

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**Featured Events**

**12.20 Endocrinology Seminar Series**

“The Paradox of Progress: Environmental Disruption of Metabolism and the Diabetes Epidemic,” presented by Robert Sargis, MD, PhD, University of Chicago

**Date:** Thursday, December 20, 4 to 5 p.m.

**Location:** Lurie Research Center — Searle
303 E. Superior St. (Chicago campus)

**Contact:** p-yim@northwestern.edu
More information

**12.20 Pediatric Grand Rounds**

“Personal Genome Sequencing,” presented by Brad Angle, MD, Feinberg

**Date:** Friday, January 4, 1 to 2 p.m.

**Location:** Ann & Robert H. Lurie Children’s Hospital of Chicago, 11-152 & 11-160
225 E. Chicago Ave. (Chicago campus)

**Contact:** bvonrueden@luriechildrens.org
More information

**12.20 Silverstein Lecture Series**

“Personal Genome Sequencing,” presented by Marc S. Williams, MD, Geisinger Health System Genomic Medicine Institute

**Date:** Thursday, January 17, 6 to 8 p.m.

**Location:** Lurie Research Center — Searle
303 E. Superior St. (Chicago campus)

**Contact:** mohney@northwestern.edu
RSVP & More information

**1.24 Feinberg Cardiovascular Institute Seminar Series**

“Systems Analysis of micro-RNA-mRNA Interactions in Experimental Heart Disease,” presented by Gerald Dorn II, MD, Washington University School of Medicine

**Date:** Thursday, January 24, 8:30 to 10 a.m.

**Location:** Lurie Research Center — Baldwin
303 E. Superior St. (Chicago campus)

**Contact:** (312)-503-0344
More information

More events

Event organizers are encouraged to submit calendar items on Plan-It Purple for consideration. Please contact the Research Office with further questions.