Breakthroughs

Feinberg School of Medicine Research Office

February 2015

Elizabeth McNally, MD, PhD, (right) talks with Lisa Castillo (left), a certified genetic counselor, in the Cardiovascular Genetics Clinic, where genetic testing identifies causes of inherited disease.

Center for Genetic Medicine's New Director Aims to Impact Disease Therapy

Technological breakthroughs have led to better, faster, and cheaper gene sequencing, and along with it, an appreciation of how different each individual human genome is from another, and how that variation can hold powerful information for understanding disease risk.

"What we'll need to build more of, going forward, is a capacity to sequence at a rapid rate, interpret the information correctly and accurately—which is no small feat—and then implement the use of this genetic information in the clinic," says Elizabeth McNally, MD, PhD, the new director of the Center for Genetic Medicine (CGM), who hopes to establish Chicago as a "mecca for genetics."

CGM was founded in 2000 as a collaboration between Northwestern University, the Ann & Robert H. Lurie Children's Hospital of Chicago, and Northwestern Memorial Hospital to facilitate development of new genetic knowledge and its application to medicine. It supports the genetic research of more than 100 faculty members from 33 departments and three schools through core facilities and services, including DNA extraction, sequencing, gene expression profiling, gene targeting, and transgenic projects.

During the past decade, CGM created one of the first biobanks of human DNA sequences, NUgene, which has allowed scientists to study the role genes play in the development of

(continued on page 2)

Northwestern Medicine®

New Center for Genetic Medicine Director Aims to Influence Field

(continued from cover page)

common and rare diseases. McNally's plan for CGM is to take the next steps towards identifying genetic defects and creating treatments to fix them.

"We're building upon the wonderful clinicians and expertise that already exist at Northwestern," McNally says. "We have great infrastructure and delivery mechanisms such as the genetic counseling program; we just have to assemble some of those pieces in between."

Defining Genetic Defects in a Meaningful Way

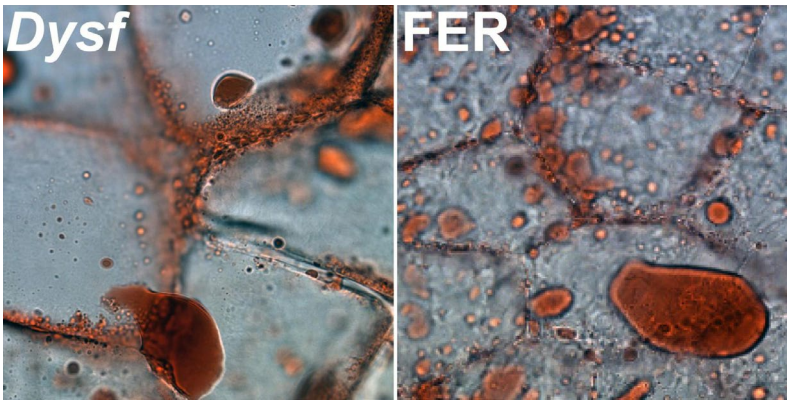
During the past decade, most research sampled a small fraction of the genome and focused on common gene variations. With the ability to sequence the whole genome, scientists can now see both common and rare gene variation. In the field of genetics, there is growing acceptance that rare genetic variation is important for inheritance.

McNally plans to move CGM towards studying common diseases by re-examining them as a constellation of rare diseases. She has selected a few targeted areas, such as heart failure, and will start to classify the diseases, match genetic changes, and eventually, develop treatments.

For example, by sequencing genomes of heart failure patients, researchers have found that approximately 20 percent of those with a weakened heart have gene variants that cut off a protein known as titin.

"Right away, the genome tells you that titin is a target, a gene we need to understand better and determine how to replace what is missing when it's truncated," McNally said. "Genetic variation will allow us to classify diseases in a way we didn't before. In the heart failure field, we used to think of it all as one disease; but now we can begin to understand this type of heart failure due to titin mutations and distinguish it from heart failure due to other mutations. Much in the same way that we don't treat all cancers the same, we will apply heart treatments more selectively and successfully. A lot of of medicine can be better understood by uncovering genetic signatures."

CONTENTS



From the McNally lab: muscles with mutations in dysferlin and the related protein myoferlin develop fat accumulation within the muscle (red).

In the future, McNally sees the Center using new molecular technologies that will fix genetic defects such as gene editing and exon skipping.

"It is in the very early days of using this kind of technology, but as it becomes more commonplace we will get better tools to correct genetic defects," she says.

Gene Modifiers in Muscle Disease

McNally brings to Feinberg not only her expertise in program direction, but also her research on inherited forms of heart and muscle disease.

Funded by grants from the National Institutes of Health and Department of Defense, McNally's lab strives to understand how gene modifiers can change the outcome of a given mutation; in particular, she studies a form of muscular dystrophy called Duchenne muscular dystrophy. This hereditary disease affects boys in their first decade and robs them of their ability to walk and breathe.

Using a mouse model of muscular dystrophy, McNally identified a gene that regulates the protein TGFβ and learned that mice carrying specific genetic variation in this gene experience a less severe form of the disease. In another study, she collaborated with investigators in Ohio and Utah and found the same gene that helped protect the mice also protected Duchenne patients. Boys with the protective gene signature walked for almost two years longer than boys without these genetic variants.

In a recent paper in *Science Translational Medicine*, McNally and her team inserted the damaging version of the human gene for this TGFβ binding protein into mice, making the disease worse, and uncovering the possibility of a new therapy that blocks the gene to decrease inflammation and muscle damage.

"These results tell us that's a pathway worth modifying," McNally says. "So now we are doing preclinical studies to develop this modifier into a therapy. That's what genetics can teach you: the victory is getting something you can manipulate therapeutically, that's the goal of finding these modifiers."

Northwestern University Feinberg School of Medicine

11th Annual Lewis Landsberg Research Day

Call for Abstracts

Submission Deadline: Tuesday, March 3 at 5:00 p.m.

The 11th Annual Lewis Landsberg Research Day will be held on April 3, 2015 from 1 to 5 p.m. on the Chicago campus, in the Robert H. Lurie Medical Research Building and at Northwestern Memorial Hospital's Conference Center.

This event features a poster competition open to researchers in the following categories:

- Faculty
- Graduate students
- MD-PhD students
- Medical students
- Postdoctoral researchers and fellows
- Clinical residents and fellows
- Research staff

Those interested in participating in the 2015 event must **submit an abstract online** **no later than 5 p.m. on Tuesday, March 3**. Registrants will not be able to enter information on the web site after that date. Space is limited and will be assigned on a first-come, first-serve basis.

Research Day is a campus-wide event to promote faculty and trainee development through the sharing of exciting research and conversation with colleagues. Junior faculty are especially encouraged to submit abstracts and to network and exchange ideas with other Feinberg faculty.

For more information, please call the Feinberg Research Office at (312) 503-1499 or e-mail **researchday@northwestern.edu**.

NORTHWESTERN UNIVERSITY FEINBERG SCHOOL OF MEDICINE

Feinberg IT Introduces Data Security Requirements for Clinical Research

As part of an effort to protect sensitive data and to help investigators comply with regulatory requirements, all clinical research studies collecting personal or health-related identifiable information will soon be required to have a documented Data Security Plan. This will be submitted through Northwestern University's Institutional Review Board (IRB) research application and workflow process.

"For the first time, we'll be integrating data security considerations into the IRB workflow," said Carl Cammarata, senior director of information security at Feinberg Information Technology. "Northwestern University Feinberg School of Medicine is working very hard to improve its information security posture to reduce our risks of disclosing patient and research participant data to the public."

The new policy will apply to new research applications, re-applications, and applications subject to renewal occurring subsequent to the effective date of this policy, which will be announced later this winter or spring.

"We should be doing everything we can to protect the data that study participants entrust us with," Cammarata said.

The plan will guard against the accidental disclosure of personal data, which could harm not only study participants, but also the university's reputation and, by extension, its research efforts.

"Exposing data could impact our ability to get grant applications approved," Cammarata said. "At the end of the day, it's the patients that are impacted—study participants and future patients who might benefit from our research."

The plan will also help investigators comply with university, state, and federal regulations. Feinberg IT has developed policy and procedure guidelines for the new Data Security Plan, as well as a template and two examples, to assist investigators.

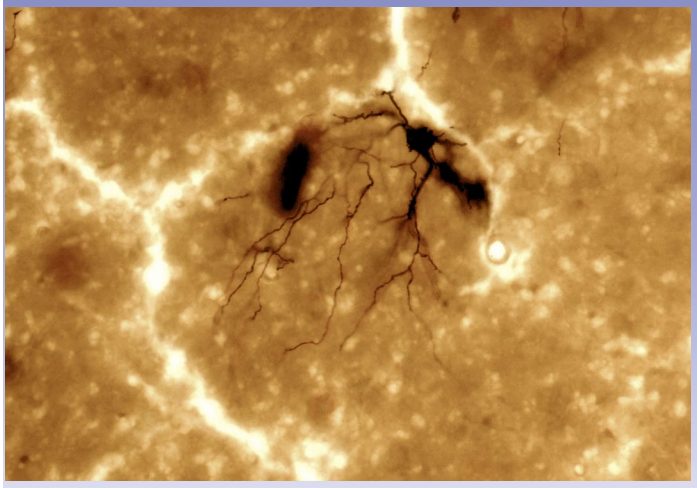
The plan contains seven parts:

- Data Custodian
- Data Sensitivity
- Data Flow and Transmission
- Data Storage
- Data Access
- Data Backup and Recovery
- Data Retention (Archiving)

Altogether, these sections include 13 short-answer and checklist questions designed to be completed by the principal investigator in one to two pages. Cammarata notes that using standardized clinical research services provided by NUCATS and/or Feinberg IT simplifies the acquisition of resources such as server and storage capacity.

When an implementation date is selected, an e-mail notification will be sent to the Feinberg community.

Feinberg Year In Review Highlights Research, Notable Achievements



Using fragile X mouse models, the lab of Anis Contractor, PhD, identified immature neurons (shown here) that resulted from a shift in the maturation of the neurotransmitter GABA. This story and more are featured in the 2014 Year in Review.

Discoveries, scientists, and students are featured prominently in Northwestern University Feinberg School of Medicine's 2014 Year in Review.

"For the medical school, 2014 was a tremendous year," said Eric G. Neilson, MD, vice president for medical affairs and Lewis Landsberg Dean. "Feinberg faculty published groundbreaking medical discoveries, while academic programs demonstrated continued excellence. We established a number of new and innovative programs and centers, recruited more world-class faculty and admitted students of the highest caliber. At the same time, the growth of the Northwestern Medicine health system cements our status as one of the nation's premier academic medical centers. I look forward to another year of noteworthy research discoveries and academic distinction in 2015."

The annual review includes high-impact research, an overview of academic activity, leadership highlights, and notable announcements.

Battling Cancer Through Scientific Discovery

Leonidas Platanias, MD, PhD, Director, Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Leonidas Platanias, MD, PhD, named permanent director of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University last October, is at the helm of Feinberg's efforts to battle cancer through scientific discovery.

Platanias's research in molecular biology and biochemistry, spanning more than 20 years and 250 published papers, focuses on signaling pathways in cancer cells and developing therapies that target those pathways to treat malignancies. He is well known for his work involving cytokines, which are specific proteins within the blood that have important links to cancer and other diseases.

Platanias joined Feinberg in 2002, as the Lurie Cancer Center's first Deputy Director and the Jesse, Sara, Andrew, Abigail, Benjamin and Elizabeth Lurie Professor of Oncology in Medicine-Hematology/Oncology. He is also a professor in Biochemistry and Molecular Genetics.

Q&A

What are your research interests?
I work in the area of signal transduction in malignant cells. I am interested in the mechanisms by which different cytokine receptors generate signals to either promote or suppress malignant cell proliferation. My laboratory also works on targeting signaling pathways to treat malignancies. We have made contributions in interferon signaling and defined different components of mTOR and MAP kinase pathways in normal and malignant hematopoiesis.

What is the ultimate goal of your research?
The goal is to further our overall understanding of the mechanisms of tumorigenesis, and to develop new targeted therapies for the treatment of selected malignancies.

What types of collaborations are you engaged in across campus?
At Northwestern, we have longstanding collaborations with colleagues in the Department of Chemistry on the Evanston campus, including the group of Tom O'Halloran. We collaborate closely with the groups of Elizabeth Eklund, MD, John Crispino, PhD, and others on Feinberg's downtown campus. Other collaborators are Eleanor Fish at the University of Toronto on the mechanisms of interferon signaling and Amit Verma at Albert Einstein University in New York on the signaling pathways in malignant hematopoiesis.

How is your research funded?
My research is funded by four R01 grants from the National Cancer Institute (NCI) and a Merit Review grant from the Department of Veterans Affairs. I am also the principal investigator of a NCI T32 training grant in signal transduction and cancer and of the American Cancer Society Institutional Review Grant, which provides funding for junior investigators at Feinberg. Finally, as director of the Lurie Cancer Center, I am the principal investigator of the Cancer Center Support Grant (CCSG) from the NCI.

Where have you recently published papers?
Our group has published articles in *Proceedings of the National Academy of Sciences USA, Blood, Cancer Research, Clinical Cancer Research, The Journal of Biological Chemistry, Nature Reviews Immunology, Oncogene, Molecular and Cellular Biology,* and more.

Which honors are you most proud of and why?
I am most proud of the Milstein Award from the International Cytokine and Interferon Society. This award is bestowed upon research scientists who have made outstanding contributions to international cytokine research, either in a basic or applied field. Awardees have made seminal advancements that have enabled the successful treatment of disease or have the potential to lead to significant health benefits. Since the Milstein Award was established in 1988, it has been widely recognized that cytokines play critical roles in the development and progression of many major diseases including cancer, viral diseases such as hepatitis and influenza, and autoimmune disorders like multiple sclerosis and lupus. Other past Milstein awardees include remarkable investigators such as Tadatsugo Taniguchi, Tom Maniatis, and Jim Darnell.

Hunting for Clues in Genomic Data

Matthew Dapas, Driskill Graduate Program in Life Sciences

Matthew Dapas, a second-year PhD student in the Northwestern University Driskill Graduate Program in Life Sciences (DGP), studies bioinformatics under Ramana Davuluri, PhD, professor in Preventive Medicine- Health and Biomedical Informatics.

Dapas received his bachelor's degree in biomedical engineering and master's degree in biotechnology from Johns Hopkins University. Prior to enrolling at Northwestern, he spent several years working as a technology consultant in pharmaceutical research and development.

Q&A

Where is your hometown?
I grew up primarily in Batavia, Illinois, which is about an hour west of Chicago on the Fox River.

What are your research interests?
My research interests lie in the domain of computational genomics: searching for causal disease mechanisms through computational analysis of genomic data. Identifying genomic disease signatures can be extremely useful both in biological research, where results can help steer the focus of genetic studies, and in clinical applications, where genomic biomarkers can be used to personalize treatment. In oncology, for example, genetic tumor subtyping can lead to the development or application of molecularly targeted therapies, as well as provide more accurate prognoses for patients.

What exciting projects are you working on?
With Ramana Davuluri, I'm studying the correlation of gene isoform expression between a number of different platforms. An ongoing challenge in bioinformatics is accurately quantifying gene expression at the gene isoform level (most genes produce multiple mRNA variants, or isoforms), yet there is an incredible amount of information that is lost when isoform dynamics are aggregated to their respective genes as single data points. We are trying to improve upon current methods to include gene isoform expression data in the study of cancer genomics.

I've also been collaborating with Geoffrey Hayes, PhD, and Andrea Dunaif, MD, in their study of the genetics of Polycystic Ovary Syndrome (PCOS). They've managed to sequence the entire genomes of many families affected by the disease. This has enabled us to study with relatively great statistical power how certain rare genetic variants are associating with the disease. We hope our results will help uncover some of the involved hereditary mechanisms and ultimately teach us more about the molecular drivers of PCOS.

What attracted you to the PhD program?
I'm encouraged by the momentum that Northwestern has in research, as an institution and in my particular focus area.

Biomedical informatics at Feinberg, although relatively small, is rapidly expanding and is very well positioned to grab and maintain a leadership role in the field. It's exciting for me to feel like I'm a part of that explosive growth and I get the sense that long after I'm gone, research at Feinberg will only continue its upward trends in terms of impact and prestige. Being a Chicago native, as well, I've enjoyed getting to stick around for at least a few more years.

What has been your best experience at Feinberg?
I get paid to learn about things that I find incredibly interesting, and my research may one day help improve the lives of unlucky people who suffer from the diseases I am studying. To me, it doesn't get any better than that.

What do you do in your free time?
I spend a lot of time in the gym or along the lakefront, depending on the time of year. As a lover of all things science, I also read a fair amount of nerdy books. On the weekends, however, I'm typically with friends, trying to have as much fun as my graduate student stipend will allow.

What are your plans for after graduation?
I want to continue driving innovation and discovery in computational genomics, but I'm not sure yet what that will look like, specifically, career-wise. I think I'd like to live in another country for a while, too.

Student Research in the News

Third year medical student in the Medical Scientist Training Program **Keith Summa, PhD candidate,** recently published an article in *Scientific American*. Summa is co-author of the article, "Molecular Clocks throughout Body, Not Just Brain, Keep Tissues Humming," with his PhD advisor, Fred Turek, PhD, professor in the Ken and Ruth Davee Department of Neurology, Psychiatry and Behavioral Sciences, and Weinberg College of Arts and Sciences.

Summa was featured in *Breakthroughs* in 2012.

Research in the News

***US News & World Report* January 27**
Watch upper number on blood pressure for younger adults: study
Donald Lloyd-Jones' research was featured.

***Chicago Tribune* January 23**
Cancer and bad luck
Leonidas Platanias was quoted.

- Platanias was also featured on WGN-TV Chicago.

CBS News (National) January 22
New study reveals healing power of voices
Theresa Pape's research was featured.

***US News & World Report* January 20**
Postpartum anxiety or normal new mom fears?
Emily S. Miller was quoted.

Chicago Tonight (WTTW-TV) January 19
Good Buddies
Sandra Weintraub was featured.

Yahoo! News January 16
Eczema linked to surprising health risks
Jonathan Silverberg's research was featured.

- This research was also featured in Reuters.

National Public Radio January 15
Even small changes made midlife can help keep your heart healthy
Bonnie Spring was quoted.

***Chicago Tribune* January 9**
Study: Pop music helps ease post-surgery pain for children
Santhanam Suresh's research was featured.

FOX News (National) December 31
Researchers use nanotechnology to engineer ACL replacements
Guillermo Ameer's research was featured.

***Chicago Magazine* December 30**
Medical wonders
Andrew Parsa's research was featured.

More media coverage available online.

Northwestern University
NUCATS
Clinical and Translational Sciences Institute

NUCATS Corner

Chicagoland CTSA Institutes Offer Shared Resources and Services

The Chicagoland Clinical and Translational Science Award (CTSA) Institutes—Northwestern University, University of Chicago, and University of Illinois at Chicago—are committed to facilitating greater integration and coordination across the institutes to provide seamless access to all relevant resources for translational researchers.

The Chicagoland CTSAs have identified a list of shared resources and services that investigators and research staff at all three institutes can use. The majority of the shared resources and services listed on the NUCATS website are offered at no charge or at the internal rate to Chicagoland CTSA affiliates.
Each month *NUCATS News* will be featuring our fellow

Chicagoland CTSA Institute's upcoming shared resources and services. In February 2015, investigators and research staff at Chicagoland CTSA affiliates have access to:

University of Chicago Institute for Translational Medicine (ITM)

- February 5, 12, 19, and 26 – Pathobiology of Disease Seminar Series

University of Illinois at Chicago Center for Clinical and Translational Science (CCTS)

- February 23, 2015 – Biomedical & Health Informatics Colloquium

For a full listing of Chicagoland CTSA shared resources and services, please click here. To stay up-to-date on upcoming Chicagoland CTSA shared resources and services, sign-up for *NUCATS News*.

Sponsored Research

PI: Hidayatullah Munshi, MD
Associate Professor of Medicine-Oncology and Otolaryngology

Sponsor: National Cancer Institute (NCI)

Title: "Targeting BET Bromodomain in Pancreatic Cancer"

Pancreatic ductal adenocarcinoma (PDAC) is a highly chemo-resistant and lethal malignancy, in part due to the activation of aberrant signaling pathways that limit the effectiveness of current therapies. Although mutant K-ras signaling—which occurs in greater than 95 percent of PDAC tumors—is one such pathway associated with PDAC chemo-resistance, targeting K-ras for therapeutic intervention has proven difficult.

Another common feature of PDAC tumors is the presence of pronounced fibrosis, which Munshi's findings have shown elicits chemotherapy resistance through epigenetic changes that, in turn, affect signaling. Specifically, Munshi and colleagues reported previously that collagen induces PDAC expression of high mobility group A2 (HMGA2), an architectural protein that regulates chromatin structure (Dangi-Garimella et al., *Cancer Research* 71:1019-28, 2011). Further, Munshi's more recent findings indicate that collagen also impacts chromatin structure and function by increasing histone H3 acetylation and histone acetyltransferase (HAT) expression in PDAC cells (Dangi-Garimella et al., *PLoS One* 8:e64566, 2013).

Importantly, the team also has found that downregulating either HMGA2 or HATs sensitized PDAC cells grown in 3D collagen to the nucleoside analog gemcitabine, which normally provides only minor therapeutic benefit in PDAC. Significantly, results of another study Munshi's team conducted indicated that inhibiting the bromodomain (BRD) and extra terminal domain (BET) family of proteins, which function as 'readers' of histone acetylation marks, decreases growth of PDAC cells in 3D collagen (Sahai et al., *Molecular Cancer Therapy* 13:1907-17, 2014). BET inhibitors (JQ1 and I-BET151) also decrease growth of pancreatic stellate cells, key mediators of fibrosis in vivo. Moreover, Munshi has evidence that treatment of PDAC cells with BET inhibitors decreases the cancer stem cell population and represses HMGA2, MYC and FOSL1 function.

The team's combined evidence strongly supports that BET proteins contribute to the fibrotic stroma and PDAC chemo-resistance. Precisely defining the underlying mechanisms and effects that inhibiting BET protein function in vivo exhibit on tumor development should lead to novel mechanism-based, clinically useful strategies to improve PDAC patient outcomes. The objective of this research is to determine how BET proteins mediate chemo-resistance and contribute to fibrosis in vivo. The central hypothesis is that BET protein inhibition will decrease PDAC tumor growth and increase chemo-sensitivity by decreasing the cancer stem cell population and HMGA2 protein function, respectively.

Based on preliminary studies, Munshi further hypothesizes that BET inhibition will lead to an attenuation of fibrosis in PDAC tumors. At the completion of these studies, it is his expectation that the team will have successfully identified the role of BET proteins in PDAC progression in vivo. Further, he anticipates having determined the in vivo efficacy of BET inhibition to increase chemotherapy sensitivity and decrease fibrosis. These studies should have important clinical-translational implications and should provide a strong evidence-based proof of principle for the development and future clinical trials of BET inhibitors for the treatment of PDAC.

PI: C. David James, PhD
Professor of Neurological Surgery and Biochemistry and Molecular Genetics

Sponsor: National Institute of Neurological Diseases and Stroke

Title: "BRAF Mutation in Malignant Astrocytoma Origin, Evolution and Response to Therapy"

Many pediatric brain tumors, including malignant astrocytomas (MA), are thought to originate from neural stem cells, which—due to the occurrence and accumulation of growth-promoting gene alterations—may give rise to various cell subpopulations, including tumor-initiating cells (TICs). TICs are considered to have increased resistance to conventional therapy for MA, and consequently are important contributors to MA recurrence.

Whereas neural stem cells undergo asymmetric cell divisions (ACD) to self-renew and differentiate at a one-to-one ratio, TICs proliferate and self-renew, failing to generate fully differentiated cells, suggestive of defective ACD.

A mutant, activated form of BRAF, BRAFVE, and concomitant homozygous deletion of CDKN2A, encoding p16, have been found in a significant fraction of pediatric MA. BRAFVE is known to promote proliferation while suppressing normal cellular differentiation. Whether increased production of self-renewing cells through increasing symmetric cell divisions (i.e., decreased

(continued on page 9)

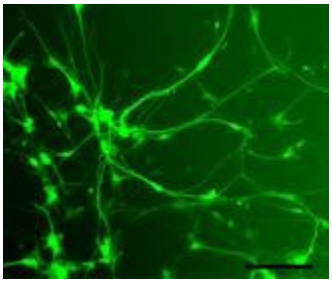
Sponsored Research

(continued from page 8)

ACD) is manifested in association with BRAFVE induced cell transformation is currently unknown.

To bridge the gap in understanding of BRAFVE-induced transformation, and its relationship with ACD, James and colleagues will examine effects of BRAFVE in p16 deficient neural stem cells, as well as in corresponding p16 deficient astrocytes of mouse and human origin. In addition, they will investigate relationships between BRAFVE-p16 deficient tumors and their adaptation to BRAFVE targeted therapy, with the primary focus directed toward tumor cell subpopulation and ACD changes resulting from treatment.

Related research will be performed in the context of the following specific aims: using genetically engineered mouse models (GEMMs), James will determine effects of BRAFVE expression on ACD, proliferation, differentiation, and survival, and association with MA tumorigenesis in neural stem cells and mature astrocytes (aim one).



Neural stem cells (Courtesy of L. Lyass)

To complement these studies, the team will suppress p16 expression and force BRAFVE expression in human neural stem cells and normal human astrocytes, using lentiviral shRNA knockdown and BRAFVE gene transfer, respectively. Modified neural stem cells and NHAs, as well as MA cells with BRAFVE expression, will be characterized, both in vitro and in vivo, for the same characteristics as for the mouse model tumors noted in aim one (aim two).

The team will also investigate BRAFVE tumor cells and tumor tissues, in vitro and in vivo, respectively, for molecular changes, TIC composition, and ACD in association with response to BRAFVE targeted therapy. This research will include comparison of effects when tumors are in a responsive phase to therapy, as well as when they have acquired resistance to therapy, and will utilize both human tumor xenograft and mouse allograft models (aim three).

This project will generate new information regarding the cellular origin of BRAFVE induced MA, provide insight about the molecular mechanisms of neoplastic transformation resulting in brain tumor development, increase our understanding of brain tumor cell subpopulations that are responsible for therapy resistance and tumor recurrence, and in so doing will ultimately lead to improved treatment outcomes for MA patients.

Funding

Core Infrastructure and Methodological Research for Cancer Epidemiology Cohorts (U01)

More information

Sponsor: Department of Health and Human Services, National Institutes of Health, National Cancer Institute

Submission deadline: April 1
Upper Amount: $2.5 million

Synopsis: This funding opportunity announcement invites grant applications for targeted infrastructure support of the core functions of Cancer Epidemiology Cohorts (CECs) and methodological research. Through this funding opportunity, the National Cancer Institute (NCI) will support infrastructure and core functions for existing or new CECs. This will also lead to support of core functions for CECs currently funded through other grant mechanisms by the Epidemiology and Genomics Research Program (EGRP) and other components of the Division of Cancer Control and Population Sciences (DCCPS) at the NCI.

Opportunities for Collaborative Research at the NIH Clinical Center (U01)

More information

Sponsor: Department of Health and Human Services, National Institutes of Health

Submission deadline: March 20
Upper Amount: $1.5 million

Synopsis: The goal of this program is to support collaborative translational research projects aligned with NIH efforts to enhance the translation of basic biological discoveries into clinical applications that improve health. It encourages high-quality science demonstrating the potential to result in understanding an important disease process or lead to new therapeutic interventions, diagnostics, or prevention strategies within the research interests and priorities of the participating NIH Institutes/Centers (ICs). Specifically, the program seeks to broaden and strengthen translational research collaborations between basic and clinical researchers both within and outside NIH to accelerate and enhance translational science by promoting partnerships between NIH intramural investigators and extramural investigators, and by providing support for extramural investigators to take advantage of the unique research opportunities available at the NIH Clinical Center by conducting research projects in collaboration with NIH intramural investigators.

View more funding opportunities

High Impact Factor Research

November and December 2014

Akay T, **Tourtellotte WG**, Arber S, Jessell TM. Degradation of mouse locomotor pattern in the absence of proprioceptive sensory feedback. *Proceedings of the National Academy of Sciences USA*. 2014 Nov 25;111(47):16877-82.

Brooks JF 2nd, Gyllborg MC, Cronin DC, Quillin SJ, Mallama CA, Foxall R, Whistler C, Goodman AL, **Mandel MJ**. Global discovery of colonization determinants in the squid symbiont Vibrio fischeri. *Proceedings of the National Academy of Sciences USA*. 2014 Dec 2;111(48):17284-9.

Burbridge TJ, Xu HP, Ackman JB, Ge X, Zhang Y, Ye MJ, Zhou ZJ, **Xu J, Contractor A**, Crair MC. Visual circuit development requires patterned activity mediated by retinal acetylcholine receptors. *Neuron*. 2014 Dec 3;84(5):1049-64.

Doroghazi JR, Albright JC, Goering AW, Ju KS, Haines RR, Tchalukov KA, Labeda DP, **Kelleher NL**, Metcalf WW. A roadmap for natural product discovery based on large-scale genomics and metabolomics. *Nature Chemical Biology*. 2014 Nov;10(11):963-8.

French CR, Seshadri S, Destefano AL, Fornage M, Arnold CR, Gage PJ, Skarie JM, Dobyns WB, Millen KJ, **Liu T, Dietz W, Kume T**, Hofker M, Emery DJ, Childs SJ, Waskiewicz AJ, Lehmann OJ. Mutation of FOXC1 and PITX2 induces cerebral small-vessel disease. *Journal of Clinical Investigation*. 2014 Nov 3;124(11):4877-81.

Gallardo G, Barowski J, Ravits J, **Siddique T**, Lingrel JB, Robertson J, Steen H, Bonni A. An α2-Na/K ATPase/α-adducin complex in astrocytes triggers non-cell autonomous neurodegeneration. *Nature Neuroscience*. 2014 Dec;17(12):1710-9.

Halo TL, **McMahon KM, Angeloni NL, Xu Y, Wang W**, Chinen AB, Malin D, Strekalova E, Cryns VL, **Cheng C, Mirkin CA, Thaxton CS**. NanoFlares for the detection, isolation, and culture of live tumor cells from human blood. *Proceedings of the National Academy of Sciences USA*. 2014 Dec 2;111(48):17104-9.

Hashizume R, Andor N, Ihara Y, Lerner R, Gan H, Chen X, Fang D, Huang X, Tom MW, Ngo V, Solomon D, Mueller S, Paris PL, Zhang Z, Petritsch C, Gupta N, Waldman TA, **James CD**. Pharmacologic inhibition of histone demethylation as a therapy for pediatric brainstem glioma. *Nature Medicine*. 2014 Dec;20(12):1394-6.

Howard JD, Gottfried JA. Configural and elemental coding of natural odor mixture components in the human brain. *Neuron*. 2014 Nov 19;84(4):857-69.

Kelley SO, **Mirkin CA**, Walt DR, Ismagilov RF, Toner M, Sargent EH. Advancing the speed, sensitivity and accuracy of biomolecular detection using multi-length-scale engineering. *Nature Nanotechnology*. 2014 Dec 3;9(12):969-980.

Kwo PY, Mantry PS, Coakley E, Te HS, Vargas HE, Brown R, Gordon F, **Levitsky J,** Terrault NA, Burton JR, Xie W, Setze C, Badri P, Pilot-Matias T, Vilchez RA, Forns X. An interferon-free antiviral regimen for HCV after liver transplantation. *New England Journal of Medicine*. 2014 Dec 18;371(25):2375-82.

Mercy KM, Gordon KB, Paller AS. Patient satisfaction and quality of life in psoriasis and psoriatic arthritis. *JAMA- Journal of the American Medical Association*. 2014 Dec 24-31;312(24):2676-7.

Park DJ, Zhang C, Ku JC, Zhou Y, Schatz GC, **Mirkin CA**. Plasmonic photonic crystals realized through DNA-programmable assembly. *Proceedings of the National Academy of Sciences USA*. 2014 Dec 29.

Rajaram R, **Chung JW**, Jones AT, Cohen ME, **Dahlke AR**, Ko CY, Tarpley JL, Lewis FR, Hoyt DB, **Bilimoria KY**. Association of the 2011 ACGME resident duty hour reform with general surgery patient outcomes and with resident examination performance. *JAMA-Journal of the American Medical Association*. 2014 Dec 10;312(22):2374-84.

Rotman E, Steven Seifert H. The genetics of Neisseria species. *Annual Review of Genetics*. 2014 Nov 23;48:405-31.

Sabharwal SS, Schumacker PT. Mitochondrial ROS in cancer: initiators, amplifiers or an Achilles' heel? *Nature Reviews Cancer*. 2014 Nov;14(11):709-21.

Sagi Y, Heiman M, **Peterson JD**, Musatov S, Kaplitt MG, **Surmeier DJ**, Heintz N, Greengard P. Nitric oxide regulates synaptic transmission between spiny projection neurons. *Proceedings of the National Academy of Sciences USA*. 2014 Dec 9;111(49):17636-41.

Weinberg SE, Chandel NS. Targeting mitochondria metabolism for cancer therapy. *Nature Chemistry Biology.* 2014 Dec 17;11(1):9-15.

Weingarten AS, Kazantsev RV, Palmer LC, McClendon M, Koltonow AR, Samuel AP, Kiebala DJ, Wasielewski MR, **Stupp SI**. Self-assembling hydrogel scaffolds for photocatalytic hydrogen production. *Nature Chemistry*. 2014 Nov;6(11):964-70.

Wood AR, et. al. (Includes **Kho AN** and **Hayes MG**). Defining the role of common variation in the genomic and biological architecture of adult human height. *Nature Genetics*. 2014 Nov;46(11):1173-86.

Yang H, Qiu Q, Gao B, Kong S, Lin Z, Fang D. Hrd1-mediated BLIMP-1 ubiquitination promotes dendritic cell MHCII expression for CD4 T cell priming during inflammation. *Journal of Experimental Medicine*. 2014 Nov 17;211(12):2467-79.

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."*

Calendar

Tuesday, February 17

Microbiology-Immunology Seminars

"Role of Liver-Specific MicroRNA miR-122 in the Hepatitis C Virus Life Cycle," presented by Peter Sarnow, PhD, Stanford University.

Time: Noon to 1 p.m.
Location: Lurie Medical Research Building — Baldwin 303 E. Superior St. (Chicago campus)
Contact: derek.walsh@northwestern.edu
More information

Tuesday, February 17

Lectures in Life Sciences

"Lipid Signaling Pathways in Physiology and Disease," by Peter Tontonoz, University of California Los Angeles and Howard Hughes Medical Institute.

Time: 4 to 5 p.m.
Location: Lurie Medical Research Building — Hughes 303 E. Superior St. (Chicago campus)
Contact: debu@northwestern.edu
More information

Monday, February 23

Preventive Medicine- Biostatistic Seminar

"Variable Selection in High-dimensional Regression Models" by Tong Wang, PhD, Shanxi Medical University.

Time: 3 to 4 p.m.
Location: 680 N. Lake Shore Dr. — Suite 1400, Stamler Conf. Rm. (Chicago campus)
Contact: JenniferBuchko@northwestern.edu
More information

Thursday, March 5

Lurie Tumor Cell Biology Seminars

"Functional genomics: From tumor suppressor genes to targeted therapy," presented by Christopher Kemp, PhD, University of Washington.

Time: 1 to 2 p.m.
Location: Lurie Medical Research Building — Baldwin 303 E. Superior St. (Chicago campus)
Contact: cancer@northwestern.edu
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.

NIH News

ASSIST now an option for R03 and R21

Applicants now have the option to use NIH's online ASSIST system to prepare and submit their R03 and R21 grant applications. ASSIST users benefit from pre-submission checks against NIH business rules and the ability to preview their application image in the NIH format prior to submission. Use of ASSIST is optional; grants.gov downloadable forms and institutional system-to-system solutions remain viable submission options.

Learn more.

Fiscal Policies for 2015

In January, NIH announced policies for fiscal operations for fiscal year (FY) 2015, implementing the 2015 Consolidated Appropriations Act signed by President Obama on December 16, 2014. NIH has a budget of $30.31 billion, an increase of approximately $240 million over the FY 2014 final budget allocations of $30.07 billion. NIH also announced stipend levels for Ruth L. Kirschstein National Research Service Awards (NRSA), and salary limits for individuals receiving salaries from an NIH grant, cooperative agreement, or contract.

Keeping with the precedent set last year, and because each NIH institute and center (IC) has a different budget, ICs are given flexibility to manage funding levels of non-competing continuation awards. Non-competing continuation awards already made for FY2015 that that were funded at reduced levels (usually at the 90 percent level) may be fully or partially restored as described in NOT-OD-15-001. Non-competing continuation grants likely will be made within the range between the commitment level indicated on the Notice of Award and three percent below that level. Grants management official will be working with institutions' grants officials on the final budget levels when issuing or reissuing these awards.

Read more about the NIH's 2015 NIH fiscal policy.

Follow Feinberg Online