EMERGING SCHOLARS PROGRAM

NEURONETWORK FOR EMERGING THERAPIES
MICHIGAN MEDICINE
The NeuroNetwork for Emerging Therapies at Michigan Medicine Emerging Scholars Program intends to assure that there is a solid future for our next generation of medical science leaders and the many cures and treatments that will be their legacy.

The NeuroNet has talented young scientists who require funding to pursue innovative approaches to the treatment of disease and build the credentials they need to secure long-term financial support for their research from private foundations and the National Institutes of Health.

Emerging Scholars funding typically involves a $150,000 commitment, which is spread equally over three years. During that time, donors receive biannual reports from their Emerging Scholar about the research they are supporting, as well as an opportunity to meet with their Emerging Scholar to learn first-hand the impact their gift has made in the battle against disease.

Support for the Emerging Scholars Program also may be made through the University of Michigan’s endowment. A gift of $500,000 allows for the establishment of a permanent Emerging Scholar Fund, which can support young scientists working in a designated field of medicine. This allows a donor’s commitment to medical research to live on in perpetuity.

Emerging Scholars Program

Dr. Brian Callaghan
Dr. Bhumsoo Kim
Dr. Benjamin Murdock
Dr. Phillipe O’Brien
Dr. Amy Rumora

Dr. Osama Kashlan
Dr. Kevin Chen
Dr. Sarah Elzinga
Dr. Claudia Figueroa-Romero
Dr. Stephen Goutman

Dr. Evan Reynolds
Dr. Amy Rumora
Dr. Bhumsoo Kim
Dr. Benjamin Murdock
Dr. McGinley has extensive experience in translational cell and gene therapies, and her major research interests lie in identifying novel therapeutics for neurodegenerative diseases, including Alzheimer’s disease (AD). With no cure or preventative measures for AD, the leading cause of dementia in the country, her work addresses a critical research area to develop effective therapies for this devastating disease. She currently leads a University of Michigan-based collaborative stem cell initiative with Neuralstem, Inc., to meet this goal.

Stem cell therapy offers a potentially transformative approach to treating AD. Dr. McGinley has published an in vitro characterization of a novel human neural stem cell line and proof-of-concept studies demonstrating that intracranial transplantation of this cell type significantly improves cognition and pathology in a mouse model of AD. In parallel, Dr. McGinley is assessing MRI-based cell tracking methods for non-invasive imaging of transplanted stem cells within the brain. Having recently received National Institutes of Health funding, Dr. McGinley is a co-investigator on a National Institutes of Aging-funded U01 grant with Dr. Eva Feldman and Dr. Geoffrey Murphy, working to complete the necessary preclinical framework required to advance stem cell transplantation therapy to human clinical trials.

Dr. McGinley is also interested in further understanding mechanisms of neurodegeneration in order to identify novel therapeutic targets for disease. Interestingly, diabetes, obesity, and metabolic syndrome all are associated with a heightened risk of developing cognitive dysfunction, including AD. In a recently established study with the National Institute of Diabetes and Digestive and Kidney Diseases, Dr. McGinley and Dr. Feldman are assessing AD and related dementias in a Pima Indian cohort with type 2 diabetes to identify patient “signatures” at the gene, protein, lipid, and metabolite levels that predict the onset, progression, and/or severity of cognitive disorders, with an emphasis on early onset AD.

“It is an honor for me to support the life-changing Alzheimer’s research taking place in Dr. Feldman’s laboratory. I have had the pleasure of learning about Dr. Lisa McGinley’s work, and I came away inspired by her passion and expertise.”

- Charlene Handleman
Sponsor of Dr. Lisa McGinley, the inaugural Handleman Emerging Scholar
Nerve cells are like factories, using sugar and fats as energy sources. Energy production in turn creates secondary waste products. These waste products, known as free radicals, accumulate in nerve cells and produce an energy crisis called oxidative stress. Oxidative stress underlies brain and nerve injury although the exact mechanisms of damage remain unknown.

Dr. Stephanie Eid is interested in understanding the molecular and cellular mechanisms by which oxidative stress injures nerves during diabetes, a condition known as diabetic neuropathy. She is studying free radical production in diabetes, and exploring its role in the onset and progression of nerve damage in diabetes. Dr. Eid uses cellular and animal models of diabetes as well as studies on patients with diabetes. Understanding how free radicals and oxidative stress contribute to nerve injury in diabetes will form the basis for mechanism-based design of new drug therapies.

“My husband, Jeff, and I consider it a privilege to support Dr. Eid and the amazing diabetes research taking place in Dr. Feldman’s laboratory. My grandparents’ philanthropic vision was to improve public healthcare through research and education. We are very excited to play a part in the breakthroughs that are being developed to treat diabetes.”

- Alene Lipshaw
Granddaughter of Rose and Nathan Milstein and Sponsor of Dr. Stephanie Eid, the inaugural Milstein Family Emerging Scholar
MEET THE CANDIDATES
Obesity, prediabetes and diabetes underlie nerve damage

Dr. Callaghan’s research has focused on the metabolic factors that are associated with neuropathy. He has completed four observational studies that have demonstrated that hyperglycemia, obesity, and the number of metabolic syndrome components (increased blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol levels), but not hypertension or dyslipidemia, are associated with neuropathy. This has led to a proposed interventional study of surgical weight loss and/or high intensity interval training to determine if either intervention can prevent nerve injury. If successful, either intervention would be the first disease modifying therapy for neuropathy. In February 2018, he published “Diabetes and Obesity Are the Main Metabolic of Peripheral Neuropathy,” in the Annals of Clinical and Translational Neurology.

Dr. Callaghan has investigated ways to improve the efficiencies of healthcare delivery within neurology with a focus on peripheral neuropathy. Additionally, he has studied the utilization and costs associated with neurologic testing, prescriptions, and neurologic visits with implications for payment reform.

As part of his research efforts, Dr. Callaghan has mentored two undergraduates, 13 neurology residents, two neuromuscular fellows, two international residents, and two graduate student research assistants. He is nationally recognized through the American Academy of Neurology (three committees and the Drug Price Task Force), American Diabetes Association (Diabetic Neuropathy Chair and grant reviewer), American Neurological Association (Health Services Research Special Interest Group co-Chair), and Neurology journal (co-section editor of health services research website).

Watch Dr. Callaghan's Profile Video: http://michmed.org/E578P
Dr. Chen has an interest in stem cells, and in particular induced pluripotent stem cells (iPS). These cells are created from tissue that is easily obtainable from patients, for example skin cells, and quickly grown in a culture dish. By genetically reprogramming these cells, they revert back to a “stem cell” state (iPS cells), and can then be formed into nerve cells. By creating these iPS cells from patients with diseases like amyotrophic lateral sclerosis (ALS), the mechanisms of a real person's disease can be directly studied. An array of potential treatments can even be tested in the laboratory. Furthermore, by engineering how iPS cells change from their stem cell state, a patient’s cells could potentially become a therapy that the patient receives back into their own body. Currently, Dr. Chen is interested in using iPS cells to form new brain connections, and is studying how these connections may impact ALS. The ability to regulate nerve activity with new nerve connections could eventually also be applied to other neurodegenerative disorders such as Alzheimer’s disease and Parkinson’s disease, as well as other conditions such as epilepsy, stroke, chronic pain, and even psychiatric diseases.

Dr. Chen is also a clinically practicing neurosurgeon with subspecialty training in stereotactic/functional neurosurgery, which utilizes techniques to precisely target specific areas in the brain. His overarching goal is to use his clinical experience with patients to inform his research, and in turn bring discoveries from the laboratory to patients in the form of new and innovative therapies.
Patients with prediabetes and diabetes are at risk for neurologic complications affecting the peripheral and central nervous systems, such as peripheral neuropathy and cognitive decline. As these patients have low levels of systemic inflammation, changes in glucose and insulin metabolism, and varying circulating fat concentrations, it is critically important to determine how these factors work together in early disease to promote nerve damage in order to develop much-needed treatments.

Dr. Sarah Elzinga’s goal is to understand how immune system pathways respond to damage at the cellular level to promote inflammation and injure the nervous system, and she is utilizing multiple models to examine nervous system injury and cognitive decline. One model includes a novel 3D culture system, developed in collaboration with the University of Michigan’s bioengineering department, that is increasing our understanding of how the different cell types in the nervous system interact. Additionally, work in other model systems has begun to uncover the underlying mechanisms and present possible treatment options for brain and nerve injury secondary to diabetes and obesity.
Although the mechanisms underlying the pathogenesis of neurodegenerative diseases like amyotrophic lateral sclerosis (ALS) and diabetic neuropathy are unknown, they likely result from a complex interplay of environmental factors and the genome. It is therefore important to determine how environmental factors drive the onset of neurological disease to facilitate earlier diagnosis and allow for early-stage therapeutic interventions to improve functional outcomes and survival.

Dr. Claudia Figueroa-Romero’s research is identifying post-translational modifications and epigenetic mechanisms that may explain how adverse environmental factors damage neurons. Using postmortem patient tissue, she is exploring how the role of the exposome (collective exposures to environmental pollutants throughout life) impacts ALS by identifying correlations between altered levels of epigenetic marks and high environmental risk scores determined from blood in ALS and control subjects. Using animal models, she is also examining how the internal environment defined by gut microbial communities, or the microbiome, affects neurodegeneration. This unique work is providing important insight into a potential link between the microbiome and aberrant expression of immune- and inflammation-related markers in ALS and diabetic neuropathy. Also of note, Dr. Figueroa-Romero is using her life experience as a Latina woman and expertise as a scientist to work with students and serve as a role model to support the next generation of minority students as they become active members of the scientific community.
Amyotrophic lateral sclerosis (ALS) is a progressive, fatal neurodegenerative disease with limited treatment options, and in the University of Michigan ALS Multidisciplinary Clinic, an ALS Association Certified Center of Excellence, Dr. Stephen Goutman leads a team of providers that strive to deliver comprehensive and compassionate care to persons with ALS and their families. Dr. Goutman is also a site principal investigator of several multi-site clinical trials focused on identifying new ALS treatments and causes, is an active participant with the Northeast ALS Consortium (NEALS) to improve care for ALS, and helps direct the University of Michigan ALS Biorepository, which provides essential resources to ALS researchers within and outside of the University of Michigan, enabling studies into areas of ALS genetics, epigenetics and immunology.

Inspired by his patients, Dr. Goutman also leads research focused on identifying causes of and treatments for ALS. His major research interest is specifically in identifying non-genetic causes of ALS and understanding why the State of Michigan has some of the highest rates of ALS in the country. With funding from the National Institutes of Health and the Centers for Disease Control and Prevention, he is discovering environmental risk factors associated with the onset of ALS by collecting epidemiologic surveys and biofluids from individuals with and without ALS. His research has shown a link between ALS and pesticides, and his recent article on this work received widespread attention, as this important finding may help solve the mystery of ALS.
Advancing neurosurgical approaches to treat Alzheimer’s disease

The unique multidisciplinary team of scientists, clinicians, and neurosurgeons in the NeuroNetwork for Emerging Therapies has been instrumental in advancing a cellular therapy from the laboratory to patients for amyotrophic lateral sclerosis. This experience is key because treating neuronal injuries and spinal or neurodegenerative diseases requires innovative strategies to develop and safely deliver effective therapies to the central nervous system without inducing further damage.

Dr. Osama Kashlan, a highly skilled neurosurgeon with a clinical practice focused on all aspects of spinal disease and a special interest in minimally-invasive spinal surgery, is partnering with Drs. Eva Feldman and Lisa McGinley on a National Institutes of Health-funded study to understand the therapeutic effect of stem cells in Alzheimer’s disease. Multiple studies have supported the feasibility and shown beneficial effects of transplanting stem cells into the brain of mouse models of Alzheimer’s disease, and Dr. Kashlan now aims utilize his extensive skill set and expertise in neurosurgical approaches to push this research further. The ultimate goal is to translate this therapy to humans, and to find a cure for this terminal illness.

Watch Dr. Kashlan’s Profile Video: http://michmed.org/QLL4b

Osama Kashlan, MD
Clinical Assistant Professor • Alzheimer’s Disease
Department of Neurosurgery

CREDENTIALS
BS, Chemical and Biomolecular Engineering, Georgia Institute of Technology, 2006
MD, Emory University, 2010
MPH, Epidemiology, University of Michigan, 2016
Residency, Neurosurgery, University of Michigan, 2017
Fellowship, Spine Surgery, Emory University, 2018

AWARDS
Scholarships for Excellence, BP/Amoco and Eastman
Exemplary Student Award, Georgia Institute of Technology Department of Chemical and Biomolecular Engineering
Member, Alpha Omega Alpha
Dean’s Scholarship, University of Michigan School of Public Health
Neurosurgery Academic Excellence Award, University of Michigan
McGillicuddy Resident Leadership Award, University of Michigan
Consultant Award, University of Michigan Department of Emergency Medicine
Nomination and selection to AANS Leadership Development Course
Third place oral presentation, Michigan Association of Neurologic Surgeons meeting
Max Peet Teaching Award

PUBLICATIONS
17
Multiple studies indicate that patients with metabolic syndrome features, such as diabetes and obesity, have an increased risk of developing cognitive decline and Alzheimer’s disease (AD). Given the increasing prevalence and impact of these conditions on an individual’s quality of life, it is important to understand the link between metabolic syndrome and AD to support the identification of much-needed therapeutic options.

Dr. Bhumsoo Kim is using cell culture and animal experimental models to examine how obesity and diabetes affect amyloid and tau proteins, two prominent pathological markers involved in the development and progression of AD. He is especially interested in how insulin resistance, a key component of the metabolic syndrome, contributes to AD. In cultured brain neurons, Dr. Kim has shown that high levels of glucose and fat, the two main factors involved in the development of diabetes and obesity, induce biochemical changes in amyloid and tau proteins that are similar to those seen in AD. In parallel, he has also shown that obesity and diabetes affect cognitive function in animal models. His continuing efforts are focused on identifying common factors affected by both metabolic syndrome and AD to support the development of more effective therapeutic approaches to treat both diseases.
Research indicates that the immune system plays a key role in the progress of amyotrophic lateral sclerosis (ALS). However, while immune cells may have a destructive role and contribute to disease progression, the immune system can also play a protective role in disease. Research is required to understand how the various immune cell types drive these destructive and protective effects so that immune mechanisms underlying neurodegeneration in ALS can be therapeutically targeted.

Dr. Ben Murdock is interested in the immune system's responses in ALS patient blood samples and ALS mouse models, and he is particularly focused on two types of cells -- natural killer (NK) cells and CD4 T cells -- and their roles in controlling ALS progression. NK cells protect the body from infection and cancer, but also kill dying cells. Research has also found that the molecule that protects the body from its own NK cells is missing in motor neurons during ALS, and that the number of NK cells increases dramatically as ALS progresses. Conversely, CD4 T cells, the master control cells of the immune system, disappear from the blood during ALS, and studies in mice demonstrate that loss of CD4 T cells dramatically accelerates the rate of disease. Dr. Murdock is therefore attempting to slow ALS progression by interfering with NK cell function or by enhancing CD4 T cells. His findings have led to preclinical ALS studies utilizing a currently FDA-approved drug, and if successful, this drug will be tested in clinical trials in ALS patients. Dr. Murdock has obtained a patent on the use of this drug in ALS patients if these trials are successful.
The current obesity and diabetes pandemic is driving a parallel increase in neurological complications including peripheral neuropathy. As peripheral neuropathy is a disease that results in loss of sensory neurons, the patients quality of life is severely impacted with patients experiencing pain or, conversely, a loss of sensation. Unfortunately, the only prescribed treatments currently available are those that manage painful symptoms. To develop effective therapeutic strategies that restore sensory nerve function, disease models that manifest the key features of peripheral neuropathy development and progression in patients are necessary to further our understanding disease.

Dr. Phillipe O’Brien’s current research specializes in identifying more clinically relevant neuropathic mouse models of diabetes and obesity that more accurately reflect the important features seen in patients. Over the last eight years, he has characterized the metabolic and neuropathy phenotypes in several mouse models of diabetes and obesity including leptin deficient BTBR ob/ob mice, mice fed high-fat plus high-sugar diet and, more recently, the Tallyho and NONcNZO polygenic mouse models. Using these robust models, Dr. O’Brien is examining how lifestyle changes, including dietary intervention, can improve metabolic health and consequently look at direct and indirect benefits on peripheral nerve function. Together, these recent studies are providing important insight into how dietary composition (fat and sugar) contributes to disease and how limiting calories can have a positive influence on restoring normal peripheral nerve function.
Patients who have prediabetes, diabetes or other metabolic syndrome (MetS) components (elevated blood pressure, high blood sugar, increased body fat and abnormal cholesterol levels) are at risk for developing nerve damage. This injury often occurs in the extremities, but also can affect the eyes, kidneys and possibly the brain.

Dr. Reynolds is a biostatistician who is working to identify risk factors associated with neuropathy by applying statistical analyses with complex data. He collaborates with U-M’s clinicians to evaluate and quantify the contrasting effects of weight loss from bariatric surgery and diet on nerve damage throughout the body. He is working to identify how brain injury is related to weight loss. Dr. Reynolds is also trying to determine whether longitudinal elevated metabolic risk factors are associated with increased rate of onset for nerve damage in a cohort of Pima Indian patients.

Dr. Reynolds is also interested in improving neurologic healthcare delivery. He utilizes information from Optum Insight, Medicare and Veterans Affairs to assess utilization, costs and trends of neurologic medication and diagnostic testing.
Patients with diabetic neuropathy experience a loss of sensation in their limbs that can ultimately lead to severe morbidity and amputation. Although the mechanisms underlying nerve injury remain elusive, recent data indicate that alterations in dietary fat may be associated with damage to peripheral nerves in type 2 diabetes and obesity.

Dr. Rumora is interested in understanding how different types of dietary fat impact the peripheral nervous system so that treatments to prevent the onset and progression of diabetic neuropathy can be developed. Using cultured cells and animal models of neuropathy, Dr. Rumora recently identified a differential effect of saturated and unsaturated fats on the neurons involved in the progression. Interestingly, she found that one type of unsaturated fat can reverse the progression of neuropathy and restore nerve function, and she is now evaluating the underlying molecular changes facilitated by this unsaturated fat that restore nerve function. Specifically, she is using advanced imaging technologies to understand how fat affects the ability of mitochondria, the energy producing powerhouse of the cell, to travel along the length of the neurons. This work will provide important insights into how nerves are damaged, as well as offer insights into potential dietary approaches to maintain nerve health.
$49 million + total funding**

83 h-index
(measures productivity and citation impact)

TRAINED:

10 DOCTORAL STUDENTS
47 PHD SCIENCE FELLOWS
60 CLINICAL FELLOWS
12 CURRENT FELLOWS
3 SABBATICAL INVESTIGATORS

348** papers

**2019 and 20-year totals will be higher at the end of the year