PATHWAYS TO CURES

April 2024

Society Commits Over $16 Million for Research to Drive Pathways to Cures

The National MS Society has recently committed $16.4 million in multi-year funding to launch important new MS research projects. This is part of our ongoing effort to align the global MS research community around the most promising areas outlined in the Pathways to Cures roadmap to stop MS, restore function and end MS.

The new projects include 9 new research grants, and 31 new fellowships and early career awards to support the MS workforce.

These are part of the Society's annual investment of over $30 million to support more than 200 new and ongoing MS research studies around the world, including support and leadership for the International Progressive MS Alliance – a global effort to accelerate the development of effective treatments for people with progressive MS to improve quality of life worldwide.

Here are a few of the newly committed research projects:

STOPPING MS in its tracks:

• A research team at Columbia University is developing immune profiles of people with MS from diverse backgrounds and ages to identify blood signatures that can guide treatment decisions. (See p.11)

RESTORING what's been lost:

• A team at Emory University is testing a method for reversing dizziness and balance problems experienced by people with MS. (See p.15)

ENDING MS forever:

• Stanford University scientists are working to understand the role of Epstein-Barr virus as a potential cause of MS to suggest ways to treat and prevent it from triggering MS. (See p.26)

NEW PROJECTS SUMMARIZED INSIDE:

Pathways to Cures:

Of Note:

Pathways to Cures: STOPPING MS

Stopping MS means achieving a state of no new disease activity or central nervous system injury, no worsening of daily living or quality of life, and no new manifestations of the disease. By doing this, we prevent disability, create an environment for myelin and axon repair and cultivate pathways that promote the restoration of function. The STOP pathway includes two major objectives: detecting MS early and precision medicine.

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Jeffrey Atkinson, PhD (Pending)
The Ohio State University
Columbus, Ohio
Award: Career Transition Fellowships
Term: 7/1/2024-6/30/2029
Funding: $619,773
Title: Age-associated glial cell dysregulation in CNS autoimmune disease
Summary: Researchers at The Ohio State University are identifying factors that impact MS-like disease in aging mice for insights into stopping progression in people with MS.

Background: In MS, many people start with a relapsing-remitting course and, with age, gradually have fewer relapses and more progression of disability. Emerging research suggests that something related to aging causes this switch. One aspect of progressive MS is that immune cells called microglia, which reside in the brain and spinal cord, are involved in inflammatory processes that are generally not responsive to the disease-modifying therapies available today. Dr. Atkinson has developed a new mouse model that enables him to explore factors that are involved in aging and the behavior of microglia in aged mice and their role in the nerve degeneration that underlies MS progressive disability.

The Study: Dr. Atkinson is taking advantage of the aged mouse model of progressive MS to explore circulating factors prevalent in aging and how they may influence microglia behavior. He will compare blood from young and aged mice to look for aging factors. He will also explore the activity of aged microglia and how they may be involved in neurodegeneration, and is manipulating microglia in the aged mice to see if their reduction can alter progression.

What is the potential impact for people with MS? Identifying circulating factors that impact the disease process in aging mice could reveal insights into ways to target them with new therapies to stop progression in people with MS.

Sidar Aydin, PhD
University of California San Diego
San Diego, California
Award: Postdoctoral Fellowships
Term: 7/1/2024-6/30/2026
Funding: $138,437
Title: The role of endothelial Stra6 in the modulation of neuroinflammation in the central nervous system
Summary: University of California San Diego researchers are investigating the role of Vitamin A on immune system function and MS-like symptoms in a mouse model of MS.

Background: Along with disease-modifying therapies to slow MS disease activity, some medications, exercise, rehabilitation and dietary supplements may improve MS symptoms. Vitamin A is a supplement commonly taken by people living with MS, and it may be beneficial, but its impact on the brain and spinal cord is unknown.

The Study: Dr. Aydin and team are investigating whether different doses of Vitamin A have beneficial or harmful effects on MS disease symptoms. They are investigating a molecule called Stra6, which helps transport Vitamin A into the brain. In mice with an MS-like disease called EAE, they are studying the effects of Vitamin A on the immune cells and the immune response in the brain and spinal cord. To do this, they are comparing normal mice with mice that lack Stra6 and that therefore cannot transport Vitamin A into the brain. This enables the team to investigate how EAE symptoms are affected by the lack of Vitamin A.

What is the potential impact for people with MS? Results from this study may increase understanding of how different doses of Vitamin A affect immune function in a mouse model of MS, and provide information that will be useful in clinical trials investigating the effect of Vitamin A on people with MS.

Estelle Bettelli, PhD
Benaroya Research Institute
Seattle, Washington
Award: Research Grant
Term: 4/1/2024-3/31/2027
Funding: $726,000
Title: Targeting subsets of memory T cells to limit neuroinflammation
Summary: A team at Benaroya Research Institute in Seattle is studying how a rogue type of immune cell may serve as a target for therapies aiming to stop MS.

Background: In MS, cells of our immune system (mainly T and B cells) that are normally in charge of protecting us against infection turn against the myelin coating that surrounds and protects nerve fibers. Sometimes these cells go “rogue” and are lodged in tissues as resident memory cells that are very resistant to immune therapies. Once generated, they stay “hidden” in the brain and spinal cord (central nervous system – CNS) and may drive further tissue damage and progression. Dr. Bettelli’s team believes

that these cells may be key players in the immune response that goes wrong in MS.

The Study: Tissue resident memory cells are difficult to study because they "hide" in CNS tissue and cannot be sampled and analyzed in the blood of individuals. Dr. Bettelli and colleagues have generated a novel mouse model that allows them to identify and manipulate these cells. In this project, they want to combine the use of these mice with models of MS-like disease. This approach will allow them to gain a maximum amount of information regarding these cells, identify novel molecules and pathways that enable these tissue resident memory cells, and test an approach to boot them out of the brain and spinal cord.

What is the potential impact for people with MS? If successful, this study may help to eliminate cells that likely fuel inflammation and progression in MS. Targeting these cells can yield therapies that more effectively stop disease activity and tissue destruction in people with MS.

Sachin Gadani, MD, PhD (Pending)
Johns Hopkins University
Baltimore, Maryland
Award: Career Transition Fellowships
Term: 7/1/2024-6/30/2029
Funding: $622,268
Title: Augmentation of IL-33–induced Amphiregulin to Regulate Pathologic Glia in MS

Summary: Researchers at Johns Hopkins are investigating ways to enhance the effects of beneficial molecules to reduce inflammation and increase repair of tissue that is damaged in progressive MS.

Background: In MS, ongoing inflammation in the brain can interfere with the body's natural ability to restore nerve-insulating myelin and also promotes disease progression. A beneficial immune-system molecule called interleukin-33 (IL-33) appears to be blocked from working in the brains of people with MS.

The Study: Dr. Gadani and team are studying how IL-33 and a molecule called amphiregulin, which IL-33 stimulates, are beneficial in MS. They are exploring the effects of enhancing IL-33 in mice with an MS-like disease called EAE and in another mouse model of myelin injury that is relevant to what is seen in people with MS. Amphiregulin may reduce inflammation and enhance the ability of cells in the brain to repair damaged myelin.

What is the potential impact for people with MS? Enhancing IL-33 and/or amphiregulin, or blocking inhibitors of these molecules, may turn out to be a novel strategy to slow MS progression and restore function.

Gustavo Gastao Davanzo, PhD
Washington University in St. Louis
St. Louis, Missouri
Award: Postdoctoral Fellowships
Term: 7/1/2024-6/30/2027
Funding: $210,938
Title: Contribution of CNS-associated regulatory T cells to the maintenance of CNS-tolerance
Summary: Researchers at Washington University in St. Louis are investigating the formation of beneficial immune cells near the border between the meninges and brain and their role in the control of MS.

Background: In MS, harmful immune cells recognize and attack the body's own "self" brain and spinal cord tissues. Normally immune cells capable of attacking self tissues are eliminated, but in MS they manage to penetrate the layers of barriers (meninges) that separate the bloodstream from the brain. These harmful cells may be eliminated or kept in check by another type of immune cell called regulatory T cells (Tregs).

The Study: Dr. Davanzo and team are investigating a new concept in terms of how these helpful Tregs are formed in the area of the border between the meninges and the brain. They are also determining the role of Tregs in mice with an MS-like disease called EAE, and its progression.

What is the potential impact for people with MS? This study may help researchers design new ways to potentiate Tregs that target harmful immune cells to treat or eliminate MS.

Martin Hsu, PhD (Pending)
University of North Carolina at Chapel Hill
Chapel Hill, North Carolina
Award: Postdoctoral Fellowships
Term: 7/1/2024-6/30/2027
Funding: $210,938
Title: Investigating a Novel Beneficial Gut Microbe for Potential MS Therapy
Summary: Researchers at the University of North Carolina at Chapel Hill are studying the ability of beneficial bacterial Bacteroidetes strains to prevent or treat MS-like disease in mice.

Background: Everyone has bacteria in their gut that can be beneficial or harmful. Research suggests that gut bacteria interact directly with the immune system and can contribute to inflammation or restore balance. Certain species and strains of bacteria, in particular strains of the bacterial species Bacteroidetes, may be beneficial in MS, but more research is needed to translate this finding into possible probiotic approaches to help treat the disease.

The Study: Dr. Hsu and team are testing the effect of Bacteroidetes strains to prevent or treat mice with an MS-like disease. They are also testing the molecules that are made by Bacteroidetes that may be responsible for their benefits. In a second study, the team is transplanting fecal bacteria from people

with progressive MS into mice to create a mouse model of the progressive MS gut bacteria and the MS-like disease that results. They are then giving Bacteroidetes to these mice to see if it prevents or improves their disease.

What is the potential impact for people with MS? This study may provide evidence that Bacteroidetes and/or its by-products may be beneficial in people with progressive MS, which would likely lead to clinical trials to test this approach.

Leslie Kirby, PhD (Pending)
Karolinska Institutet
Stockholm, Sweden
Award: Career Transition Fellowships
Term: 7/1/2024-6/30/2029
Funding: $609,896
Title: Defining the spatial cellular landscapes in MS to decode the underlying mechanisms of chronic inflammation and disease progression
Summary: Karolinska researchers are unraveling steps in the damaging inflammation in a structure that surrounds the brain for clues to new approaches to stop MS progression.

Background: Although therapies exist for the treatment of relapsing forms of MS, few treatments are available for treating progressive MS. Recent research points to a damaging role of inflammation of the leptomeninges, a thin covering on the surface of the brain. This structure can develop pockets of immune cells that can promote disease activity and nerve damage. Exactly how these pockets ("ectopic lymphoid follicle-like structures" - ELFLS) contribute to tissue damage and disease progression is not yet understood.

The Study: Dr. Kirby and team are using a mouse model of MS and advanced lab tools to explore how the ELFLSs form, how long they persist, and how they interact with nearby brain tissues. She is also examining how damaged nerve cell signals may fan additional inflammation and contribute to disease progression. Taken together, these sophisticated studies using advanced technologies should bring new understanding to the complex interactions underlying this destructive inflammation in MS.

What is the potential impact for people with MS? Ultimately this study could uncover mechanisms that help drive MS progression, and potential targets for the development of therapies to stop tissue damage.

Jacob Loeffler, MD (Pending)
Stanford University
Stanford, California
Award: Clinician Scientist Development Awards
Term: 7/1/2024-6/30/2027
Funding: $232,168
Title: Integrated Single Cell Analysis to Investigate CD8 T cell Responses to EBV EBNA1 and Self-Antigen Mimics in MS
Summary: Researchers at Stanford University are investigating the importance of immune T cells from people with MS that incorrectly recognize proteins in the brain and spinal cord that are similar to Epstein-Barr virus proteins.

Background: Epstein-Barr virus (EBV) may play a role in triggering MS and in perpetuating disease activity. The immune system in people with MS may mistake some of its own brain and spinal cord proteins for the virus, leading to abnormal immune attacks against the body's own proteins.

The Study: Dr. Loeffler and team are investigating immune cells called T cells that may mediate this mistaken identity. To identify which normal EBV-like proteins abnormally activate T cells, they are using T cells from people with MS and stimulating them with normal proteins and proteins from EBV. They are then isolating individual T cells, determining the identity of the reactive T cells, and analyzing which genes were switched on by the stimulation.

What is the potential impact for people with MS? If mistaken identity is at the root of immune attacks in MS, therapies that specifically target harmful T cells may be beneficial to people with MS.

Kristin O'Grady, PhD
Vanderbilt University Medical Center
Nashville, Tennessee
Award: Harry Weaver Scholar Awards
Term: 7/1/2024-6/30/2029
Funding: $660,712
Title: Structural and functional MRI of lumbosacral spinal cord pathology in progressive MS
Summary: Researchers at Vanderbilt University Medical Center are testing tools to image the lower spinal cord to better understand symptoms and to track progression in people with MS.

Background: People living with progressive MS experience worsening neurologic function and disability, and symptoms such as difficulty with walking and bladder and bowel problems significantly affect their quality of life. Researchers have made advances in studying the effects of progressive MS on the brain and upper spinal cord using new MRI methods. However, the lower regions of the spinal cord have been understudied despite their importance to lower limb, bladder, and bowel function, due to technical challenges. Dr. O'Grady and colleagues believe that disease activity in the lower spinal cord is an important contributor to clinical disability in

progressive MS. They have optimized MRI methods specifically for studying the lower spinal cord and are now working to apply them to people living with progressive MS.

The Study: This study is using 3-Tesla research MRI scanners that are the same type as those used in many hospitals. The team will recruit people with and without MS. Participants will undergo MRI scans using the novel methods developed for the lower spinal cord. They will also have assessments of walking and lower limb function and bladder and bowel symptoms. The researchers will determine how imaging results relate to individuals' clinical symptoms.

What is the potential impact for people with MS? The results of this work may improve our understanding of progressive disease and provide new measurements known as "imaging biomarkers" that can track disease activity, predict disease course, and evaluate the response to therapies.

Carolina Polonio, PhD (Pending)
Brigham and Women's Hospital
Boston, Massachusetts
Award: Postdoctoral Fellowships
Term: 7/1/2024-6/30/2027
Funding: $206,011
Title: Control of T cells in EAE and MS by HIF1α-NDUFA4L2-XBP1 axis in DCs
Summary: Researchers at Brigham and Women's Hospital are investigating molecules that control the immune cells involved in immune attacks on the brain and spinal cord in MS.

Background: In MS, immune cells called T cells play a role in attacking the body's own "self" tissues in the brain and spinal cord, leading to inflammation and tissue injury. Another type of immune cell called dendritic cells control T cells.

The Study: Dr. Polonio and team are determining the role of a series of molecules that control dendritic cells and that may therefore limit their activation of harmful T cells. The team is using mice with an MS-like disease called EAE. They are also studying dendritic cells and T cells from the blood of people with MS and people who don't have MS to explore differences.

What is the potential impact for people with MS? Better understanding of how dendritic cells are controlled may provide insights to new approaches to treating and stopping MS.

Fernanda Schumacher, PhD (Pending)
The Ohio State University
Columbus, Ohio
Award: Biostatistics/Informatics Junior Faculty Award
Term: 7/1/2024-6/30/2027
Funding: $170,162
Title: Epigenetics in MS: An evaluation of biological aging and disease severity
Summary: Researchers at The Ohio State University are analyzing how MS progression is affected by accelerated aging, for clues to stopping progression in its tracks.

Background: Aging is linked to MS disease severity. Biological aging differs from chronological aging as it considers cumulative damage in body systems. There are several markers of biological age. Dr. Schumacher and colleagues are investigating the use of "epigenetic clocks" in people with MS. These are algorithms that estimate the biological age by analyzing changes in DNA activity. They aim to clarify how epigenetic clocks work for people with relapsing-remitting MS and secondary progressive MS and explore associations between biologic aging, MS disease outcomes and disease progression.

The Study: To achieve these aims, Dr. Schumacher is analyzing data collected in an ongoing clinical study that is currently enrolling participants. This study has the goal of testing the idea that people with MS may age faster than people without MS, by comparing several measures of biological aging between people with relapsing MS, progressive MS, and people without the disease. Dr. Schumacher will revisit this existing data to look at how chronological age compares to biological age in each group and how any differences compare to disease activity and outcomes.

What is the potential impact for people with MS? Results could eventually allow healthcare providers to identify individuals at greater risk of disease progression who may benefit from more aggressive treatment options. The ultimate goal is to stop disease progression.

Patrick Sheehan, PhD (Pending)
University of Massachusetts Medical School
Worcester, Massachusetts
Award: Postdoctoral Fellowships
Term: 7/1/2024-6/30/2027
Funding: $206,011
Title: A molecular dissection of complement in demyelinating disease
Summary: Researchers at the University of Massachusetts Medical School are investigating the importance of "complement" proteins in the destruction of nerve connections in MS.

Background: In MS, immune cells that reside in the brain, called microglia, play many beneficial and potentially damaging roles, depending on conditions. Research suggests microglia can destroy the points of communication, called synapses,

between nerve cells. Destruction of synapses can cause problems with thinking in people with MS. Proteins called complement are made by microglia and other cells and may drive destruction of synapses.

The Study: Dr. Sheehan and team are investigating the role of complement proteins in synapse destruction in MS. They are using mice with an MS-like disease called EAE that have been engineered not to have complement produced in microglia. They are asking if synapses are preserved in these mice. There are many types of complement proteins, and the team is also mapping which brain cells make which complement proteins and where.

What is the potential impact for people with MS? Because preserving synapses can protect from symptoms in mouse models of MS, drugs that target complement, many of which are approved for other conditions, may be beneficial in people with MS.

Dinesh Keran Sivakolundu, MD, PhD (Pending)
Weill Cornell Medical College
New York, New York
Award: Clinician Scientist Development Awards
Term: 7/1/2024-6/30/2027
Funding: $232,668
Title: Investigating the Role of Brain Lymphatics in Cognitive Decline in MS
Summary: Researchers at Weill-Cornell Medicine are investigating whether problems in clearing waste products from the brain may be related to issues with cognition experienced by many people with MS.

Background: Many people with MS eventually experience cognitive decline, specifically a decrease in their rate of thinking, remembering, and processing information. A system in the brain called the lymphatic system rids waste products from the brain. This is an important process that usually keeps the brain running smoothly.

The Study: Dr. Sivakolundu and team are investigating the idea that problems with the lymphatic system in MS are related to cognitive decline. The team is studying MRI scans of people with MS and comparing them to people who don't have MS, to see how well waste removal works in their brains. They are also determining if there is a relationship between waste removal in the brain and cognitive problems.

What is the potential impact for people with MS? If poor clearance of waste products is indeed responsible for cognitive issues in MS, growing knowledge of the brain's lymphatic system may lead to treatments to increase clearance to improve and maintain cognitive abilities and quality of life for people with MS.

Peter Tessier, PhD (Pending)
Regents of the University of Michigan
Ann Arbor, Michigan
Award: Research Grant
Term: 4/1/2024-3/31/2027
Funding: $726,000
Title: Non-invasive Delivery of Anti-inflammatory Cytokine Depots to the Myelin Sheath
Summary: University of Michigan scientists are creating novel proteins and testing their ability to stop inflammation in mice and prevent disease progression.

Background: MS occurs when the immune system attacks the brain and spinal cord. Nerve cells and the myelin that surrounds their wire-like axons are damaged. While the brain and spinal cord produce natural immune proteins such as interleukin-10 (IL-10) to combat inflammation, the levels are too low to stop MS progression. Professor Tessier aims to develop protein-based agents that can deliver IL-10 precisely to myelin-making cells with the goal of stopping MS progression.

The Study: The team is performing a series of investigations in mouse models of MS. First, so-called "antibody-IL10 fusion proteins" will be generated and labeled with radioactive compounds that enable ultrasensitive protein detection. The labeled proteins will be injected into the blood stream, and – at different time points – the concentrations of the radioactive proteins in the blood, brain and spinal cord will be measured to confirm delivery to the central nervous system. The antibody-IL10 proteins will be administered to mice that have an MS-like disease. The team will evaluate symptoms over time to see if antibody-IL10 proteins prevent disease progression.

What is the potential impact for people with MS? The results of this study may establish an effective method for reducing inflammation in the brain, and stopping MS progression in its tracks.

Hanane Touil, PhD
Columbia University
New York, New York
Award: Career Transition Fellowships
Term: 7/1/2024-6/30/2029
Funding: $614,784
Title: Immunosenescence in Multiple Sclerosis: A pursuit of disease progression Biomarkers
Summary: Columbia University researchers are developing immune profiles from people with MS from diverse backgrounds and ages to identify blood signatures that can guide treatment decisions.

Background: An emerging idea in MS research is that the immune system of people with MS undergoes premature aging, potentially contributing to disease progression. Research to explore this phenomenon more deeply may reveal new approaches to stopping MS progression.

The Study: Dr. Touil and team are investigating the evolution of immune cell aging (called immunosenescence) by using advanced technologies to compare blood samples from a diverse group of people living with MS who are from different age groups, ethnicities/races, and people with MS who are treated with the disease-modifying B cell therapy (ocrelizumab) or not. They are also comparing their immune cell findings to those of a group of people who do not have MS. The team's goals are to determine if therapy can prevent immune cell aging, thought to take place prematurely in MS. They also aim to identify immune cell "signatures" that in the future could identify people likely to progress faster, to help guide treatment decisions.

What is the potential impact for people with MS? This research can contribute to the goal of providing precision medicine to people with MS and effectively stop disease progression.

Training Trial Specialists: The Sylvia Lawry Fellowship

Without clinical trials, there would be no disease-modifying therapies for MS – these are how new treatments are tested. Without clinicians trained in conducting these studies, they cannot proceed. Seeing this need, the Society established the Sylvia Lawry Physician Fellowship, named in honor of its founder. This program provides formal clinical trial training with established investigators. Six new trainees have been awarded this fellowship in 2024:

Angeliki Filippatou, MD: During this fellowship, Dr. Filippatou will obtain specialized clinical and research training at the Johns Hopkins MS Center. She will have several roles in ongoing clinical trials, including treating physician, disability rater, and co-investigator. This will allow her to become familiar with the nuances of designing and conducting clinical trials. Additionally, she will pursue formal coursework in biostatistics, epidemiology, and clinical trial design.

Claudia Gambrah-Lyles, MD: The fellowship will take place at both the pediatric and adult MS centers at Washington University in St. Louis (WUSTL). It will comprise hands-on experience in clinical trials, and inpatient and outpatient clinical activities. A master's program will allow Dr. Gambrah-Lyles to become familiar with the intricacies of clinical trial design and implementation, as well as the measurement of common clinical, biomarker and imaging outcomes used in these trials.

Jeffrey Lambe, MBBCh, MRCPI: The Neuroimmunology Fellowship at the Cleveland Clinic will provide rigorous training in clinical and translational MS research. The fellowship will involve serving various roles in conducting clinical trials to gain a diverse exposure to different aspects of running trials. Dr. Lambe also will be participating in coursework and a thesis project leading to a Master of Science in Clinical Research at Case Western Reserve University.

Vivek Mehta, MD: To develop clinical trials proficiency, Dr. Mehta will spend time caring for people with MS at the John L. Trotter MS Center in WUSTL and will see patients with all subtypes of MS and at all stages of disease progression. Dr. Mehta will be an active investigator in clinical trials. He will participate as an examining physician in several of these trials and learn commonly utilized clinical study outcome measures. He will complete a Master of Science in Clinical Investigation.

Farris Taha, MD: During this WUSTL fellowship, Dr. Taha will actively participate in clinical trials at all stages, both industry-sponsored and investigator-initiated. In addition to seeing people with MS in the clinic, he will spend a substantial amount of time being involved in clinical trials at every stage from startup through conclusion. Dr. Taha will also apply learned knowledge from master's coursework to become skilled at study design, recruiting participants, and measuring outcomes.

Akash Virupakshaiah, MD: Dr. Virupakshaiah will receive three years of training at the University of California, San Francisco, in performing clinical trials and caring for people with MS. This will include a Master's Degree in Clinical Research. Dr. Virupakshaiah will be involved in several ongoing clinical trials in relapsing-remitting and progressive MS at different stages of their development and conduct. He will also be involved in studying treatments for children diagnosed with MS.

Pathways to Cures: RESTORING FUNCTION

Restoring what has been lost means reversing MS symptoms and recovering function. While disease-modifying therapies (DMTs) can limit relapses and delay disease progression, they do not truly restore cognitive or physical abilities. By focusing on an integrated approach to regeneration and remyelination, as well as better understanding how wellness and lifestyle choices affect symptoms, those living with MS can have an improved quality of life free from the burden of MS symptoms. The RESTORE pathway includes two major objectives: regeneration and restoration of activity.

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Riley Bove, MD (Pending)
University of California, San Francisco
San Francisco, California
Award: Mentor-Based Postdoctoral Fellowships
Term: 7/1/2024-6/30/2029
Funding: $529,515
Title: Novel Digital Approaches to Rehabilitation in MS
Summary: Experienced mentors/researchers are training promising professionals to conduct MS rehabilitation research.

Background: Rehabilitation science plays a critical role in MS. Rehabilitation can stabilize disease and improve function and quality of life. Digital tools are increasingly used to evaluate, track and treat people with MS, so there is a need to train experts in using these tools. UCSF provides an ideal environment for this training. There is strong collaboration between rehabilitation and neurology departments, digital innovators, and other types of scientists.

The Study: This Program lasts five years in total and supports postdoctoral researchers for one or more years. For their research project, Fellows can select a novel aspect of MS rehabilitation. They will work with experts in MS research and repair, remote monitoring and rehabilitation and remote cognitive assessments and interventions. Training will be multifaceted. They will gain practical research skills while they are directly immersed in studies to observe or treat MS. They will have exposure to a wide variety of individuals with MS and have opportunities to engage with scientists to present and publish their research. Mentoring will also include how to advance their careers. Fellows will publish at least one high-impact paper and apply for at least one grant during their training period. Co-mentoring will be provided as relevant by Dr. Joaquin Anguera (cognition) and Dr. Valerie Block (physical therapy).

What is the potential impact for people with MS? Overall, the training goal is for Fellows to become experts in advancing novel and impactful research on how to evaluate, track and improve function of individuals living with MS.

Alexander Gow, PhD
Wayne State University
Detroit, Michigan
Award: Research Grant
Term: 4/1/2024-3/31/2027
Funding: $644,827
Title: Metabolic stress and oligodendrocyte pathophysiology
Summary: Researchers at Wayne State are looking at a novel mechanism for preventing damage and promoting repair of nerve-insulating myelin in MS.

Background: MS can involve damage to several parts of the brain and spinal cord, and that damage appears to go beyond what might be blamed on the immune attacks that occur. Another possible type of biological activity that could lead to nervous system damage is called metabolic stress. Metabolic stress in cells encompasses a variety of problems including energy deficits and failure to recycle and break down unneeded or damaged proteins. There is growing evidence that metabolic stress in cells is associated with MS.

The Study: Professor Gow and colleagues have identified a protein in cells that make nerve-insulating myelin, called oligodendrocytes. The protein (Trb3) appears to drastically reduce metabolic stress and its negative impact on health in mice. In this project they are testing this protein and other proteins that Trb3 seems to interact with, by "deleting" them in mouse models. They are studying these models to see how each protein affects metabolic stress. They also are studying how the process of myelin formation is affected.

What is the potential impact for people with MS? This project may yield several small compounds to further optimize for pre-clinical testing and possibly clinical trials of treatments that can prevent damage and promote repair in MS.

Colin Grove, DPT, PhD (Pending)
Emory University
Atlanta, Georgia
Award: Research Grant
Term: 4/1/2024-3/31/2027
Funding: $659,896
Title: DIIVA-MS: Daily versus Intermittent Incremental Vestibulo-ocular Reflex Adaptation as a Novel Treatment for Dizziness in People with Multiple Sclerosis
Summary: A team at Emory University is testing a method for improving dizziness and balance problems in people with MS.

Background: Many people with MS experience dizziness during the course of their disease. People with MS who have dizziness or imbalance also have difficulty keeping their eyes looking at a target while their head is moving. This problem, known as gaze instability, can prevent people from seeing clearly whenever their head is moving, such as while walking or driving, which can lead to serious consequences. Traditional gaze stabilization exercises (which involve holding one's gaze on a

target while moving one's head) can reduce dizziness, restore balance, and improve visual acuity. Dr. Grove's team has developed a technology that can rapidly improve gaze stability using a gradual approach to increasing the difficulty of the exercises.

The Study: Now they are using this technology in an 18-week study to compare the effectiveness of daily versus every-other-day gaze stability exercises in 92 people with MS who have dizziness and/or imbalance. All participants will receive six weeks of exercises. For each participant, investigators will assess gaze instability before and after the exercises, and determine whether either dosage of gaze stability exercise has effects that last up to three months after stopping these exercises. Participants will also complete questionnaires related to disability, balance-related confidence, the impact of dizziness on daily life, and quality of life.

What is the potential impact for people with MS? This line of research may improve the treatment of dizziness, imbalance, and gaze instability. Ultimately, if people with MS have access to effective treatments for these problems, they may be able to remain actively engaged in the activities they enjoy most with less concern about becoming dizzy or falling.

Jingwen Hu, PhD
Johns Hopkins University
Baltimore, Maryland
Award: Postdoctoral Fellowships
Term: 7/1/2024-6/30/2027
Funding: $202,747
Title: The Role of Inflammatory Oligodendrocyte Lineages in MS
Summary: Johns Hopkins researchers are investigating the role of rogue cells in the brain that may contribute to inflammation in MS.

Background: There are stores of spare cells lodged in parts of the brain and spinal cord that are ready to move into action to help repair nerve-insulating myelin after it has been injured, such as what occurs in MS. Recent research from the lab of Dr. Hu's mentor at Johns Hopkins has discovered that in some circumstances, some of these cells can go rogue and participate in inflammation instead of repair. These are called "inflammatory oligodendrocyte lineage cells," and they may play a role in making MS worse. Very little is known about these cells.

The Study: Dr. Hu and team are investigating the roles of inflammatory oligodendrocyte lineage cells, the circumstances in which they act as immune cells, and how this impacts their usual repair functions. In mouse models of MS, they are investigating the importance of an immune molecule called MHC that is displayed by these cells. They are also

asking whether blocking MHC can restore their repair abilities in mouse models.

What is the potential impact for people with MS? This study will provide new insights into the role of these newly discovered cells in MS development and recovery. If they prove to be a viable target, this could lead to improved MS therapies that block inflammation and repair myelin.

Yasmine Kamen, PhD
Trustees of Dartmouth College
Hanover, New Hampshire
Award: Postdoctoral Fellowships
Term: 7/1/2024-6/30/2027
Funding: $206,011
Title: Impact of demyelination and remyelination on axonal structural plasticity and function
Summary: Dartmouth researchers are investigating how the loss of nerve-insulating myelin and its repair affect the ability of nerve cells to communicate with each other.

Background: Communication between nerve cells occurs through electrochemical signals. For optimal communication, nerve cell fibers are protected by a fatty, insulating structure called myelin. Myelin is destroyed in MS, and people with the disease experience various symptoms due to loss of myelin and the impaired ability of nerve cells to communicate. The nerve cells themselves can also degenerate during the course of MS.

The Study: Dr. Kamen and team are using a novel method to study the loss of myelin in mice. They are investigating how myelin loss and later myelin repair (which is often incomplete in MS) affect the ability of nerve cells to transmit signals, change the shape of existing connections between nerve cells, and form new connections. These experiments should provide a better understanding of how myelin loss and repair affects nerves and nerve transmission.

What is the potential impact for people with MS? This study may suggest new ways to protect or restore communication between nerve cells after myelin has been damaged in MS.

Anna Kratz, PhD (Pending)
Regents of the University of Michigan
Ann Arbor, Michigan
Award: Mentor-Based Postdoctoral Fellowships
Term: 7/1/2024-6/30/2029
Funding: $492,176
Title: Training to Advance Rehabilitation Research in Multiple Sclerosis
Summary: Experienced mentors/researchers at University of Michigan are training promising professionals to conduct MS rehabilitation research.

Background: Chronic pain, fatigue, and cognitive dysfunction (thinking problems) remain some of the most common, distressing, and disabling symptoms in MS,

despite decades of research on these problems. For MS research on symptom management to progress, the next generation of rehabilitation researchers needs to be trained in state-of-the-art research methods and to engage effectively in interdisciplinary team science. Innovative research that increases our understanding of the mechanisms that underlie MS symptoms and the best approaches to treating them is sorely needed to help people live their best lives.

The Study: This postdoctoral training program will leverage completed, ongoing and upcoming research studies that are led by members of the mentor team. More than 15 research studies focused on symptoms and functional outcomes in rehabilitation populations are available to the fellows. Trainees will have an opportunity to work on cutting-edge projects. In one ongoing study, researchers are comparing traditional tests of cognitive and motor symptoms to tests administered via a smartphone application at home to see if the mobile tests provide more sensitive measures of functional change. Fellows can work with data from a recently completed clinical trial to compare modafinil (a wake promoting drug), telephone-delivered cognitive behavioral therapy, and a combination to reduce fatigue in MS. Trials of cannabinoids or self-administered acupressure for chronic pain in MS are also available to fellows.

What is the potential impact for people with MS? With the support of the mentor team, fellows in this program will be ready to conduct their own research relevant to the understanding and treatment of symptoms, and to restoring function in people with MS.

Mable Lam, PhD (Pending)
Stanford University
Stanford, California
Award: Career Transition Fellowships
Term: 7/1/2024-6/30/2029
Funding: $614,784
Title: Investigating mechanisms of activity-dependent myelin growth
Summary: Researchers are investigating the importance of a process called exocytosis in stimulating myelin repair in cells grown in a dish and in mice with myelin loss.

Background: In MS, a fatty substance called myelin, which surrounds and protects the fibers of nerve cells, is attacked and destroyed. Nerve cells that have lost their myelin do not function properly, leading to symptoms in people with MS. Natural myelin repair by brain cells called oligodendrocytes often fails in MS.

The Study: Dr. Lam and team are investigating the idea that nerve cell activity stimulates oligodendrocytes to repair myelin via a process called exocytosis. To study this, they are using advanced tools to image exocytosis in

oligodendrocytes and nerve cells grown together in lab dishes. They are also manipulating exocytosis and nerve stimulation in mice with myelin loss, and determining if exocytosis is required for myelin repair in these mice.

What is the potential impact for people with MS? Knowledge from this study should inform whether nerve stimulation that enhances exocytosis has potential to improve myelin repair and restore function in people with MS.

Sonia Nocera, PhD
University of California, San Francisco
San Francisco, California
Award: Postdoctoral Fellowships
Term: 7/1/2024-6/30/2027
Funding: $210,938
Title: Cholinergic neuro-immune interaction that inhibits remyelination
Summary: Researchers are testing whether and how immune molecules in MS lesions may inhibit repair of nerve-insulating myelin and strategies to neutralize them.

Background: In MS, a fatty substance called myelin, which surrounds and protects the fibers of nerve cells, is attacked and destroyed. The body's natural ability to restore damaged myelin often fails. The cells in the brain that repair myelin are called oligodendrocytes. In MS, these cells appear to encounter something in MS lesions that inhibits their ability to fully mature and repair myelin.

The Study: Dr. Nocera and team are investigating whether immune system molecules in MS lesions are responsible for inhibiting oligodendrocyte maturation and myelin repair. They are characterizing the immune cells and the inhibitory molecules they make by evaluating nervous system tissues from people who had MS in their lifetimes. They are then examining how these inhibitory factors affect oligodendrocytes and nerve cells grown together in a dish and in mice with an MS-like disease.

What is the potential impact for people with MS? This study may uncover potential targets to block inhibitors of myelin repair to restore function in people with MS.

Davin Packer, MD, PhD
University of Colorado Anschutz Medical Campus
Aurora, Colorado
Award: Postdoctoral Fellowships
Term: 7/1/2024-6/30/2027
Funding: $206011
Title: Regional Heterogeneity of mTOR-Endosomal/Lysosomal Regulation in Oligodendroglia from the Brain and Spinal Cord During Normal Development and Inflammatory Pathology
Summary: Researchers at the University of Colorado are investigating the role of a molecule called mTOR in myelin repair in the brain compared with the spinal cord.

Background: In MS, a fatty substance called myelin, which surrounds and protects the fibers of nerve cells, is attacked and destroyed. Nerve cells that have lost their myelin do not function properly and are vulnerable to degeneration. The cells in the brain and spinal cord that repair myelin are called oligodendrocytes, and in MS, sometimes they stall before completing the task of restoring myelin.

The Study: Dr. Packer and team are examining a molecule called mTOR and related molecules, which may play a role in how these oligodendrocytes respond to stress and their ability to repair myelin. mTOR and related molecules may be different in the brain compared with the spinal cord. The team is using mice with myelin abnormalities and cells grown in lab dishes to further understand the importance of mTOR and related molecules in oligodendrocytes from the brain compared to those from the spinal cord.

What is the potential impact for people with MS? Understanding how mTOR and related molecules are important for myelin repair may lead to new targeted treatments to restore myelin and improve function in MS.

Amber Philp, PhD
University of California, San Francisco
San Francisco, California
Award: Postdoctoral Fellowships
Term: 7/1/2024-6/30/2027
Funding: $206,011
Title: Investigating the aging matrisome as a driver of impaired remyelination
Summary: University of California, San Francisco researchers are investigating the importance of molecules near cells that make myelin and how the molecules change during aging to find clues to repairing myelin in MS.

Background: In MS, a fatty substance called myelin, which surrounds and protects the fibers of nerve cells, is attacked and destroyed. Nerve cells that have lost their myelin do not function properly and are vulnerable to degeneration. The body can naturally repair myelin, but at some point in MS this process tends to fail, and myelin repair also decreases with age.

The Study: Dr. Philp and team are investigating the idea that age-related changes in the tissues and related molecules around myelin-making cells (called the extracellular matrix or ECM) may block myelin repair. The team is comparing ECM molecules during myelin repair in young versus old mice. They are also assessing the importance of a specific ECM protein called Hapln2 to see if decreasing Hapln2 improves myelin repair.

What is the potential impact for people with MS? Better understanding of the role of the extracellular matrix in myelin repair may lead to new therapies that can restore myelin with age and in progressive phases of MS.

Prudence Plummer, PhD, PT
MGH Institute of Health Professions
Boston, Massachusetts
Award: Mentor-Based Postdoctoral Fellowships
Term: 7/1/2024-6/30/2029
Funding: $481,686
Title: Training Rehabilitation Scientists in Multiple Sclerosis
Summary: Mass General researchers are training fellows in evaluating mobility, balance, and how attention affects movement performance and rehabilitation outcomes.

Background: Rehabilitation is an essential element of managing MS symptoms, with studies revealing the potential to restore function in individuals with MS. There is a need to ensure comprehensive training of rehabilitation scientists who can develop the evidence to further advance such interventions for people MS. This project involves a rigorous training plan in clinical and rehabilitation research for new investigators that will include studies that focus on mobility, balance, and fatigue, especially in complex, real world settings.

The Study: The training program will comprise work on MS-related clinical and rehabilitation projects, professional development of the fellow, and coursework. Individuals with all types of MS will be recruited for a variety of studies that are already ongoing in the mentor's lab. These include studies that measure how physical therapy with or without medication works to improve walking speed and fatigue. Other research that will be part of this training program is intended to better understand what factors limit the ability or motivation for people with MS to access rehabilitation, as well as how difficulties with posture and balance affect fatigue. The research involves recruiting individuals with MS and also examining existing data and data extracted from the electronic health record.

What is the potential impact for people with MS? Fellows will obtain expertise in evaluating mobility, balance, and how attention affects movement performance and rehabilitation outcomes. Their training will enable them to conduct independent research that contributes to improved health and functional outcomes for people living with MS.

Milap Sandhu, PhD
Shirley Ryan AbilityLab
Chicago, Illinois
Award: Research Grant
Term: 4/1/2024-3/31/2027
Funding: $718,104
Title: Efficacy and Neurophysiological Mechanisms of Acute Intermittent Hypoxia Therapy in MS
Summary: Researchers at the Shirley Ryan AbilityLab are exploring whether a treatment called acute intermittent hypoxia can improve nerve connections and upper muscle strength in people with MS.

Background: The immune system attacks in MS can damage the connections between the brain, spinal cord, and limbs. This damage can lead to mobility problems and other symptoms that reduce a person's quality of life. Dr. Sandhu has been exploring the benefits of a therapy known as acute intermittent hypoxia (AIH) which involves brief, controlled periods of breathing air with lower oxygen levels alternating with normal oxygen levels. This treatment stimulates neuroplasticity—the brain's ability to adapt and strengthen nerve connections—and improves the function of nerve pathways. Dr. Sandhu's prior work in people with spinal cord injuries has shown AIH's potential in improving function and the team is now applying it to people with MS.

The Study: In this study, Dr. Sandhu is exploring how AIH can be utilized to strengthen nerve connections that are important for upper body strength in individuals with MS and to understand the mechanisms behind this effect. This process involves giving short bouts (about 60 seconds) of modestly low oxygen through a mask. The team plans to recruit 22 people with relapsing-remitting MS. Participants will attend several sessions where they will receive either AIH or a sham (placebo) treatment. Before and after these sessions, assessments will be done to determine whether the therapy has made the hand muscles stronger and improved the transmission of nerve signals from the brain to the hands.

What is the potential impact for people with MS? If this study shows significant benefits of AIH, it could pave the way for a larger trial. This future research might combine AIH with physical training to develop a new approach for improving upper body strength in people with MS.

Catherine Siengsukon, PhD, PT (Pending)
University of Kansas Medical Center
Kansas City, Kansas
Award: Research Grant
Term: 4/1/2024-3/31/2027
Funding: $724,801
Title: Efficacy of Cognitive Behavioral Therapy for Insomnia to Treat Insomnia Symptoms and Fatigue in Individuals with Multiple Sclerosis
Summary: Researchers at the University of Kansas Medical Center are testing whether online cognitive behavioral therapy can improve insomnia symptoms, fatigue, and quality of life in people with MS.

Background: Insomnia is a common issue in people with MS and has been linked with MS-related symptoms, including fatigue and reduced quality of life. Cognitive behavioral therapy for insomnia (CBT-I) is the recommended treatment for chronic insomnia and addresses behaviors and thoughts that negatively impact sleep. In previous studies, Dr. Siengsukon and colleagues found that one-on-one CBT-I (in-person and by video conference) is feasible in people with MS. Now they are seeking to answer whether CBT-I can improve insomnia symptoms, fatigue, and quality of life.

The Study: Individuals who enroll in this study will be randomly assigned (like flipping a coin) to one of two groups. One group will receive CBT-I provided via video conferencing one-on-one with a trained provider once a week for six weeks. The second group will receive basic sleep and lifestyle education with a trained provider once a week for 6 weeks. Before and after the program, and after six months, the participants will answer questionnaires to assess disability level, anxiety, depression, sleep self-efficacy level (the confidence that they are capable of changing their sleep), and adherence to the intervention. This study is conducted online so no in-person visits are required, and participants can live anywhere in the United States.

What is the potential impact for people with MS? Addressing insomnia symptoms through CBT-I could represent a low-cost, non-pharmacological option for improving sleep quality, fatigue, and quality of life in individuals with MS.

Glenn Wylie, PhD
Kessler Foundation Research Center
West Orange, New Jersey
Award: Research Grant
Term: 4/1/2024-3/31/2027
Funding: $722,602
Title: Establishing a clearer measure of cognitive fatigue in Multiple Sclerosis: State vs. Trait
Summary: Researchers at the Kessler Foundation in New Jersey are testing behavioral and imaging methods to measure MS-related fatigue to enable the development of solutions for this troublesome symptom.

Background: Many people with MS experience fatigue, and they report that

fatigue is amongst their most troubling symptoms. However, it is difficult to objectively measure fatigue, and current measures typically assess fatigue that results from sleep problems or depression rather than from MS itself. Dr. Wylie has developed behavioral and imaging methods to evaluate MS fatigue and is conducting tests to further validate their use in research.

The Study: Dr. Wylie and team are using challenging and well-studied thinking tests to induce cognitive fatigue in people with MS. They will then use their behavioral and imaging methods to better understand differences in fatigue between people with MS and people who don't have MS. The imaging looks at areas of the brain that are activated during tasks, and the team is also looking at how different parts of the brain are connected when people experience fatigue.

What is the potential impact for people with MS? Validation of objective measures of fatigue will enable clinicians and researchers to better study and find solutions for MS fatigue, for which there are few reliable treatments.

Weiquan Zhu, PhD
University of Utah
Salt Lake City, Utah
Award: Research Grant
Term: 4/1/2024-3/31/2027
Funding: $723,875
Title: Inhibiting EndoMT to Promote Remyelination and Functional Recovery in Mouse Models of Multiple Sclerosis
Summary: University of Utah researchers are investigating the role of a protein called ARF6 in blocking repair of nerve-insulating myelin in mice for clues to how to overcome it to restore function in MS.

Background: In MS, a fatty substance called myelin, which surrounds and protects the fibers of nerve cells, is attacked and destroyed. Nerve cells that have lost their myelin do not function properly and are vulnerable to degeneration. The body can normally restore damaged myelin but in MS myelin repair is incomplete. One possible reason for this is that the tissue and related molecules around the cells that repair myelin create an environment that inhibits repair.

The Study: Dr. Zhu and team are investigating the idea that a molecule called ARF6, which is activated by MS inflammation, creates an environment that blocks myelin repair. In particular, ARF6 may allow other harmful molecules to leak into the brain from the bloodstream and may also help create a "scar" in the brain that inhibits repair.

They are using two types of mice with MS-like disease to test these ideas. They are also testing whether blocking ARF6 in these mice restores the mouse's ability to repair myelin.

What is the potential impact for people with MS? These studies may offer insights into how to develop therapies that overcome blockages to myelin repair in MS.

J. Bradley Zuchero, PhD (Pending)
Stanford University
Stanford, California
Award: Research Grant
Term: 4/1/2024-3/31/2027
Funding: $665,435
Title: An unexplored pathway for demyelination and remyelination by surviving oligodendrocytes
Summary: Researchers at Stanford University are investigating the importance of a protein secreted by astrocyte cells that converts oligodendrocytes to a cell type that cannot repair myelin.

Background: In MS, a fatty substance called myelin, which surrounds and protects the fibers of nerve cells, is attacked and destroyed. Nerve cells that have lost their myelin do not function properly and are vulnerable to degeneration. The cells in the brain and spinal cord that make myelin are called oligodendrocytes. Researchers long thought that myelin repair was incomplete in MS because oligodendrocytes died.

The Study: Dr. Zuchero and team are investigating the idea that instead of dying, oligodendrocytes in MS switch to a different type of cell that cannot make myelin following exposure to a molecule that is induced and released from astrocytes cells in MS. The team is using sophisticated tools to determine if this secreted signal can cause this cellular switch in mice and how this switching process works.

What is the potential impact for people with MS? If this study confirms that the switching process is indeed responsible for myelin repair failure, it would set the stage for developing therapies that could either prevent the switching or promote myelin repair in oligodendrocytes that have switched. Either approach could lead to restoring myelin and function in people with MS.

Pathways to Cures: ENDING MS

Ending MS means no one else hears the words, "you have MS." There is growing evidence that MS may be preventable. The two main objectives of the END pathway are preventing MS in the general population and identifying MS in its earliest (prodromal) stages to delay or prevent the onset of signs or symptoms, defined as secondary prevention.

* * *

Frederik Bartels, MD (Pending)
Stanford University
Stanford, California
Award: Postdoctoral Fellowships
Term: 8/1/2024-7/31/2027
Funding: $241,652
Title: Characterization of Epstein-Barr Virus infected B cells in Multiple Sclerosis Patients
Summary: Researchers at Stanford University are working to understand the role of Epstein-Barr virus as a potential cause of MS to suggest ways to treat and prevent it.

Background: Most people, and nearly everyone with MS, have been infected with the Epstein-Barr virus (EBV), which causes a mild illness in childhood and mononucleosis in adolescents, and may play a role in causing MS. During a person's life, EBV remains inactive in immune cells called B cells. Therapies such as ocrelizumab and ofatumumab that deplete B cells are effective treatments for MS, suggesting that B cells are important in this disease.

The Study: To further understand how EBV may trigger MS, Dr. Bartels and team are investigating how EBV changes B cells in people with MS. They are also looking at the antibodies that B cells produce, which are "flags" in the blood that can tag a target - for example, a virus - for the immune system. The team is comparing blood and spinal fluid from people with MS, people without MS, and people with other disorders. They are also examining tissue samples from brains donated from people who had MS in their lifetime. The team will then study the antibodies produced by B cells and identify their targets, which could include parts of EBV and parts of the brain.

What is the potential impact for people with MS? Uncovering the mechanisms that underlie the link between MS and EBV will help find new therapies for MS and even help formulate strategies to prevent MS before it begins.

Kathryn Fitzgerald, DSc
Johns Hopkins University
Baltimore, Maryland
Award: Harry Weaver Scholar Awards
Term: 7/1/2024-6/30/2029
Funding: $769,382
Title: A genomics-informed pipeline to refine multiple sclerosis risk and identify drug targets for potential repurposing
Summary: Researchers at Johns Hopkins are undertaking an extensive cutting-edge data analysis to understand factors that may help to stop the development of MS or its progression.

Background: The cause of MS is not yet known, but a person's genetic makeup and other factors combine to increase a person's likelihood of developing MS. Dr. Fitzgerald and colleagues are using genetic information to better understand what triggers MS and to identify therapies that may address MS progression. There are intermediate steps in between a person's genetic risk for MS and actually developing the disease. This project will try to identify some of the intermediate steps and potential biomarkers in the blood that may point to conversion to MS. Knowing lifestyle or environmental factors could suggest ways that a person with a high genetic risk for MS, like a family member, might be able to prevent MS. Also, there are limited treatments that target disability progression. Genetic factors can also affect how well certain medicines for other conditions outside of MS work.

The Study: Dr. Fitzgerald and colleagues will use large data sets ("cohorts") of people with and without MS from three different countries: Canada, the United Kingdom, and the United States. In these cohorts, they can identify people who have MS and those who do not, and study individuals' genetic information. They will then use a new data analysis technique to try to identify possible intermediate factors, starting with people with a family history of MS. Then they will study large cohorts that have genetic information and brain imaging to identify possible new therapies for MS progression. They will then check to see if people with MS in separate populations who have used these therapies (for indications other than MS) have less disability.

What is the potential impact for people with MS? The results of this study may suggest new factors underpinning MS development, and treatments that can target MS progression and might be one way clinicians can help improve health outcomes in people with MS.

Funding Clinical Training to Improve Care

2024 Clinical Care Fellowships

These awards provide one year of post-residency training with experienced mentors to optimize access to quality care and solutions for people with MS.

Fellow	Mentors	Institution
Matthew Doerfler, MD	Robert Gross, MD Teri Schreiner, MD	University of Colorado Denver
Daniel Gratch, MD	Fred Lublin, MD	Icahn School of Medicine at Mount Sinai
Madeleine Hebert, MD	Grace Gombolay, MD	Emory University
Zarmina Javed, MBBS	Jeffery Cohen, MD	Cleveland Clinic Foundation
Alexander Jonokuchi, MD	Ilya Kister, MD	New York University Grossman School of Medicine
Parisa Khosravi, DO	Leorah Freeman, MD, PhD	University of Texas at Austin
Florina Kralter, DO	Scott Newsome, DO Ellen Mowry, MD	Johns Hopkins University
Iwalewa Oloworporoku, MD	Tirisham Gyang, MD Benjamin Segal, MD	The Ohio State University
Atika Paracha, MBBS	Annette Wundes, MD Jodie Haselkorn, MD, MPH	University of Washington
Paridhi Shah, MD	Tiffany Braley, MD Andrew Romeo, MD	Regents of the University of Michigan
Elle Wade, MD	Robert Gross, MD	University of Colorado Anschutz Medical Campus

2024 Institutional Clinician Training Awards

These awards go to mentors and institutions to provide training for board-certified/eligible neurologists and physiatrists in MS care.

Mentors	Institution
Jeffrey Cohen, MD	Cleveland Clinic Foundation
Claire Riley, MD	Columbia University
John Rinker, II, MD	University of Alabama at Birmingham

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