NEW RESEARCH

STOP. RESTORE. END.

Spring 2018

Society Commits $14.2 Million for 45 New MS Research Projects

The National Multiple Sclerosis Society has just committed more than $14.2 million to support 45 new MS research projects. This financial commitment is the latest in the Society's relentless research effort, investing a projected $34 million in 2018 alone to support new and ongoing studies around the world.

These new research projects and training awards strengthen the Society's comprehensive approach addressing critical research and scientific workforce priorities.

The Society is the largest private funder of MS research in the world and is recognized as a global leader in driving MS research. We stimulate studies worldwide, leverage opportunities, foster collaboration a, and shape the research landscape to find solutions for the urgent needs of people with MS.

To stop MS in its tracks, restore what has been lost, and end MS forever, there are still critical questions we must answer that drive the Society's research priorities:

- Why does MS affect certain people and not others?
- What is the cause of MS?
- How do we stop MS progression?
- How do we repair the damage caused by MS?
- How do we reverse symptoms and promote wellness?

The 45 new projects seek answers to these questions. For example, several investigators are exploring the increasing evidence that **gut bacteria** differ in people with MS and play a role in triggering MS and progression (p. 3). Others are investigating how to promote the **repair of nerve-insulating myelin** using existing medications (p. 13) and testing how to bolster **cell therapy** strategies (p.17). Others are focusing on addressing troublesome symptoms, including a team testing two non-pharmacological approaches to **managing pain** in people with MS (p.21).

National Multiple Sclerosis Society

Inside…

Risk Factors: Why do some people get MS and others don't?

Although tremendous progress has been made in identifying key biological pathways that contribute to MS risk, the cause is still unknown. Preventing MS for future generations requires a deep understanding of what triggers MS, how triggers lead to the development of the disease, and how to protect against it.

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Amir-Hadi Maghzi, MD
Brigham and Women's Hospital
Boston, Massachusetts
Award: Clinician Scientist Award
Category: Stopping MS
Term: 7/1/2018-6/30/2021 **Funding:** $206,246
Title: Investigation of the microbiome in multiple sclerosis and its relationship to immunologic and clinical features of disease
Summary: Investigators are researching gut bacteria in MS and its relationship to immune activity and other features of the disease.

Background: The tiny universe of bacteria and other microbes that inhabit the intestines, known as the gut microbiome, has been shown to differ in people with MS compared to people who do not have MS, and the microbiome also changes with MS disease-modifying treatment. A central question is the degree to which the changes in the microbiome are linked to clinical, immunologic and MRI measures of the disease, and whether there is a way to positively change the microbiome in a way that mitigates disease activity.

The Study: In this study, Amir-Hadi Maghzi, MD, and colleagues aim to understand how the immune system interacts with the microbiome in MS, and assess the effect of components of the microbiome on clinical measures of MS disability, MRI activity and response to treatments. His team will also study the effect of MS gut bacteria in a mouse model of MS.

What's Next: Better characterization of these aspects of the gut microbiome in MS holds potential for understanding the disease process and developing therapeutics that target the microbiome.

Jorge Oksenberg, PhD
University of California, San Francisco
San Francisco, California
Award: Research Grants
Category: Ending MS
Term: 4/1/2018-3/31/2020 **Funding:** $595,690
Title: Maintenance and enhancement of a core DNA repository for multiple sclerosis
Summary: Researchers are maintaining and enhancing a blood biospecimen bank as a shared resource to identify genetic variants and other factors that contribute to risk and genetic susceptibility in MS.

Background: MS is a complex disease. Accessibility to human biological materials and linking these materials to clinical and laboratory data is critical to support the basic and translational research efforts needed to bring significant improvements in diagnosis, treatment, and prevention of MS. The MS DNA Biobank was established two decades ago as a result of transformative advances in human genetics to enable studies of MS susceptibility. Supported by the National MS Society, this repository has contributed thousand of high quality de-identified biological samples to studies with different research goals. However, the task of acquiring and managing centralized collections of

Risk Factors, cont.

biospecimens is evolving in response to the changing landscape of research priorities and technological advances. Now the biospecimen bank is expanding its size and scope to allow the completion of genetic screens, the discovery of biomarkers of disease severity, and testing novel hypotheses focused on disease progression.

The Study: The team is maintaining and expanding its core biological repository of people living with MS, family members and unrelated controls, linking it to a sophisticated database system for storing and pairing detailed sample inventory, clinical, demographic, and laboratory data. Blood samples are drawn for storage of serum, cells, DNA and RNA. The team also assembles questionnaires and interviews to provide context for the biological samples. These evaluations assess historical as well as contemporary exposures to potential risk factors and document co-morbidities, and clinical history.

What's Next? This resource offers outstanding opportunities for researchers to identify and characterize genes and other factors that influence MS susceptibility and disease course, which should translate into clinically useful biomarkers and reveal targets for new therapies.

Nikos Patsopoulos, MD, PhD
Brigham and Women's Hospital
Boston, Massachusetts
Award: Research Grants
Category: Ending MS
Term: 4/1/2018-3/31/2021 **Funding:** $599,277
Funded in part by the Al Otaiba Family
Title: Sex specific genetics of multiple sclerosis
Summary: Researchers are analyzing large sets of genetic data to identify genes that explain why women are more susceptible to multiple sclerosis than men.

Background: MS affects females at least twice as frequently as males, but the reasons for this are not well understood. Over 200 gene variations have been linked to increasing people's susceptibility to getting MS, but so far none explain why women are more susceptible.

The Study: Dr. Patsopoulos and his team are collecting large amounts of genetic data to look for genetic differences between males and females that may play a role in susceptibility to MS. This information is being collected from publicly available databases as well as that of the International MS Genetics Consortium, in which this team is involved. The team is using advanced mathematical modeling and analysis of single cells to look for sex-related differences that may be important in MS.

What's Next: Results from this study may lead to a better understanding of the cause of MS, as well as personalized predictions that will allow better selection of therapies and improved prediction of disease progression.

Anne-Katrin Pröbstel, MD
University of California, San Francisco
San Francisco, California
Award: Postdoctoral Fellowships
Category: Stopping MS
Term: 7/1/2018-6/30/2021 **Funding:** TBD
Title: Gut-Brain-Axis: Dissecting the crosstalk between B cells and the gut microbiota in multiple sclerosis
Summary: Researchers at the University of California, San Francisco are identifying harmful gut bacteria in people with MS and testing their role in disease triggering and progression.

Risk Factors, cont.

Background: Types of immune cells called B cells play an important role in MS. There is growing awareness that the bacteria in the gut of people with MS are different from bacteria in people without MS, and that harmful bacteria found in the gut of people with MS may have detrimental effects on MS disease activity and possibly on B cell function.

The Study: Dr. Pröbstel and her team are investigating the role of gut bacteria in MS on B cells and inflammation. They are working to identify the gut bacteria in people with MS that may be harmful. They are transferring these harmful bacteria to mice to see if they make the MS-like disease called EAE worse. They are also testing whether eliminating these harmful bacteria improves EAE. Finally, they are determining whether these harmful bacteria are present in the blood or spinal fluid in people with MS.

What's Next: Exploring the impacts of gut bacteria on MS disease initiation and activity may inform the development of probiotic strategies to treat people with MS.

Howard Weiner, MD
Brigham and Women's Hospital
Boston, Massachusetts
Award: Research Grants
Category: Stopping MS
Term: 4/1/2018-3/31/2021 **Funding:** $551,752
Title: The role of fecal microRNAs in CNS autoimmune inflammatory disease
Summary: Researchers at Harvard Medical School are investigating a type of molecule called microRNA that is found in the gut and that may someday be a treatment for MS.

Exploring the impacts of gut bacteria on MS disease initiation and activity may inform the development of probiotic strategies

Background: MS is an immune-mediated disease. Growing evidence suggests that the bacteria and the immune system in the gut may modulate the immune attack on the brain in MS. A type of genetic material present in the gut (and elsewhere) called microRNA is different in people with MS and in mice with an MS-like disease called EAE, compared to people and mice that don't have MS.

The Study: The team is developing a novel therapy approach for MS based on microRNA obtained from feces. They are examining how fecal microRNAs change in MS and EAE and are then testing if these microRNAs can treat or prevent EAE. They are also working to understand how these microRNAs work.

What's Next: The results of this study may lead to development of synthetic microRNAs that could be used to treat people with MS.

Pathology: What is the cause of MS?

Much has been learned about immune system activity in the relapsing-remitting phase of MS and this knowledge has led to the development of effective disease-modifying therapies. Less understood is the relationship between initial immune activity and progressive neurodegeneration and how other immune factors participate in the progressive phase of MS. Identifying the causes of MS, and the underlying mechanisms and biological pathways involved in MS injury to the brain and spinal cord, will expose new targets for the development of treatments to stop the damage that causes disability.

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Elizabeth Frost, PhD
University of Virginia
Charlottesville, Virginia
Award: Postdoctoral Fellowships
Category: Stopping MS
Term: 7/1/2018-6/30/2021 **Funding:** $181,754
Title: Spleen tyrosine kinase regulation of microglial functions in experimental autoimmune encephalomyelitis
Summary: Researchers are investigating whether an enzyme plays helpful roles in regulating the function of a cell type called microglia in MS.

Background: New strategies are needed to treat people with MS. One potential strategy is to target a type of immune cell called "microglia," which are normally found in the brain and spinal cord, but which may function abnormally and cause harm in MS. The normal roles of microglia in the healthy brain are to clean up cellular debris and to regulate other immune cells.

The Study: Dr. Frost's team is investigating how an enzyme called SYK (spleen tyrosine kinase) regulates the function of microglia in the brain. The group has shown that SYK in microglia regulates inflammation and tissue damage in the brain and contributes to the stabilization of MS-like disease in mice. Now they are testing whether SYK controls the ability of microglia to clean up cellular debris and whether SYK dampens harmful autoimmune reactions in the brain. To test these ideas, they are using a mouse model of MS in which the microglia lack SYK.

What's Next: Better understanding the biological activity of microglia and SYK may lead to the development of novel approaches to stop MS.

Roland Henry, PhD
University of California, San Francisco
San Francisco, California
Award: Research Grants
Category: Stopping MS
Term: 4/1/2018-3/31/2021 **Funding:** $738,084
Title: Enabling Multicenter MRI Studies of Neurodegeneration in Multiple Sclerosis
Summary: Researchers are gathering and standardizing existing MRI and genetic information from people with MS across the globe to accelerate research into progressive MS.

Background: Neurodegeneration, which is damage and loss of nervous system tissues, occurs in MS, especially in progressive forms of the disease. Therapies are needed to stop neurodegeneration, but research is hindered in part because neurodegeneration varies among people, and ways of detecting brain shrinkage, or atrophy, are not standard. In addition, various genes may play a role in neurodegeneration. To understand neurodegeneration and accelerate development of better therapies, researchers need to analyze the genetic factors and imaging results obtained from many people with MS worldwide.

Pathology, cont.

The Study: Not all institutions perform imaging and genetic analysis the same way. Thus, trying to combine information obtained from multiple locations is difficult and time-consuming. Dr. Henry and his team are using existing imaging and genetic data that have been gathered worldwide to find ways to quantitate neurodegeneration and perform the first investigation of the relationship between genes and neurodegeneration in MS. They are developing ways to standardize existing data from multiple locations so that they can be compared. They are also collecting MRI scans from locations worldwide into a central database where they can then be standardized. Genetic information relevant to multiple sclerosis is also being gathered from multiple sites for analysis.

What's Next: Gathering and standardizing imaging and genetic data will allow researchers to more quickly answer questions, without the need to acquire and standardize the information each time. These efforts will accelerate research in progressive MS.

Xiaoxia Li, PhD
Cleveland Clinic Foundation
Cleveland, Ohio
Award: Research Grants
Category: Stopping MS
Term: 4/1/2018-3/31/2021 **Funding:** $732,861
Title: Cellular and molecular mechanisms of the inflammasome in CNS inflammation
Summary: Researchers at the Cleveland Clinic are investigating the importance of harmful immune system molecules in an animal model of MS.

Background: In MS, the immune system attacks components of the brain and spinal cord, causing damage and often devastating neurological symptoms. One component of the immune system, called "Th17" T cells, is thought to play a harmful role in MS. The activity of Th17 cells is controlled by a group of messenger molecules called "cytokines." One cytokine, IL-1beta, may play a key role in the harmful activity of Th17 cells in MS, but the importance of IL-1beta and how IL-1beta is produced are not known.

The Study: Dr. Li and her team are using a model of MS in mice called EAE. They are testing the idea that proteins found in various immune cells control the production of IL-1beta, which then leads to activation and maintenance of Th17 cells, thus worsening EAE and MS. To explore this, they are using mice that lack various members of this group of proteins, or IL-1beta or its docking site, the IL-1beta receptor.

What's Next: Understanding which molecules are responsible for causing harmful inflammatory events in EAE, and by implication in MS, will suggest new therapeutic targets to treat MS that are more specific.

Pathology, cont.

Andrew Mendiola, PhD
The J. David Gladstone Institutes
San Francisco, California
Award: Postdoctoral Fellowships
Category: Stopping MS
Term: 7/1/2018-6/30/2021 **Funding:** $177,243
Title: In vivo imaging and profiling of mechanisms of T-cell recruitment and activation during neuroinflammatory disease
Summary: Researchers are investigating how a protein found in the blood called fibrinogen promotes a damaging immune response in MS.

Background: In MS, the blood-brain barrier (BBB) does not function properly and as a result, proteins found in the blood leak out of blood vessels into the brain and spinal cord. Fibrinogen is a protein normally found in the blood and is kept out of the brain due to the BBB. However in both early and progressive forms of MS, fibrinogen is detected in the brain and may interact with immune cells leading to a damaging inflammatory response by the immune system.

The Study: Using a mouse model of MS called EAE, Dr. Mendiola and his team are testing how fibrinogen works to stimulate harmful cells. They are using mice in which individual types of immune cells are labeled with fluorescent dyes. This allows cells in the spinal cord of living mice to be viewed in a microscope. The fibrinogen in these mice has been genetically inactivated, so they are comparing mice with functional vs. non-functional fibrinogen. The team is able to study labeled immune cells as EAE develops over time in the presence or absence of fibrinogen.

What's Next: Understanding how fibrinogen influences immune cell functions in a mouse model of MS may lead to new MS therapies.

Zahra Moinfar, MD, PhD
University of California, San Francisco
San Francisco, California
Award: Postdoctoral Fellowships
Category: Stopping MS
Term: 7/1/2018-6/30/2021 **Funding:** $177,243
Title: Pathogenic T cells that target NMO autoantigen aquaporin-4
Summary: Researchers are investigating similarities and differences between MS and a related but distinct disease called NMO.
Background: A disease called neuromyelitis optica (NMO) has certain similarities and certain differences compared to MS. Studying NMO can reveal fundamental differences between the two diseases, which is important for proper diagnosis and treatment of each. Understanding similarities can help increase understanding of both diseases.

The Study: Dr. Moinfar and her team are examining how a class of immune cells called T cells that can be harmful are activated in NMO. The team is using mice with genetic deletions in NMO-related molecules to answer questions about T cells in NMO. They are also testing to what extent bacteria found in the gut can impact NMO or MS. To test this, they are transferring stool samples from people with MS or NMO into mice and evaluating how the T cells in the mice are affected by these transfers.

What's Next: These studies will increase understanding of the harmful biological steps that lead to NMO and provide insight into what activities distinguish NMO and MS.

Pathology, cont.

Russell Shinohara, PhD
University of Pennsylvania
Philadelphia, Pennsylvania
Award: Research Grants
Category: Stopping MS
Term: 4/1/2018-3/31/2021 **Funding:** $585,061
Title: A traveling subject study of replicability in conventional and advanced MRI MS biomarkers
Summary: Researchers are developing statistical methods to reduce differences in images obtained on different MRI scanners to improve the accuracy of MRI data from people with MS.

Background: Magnetic resonance imaging (MRI) is widely used in people with MS to look for lesions and other changes in the brain, and it is also one tool used to determine outcomes in clinical trials for MS. However, because imaging scanners differ from location to location, comparing images taken in different places is difficult.

The Study: To address this need, the team is sending 12 people with MS to undergo MRI at four different locations (University of Pennsylvania, Johns Hopkins University, Brigham and Women's Hospital, and the National Institutes of Health). The images obtained for an individual person on different scanners within a short time frame should be the same, but the team knows that they are not. Thus, they will analyze differences among images taken on different scanners and then develop statistical approaches to harmonize the images.

What's Next: Results from this study will improve the accuracy of interpretation of imaging data obtained in multi-site clinical trials, allowing more accurate assessment of the effectiveness of new MS treatments.

Ari Waisman, PhD
University Medical Center of the Johannes Gutenberg-University Mainz
Mainz, Germany
Award: Research Grants
Category: Stopping MS
Term: 4/1/2018-3/31/2021 **Funding:** $484,464
Title: The role and mode-of-action of IL-17 in the CNS
Summary: Researchers are identifying the destructive activities that are launched by an immune messenger for clues to stopping MS.
Background: The neurological problems that people with MS experience are a result of damage to brain and spinal cord (central nervous system – CNS) tissues by their own immune systems. Prof. Waisman's group and others have found that specific immune cells that produce a messenger protein called IL-17 are involved in this damaging process. It is not clear yet how IL-17 facilitates this damage.

The Study: Prof. Waisman and team are identifying which cell types in the brain and spinal cord respond to IL-17 during the inflammatory immune response in MS, and exactly how they do it. They are using mice with the MS-like disease EAE to answer these questions. By genetic manipulation they will make certain cells of the CNS incapable of sensing IL-17, which will or will not have consequences for their participation in the overall disease progression. This way, they will tease out how nerve and other cells respond during inflammation.

What's Next: Better understanding of mechanisms that lead to nervous system damage will enable the design of new strategies to stop MS.

Progression: How do we stop MS progression?

MS progression often occurs early in the disease, even while the brain compensates for injury and even in people successfully treated for relapses. Progression is not easily measured and usually happens over long periods of time, making it hard to quickly detect whether a therapy is impacting the course of disease. This has made the development of therapies for progressive stages of MS a challenge. Diagnosing progressive disease based on biomarkers, in addition to clinical presentation, would enable the testing of therapies earlier, promising better ways of protecting the nervous system from MS injury.

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Pavan Bhargava, MD
Johns Hopkins University
Baltimore, Maryland
Award: Research Grants
Category: Stopping MS
Term: 4/1/2018-3/31/2020 **Funding:** $355,455
Title: Bile acid supplementation for Multiple Sclerosis
Summary: Researchers are investigating whether a dietary supplement can be beneficial for the immune system, gut bacteria and MS.

Background: People with MS may have abnormalities in the way they process energy and other maintenance activities (metabolism). One metabolic pathway identified by this team is bile acid metabolism. Bile acids are produced by the liver and help in the absorption of fats (lipids) in the gut, and can influence the composition of gut bacteria. Bile acids can also interact with immune cells and brain cells and influence their function. Abnormalities in gut bacteria have been identified in people with MS and may be related to the observed abnormalities in bile acid metabolism. Now Dr. Bhargava's team is investigating whether supplementing bile acids in people with MS will lead to beneficial effects on the immune system, gut bacterial composition or other disease-related parameters.

The Study: The team will identify and recruit 60 people with progressive MS who have abnormal bile acid metabolism. They will be given a bile acids supplement or a placebo for four months. The team will monitor blood samples and stool specimens before, during and after this intervention, and also look for the development of any new neurological symptoms during the trial. They will then analyze whether this treatment improved circulating bile acid levels and altered composition of gut bacteria or immune function.

What's Next: This study has the potential to optimize a method to identify people with MS who have abnormalities in bile acid metabolism and a potential treatment that would potentially impact the composition of gut bacteria, the peripheral immune system and have neuroprotective effects.

Emily Evans, MD
Washington University School of Medicine
St. Louis, Missouri
Award: Sylvia Lawry Physician Fellowship
Category: Stopping MS
Term: 7/1/2018-6/30/2020 **Funding:** $130,000
Title: Sylvia Lawry Clinical Trials Research Training Fellowship
Summary: A promising doctor will develop the skills involved in the design, implementation, and analysis of clinical trials in MS.

Physicians Receive Training Awards for Specialized MS Care

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

Awardee	Location	Mentor
Brooke Guerrero, MD	Cedars-Sinai Medical Center	Nancy Sicotte, MD
Amanda Thuringer, DO	University of Kansas Medical Center	Sharon Lynch, MD
Asya Wallach, MD	New York University School of Medicine	Ilya Kister, MD
Kelly Tisovic, MD	University of Southern California	Lilyana Amezcua, MD
Douglas Juvinall, MD	Northwestern University	Roumen Balabanov, MD
Frank Benesh, MD, PhD	University of Alabama at Birmingham	John Rinker, MD

The Study: To develop her clinical skills, Dr. Evans will spend time evaluating patients in the John L. Trotter Multiple Sclerosis Center where she will see both new patients and follow-ups. She will also spend time rotating through the pediatric MS clinic. These clinical experiences will allow her to treat MS in all of its stages and throughout the lifespan. She will also spend time in the neuro-rehabilitation department to develop a multidisciplinary approach to managing MS-related symptoms. To develop her clinical investigation skills, Dr. Evans will be an active investigator in clinical trials at the MS Center. She will participate as an examining physician in these trials and learn commonly utilized clinical study measures. She will also pursue a Master of Science in Clinical Investigation, a degree program geared towards helping young investigators prepare for academic research.

What's Next: By the end of their training, Sylvia Lawry fellows emerge fully ready to plan and conduct studies of promising new treatments for multiple sclerosis.

Progression, cont.

Jenny Feng, MD
Cleveland Clinic Foundation
Cleveland, Ohio
Award: Sylvia Lawry Physician Fellowship
Category: Stopping MS
Term: 7/1/2018-6/30/2021 **Funding:** $195,000
Title: Training in multiple sclerosis diagnosis, management, and clinical trials
Summary: A promising doctor will develop the skills involved in the design, implementation, and analysis of clinical trials in MS.

The Study: Dr. Feng is completing a three-year training plan as a fellow in neuroimmunology at the Mellen Center for MS at the Cleveland Clinic. She will directly participate as a co-investigator in multiple clinical trials being conducted at the Mellen Center, gaining first-hand experience in designing, executing, and analyzing clinical trials, as well as the intricate administrative responsibilities involved in being a principal investigator. At the same time, she will be enrolled in graduate courses at Case Western University with the goal of obtaining a Masters' degree in Clinical Research. She will also see patients in both outpatient and inpatient settings to strengthen her skills as a clinician in the diagnosis and management of MS and related disorders.

What's Next: By the end of their training, Sylvia Lawry fellows emerge fully ready to plan and conduct studies of promising new treatments for multiple sclerosis.

Christopher Langston, MD, PhD
Icahn School of Medicine at Mount Sinai
New York, New York
Award: Sylvia Lawry Physician Fellowship
Category: Stopping MS
Term: 7/1/2018-6/30/2020 **Funding:** $130,000
Title: Sylvia Lawry Physician Fellowship
Summary: A promising doctor at Icahn School of Medicine at Mount Sinai Hospital will develop the skills involved in the design, implementation, and analysis of clinical trials in MS.

The Study: During this training, Dr. Langston will help to create comprehensive treatment plans for people with MS. He will work with neuroradiologists who have access to state of the art imaging technology to understand the signature findings of the various subtypes of MS and to distinguish MS from other conditions. He will work with research coordinators to recruit people with MS for clinical trials, collect data, analyze results, and generate novel conclusions that will improve MS care. Dr. Langston also will have the opportunity to work in a basic science laboratory examining models that reflect specific aspects of MS pathology to identify potential targets for therapy in MS.

What's Next: By the end of their training, Sylvia Lawry fellows emerge fully ready to plan and conduct studies of promising new treatments for multiple sclerosis.

Progression, cont.

Muhammad Taimur Malik, MD
Johns Hopkins University
Baltimore, Maryland
Award: Sylvia Lawry Physician Fellowship
Category: Stopping MS
Term: 7/1/2018-6/30/2020 **Funding:** $130,000
Title: MS Clinical Trials Fellowship
Summary: A promising doctor at Johns Hopkins University will develop the skills involved in the design, implementation, and analysis of clinical trials in MS.

The Study: Dr. Malik will be extensively involved in clinical trials, including investigator-initiated and industry-sponsored studies. He will also learn the necessary skills needed to become an academic neurologist specializing in the care of people with MS. The Johns Hopkins MS Center investigators have an established track record for conducting large-scale prospective and retrospective studies. Dr. Malik will have access to large MS datasets to perform clinical research projects. The Center also is equipped with fourth generation state-of-the-art OCT (optical coherence tomography) scanners, and Dr. Malik will use these to investigate the relationships between nerve tissue loss in the eye and MS disease activity and progression. Dr. Malik also will complete the Science of Clinical Investigation Training Program at Johns Hopkins Bloomberg School of Public Health.

What's Next: By the end of their training, Sylvia Lawry fellows emerge fully ready to plan and conduct studies of promising new treatments for multiple sclerosis.

Michael Robers, MD
University of Southern California
Los Angeles, California
Award: Sylvia Lawry Physician Fellowship
Category: Stopping MS
Term: 7/1/2018-6/30/2020 **Funding:** $130,000
Title: MS Fellowship
Summary: A promising doctor at the University of Southern California, Los Angeles, will develop the skills involved in the conduct, design, implementation, and analysis of large epidemiological and clinical trials in MS.

The Study: This fellowship will include several half days per week in an MS clinic as well as inpatient consultations as needed. The clinical research aspects will include clinical trials as well as large scale epidemiologic studies. Dr. Robers's responsibilities on these trials will include recruitment, measuring endpoints, safety monitoring, managing protocols and troubleshooting issues as they arise. Dedicated coursework will result in a Master of Science degree in Clinical, Biomedical, and Translational Investigations which is a unique program designed to train professionals in the required statistics and foundations of trial design to be successful in clinical research.

What's Next: By the end of their training, Sylvia Lawry fellows emerge fully ready to plan and conduct studies of promising new treatments for multiple sclerosis.

Progression, cont.

Margot Woodroofe, PhD
Sheffield Hallam University
Sheffield, United Kingdom
Award: Research Grants
Category: Stopping MS
Term: 4/1/2018-3/31/2020 **Funding:** $134,514
Title: Lipidomics in progressive MS
Summary: Investigators are mapping changes in the fatty composition of the brain for clues to finding ways to stop progressive MS.

Background: All of the factors that drive MS progression (gradual worsening of disability) are not fully known. In both primary and secondary progressive MS, the role of changes in brain composition, and in particular changes in fatty substances (lipids), are poorly understood.

The Study: Professor Woodroofe and team will identify regional differences and specific changes in lipid composition of the normal, apparently unaffected white matter part of the brain in people with primary and secondary progressive MS, compared to control samples, using post mortem tissue from the MS Tissue Bank, Imperial College London, UK. The unique lipid species identified will be mapped across the tissue sections using a mass spectrometry imaging technique that allows identification of regional variations in the lipids in progressive MS.

What's Next: This research will provide understanding of lipid changes during the course of MS and possible new treatment strategies – possibly even dietary changes.

Neuroprotection/Repair: How do we repair the damage caused by MS?

The hopes of people living with MS today rest on finding a way to stop disease worsening by preventing neurodegeneration and reversing the damage to restore lost function. The brain can repair myelin and also rewire itself around damaged areas, but in order to significantly impact disease, this natural ability needs to be enhanced. In addition to developing treatment strategies, there is a crucial need for non-invasive ways to determine quickly whether neuroprotective and repair strategies are working.

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Riley Bove, MD
University of California, San Francisco
San Francisco, California
Award: Research Grants
Category: Restoring what's been lost
Term: 4/1/2018-3/31/2021 **Funding:** $578,719
Title: Functional validation of SERMs as remyelinating agents
Summary: Researchers are determining the potential of SERMs (selective estrogen receptor modulators) medications for stimulating repair of nerve-insulating myelin.

Background: MS destroys the myelin casing on nerve fibers in the brain and spinal cord. This leaves them vulnerable to damage, and causes a variety of symptoms. Treatments that promote myelin repair represent a major unmet need for people living with MS.

The Study: Dr. Bove and colleagues are focusing on the potential of a category of medications called SERMs (selective estrogen receptor modulators). SERMs have been developed to treat a number of medical problems, such as osteopo-

28 New High-Risk Pilot Projects Take Aim at MS

One way the Society propels MS research is by funding high-risk, high-potential pilot projects to investigate untested ideas. These one-year grants allow researchers to quickly gather data to determine if ideas are worth pursuing.

STOPPING MS

Tanuja Chitnis, MD (Massachusetts General Hospital, Boston, MA) is evaluating what proportion of children with MS experience a severe course of the disease.

Marc Horwitz, PhD (University of British Columbia, Vancouver, British Columbia, Canada) is testing whether Epstein-Barr Virus specifically acts as an important factor in developing MS.

Yong Chan Kim, PhD (Henry M. Jackson Foundation, Bethesda, MD) is developing an innovative therapeutic strategy to treat an MS-like disease.

Pawan Kumar, PhD (State University of New York at Stony Brook) is testing a therapeutic approach using molecules that regulate gut bacteria to reduce severity of MS-like disease.

Sharon Lynch, MD (University of Kansas Medical Center, Kansas City, KS) is studying older people with MS and without MS and comparing measurements of disability.

Yungki Park, PhD (The State University of New York at Buffalo, Buffalo, NY) is focusing on how genetic variations may contribute to MS risk, using cutting-edge technology.

Miguel Paz Soldan, MD, PhD (Western Institute for Biomedical Research (WIBR), Salt Lake City, UT) is studying whether differences in brain/spinal cord cells contribute to MS progression.

Bart Rypma, PhD (The University of Texas at Dallas, Dallas, TX) is using neuroimaging methods to determine mechanisms of cognitive dysfunction in MS.

Nancy Sicotte, MD (Cedars-Sinai Medical Center, Los Angeles) is investigating what factors contribute to the development of MS-like disease after administration of TNF-alpha blockers.

Mary Stevenson, PhD (McGill University, Toronto, Ontario, Canada) is investigating the effectiveness of proteins derived from parasitic worms as therapy for mice with MS-like disease.

Carles Vilarino-Guell, PhD (University of British Columbia, Vancouver, British Columbia, Canada) is developing and testing a new lab model of MS-like disease.

Li Wen, MD, PhD (Yale University School of Medicine, New Haven, CT) is identifying which gut bacteria can stimulate the immune system and possibly promote the development of MS.

Junqian Xu, PhD (Icahn School of Medicine at Mount Sinai, New York, NY) is optimizing tools to prepare for the investigation of the effects of rehabilitation in MS.

Yuhong Yang, MD (The Ohio State University, Columbus, OH) is targeting a novel pathway for stopping the immune attack in MS.

RESTORING WHAT'S BEEN LOST

Brett Fling, PhD (Colorado State University, Fort Collins) is testing how changes in communication between the two sides of the brain contribute to differences in the lower limbs in MS.

Nader Ghasemlou, PhD (Queen's University, Kingston, Ontario, Canada) is identifying new therapeutic targets that can be used to block or reduce pain in those living with MS.

Jacob Hines, PhD (Winona State University, Winona, MN) is learning what properties of the nerve fiber enable successful formation of myelin sheaths.

Sherri LaVela, PhD, MPH (CARES - Chicago Association for Research and Education in Science) is evaluating whether a novel therapy strengthens the ankle and muscles in MS.

Victoria Leavitt, PhD (Columbia University, New York, NY) is testing an online format to deliver the benefits of support groups to people with MS.

Steven LeVine, PhD (University of Kansas Medical Center - Kansas City) is investigating whether high dose biotin therapy might promote myelin repair processes in people with MS.

PILOT SPOTLIGHT: Neurostimulation to Improve Mobility

Weakness on one side of the body is a hallmark of MS, and is a significant cause of progressive worsening of walking abilities. Transient direct current stimulation (tDCS, a form of neurostimulation that uses constant, low direct current delivered via electrodes on the head) has been consistently shown to enhance motor performance in stroke patients and others. Thorsten Rudroff, PhD, and colleagues at Colorado State University, Fort Collins are seeking to determine whether applying tDCS will increase walking distance in 30 people with MS. The use of tDCS as a supplementary application in addition to rehabilitative exercise training may help to improve muscle weakness, bilateral asymmetries and mobility impairments in people with MS.

Jeri-Anne Lyons, PhD (University of Wisconsin-Milwaukee) is conducting clinical trial to determine the effectiveness of a form of light therapy to treat muscle fatigue in people with MS.

Bardia Nourbakhsh, MD (Johns Hopkins University, Baltimore, MD) is performing a clinical trial to find out if ketamine can alleviate the severity of fatigue in people with MS.

Catherine Siengsukon, PhD (University of Kansas Medical Center - Kansas City, KS) is assessing the feasibility of using cognitive behavioral therapy to improve MS symptoms of reduced sleep quality and fatigue in individuals with MS who have insomnia.

Fraser Sim, PhD (The State University of New York at Buffalo) is establishing a new lab model of demyelination to determine whether human cell therapy can restore lost myelin.

Caila Vaughn, PhD, MPH (The State University of New York at Buffalo) is conducting a trial to determine whether an application for smart devices improves communication in MS.

Brooks Wingo, PhD (University of Alabama at Birmingham, AL) is testing a web-based lifestyle intervention in people with MS that includes both diet and exercise components.

Ann Yeh, MD (The Hospital for Sick Children, Toronto, Ontario, Canada) is investigating how sleep habits, physical activity, and MS symptoms are related in children with MS.

Neuroprotection/Repair, cont. from p. 13

rosis and breast cancer. There have also been suggestions that SERMs may promote the repair of myelin, which is damaged by MS. Dr. Bove's team will look at the myelin repair potential of SERMs in human cells as well as rodent models, testing a variety of them to find those with the best overall benefit:risk profiles. The team will also determine whether SERMs promote remyelination by working on estrogen receptors (docking sites), or on other targets in cells.

What's Next: The ability to promote myelin repair represents one of the central priorities for people with MS. By the end of the study, they should have a clear understanding of which SERMs are the best candidates to test for promoting myelin repair in people with MS.

Emily Harrington, MD, PhD
Johns Hopkins University
Baltimore, Maryland
Award: NMSS-ABF Clinician Scientist Development Award
Category: Stopping MS
Term: 7/1/2018-6/30/2021 **Funding:** $276,697
Title: The role of oligodendrocyte progenitors as immune cells in MS models
Summary: Johns Hopkins researchers are observing interactions between the immune system and myelin making cells for clues to stopping myelin loss and promoting myelin repair.

Background: The majority of the therapies that are used to treat multiple sclerosis work through mechanisms of suppressing the immune system. Oligodendrocytes are the cells in the brain and spinal cord that wrap nerve fibers with myelin sheaths that allow for rapid conduction of signals. A largely unexplored role of oligodendrocyte precursors (immature oligodendrocytes) is how they interact with immune cells and how these interactions influence the immune response and oligodendrocyte function and survival.

The Study: This project focuses on defining the interactions between early oligodendrocytes and T cells, immune cells that drive MS. Dr. Harrington's team is isolating T cells from mice that are stimulated to form an inflammatory response to myelin proteins and transferring them into mice that have genetically labelled oligodendrocyte precursors. After myelin has been damaged, the team will observe the interaction between T cells and oligodendrocyte progenitors in the brain using imaging. They will then determine how that interaction influences the inflammatory response and the loss of oligodendrocyte progenitors. Inhibitors of this interaction will be assessed for their ability to block oligodendrocyte progenitor loss and promote myelin repair.

What's Next: Results from this study may help guide the development of therapies for MS that promote oligodendrocyte progenitor survival and promote myelin repair.

Yang Hu, MD, PhD
Stanford University
Stanford, California
Award: Research Grants
Category: Stopping MS
Term: 4/1/2018-3/31/2021 **Funding:** $467,623
Title: Combined Neuronal Soma and Axon Protection by Manipulation of Both ER Stress and NAD+ Metabolism in EAE/Optic Neuritis
Summary: Researchers at Stanford University are using a strategy of combination therapy in a mouse model of MS to protect the nervous system from a type of damage that occurs in MS.

Neuroprotection/Repair, cont.

Background: Neurodegeneration is common in MS and includes damage and loss of nervous system tissues. Nerve cells, which transmit signals, are lost in the process of neurodegeneration. They contain two important parts, a cell body, and a wire-like axon. Therapies aimed at protecting both parts of the nerve cell may work best.

The Study: The visual system and its nerve cells are affected in both MS and a mouse model of MS called EAE, causing vision problems. Dr. Hu and his team are using mice with EAE and are testing a combination of two treatment strategies: one is aimed at protecting the cell body from damage and one is aimed at protecting the axon of nerve cells. The team is monitoring the back of the eye, called the retina, to detect the impact of these treatment strategies.

What's Next: Combination strategies aimed at protecting the nervous system and preventing neurodegeneration may eventually be developed to treat people with MS to stop MS progression and preserve functions.

Yevgeniya Mironova, PhD
Johns Hopkins University
Baltimore, Maryland
Award: Postdoctoral Fellowships
Category: Restoring what's been lost
Term: 7/1/2018-6/30/2021 **Funding:** $181,754
Title: Non-progenitor functions of oligodendrocyte precursor cells in the brain
Summary: Researchers at Johns Hopkins University are studying how oligodendrocyte precursor cells in the adult brain play multiple roles in repair of myelin damage.

Background: In MS, the immune system attacks and destroys myelin, the fatty substance that surrounds and protects nerve fibers. Nerve fibers that have lost their myelin do not function properly and are vulnerable to damage, causing symptoms in people with MS. The brain is only able to partially repair myelin, and therapies to enhance this repair are needed.

The Study: Oligodendrocyte precursors (OPCs) are a group of immature glial cells that can mature into myelin-making oligodendrocytes. Dr. Mironova and her team are testing the idea that OPCs have other functions that may be important in myelin repair. Specifically, they are testing whether OPCs play a role in the removal of myelin debris and if this clearance is used to regulate immune cells in the brain. They are studying these questions in mice with myelin damage. The team can label different cell populations such as OPCs and mature myelin-making cells, allowing them to see the cells in action and the roles they play in the myelin repair process.

What's Next: These studies may lead to novel approaches to facilitating myelin repair to protect nerve fibers and restore function in people with MS.

Hiroko Nobuta, PhD
Albert Einstein College of Medicine
Bronx, New York
Award: Career Transition Fellowship
Category: Restoring what's been lost
Term: 7/1/2018-6/30/2023 **Funding:** $562,908
Title: Development of a Human Compatible Platform to Study Oligodendrocyte Biology
Summary: Researchers are optimizing ways of producing human myelin-making cells to speed efforts to find strategies to repair nerve-insulating myelin and restore function in MS.

Neuroprotection/Repair, cont.

Background: One of the unsolved problems in MS treatment is to repair the nerve-insulating myelin that is damaged in hopes of protecting nerves and restoring function. Some natural repair occurs in MS, but there is a need to find ways to stimulate myelin-making cells (oligodendrocytes) to conduct more reliable repair. Much of what is known about myelin repair has involved rodents, rather than people. To gain more ground, there is a need for ways to identify promising myelin repair strategies that more readily translate to treating people.

The Study: Dr. Nobuta aims to develop methods to study human oligodendrocytes by cultivating human cells and using them to test drugs or cell therapies that will promote myelin repair. Her team is establishing culture conditions that allows the observation of genes, mechanisms, and signals that facilitate myelin repair. The team will establish and share with other investigators a database of information to speed progress. Ultimately the findings will be used to generate transplantable human oligodendrocytes for future therapies.

What's Next: Having and sharing rich information about human myelin-making cells and optimal conditions for their growth and transplantation will speed efforts to restore function in people with MS.

Lu Sun, PhD
Stanford University
Stanford, California
Award: Career Transition Fellowship
Category: Restoring what's been lost
Term: 7/1/2018-6/30/2023 **Funding:** $589,886
Title: Identification of a novel pathway that regulates CNS myelination and remyelination

Summary: Stanford University researchers are investigating mechanisms involved in the loss of cells that make nerve-insulating myelin, and potential ways to promote their survival and myelin repair.

Background: An important unmet need in MS is finding a way to repair the myelin coating on nerve fibers damaged as a result of immune system assaults of the brain and spinal cord. Nerve fibers stripped of their myelin are vulnerable to loss. Repairing myelin may protect from nerve loss and restore nerve signaling to improve functional abilities. The cells that repair myelin in the central nervous system are called oligodendrocytes. They reside in the brain in immature states, and they are called up when injury occurs, when they begin to mature and move to the areas of damage and start the myelin regeneration process.

The Study: Dr. Sun and team have identified a natural molecule in the brain that is active during early development to help determine when and where myelin grows. This molecule, called TFEB, inhibits the survival of immature oligodendrocytes so that myelin develops in the proper amounts and places. In this project, Dr. Sun is conducting lab studies to understand signals that influence TFEB, with the goal of determining whether therapies that block TFEB would be a promising strategy for protecting oligodendrocytes from loss and promoting repair in MS.

What's Next: This study will provide important fundamental information about amechanisms involved in myelin loss and potential ways to promote its repair to restore function in people with MS.

Neuroprotection/Repair, cont.

William Talbot, PhD
Stanford University
Stanford, California
Award: Research Grants
Category: Restoring what's been lost
Term: 4/1/2018-3/31/2021 **Funding:** $436,224
Title: Role of RagA in Lysosome Function and Myelination in Oligodendrocytes
Summary: Researchers at Stanford University are investigating two genes that affect the growth of nerve-insulating myelin, for clues to finding ways to repair myelin in people with MS.

Background: In MS, the immune system attacks and destroys myelin, the fatty substance that surrounds and protects nerve fibers. Nerve fibers that have lost their myelin do not function properly and are vulnerable to damage, leading to symptoms in people with the disease. Myelin repair improves function, however, natural myelin repair is incomplete in MS, and therapies are needed to enhance myelin repair in MS.

The Study: Dr. Talbot's team is investigating the role of a part of the cell called the lysosome. Lysosomes are responsible for the breakdown and recycling of cellular debris, which may be important for proper myelin repair. They are investigating genes that control how lysosomes work in myelin-making cells using zebrafish as their experimental model. The larvae are transparent, allowing the team to see changes in myelin. They have discovered two genes in these fish that affect lysosomes and myelin synthesis, and have obtained evidence that these genes may not function correctly in people with MS.

What's Next: Understanding the function of genes that affect myelin synthesis will provide clues to improving myelin repair in MS.

J. Bradley Zuchero, PhD
Stanford University
Stanford, California
Award: Harry Weaver Neuroscience
Category: Restoring what's been lost
Term: 7/1/2018-6/30/2023 **Funding:** $772,639
Title: How does the actin cytoskeleton control myelination and remyelination?
Summary: Stanford University researchers are investigating how scaffold-like structures inside cells change during the formation of myelin, for clues to stimulating myelin repair in MS.

Background: One hallmark of MS is the destruction of the myelin sheath, the insulating layer that surrounds wire-like axons throughout the brain and spinal cord. Myelin is formed by oligodendrocytes, cells that extend long processes that wrap around axons. In chronic MS lesions that fail to regenerate myelin, oligodendrocytes are present and even can extend their processes toward axons but the step in which they wrap around axons to form mature myelin is blocked, for unknown reasons. Dr. Zuchero aims to determine why oligodendrocytes may not wrap around axons in people with MS. Specifically, his team is investigating the role of structural scaffolding, called the cytoskeleton, which exists inside oligodendrocytes.

The Study: First, the team is studying myelin wrapping as it occurs normally in lab dishes and in a mouse model. Next, they are studying myelin wrapping during the myelin repair process in mouse models of MS. Finally, they will use novel tools developed in Dr. Zuchero's laboratory to stimulate or block the disassembly of the cytoskeleton to determine the impacts on repair.

What's Next: This project may uncover novel insights into why myelin repair fails in MS.

Symptoms, Rehab, Wellness: How do we reverse symptoms and promote wellness?

Emerging evidence suggests that wellness behaviors and lifestyle factors can influence the risk for developing MS, disease course, severity of symptoms and quality of life. Finding ways to understand and address the variable and unpredictable symptoms caused by MS will have a profound impact on people's quality of life. In addition, people with MS often live with other chronic medical conditions. Understanding how these other health conditions affect MS disease course and symptoms represents an important research opportunity. Opportunities to improve the design and conduct of clinical trials and providing strategies people can incorporate to enhance their wellbeing are a priority.

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Valerie Block, DSc, PT
University of California, San Francisco
San Francisco, California
Award: Postdoctoral Fellowships
Category: Stopping MS
Term: 7/1/2018-6/30/2021 **Funding:** $177,243
Title: Incorporating Continuous Daily Assessment of Remote Step Count Monitoring with Quantitative Spinal Cord and Brain MRI
Summary: Researchers are determining whether a person's average daily step count can be used to measure and track progression of MS.

Background: Walking is a major form of physical activity for people with MS, and walking impairment is one of the most limiting aspects of the disease. Reliable, valid measures of walking impairment that reflect real-world daily activity on an individual level are needed. Dr. Block and colleagues are using a non-invasive, continuous measure of daily physical activity to determine a person's average daily step count (STEPS) in conjunction with sophisticated MRI measures to define more sensitive measures of MS disability.

The Study: The team is using the wearable Fitbit device to capture STEPS data for one year and at least two follow-up MRI measures for 50 people with MS. They are determining whether a strong association exists between STEPS and advanced MRI measures. They are also evaluating whether they can predict changes in disease progression in MRI scans, clinic-based outcomes, or change of medication. They are also evaluating differences between people with relapsing and progressive MS, men and women, and people with different durations of disease.

What's Next: Results from this project could improve detection of MS progression and enhance clinical trials.

Nina Bozinov, MD
Stanford University
Stanford, California
Award: Sylvia Lawry Physician Fellowship
Category: Restoring what's been lost
Term: 7/1/2018-6/30/2020 **Funding:** $130,000
Title: Imaging and immunopathologic biomarkers of cognitive impairment in MS
Summary: A promising doctor will develop the skills involved in the design, implementation, and analysis of clinical trials in MS.

The Study: Throughout this fellowship, about 40% of Dr. Bozinov's time will be spent in the MS/Neuroimmunology Clinic. She will provide direct patient care including diagnosis, initiation and optimization of disease modifying therapies, safety monitoring, symptomatic manage

ment and counseling. Dr. Bozinov will participate in clinical trials of various phases and types. Her role will involve patient screening, safety monitoring, and outcome measures. Finally, Dr. Bozinov is enrolling in the Master of Science Program in Epidemiology & Clinical Research to receive training in clinical research.

What's Next: By the end of their training, Sylvia Lawry fellows emerge fully ready to plan and conduct studies of promising new treatments for multiple sclerosis.

Chung-Yi Chiu, PhD
University of Illinois at Urbana-Champaign
Springfield, Illinois
Award: Research Grants
Category: Restoring what's been lost
Term: 4/1/2018-3/31/2021 **Funding:** $548,359
Title: Developing A Person-centered Internet-based Health Action Process Approach to Promoting Physical Activity in People with MS
Summary: Researchers are testing a program aimed at increasing physical activity among people with MS to promote healthier lifestyles.

Background: There is a strong tendency for people with MS to decrease their physical activity over time, leading to sedentary lifestyles that worsen secondary health conditions like cardiovascular disease, diabetes, and obesity. The goal of this project is to increase physical activity in people with MS.

The Study: Dr. Chiu's team is consulting with an advisory board of people living with MS to develop an online, 8-week intervention to attempt to increase physical activity. This intervention centers on how people become self-motivated to engage in activity in a way that sustained lifestyle changes occur. They will test the program in a controlled trial to see whether the treatment was effective and capable of inspiring lasting changes that increase individuals' activity levels.

How can people become self-motivated to engage in physical activity in a way that sustained lifestyle changes occur?

What's Next: Findings will generate an effective online intervention that promotes a physically active lifestyle among people with MS. A physically active lifestyle is important to control MS and to help manage individuals' overall health.

Dawn Ehde, PhD
University of Washington
Seattle, Washington
Award: Research Grants
Category: Restoring what's been lost
Term: 4/1/2018-3/31/2022 **Funding:** $879,991
Title: Mindfulness based Cognitive Therapy and Cognitive Behavioral Therapy for Pain in MS
Summary: Researchers are conducting a clinical trial testing two non-pharmacological approaches to managing pain in people with MS.

New Collaborative MS Research Award Stimulates Research On Healthy Aging in MS

Title: "Healthy Aging through LifesTyle in MS: The HALT MS Research Center "
Term: 4/1/18-3/31/23 **Grant Amount:** $816,557
Lead investigators: Robert W. Motl, PhD, Cynthia Brown, MD, Marcas Bamman, PhD, John Rinker, MD, Gary Cutter, PhD, James Rimmer, PhD, Univ. of Alabama at Birmingham

Background and details: The growing cohort of older adults with MS undergoes normal age-related declines in physical and psychological functioning that are seemingly compounded by the disease and its progression. Older adults with MS often report poor health status and functioning, depression, loneliness, cognitive difficulty, and that they depend on others for activities of daily living. This Center will facilitate collaboration among a core of six established UAB faculty members who work in MS, gerontology, or disability. The team has the express mission of stimulating interdisciplinary research on lifestyle and wellness for healthy aging in people living with MS. The HALT MS Research Center will attract investigators from diverse disciplines through interdisciplinary, collaborative pilot research grants.

Prof. Motl is the lead investigator, uniting members who will support transformative research on healthy aging with MS.:

- Dr. Cynthia Brown is a Professor of Medicine and Director of the Division of Gerontology, Geriatrics and Palliative Care at UAB. Her research has focused on mobility-related issues among older adults, including falls.
- Dr. Marcas Bamman is Director for the UCEM and the REACT Center. His work has focused on skeletal muscle and exercise biology.
- Dr. John Rinker is an Associate Professor of Medicine. He has interests in clinical trials in MS and mental health concerns.
- Dr. Gary Cutter is a Professor of Biostatistics at the UAB School of Public Health. He has substantial expertise in the design and analysis of clinical trials.
- Dr. James Rimmer is a Chair in Health Promotion and Rehabilitation Sciences. His focus is the use of technology for promoting physical activity in people with disabilities.

The center will engage in two general lines of research. The first aims to examine the factors that predict physical and psychological functioning, quality of life and disability and disease progression in older adults with MS. The second aims to use this information to determine the effect of behavioral interventions on physical and psychological functioning, quality of life, disability and disease progression in older adults with MS. This is an exciting opportunity for transforming the lives of older adults with MS through a collaborative, interdisciplinary focus on health, wellness, and successful aging.

Symptoms, Rehab, Wellness, cont. from p.21

Background: Chronic pain is one of the most prevalent, disabling, and persistent symptoms associated with MS, and current pharmacologic agents rarely provide complete relief. One non-pharmacologic approach to pain management, cognitive-behavioral therapy (CBT), has been shown to reduce pain intensity in people with MS. CBT focuses on reducing negative pain-related thoughts and coping behaviors. Another approach, mindfulness-based cognitive therapy (MBCT) integrates mindfulness meditation within a CBT-oriented framework to address not only unhelpful thoughts and behaviors but also attentional control, decoupling of attention from emotion, and meditative behavior.

The Study: Prof. Ehde's team is comparing MBCT, CBT, and "usual care" in adults with MS who have chronic pain. Both interventions will be delivered via groups (8 sessions) using video-conferencing. Pain intensity, pain interference, depression, fatigue, and sleep will be assessed before, during and after treatment, and six months later. Looking at pain severity, MS characteristics, and other factors thought to influence outcomes will help investigators identify who does best with which type of treatment.

What's Next: This study may provide important evidence for best options for managing MS pain.

Stefan Gold, PhD
Charité - Universitätsmedizin Berlin
Berlin, Germany
Award: Mentor-Based Postdoctoral Fellowships
Category: Restoring what's been lost
Term: 7/1/2018-6/30/2023 **Funding:** $414,685
Title: Neurobiological Mechanisms of Rehabilitation in MS

Summary: Researchers are training promising professionals to advance MS rehabilitation research by applying molecular biology techniques.

Background: MS symptoms such as fatigue, depression, and cognitive impairment have a major impact on quality of life. There is substantial evidence that these symptoms are related to both biological aspects of the disease as well as psychological factors, but few studies look at how biological and psychological factors in MS interact and whether rehabilitation strategies that improve MS symptoms also have the potential to change the underlying biology. To help tackle this question, this program is designed to train scientists to combine methods from neuroscience and rehabilitation.

The Study: The program is set up to attract young scientists with a doctorate in biology, neuroscience, or related fields to MS rehabilitation research. Dr. Gold has assembled a team of mentors and supervisors from neurology, neurorehabilitation, psychiatry, as well as molecular and cellular immunobiology, who will jointly train the fellows under his guidance. Fellows will receive advanced training in molecular biology and apply these techniques in their own research projects within the group's rehabilitation studies. Fellows will also receive in-depth training on designing and conducting MS studies.

What's Next: This mentor-based fellowship program will train scientists in cutting-edge methods from molecular biology and enable them to apply these to clinical research projects with relevance to improving quality of life through rehabilitation.

Symptoms, Rehab, Wellness, cont.

Audrey Hicks, PhD
McMaster University
Hamilton, Ontario, Canada
Award: Research Grants
Category: Restoring what's been lost
Term: 4/1/2018-3/31/2019 **Funding:** $96,500
Title: Exercise and Brain Health in MS
Summary: Researchers are investigating the impact of exercise on brain health in MS.

Background: Some MS symptoms are outwardly obvious, whereas other symptoms are less obvious, such as fatigue, depression, and cognitive impairment. As MS is an inflammatory disease that attacks cells in the brain (and spinal cord), it is possible that some of these invisible symptoms are related to the state of inflammation in the brain. This project will explore the effectiveness of an exercise intervention on inflammation and brain health.

The Study: Dr. Hicks's team will conduct a small trial to test the potential beneficial role of exercise in reducing symptoms associated with negative brain health. The team will evaluate symptoms before and after the exercise program, and take blood samples to measure factors that reflect inflammation.

What's Next: This project will set the stage for a larger study on the impact of physical activity on symptoms related to MS brain health.

Aaron Turner, PhD
University of Washington
Seattle, Washington
Award: Mentor-Based Postdoctoral Fellowships
Category: Restoring what's been lost
Term: 7/1/2018-6/30/2023 **Funding:** $401,426
Title: The Seattle Collaborative Fellowship

Summary: Researchers are training a series of promising professionals in how to conduct MS rehabilitation research.

Background: The VA MS Center of Excellence West and the University of Washington are jointly running a fellowship program in MS rehabilitation research. This "Seattle Collaborative Fellowship" has a dedicated team of professionals who have over 50 years of combined experience in MS research, examining psychosocial issues that impact the process of living well with illness and with quality of life.

The Study: The program emphasizes psychosocial aspects of MS, including such areas as self-management, health behavior change, depression, pain, fatigue and cognition. Fellows will develop training plans in coordination with their mentors. The plans will include research based on developing skills in clinical trials, the use of large administrative databases and the analysis, dissemination, and presentation of scientific knowledge. The goal is to train the next generation of MS rehabilitation researchers.

What's Next: This program will train scientists in cutting-edge methods and enable them to apply these to clinical research projects to improve quality of life through rehabilitation.

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