



# NEW RESEARCH

Newly Funded Projects/ Fall 2011

## \$16 Million for 32 New MS Research Projects

The National MS Society has just launched 32 new MS research projects representing multiyear commitments of \$16 million. These new projects are part of our comprehensive research program that will invest \$45.2 million in 2012 for new and ongoing research projects and Fast Forward partnerships aimed at stopping MS, restoring what's been lost, and ending MS forever.

The scope of this current launch is made possible by generous support of Society chapters and individual donors. When the National MS Society makes research commitments that span into future years, the money is not yet in hand to meet those needs. Contributions to the Society to help support these projects are essential to ensure that this important research proceeds in future years.

The new projects include explorations of new approaches to promote nervous system protection and repair; a clinical trial of a training technique to enhance cognitive function; and a study looking at how common bacteria that live in the human body might trigger immune attacks on the nervous system in MS. The new projects address research goals outlined in the Society's Strategic Response (page 10).

Following are brief summaries of the new research projects, grouped according to the categories of STOPPING, RESTORING, and ENDING.

### STOPPING MS

#### Tracking MS

To better understand the course of MS and factors that may influence that course, researchers are using advances in imaging and other techniques. This vital information may eventually be used to diagnose MS earlier, and to help track disease changes, either progression of disease, or improvements due to experimental treatments, before they are apparent clinically.

The Society has current, multi-year commitments of about \$8 million to support research projects focusing on ways of tracking disease activity in MS.

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## **Bart Rypma, PhD**

University of Texas SW Medical Center  
Dallas, TX

Chapter area: South Central

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$471,063

“Hemodynamic response function changes  
In multiple sclerosis” Developing ways to  
measure changes in blood flow in the brain  
due to MS lesions.

Cognitive problems – difficulties with remembering or processing information – are experienced by many people with MS. Although cognitive problems can cause substantial changes in the ability to deal with daily activities, relatively little is known about how tissue damage caused by MS contributes to the cognitive difficulties that people experience.

Bart Rypma, PhD, is using fMRI (functional MRI, a type of MRI that can measure changes in blood flow in the brain) to identify the neural factors that may contribute to MS-related cognitive problems. The study will involve 30 people who have MS and cognitive problems, 30 people with MS who do not have cognitive problems, and 30 people who do not have MS. Dr. Rypma and colleagues will compare the performance of the three groups on tests while changes in blood flow (hemodynamic response) are measured with fMRI, and correlate these with the extent of tissue damage revealed by MRI.

This research should improve our understanding of how MS damage contributes to cognitive deficits, and yield clues for treating this MS symptom.

## **Nancy Sicotte, MD**

University of California, Los Angeles  
Los Angeles, CA

Chapter area: So. California & Nevada/West

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$506,341

“Differential hippocampal vulnerability as a  
mechanism for major depression in MS”  
Looking for the underlying cause of MS-  
related depression.

Depression in its various forms is common during the course of MS and can have a major impact on quality of life, cognition, and long-term health. In previous studies of people with MS, Nancy Sicotte, MD, and colleagues found evidence of tissue loss in an area of the brain called the hippocampus, a region deep in the brain known to be important in memory processes.

Now Dr. Sicotte is using magnetic resonance imaging (MRI) to compare shrinkage of sub-regions of the hippocampus in four groups. The study includes people who have MS and are depressed, people with MS who are not depressed, people with major clinical depression from other causes, and a control group without MS or depression. Dr. Sicotte and colleagues are looking for correlations between the shrinkage of specific regions of the hippocampus, the level of cortisol (a stress hormone) in the blood, and the degree of depression.

These studies could help lay the groundwork for the development of therapies that will specifically target major depression in MS.

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## Sheng-Kwei “Victor” Song, PhD

Washington University

St. Louis, MO

Chapter area: Gateway Area/Midwest

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$485,100

“Noninvasive quantification of axon injury in EAE and MS” Testing a new imaging technique for its ability to provide a window to disease activity, damage and treatment in people with MS.

MS causes differing types and levels of damage to the brain and spinal cord in different people, but there is no way to directly identify or visualize the underlying disease activity. Standard MRI can pinpoint sites of inflammation in the brain but cannot differentiate areas of myelin or nerve fiber (axon) damage.

Sheng-Kwei “Victor” Song, PhD, has explored diffusion tensor imaging (DTI) to detect types of nervous system damage in rodents, but thus far, DTI hasn’t been able to consistently discern axon and myelin injury in people with MS. Dr. Song believes that inflammation complicates imaging with DTI. In this project, his team is exploring the newly developed “diffusion basis spectrum imaging” (DBSI) to overcome the interference of inflammation. They are using DBSI to detect inflammation, axonal injury, and myelin damage in mouse models of both progressive and relapsing MS. They are also testing DBSI in autopsied brain and spinal cord to see if their findings are translatable to people.

If successfully verified, DBSI may become an important tool for detecting MS damage and tracking its repair in future clinical trials.

Advances in imaging technologies are creating windows for watching disease activity, damage, and the results of therapies.

## RESTORING FUNCTION

### Psychosocial Issues

People with MS face daily challenges while coping with its unpredictable effects and symptoms. An important aspect of the Society’s research program is to understand how MS impacts psychosocial aspects of people’s lives — not only how it impacts those with the disease, but their family members and friends as well. About half of people with multiple sclerosis may experience some degree of cognitive dysfunction affecting the ability to think, reason, concentrate or remember.

One new project focuses on the social impacts of MS.

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## **Albert Lo, MD, PhD**

Brown University

Providence, RI

Chapter area: Rhode Island/Northeast

Award: Research Grant

Term/Amount: 10/1/11-9/30/13; \$713,735

"Multiple sclerosis: prevalence and social functioning by disease and subtype" A comprehensive study of the impact of MS on employment, interpersonal relations and daily living.

Because MS affects many functions of the nervous system and follows a variable course, it is difficult to predict what the disease will do to any individual. This uncertainty on how MS will affect people's lives is a major concern for many people with MS and their physicians.

Albert Lo, MD, PhD, and colleague Stephen Buka, ScD, are conducting a comprehensive study of how MS affects the social functioning of individuals in Rhode Island, (the Rhode Island MS Study, RIMSS). They will conduct extensive investigations to obtain an accurate count of all individuals in the state along with their fundamental demographic and clinical information. Later phases of the study will include interviews along with mental and physical testing with nearly 500 people newly diagnosed with MS to determine how MS affects important aspects of adult social functioning and quality of life.

This research project, which intends to follow people over a long period of time, should help identify treatable factors to positively influence the course of MS and provide insight on how independence and quality of life can be optimized.

## **RESTORING FUNCTION**

### **Rehabilitation**

Rehabilitation regimens that can help people with MS achieve maximal physical, psychological, social and vocational potential have gained increasing acceptance in recent years. But to convince doctors and insurers that rehabilitation really does help, there needs to be scientific evidence that can only come from carefully designed and conducted studies.

The National MS Society has current, multi-year commitments of over \$6 million to support research projects focusing on rehabilitation in MS, including mentor-based postdoctoral fellowships in rehabilitation research.

### **Nancy Chiaravalloti, PhD**

Kessler Foundation Research Center

West Orange, NJ

Chapter area: New Jersey Metro/Northeast

Award: Research Grant

Term/Amount: 10/1/11-9/30/12; \$62,519

"Speed of Processing Training for Improving Processing Speed in Persons with MS"

Testing the ability of a technique for improving cognition in people with MS.

Slowed speed of taking in and processing information is one of the most common problems in individuals with MS who have cognitive problems. These difficulties can have a significant negative impact on many aspects of everyday life and work, but to date few studies have attempted to treat processing speed difficulties to improve function in MS.

Nancy Chiaravalloti, PhD, and team are conducting a preliminary pilot clinical trial in 20 people with MS who have impairment

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in processing speed to test whether a training program shows signs of being beneficial. This program, called Speed of Processing Training, has been used successfully in other populations with this problem.

If the program appears to be beneficial in this pilot study, a larger clinical trial may be warranted to validate this training program's ability to reverse deficits that can have a profound impact on the lives of people with MS and their families.

**Matthew Plow, PhD**

Cleveland Clinic Foundation

Cleveland, OH

Chapter area: Ohio Buckeye/East

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$589,585

**Funded by the National MS Society's South Central Region**

"Evaluating the effects of physical activity and fatigue management strategies"

Developing methods for teleconferencing-based support to help people with MS manage fatigue and improve physical activity.

Many people with MS describe fatigue as one of their most disabling symptoms. MS fatigue can be chronic, severe, and it often interferes with the ability to maintain employment or engage in leisure activities. The reduced physical activity that results from MS fatigue can lower physical conditioning. This can lead to higher than normal levels of fatigue from normal activities of daily living, setting up a "vicious cycle" in which fatigue and physical inactivity enhance each other.

In this research project, Matthew Plow, PhD, is conducting a randomized controlled

**Rehabilitation can help restore function to people with MS. Gathering data on the best regimens is an important goal of this research.**

trial to see whether methods of fatigue management and increasing physical activity that are often provided by physical therapists at medical centers can be distributed with a series of teleconferences and phone interviews. Nearly 200 people with MS will be randomly assigned to one of three groups receiving support through teleconferencing: an educational program that combines fatigue management with physical activity promotion; a physical activity promotion program alone; or a standard support group. Activity and fatigue levels are being measured and compared among the groups.

This research could provide the basis for improving fatigue management and increasing physical activity in people with MS, particularly those who live far from major treatment centers.

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## About the Investigators

Read biographical sketches about each of these researchers starting on page 22.

### **Kathleen Zackowski, PhD, OTR**

Johns Hopkins University  
Baltimore, MD

Chapter area: Maryland/East

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$570,210

**Funded by the National MS Society's South Central Region**

“Predicting intervention responsiveness to improve rehabilitation in people with multiple sclerosis” Determining whether it is possible to predict the usefulness of exercise interventions in people with MS.

Multiple sclerosis is an inflammatory disease of the brain and spinal cord. The clinical course of the disease varies considerably from one person to another, depending in part on the location of tissue damage. Rehabilitation might help to restore function, but because MS is so variable, the details of how and why individuals are responsive (or not responsive) to rehabilitative interventions may be critical for identifying characteristics that are treatable.

Kathleen M. Zackowski, PhD, OTR, and a collaborating team of colleagues are performing a 12-week progressive resistive training intervention in a group of 30 people

with MS and 30 control subjects without MS. They are quantifying sensory and motor impairments, walking ability, and function before and after the intervention. They also are using a powerful MRI technique called diffusion tensor imaging before treatment to assess the integrity of two of the major motor (corticospinal) and sensory (dorsal column-medial lemniscus) tracts in the spinal cord and brain. The team is determining the extent to which combining quantitative information from sensory, motor and DTI tests can predict participants' responsiveness to progressive resistance training.

This novel study can help to determine which rehabilitation strategies are appropriate for specific individuals with MS.

### **STOP & RESTORE**

**Health Care Delivery/Policy Research to Improve Care Standards**

What if the cure were found today but insurers refused to pay for it? Access to high quality health care is one of many issues tackled by the Society's Health Care Delivery and Policy Research Program, providing data that can serve as the basis for influencing public policy and improving the quality of MS health care and the quality of life of people with MS and their families.

The National MS Society has current, multi-year commitments of about \$7 million to research projects focusing on health care delivery for people with MS.

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### **Eric Chamot, MD, PhD, MPH**

University of Alabama at Birmingham  
Birmingham, AL

Chapter area: Alabama-Mississippi/Southeast

Award: Healthcare Delivery & Policy Contract

Term/Amount: 10/1/11-9/30/12; \$80,960

“Unifying interpretation of clinical outcome measures of MS progression via IRT calibration” Developing methods to evaluate the impact of therapies intended to slow or prevent progression of MS.

A number of therapies that reduce the frequency of MS attacks have been developed in recent decades. But there are unmet needs for treating progressive MS. Clinical measures used in MS trials have limitations for accurately evaluating a person's disability. As novel strategies are being evaluated to prevent MS progression or nerve damage, current clinical measures may be inadequate for evaluating them.

In this research project Eric Chamot, MD, PhD, MPH, is using a form of measurement evaluation known as Item Response Theory (IRT) to combine and modify several current MS clinical scales to improve their utility for tracking MS progression. In consultation with MS experts and by tapping into patient databases, the team is in particular focusing on enhancing the MSFC (Multiple Sclerosis Functional Composite) scale, which numerically combines the results of three functional tests (walking speed, arm and hand dexterity and concentration and information processing speed).

The results of this research project could provide a set of measures that will be useful in speeding clinical trials of therapies designed to reduce or prevent progression of MS.

### **Eric Cheng, MD, MS**

University of California, Los Angeles  
Los Angeles, CA

Chapter area: So. California & Nevada/West

Award: Healthcare Delivery & Policy Contract

Term/Amount: 10/1/11-9/30/12; \$109,616

“The impact of cost-sharing among persons with multiple sclerosis” Calculating the amount of money paid out-of-pocket for health care by people with MS.

Even when they have health insurance, persons with MS report that they face financial barriers obtaining the health care they need., including treatment that may delay the onset of disability.

In this study, Eric Cheng, MD, MS, and a team of neurologists, physicians who study health care, and a health economist will calculate the amount of money paid for health care among persons with MS compared to persons without MS. The team is analyzing data collected in the Medical Expenditure Panel Survey (MEPS), conducted annually by the government on a random sample of 15,000 households in the U.S. MEPS collects demographic characteristics, health conditions, use of medical services, charges and source of payments, access to care, satisfaction with care, health insurance coverage, employment and other factors. The team is analyzing whether the amount of out-of-pocket costs paid by patients in a given year affects how much health care they receive in the following year, and whether that relationship is different among persons with and without MS.

Study results should help inform advocacy efforts aimed at ensuring that people with MS receive the health care that they need.

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## **Sarah Minden, MD**

Brigham and Women's Hospital  
Boston, MA

Chapter area: Grtr. New England/Northeast

Award: Healthcare Delivery & Policy

Contract

Term/Amount: 10/1/11-9/30/13; \$329,613

"The impact of out of pocket health-related costs on people with MS and their families"

A detailed analyses of what people with MS spend on out-of-pocket health care costs and how this affects care and quality of life.

Although most people with MS have at least some health insurance, many are at risk of losing it, or find that their insurance does not pay for a sizable portion of their health care costs. Out-of-pocket healthcare costs create a substantial burden for many people with MS and their families.

In this study, Sarah Minden, MD, and colleagues are examining data from the National MS Society-funded Sonya Slifka Longitudinal MS Study to provide a detailed and coherent picture of the extent, nature, and impact of out-of-pocket costs. The team is examining whether costs are different between subgroups of patients and trying to identify factors that contribute to differences in costs. They are also assessing the impact of costs on overall and MS-specific health status and quality of life.

These data will support the Society's advocacy efforts and help inform people with MS and their families and healthcare providers. They will also provide evidenced-based guidance for making good decisions on health care spending, particularly on the negative impact of delaying or foregoing care and treatment.

## **Sarah Shoemaker, PharmD, PhD**

Abt Associates Inc.

Cambridge, MA

Chapter area: Grtr. New England/Northeast

Award: Healthcare Delivery & Policy

Contract

Term/Amount: 10/1/11-9/30/12; \$85,403

"Medication quality and safety in multiple sclerosis" Examining the quality and safety of medication use in MS populations.

Since medications help people manage MS, it is important to understand their use and safety. The aim of this study by Sarah J. Shoemaker, PharmD, PhD, is to use the Sonya Slifka Longitudinal MS Study data to examine the use of disease-modifying therapies, and other prescription, non-prescription medicines, and complementary and alternative medicines used by people to control their MS and symptoms. She is collaborating with Dr. Alyssa Pozniak, an Associate/Scientist at Abt, who has worked on the Slifka Study and a financial modeling study of MS medical care.

The team is looking at the safety of medication use in people with MS and in sub-groups such as by age, race, ethnicity, and length of diagnosis. For example, to assess safety the team will look at potential drug interactions and interactions between prescribed and complementary medicines that could cause serious side effects. The team will also look at the quality of medication management in MS.

This study will help to identify potential problems in medication management and identify groups of persons with MS that may be at greater risk for certain problems, and set the stage to consider solutions that will ensure medicines are effective and safely used by people with MS.

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## STOPPING MS

### Why the Immune System Goes Awry

The current therapies for MS emerged from our growing understanding of how the immune system works and how it can be manipulated to suppress or regulate immune attacks. We especially need to know more about the molecules that the immune system uses to attack the nervous system, because each of these serves as a potential therapeutic target for new therapies.

The National MS Society has current, multi-year commitments of about \$30 million to support research projects focusing on stopping the immune system attack in MS.

#### **Stefan Brocke, MD, PhD**

University of Connecticut Health Center  
Farmington, CT

Chapter area: Connecticut/Northeast

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$612,252

“The Role of PDE8 in EAE” Investigating a new way to potentially prevent the immune system attack that damages the nervous system in a model of MS.

The initial symptoms of MS result from an attack by immune system cells that damages and destroys myelin in the brain and spinal cord. Myelin surrounds and protects nerve fibers, which are also damaged in MS. In order to attack myelin, immune system cells have to move out of the blood stream and leave the blood vessels that run through the brain and spinal cord, and enter into the surrounding tissue causing injury.

In this research project, Stefan Brocke, MD, PhD, is testing the effects of a new drug that inhibits the action of a relatively recently discovered molecule known as

phosphodiesterase 8 (PDE8) in EAE, an MS-like disease. PDE8 is one of several molecules involved in the movement of immune system cells and could play a role in their accumulation in the brain and spinal cord leading to the immune system attacks in MS. Dr. Brocke and his colleagues are working to see whether blocking the action of PDE8 will limit or stop the activity of immune system cells in EAE, as a prelude to its potential testing in MS.

The results of this research project could provide clues for the development of new treatments to stop the immune system attack in its tracks in people with MS.

#### **Robyn Klein, MD, PhD**

Washington University

St. Louis, MO

Chapter area: Gateway Area/Midwest

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$557,305

“Cytokine control of homeostatic chemokines within during CNS autoimmunity” Exploring the roles of immune messengers that can rev up and attract immune activity to specific areas of the brain in MS-like disease.

In MS, immune cells mistakenly attack and destroy the myelin sheaths on nerve fibers, and the nerve fibers themselves are also damaged. One aspect of disease activity is the breakdown or leaking of the blood-brain barrier (BBB), which occurs at blood vessels in the brain and spinal cord (central nervous system, or CNS). The BBB usually prevent immune cells from gaining inappropriate access to the CNS with the use of proteins that prevent immune cells from entering.

In this project, Robyn Klein, MD, PhD, and colleagues are examining what goes wrong

## National MS Society Research Facts

The National MS Society is committed to freeing the world of MS. Our global support of MS research and treatment focuses on three key areas: STOPPING the progression of the disease, RESTORING function that's been lost, and ultimately ENDING MS forever.

We do this by:

- Funding the most promising avenues
- Engaging the best and brightest minds
- Acting as a vital connector for people, resources and ideas
- Developing more and effective treatments faster
- Identifying and filling gaps in MS research

### Research Objectives Outlined in Our Strategic Response to MS 2011-2015

- We better understand the scientific mechanisms that lead to disease progression and we accelerate the development of new therapies.
- We pursue new avenues to discover how nerve cells are damaged and potentially repaired.
- We pursue new rehabilitation techniques and symptomatic treatments to restore neurological function and enhance quality of life.
- We identify risk and triggering factors that cause MS, and understand the biological interactions that lead to its development so that MS can be prevented.
- We expand and strengthen the quantity and quality of MS research worldwide to accelerate new discoveries and treatments for people with MS.

### Society Research Spending:

\$45.2 million in 2012 for research projects and Fast Forward partnerships

### Cumulative Investment:

\$761 million since first 3 grants in 1947

### Major Types of Society Research Support:

Grants: multiyear investigations by university-based scientists for basic and clinical research

Collaborative Centers: 5-year awards to teams joining together for the first time to work together on MS research projects

High risk/high potential Pilot grants: one-year awards to test innovative, cutting-edge ideas

Industry Partnerships: milestone-driven drug development funding for private companies

Fellowships: to attract and train promising investigators and doctors to focus on MS

Rehabilitation Research Fellowships: to meet the unmet need for specialists trained to conduct quality rehabilitation research

Health Care Delivery and Policy Contracts: to inform advocacy efforts and enhance quality of life for people with MS

**Our Research Fundraising Goal: We will raise \$250 million for MS research by 2015**

Learn more about NOW — An MS Research Revolution: [nationalmssociety.org](http://nationalmssociety.org)

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at the BBB during immune responses, and how immune cell proteins alter its permeability. The team is using several state-of-the-art approaches with genetically engineered mice to gain specific information about the roles of immune proteins and messengers that can rev up and attract immune activity to specific areas. The team is also looking at how immune cell proteins affect the barrier in different brain regions, causing inflammation and lesions at different sites.

This series of studies should more clearly define the processes that drive inflammation in different areas of the brain and spinal cord, and guide strategies for stopping inflammation in specific regions in MS.

**M. Edward Medof, MD, PhD**

Case Western Reserve University  
Cleveland, OH

Chapter area: Ohio Buckeye/East

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$540,201

“Modifying effector and regulatory cells in EAE by controlling local complement”

Exploring a newly discovered aspect of immune activity that may lead to development of new strategies to stop immune attacks in MS.

MS is known to involve misdirected immune attacks against the brain and spinal cord. Some immune cells inflame the attack while others can turn it off. Over the last few years regulatory T cells have been shown to be capable of turning off the attack, and for some reason these are not adequately functioning in MS.

M. Edward Medof, MD, PhD, and colleagues have uncovered a previously

unrecognized process that plays a central role in immune responses involving regulatory T cells. The team has recently learned how to shut down immune responses that are connected with autoimmune attacks in models of MS. In this study, the team will further characterize this process in different models of MS and explore its activity in blood samples from people with MS to determine whether they can apply this methodology to slow or even stop disease progression in MS.

Their results, if successful, would represent a new approach for suppressing disease in people with MS.

**Gabriel Rabinovich, PhD**

Universidad de Buenos Aires

Buenos Aires, Argentina

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$412,010

“Capitalizing on glycomics for the design of novel therapeutic strategies in MS”

Designing and testing a novel therapy aimed at turning off immune attacks such as those involved in MS.

In multiple sclerosis, immune cells attack the brain and spinal cord, destroying the protective sheath (myelin) that surrounds nerve fibers and leading to progressive disability. The disease is believed to be initiated and aggravated by aggressive cells that cause damage (T cells) and is controlled by suppressive cells (called regulatory T cells) which counteract pathogenic T cells and silence harmful inflammation.

A new field is emerging thanks to emerging technology (called glycomics) that has enabled investigation of sugar structures that may influence biological processes.

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Gabriel Rabinovich, PhD, and colleagues have recently demonstrated that galectin-1 (a protein that binds to sugars, which is found at sites of brain injury and inflammation) can selectively bind to and destroy aggressive T cells. They have observed that distinct populations of immune cells have different sugar structures on their surfaces, and now the team is studying these differences on the surfaces of aggressive immune cells versus those that can calm immune attacks. They aim to capitalize on this information for the design of novel therapeutic agents that will be tested in a mouse model of MS and in immune cells isolated from MS patients.

This research may lead to a novel strategy for stopping MS in its tracks.

### **Richard Ransohoff, MD**

Cleveland Clinic Foundation

Cleveland, OH

Chapter area: Ohio Buckeye/East

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$434,167

"Monocytes and microglia in EAE"

Differentiating the role of specific brain cells that contribute to both nervous system damage and repair, for clues to stopping MS and restoring function.

MS is known to involve immune system attacks against the brain and spinal cord, but the sequence of events and immune cells involved in the ensuing damage are not completely clear. A type of immune cell can be found in lesions, or spots of damage/disease activity, and such cells can either cause damage or help repair tissue, so distinguishing these roles is an important goal. In the bloodstream, these cells are called monocytes, and in the inflamed brain, they are called as microglia or macrophages.

Microglia enter the central nervous system during early development stay within the brain or spinal cord thereafter. Macrophages originate in the blood. Once both cells are participating in the destruction of nervous system tissues, they can't be told apart.

In this project, a team led by Richard M. Ransohoff, MD, is using newly available genetic models to distinguish these two similar but distinct cell types and their respective roles in the nervous system damage that occurs during the MS-like disease EAE in mice. They will address, for the first time, how each cell participates in tissue damage and – importantly -- tissue repair.

This novel approach should lead directly to effective new therapeutic approaches to stop damaging disease activity in MS.

### **Anthony Reder, MD**

University of Chicago

Chicago, IL

Chapter area: Greater Illinois/Midwest

Award: Research Grant

Term/Amount: 10/1/11-9/30/15; \$845,350

"Interferon resistance in MS" Evaluating how immune system signals may serve as biomarkers of future disease activity.

MS involves an immune system attack on the brain and spinal cord. Inflammation can be suppressed by interferon (IFN-beta) therapy, currently approved for the treatment of MS. Anthony Reder, MD, and colleagues have found that, before any therapy, immune cells from people with MS have abnormal, low responses to interferon. This deficiency becomes worse during the progressive stages of MS.

Dr. Reder's team is now studying mechanisms of how IFN signaling becomes abnormal in people with different forms of

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MS. They are also using cutting-edge technology to analyze the genes that are involved in IFN signaling in patients to determine what might cause abnormalities, and then to analyze whether signals are related to future disease activity.

This research may define new biomarkers to help with early diagnosis, to predict future attacks, and to help predict how patients will respond to interferon therapy.

### **Jack Strominger, MD**

Harvard University  
Cambridge, MA

Chapter area: Grtr. New England/Northeast

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$466,814

“Targeting the J5 peptide 15mer to dendritic cells for therapy of demyelinating diseases”

Investigating a substance related to Copaxone that may improve treatment of MS.

In MS, cells of the immune system attack, damage, and destroy myelin, the material that surrounds and protects nerve fibers, in the brain and spinal cord. The immune system consists of a number of cell types, some of which enhance an attack, while others can suppress immune activity. Copaxone, one of the injected drugs currently used to treat MS, appears to increase the number of regulatory immune cells that act to suppress the attack on myelin.

In this project a team led by Jack Strominger, MD, is studying the effects of a molecule known “J5 peptide 15mer” (J5) that is similar in some ways to Copaxone, but has a defined sequence and is much smaller in size. This molecule can stimulate dendritic cells -- immune system cells that activate

other immune cells -- to produce the regulatory cells that shut off immune attacks. The team is using mice with EAE, a model of MS, to find the most effective ways to target J5 to the immune system to block the disease.

The results of this research could lead to the development of a therapy with the potential to require much smaller amounts of drug and much less frequent injections to more effectively inhibit MS immune attacks.

### **Jenny Ting, PhD**

University of North Carolina at Chapel Hill  
Chapel Hill, NC

Chapter area: Eastern NC/Southeast

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$526,789

“The roles of new innate immune mediators in neuroinflammation” Studying new ways to prevent the immune system from attacking myelin in animal models of MS.

In MS, immune cells mistakenly attack myelin, the material that surrounds and protects nerve fibers, in the brain and spinal cord. The immune system has a number of different cell types that interact to either turn an immune response, such as inflammation, on or off. Some immune cells have “pathogen sensors” that recognize portions of triggers – such as viruses or bacteria – inducing the cells to launch an attack against the pathogen. The pathogen sensors on some immune cells may contribute to the attack in MS. More recent data suggest that these sensors are also important during “sterile inflammation” where inflammation occurs despite the absence of microbes. This type of inflammation is important in an array of autoimmune disorders.

## Convening Experts

The National MS Society speeds progress in research in part by working globally with partners such as the MS International Federation, ECTRIMS, and others to explore new opportunities. One way is to convene experts from different fields to focus on particular topics. Recent and upcoming conferences include:

- International Conference on Disability Outcomes in MS, 6/11  
Map out steps for developing better tools to gauge success of clinical trials.
- Tykeson Fellows Conference, 11/11  
Convene trainees from the U.S. and Canada to solidify their commitment to studying and treating MS.
- International Workshop on Vitamin D and MS Prevention, 12/11  
Begin to explore the design of an MS prevention trial.

Jenny Ting, PhD, and colleagues were among the teams that first described the NLR pathogen sensors. Now they are studying them further in two models that mimic MS. In one model, the MS-like disease is caused by an immune attack and in the other, a process of myelin damage followed by myelin repair is induced by a neurotoxin.

The results of this research should lead to better understanding of processes that trigger immune attacks in MS, and offer new targets for developing therapies to better turn off those attacks.

## RESTORING FUNCTION

### Nervous System Repair

Decades of research into nerve physiology and the biology of myelin and glial cells that support nerve cells have been laying the groundwork for finding ways to restore normal function in individuals with MS.

The National MS Society has current, multi-year commitments of about \$13 million to support research projects focusing on finding ways to repair the nervous system and restore lost function in people with MS. In addition, our \$15 million investment toward understanding myelin growth, function and repair (described in the next section) also feed this effort.

### David Baker, PhD, DSc

Barts and The London, Queen Mary's School of Medicine & Dentistry  
London, United Kingdom

Award: Research Grant

Term/Amount: 10/1/11-9/30/13; \$384,064

“Engineered precursors as a delivery mechanism for neuroprotective therapies”

Developing a new strategy to deliver a myelin-repair therapy to protect the nervous system from MS damage.

MS involves an immune system attack that destroys myelin, the protective material that surrounds nerve fibers in the brain and spinal cord. Nerve fibers are damaged as well, contributing to disability. Current therapies for MS reduce immune system attacks and slow disease progression, but their impact on the long-term progression of damage is less clear. Repairing damaged myelin may reduce or prevent long-term damage to nerve fibers, but molecules that may enhance myelin

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repair are difficult to get into lesion areas.

In this research project, David Baker, PhD, DSc, is attempting to develop a new method to deliver molecules that enhance myelin repair to the brain and spinal cord. Dr. Baker and colleagues are modifying oligodendrocyte precursor cells (OPCs, the cells that develop into myelin-making cells) so that they release substances that enhance myelin repair. They are testing whether these modified OPCs are capable of enhancing myelin repair in cells grown in the laboratory, as a prelude to future testing in mice and if promising, eventually in people with MS.

This work could lay the groundwork for new ways to deliver therapies to areas of damage and protect against nervous system damage in MS.

**Christopher Bever, MD, MBA**

University of Maryland

Baltimore, MD

Chapter area: Maryland/East

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$495,000

“Combination therapy with interferon beta and brain derived neurotropic factor in experimental allergic encephalomyelitis”

Studying an experimental combination therapy for its ability to slow or halt long-term nerve damage in an animal model of MS.

Cells from the immune system damage and destroy myelin, the protective material surrounding nerve fibers, in the brain and spinal cord of people with MS. Nerve fibers are damaged as well. Current treatments for MS limit the number and severity of immune system attacks, but do not completely prevent nerve fiber damage.

In this research project, Christopher Bever, MD, MBA, is studying whether combining a substance known as brain derived neurotropic factor (BDNF) with interferon beta, one of the current MS treatments, will prevent or slow nerve fiber damage in mice with EAE, an MS-like disease. In laboratory studies, BDNF can slow or halt the degeneration of nerve fibers, encourage their regrowth and enhance the repair of their myelin coating. Dr. Bever and colleagues hope that the combination of interferon beta and BDNF will prevent both the immune system damage to myelin and the degeneration of nerve fibers.

If this combination is effective in mice, it could pave the way for the testing of this treatment combination aimed at neuroprotection in people with MS.

**Steven Goldman, MD, PhD**

University of Rochester Medical Center

Rochester, NY

Chapter area: Upstate New York/Northeast

Award: Research Grant

Term/Amount: 10/1/11-9/30/15; \$851,630

“Molecular determinants of human glial progenitor cell-based remyelination”

Studying human myelin repair cells in action for clues to stimulating nervous system repair in MS.

MS targets and damages myelin, the sheath that encases nerve fibers and supports nerve transmission. One strategy to protect the underlying nerve fibers is to repair myelin. It is difficult to study myelin repair and manipulate myelin-making cells (oligodendrocytes) in people. To address this problem, Steven A. Goldman, MD, PhD, and colleagues have established methods

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for extracting progenitor, or immature, oligodendrocytes from human brain tissue and transplanting them in mice. They have shown that transplanting oligodendrocyte progenitors into these mice results in almost complete restoration of their previously lost neurological function.

In this project, Dr. Goldman's team is following up on studies conducted in the context of the Society's Promise: 2010 Nervous System Repair initiative. They are using this innovative "humanized" model to further manipulate and understand the behavior of human progenitors during the process of repeated myelin damage and myelin repair, similar to what occurs in MS.

The ability to study the behavior of human progenitor cells in the process of myelin destruction and repair will provide novel information that should better inform potential repair therapies for people with MS.

### **Alexander Gow, PhD**

Wayne State University  
Detroit, MI

Chapter area: Michigan/Midwest

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$775,675

"Akt signaling in stressed oligodendrocytes"  
Investigating factors that lead to the destruction of myelin-making cells, for clues to inducing repair.

Oligodendrocytes are the cells that make myelin, the sheath that supports and insulates nerve fibers. In MS, an immune response that normally targets only harmful invaders, such as bacteria, instead targets myelin and leads to its destruction and also to the eventual death of oligodendrocytes. The underlying nerve

fibers are also damaged.

The exact mechanism underlying the loss of oligodendrocytes in MS is unknown, but Alexander Gow, PhD, hypothesizes that "metabolic stress" may trigger pathology in oligodendrocytes that leads to the immune system attacking myelin. As a result, an automated sequence of events that causes the cell to self-destruct (known as "apoptosis") becomes activated. Dr. Gow's team has identified genes and proteins that may be important in this process. They are now investigating these genes and proteins in a mouse model to determine their effects on oligodendrocyte function. The eventual goal is to develop therapies that reduce the metabolic stress and halt the disease process.

Finding a way to interrupt the loss of oligodendrocytes in people with MS may help preserve their natural ability to repair myelin and reverse symptoms.

### **Akiko Nishiyama MD, PhD**

University of Connecticut  
Storrs Mansfield, CT

Chapter area: Connecticut/Northeast

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$591,645

"Promoting remyelination from endogenous NG2 cells" Looking for ways to enhance repair of damaged myelin in an animal model of MS.

MS involves an immune system attack that damages and destroys myelin, the material that surrounds and protects nerve fibers, in the brain and spinal cord. The cells that manufacture and repair myelin, oligodendrocytes, are also lost in this attack. When their myelin sheath is lost, nerve fibers fail to carry signals properly,

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and eventually they die, causing long-term deficits. There are cells in the adult nervous system that can develop into new oligodendrocytes and naturally repair damaged myelin, but they fail to keep up with the damage in MS.

In this research project Akiko Nishiyama, MD, PhD, is studying NG2 cells, which are found throughout the brain and spinal cord and are capable of developing into new oligodendrocytes. Dr. Nishiyama and her colleagues use a method that allows them to follow the stages of development of the NG2 cells as they change into oligodendrocytes and form new myelin in mice with EAE, a model of MS. They are attempting to find molecules that enhance the transformation of NG2 cells into oligodendrocytes, and increase the amount of myelin repair.

This research could lead to new ways to speed the repair of myelin and reduce the damage to nerve cells in MS.

## **RESTORING FUNCTION**

### **Myelin's Growth, Injury and Repair**

Myelin insulates the wire-like extensions of nerve cells, speeding nerve conduction and protecting the nerve from harm. Because myelin is thought to be the main target of the immune attack that underlies MS, it's vital that we understand its development, function and repair.

The National MS Society has current, multi-year commitments of about \$15 million to support research projects focusing on myelin biology in MS.

### **Manzoor Bhat, PhD, MedScD**

University of North Carolina at Chapel Hill  
Chapel Hill, NC

Chapter area: Eastern NC/Southeast

Award: Research Grant

Term/Amount: 10/1/11-0/30/14; \$621,344

“Disorganization and re-organization of axonal domains in myelinated axons”

Studying changes in nerve fiber structure that affect the function of nerves for clues to preventing disability in MS.

MS involves an attack by immune system cells directed against myelin, the material that surrounds and protects nerve fibers (axons) in the brain and spinal cord. When myelin is damaged, axons fail to carry nerve signals correctly, resulting in neurological symptoms. Unlike the smooth insulation around an electrical wire, myelin is distributed in clumps along axons with short regions known as the nodes of Ranvier between successive clumps, giving the appearance of a string of sausages. Myelin damage disturbs the organization of the nodes and the flanking regions, contributing to changes in nerve function.

In this research grant, Manzoor Bhat, PhD, is studying mice that have been genetically modified to make them deficient in key proteins that contribute to the organization of the nodes and related regions in myelinated axons. This will allow investigations to understand the processes of how the axonal domains are organized and how these proteins affect the function of axons when myelin is damaged.

This could lead to important clues about how to prevent nodal disorganization or treat the impacts of axon degeneration that leads to neurological deficits in MS.

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**Jonah Chan, PhD**

University of California, San Francisco  
San Francisco, CA

Chapter area: Northern California/West

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$680,625

“Initiating myelination: a matter of membrane curvature” Using advanced technology to understand how myelin forms, for clues to its repair.

Multiple sclerosis involves an immune attack against myelin, the substance that surrounds nerve fibers. When myelin is damaged, nerve fibers fail to conduct impulses properly, leading to neurological symptoms. Nerve fibers are damaged as well in the attack, leading to disability. It is extremely important to broaden our understanding of how myelin develops and is formed, in order to decipher potential therapeutic targets for myelin repair.

Jonah Chan, PhD, and colleagues have shown that signals from myelin proteins can determine how myelin wraps around the nerve fiber. His team is using advanced technology to study how this occurs, such as nerve fibers engineered in the laboratory and advanced imaging capable of providing great structural details of these tiny proteins.

Understanding myelin formation can yield vital clues to ways to stimulate myelin repair to restore function to people with MS.

**Susan Gauthier, DO, MPH**

Cornell University Medical College  
New York, NY

Chapter area: NYC-Southern NY/Northeast

Award: Research Grant

Term/Amount: 10/1/11-9/30/15; \$623,985

“Developing a quantitative imaging biomarker for remyelination in multiple sclerosis” Investigating a method of measuring myelin repair in people with MS, which may be useful for tracking repair during clinical trials.

In MS, the myelin that surrounds the nerves in the brain and spinal cord is damaged. Myelin enables nerves in the brain and spinal cord to efficiently transmit their signals. With the loss of myelin and damage to underlying nerve fibers, people with MS experience loss of neurological function. As agents that could potentially repair myelin are developed, tools to measure the benefit of these novel therapies on myelin health are needed.

Susan Gauthier, DO, MPH, and a team of collaborators are attempting to develop such a tool utilizing an MRI technique called T2 relaxometry. Individuals would only have to spend an additional five minutes in the MRI machine to complete this test. Dr. Gauthier is developing specific methods for using T2 relaxometry, and studying its ability to detect myelin change in rodents with myelin damage. Then the team is testing its ability to detect differences between people with MS and controls without the disease.

Study results should help facilitate the translation of novel therapies that can restore function in people with MS.

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**Jianrong Li, PhD**

Texas A&M University

College Station, TX

Chapter area: South Central

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$402,478

“Role of astroglial galectin-9 in CNS demyelination and remyelination”

Investigating a molecule that may contribute to myelin damage, for clues to repair strategies in MS.

The primary targets of the immune attack in MS are myelin – the substance that surrounds nerve fibers -- and oligodendrocytes – the cells that make myelin. The major players in this attack are immune T cells, but Jianrong Li, PhD, and colleagues propose that abnormal regulation of other brain cells, such as microglia and astrocytes, occurs early and contributes to the development of MS.

This team has found that astrocytes produce galectin-9, a protein that enhances production of inflammatory immune messenger proteins. They observed high levels of galectin-9 in astrocytes in areas of damage in MS models and in tissue from people with MS. Now Dr. Li’s group is using genetically modified mice and an animal model of myelin damage to investigate the specific impact that galectin-9 has on myelin destruction.

This study should offer new insight into what causes myelin damage, and provide clues for new strategies to promote repair and restore function in people with MS.

**Decades of Society-  
supported research have  
been laying the  
groundwork for finding  
ways to restore function in  
people with MS**

**Pablo Paez, PhD**

University of California, Los Angeles

Los Angeles, CA

Chapter area: So. California & Nevada/West

Award: Research Grant

Term/Amount: 10/1/11-9/30/13; \$471,291

“Modulation of oligodendrocyte function and myelination by the golli proteins”

Studying ways to enhance the manufacture and repair of myelin in an animal model of MS.

In MS, repeated immune attacks damage the nerve fiber-insulating myelin in the brain and spinal cord. Nerve fibers are also damaged, and many believe that rebuilding their myelin coating will protect them and restore function. An important aspect of MS is the gradual failure of oligodendrocytes (myelin-making cells) to naturally generate new myelin. Immature oligodendrocytes are present in the brain, but fail to develop into mature cells to fully repair the damaged myelin in people with MS.

Pablo M. Paez, PhD, and colleagues are studying “golli” proteins, which are produced by both the immune system and by

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oligodendrocytes; thus, golli may be involved in MS-related immune mechanisms and may also be instrumental in the manufacture of myelin. They are investigating how golli proteins regulate the amount of calcium in oligodendrocytes. Calcium levels influence the development of immature oligodendrocytes, the survival of oligodendrocytes and their ability to make myelin. Dr. Paez and colleagues are using genetically modified mice to determine the effects of excess or lack of golli proteins on myelin repair in a model of MS.

The results of this research could lead to new ways to repair myelin and restore function to people with MS.

### **Barbara Ranscht, PhD**

Burnham Institute for Medical Research  
La Jolla, CA

Chapter area: Pacific South Coast/West

Award: Research Grant

Term/Amount: 10/1/11-9/30/15; \$754,279

“Contactin functions in oligodendrocyte-mediated myelination and remyelination”  
Exploring a key molecule that influences the formation and repair of nerve-insulating myelin, for clues to restoring myelin in MS.

Disruption of myelin, the supportive casing that surrounds nerve fibers (axons), during immune attacks on the brain and spinal cord in MS results in a variety of disabling symptoms. Myelin is formed by cells called oligodendrocytes. Myelin formation and function require continuous “cross-talk” between oligodendrocytes and the contacted axons. Understanding the molecular language of this communication is critical for identifying molecular targets for treatments aimed at preserving myelin in MS and achieving repair.

Barbara Ranscht, PhD, is studying Contactin, a cell surface molecule on nerve cells and oligodendrocytes that has emerged as a key signal involved in neuron-glia communication in myelin. Recent studies in her lab suggest that Contactin is involved in regulating maturation of oligodendrocytes and myelin formation. Her team has generated a new mouse genetic model that allows teasing out of Contactin’s role in oligodendrocytes.

Dr. Ranscht’s project will clarify the role of Contactin as a contributor to the development and function of myelin. If successful, this work will form the basis for developing strategies that protect neurons and foster myelin repair in MS.

### **ENDING MS FOREVER**

#### **Seeking Risk Factors**

Because MS is thought to occur in people whose genes make them susceptible, researchers have been exploring the possibility that viruses or bacteria could act as disease triggers for MS. Other factors, such as exposure to sunlight or something else in the environment, could also play a role. The Society has multi-year investments totaling about \$10 million in research projects focusing on these questions. This includes \$2 million in epidemiology studies, over \$5 million in studies focusing on identifying MS genes, and nearly \$3 million on projects focusing on identifying possible infectious triggers.

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**Robert Clark, MD**

University of Connecticut Health Center  
Farmington, CT

Chapter area: Connecticut/Northeast

Award: Research Grant

Term/Amount: 10/1/11-9/30/14; \$650,846

“Novel bacterial lipids of commensal organisms promote EAE” Looking at how lipids from bacteria that live in humans might trigger the immune system to attack myelin in MS.

The immune system normally protects against infectious agents, such as viruses or bacteria, by attacking and destroying them. In MS, however, immune system cells attack myelin, the material that surrounds and protects nerve fibers. Similar immune system cells, potentially capable of attacking myelin, are found in people who do not have MS. An important question is what causes the cells to attack myelin in people with MS but not in others.

In this research project, Robert Clark, MD, is studying a class of lipids (fatty substances) produced by bacteria in the human body. Each person has millions of harmless bacteria, known as "commensal" bacteria, living inside of them. Dr. Clark and colleagues have found that some lipids produced by these bacteria increase the severity of EAE, an MS-like disease, in mice. Now they are looking at the precise molecular pathways by which these lipids affect EAE, and whether specific patterns of the lipids are unique in blood and spinal fluid taken from people with MS.

This research could shed new light on the question of what triggers the immune system to attack myelin, and could lead to new treatments that slow or prevent the attack in MS.

**Thomas Aune, PhD**

Vanderbilt University  
Nashville, TN

Chapter area: Mid South/Southeast

Award: Research Grant

Term/Amount: 10/1/11-9/30/13; \$300,000

“Genome copy number variants in multiple sclerosis” Understanding how alterations in DNA may contribute to a person’s susceptibility to MS and their role in spurring immune attacks.

Although the origins of MS are incompletely understood, there is clearly a genetic contribution. Genetic studies thus far suggest that additional genetic variants exist that may explain the genetic basis of susceptibility to MS. The idea to be tested in this project is that these additional genetic variants are DNA amplifications and deletions in the human genome, called copy number variations (CNV), and are specifically associated with MS. Since CNV are large, they can cause either an increase or decrease in the levels of message, or transcription, of genes within CNV areas, and may thus produce changes that could increase the likelihood of developing MS.

Through a pilot grant funded by the National MS Society, Thomas Aune, PhD, and team has identified specific CNVs in people with relapsing-remitting MS. In this project, they are evaluating the presence or absence of these CNVs in other forms of MS including primary-progressive, secondary-progressive, and other diseases. They also are studying the impact of these CNVs have on immune activity that may contribute to the disease.

Knowledge of the CNVs that are associated with MS will contribute to efforts to prevent MS and sharpen the ability to identify potential therapeutic targets.

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## ABOUT THE INVESTIGATORS

**Thomas Aune, PhD**, is Professor of Medicine in the Division of Rheumatology at Vanderbilt University School of Medicine. He began his distinguished career with a PhD in biochemistry from the University of Tennessee in Memphis. He was Assistant Professor in the Pathology Department of Washington University in St. Louis before moving into industry, first as a scientist at Genentech in South San Francisco, and then as a Senior Staff Scientist and Head of the Immunology Section at Miles, Inc. in West Haven, CT. He moved back to academia in 1995 as an Associate Professor at Vanderbilt. Has served as a scientific peer reviewer for the NIH, and is on the editorial board of *Personalized Medicine*.

**David Baker, PhD, DSc**, is a Professor of Neuroimmunology at Queen Mary University of London (United Kingdom). He received his PhD in Immunology/ Pathology at the Hunterian Institute, University of London. Dr. Baker was a member of Dr. Gavin Giovannoni's Nervous System Repair and Protection team, funded by the National MS Society. Dr. Baker has served on the MS Society (United Kingdom) Grant Review Panel for the past five years. His research interests include the development of animal models that better represent progressive MS. His present research involves developing engineered myelin-making cells ultimately to test their therapeutic utility in models of demyelination and MS.

**Christopher Bever, MD, MBA**, is a highly regarded Professor of Neurology at the University of Maryland, Associate Chief of Staff for Research and Development at the

Baltimore Veterans Administration Medical Center, and Director of its MS Center of Excellence, East. He earned his medical degree with Distinction in Research at the University of Rochester, and completed a residency in Neurology at Columbia University in New York City. He did fellowships in Immunology and Neuroimmunology at the National Institutes of Health in Bethesda, Maryland. Dr. Bever then completed an MBA at John Hopkins University in Baltimore. He has had a long interest in developing new therapies for people with MS.

**Manzoor Bhat, PhD, MedScD**, is a respected neuroscientist who is Professor in the Department of Cell and Molecular Physiology and Neuroscience Center at UNC Chapel Hill, and also Director of Graduate Studies. He earned his Master's degree at the University of Kashmir, India, and also studied at the Indian Institute of Science, Bangalore. He went on to earn his doctoral degree from Shiga University Medical School in Japan, and he was a Howard Temin Fellow, completing a fellowship in Neurogenetics at Baylor College of Medicine in Houston, Texas. He started as an Assistant Professor at the Mount Sinai School of Medicine in New York and was Hirschl Scholar at Mount Sinai before moving to UNC. Dr. Bhat understands the importance of sharing knowledge and has mentored many graduate students and postdoctoral fellows in his laboratory.

**Stefan Brocke, MD, PhD**, is Assistant Professor of Immunology and a member of the Center of Pharmacology at the University of Connecticut Health Center. He received

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his medical degree from the Free University Berlin, Germany and went on to earn a PhD in Immunology there. Dr. Brocke did his postdoctoral studies in Neurology and Neurological Sciences at Stanford University School of Medicine. He was a Visiting Scientist at the National Institutes of Health and at Israel's Weizmann Institute of Science, and took a faculty position at UConn Health Center in 2004. The overall goal of his research is to develop new therapies for MS.

**Jonah Chan, PhD**, is an accomplished neuroscientist who is Associate Professor of Neurology at UCSF. He received his training in Neuroscience at the University of Illinois and held a postdoctoral fellowship in Neurobiology at Stanford University. He earned a PhD in neuroscience at the University of Illinois at Urbana-Champaign. Dr. Chan was awarded a National MS Society career transition fellowship that successfully took him to his first faculty position at the Keck School of Medicine, University of Southern California, where he also won a National MS Society Harry Weaver Neuroscience Award. He moved to UCSF in 2010. Dr. Chan serves as a scientific peer reviewer for the Society, and on the Board of Directors for its Northern California chapter.

**Eric Chamot, MD, PhD, MPH**, is an Associate Professor in the Department of Epidemiology, School of Public Health, at the University of Alabama at Birmingham. He earned his medical degree from Lausanne University Medical School in Switzerland, a Master's degree in Parasitology from Neuchatel University Zoology Institute, Switzerland, and a Diploma in Tropical Medicine and Hygiene from the Swiss Tropical Institute in Basel. After moving to

the U.S., he received a PhD degree in Epidemiology from Tulane School of Public Health & Tropical Medicine. Before taking a faculty position at UAB, he was Assistant Professor of Public Health at Geneva University Medical Center in Switzerland. He specializes in measurement methodology, and has extensive experience in clinical and health service research.

**Eric Cheng, MD, MS**, is an Associate Professor of Neurology at UCLA and the VA Los Angeles Healthcare System. Dr. Cheng received his MD from the University of Chicago and completed his neurology residency at UCLA. He completed a fellowship at UCLA's Robert Wood Johnson Clinical Scholars Program and earned a Master's degree in Health Services from the UCLA School of Public Health. His research focuses on the quality of care received by persons with neurological conditions, and he has chaired several committees and sessions on this topic for the American Academy of Neurology and the Veterans Administration.

**Nancy Chiaravalloti, PhD**, is Director of the Neuropsychology and Neuroscience Laboratory at the Kessler Foundation Research Center and Associate Professor in the Department of Physical Medicine & Rehabilitation at the University of Medicine & Dentistry of New Jersey. She received her PhD in clinical psychology and neuropsychology at MCP Hahnemann University in Philadelphia. She received further training at Brown University and at the University of Medicine & Dentistry of New Jersey. Dr. Chiaravalloti is a licensed psychologist who conducts research in cognition and mechanisms for improving cognition across various neurological

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populations. Dr. Chiaravalloti has been the recipient of several early career awards, and also serves as a mentor to fellows learning how to do research in this important field.

**Robert Clark, MD**, is a highly regarded Associate Professor of Medicine at the University of Connecticut School of Medicine, and also Associate Professor in the Department of Immunology, Center for Immunotherapy of Cancer and Infectious Diseases at UConn. Dr. Clark received his medical degree from Stanford University, and did his internship and residency in internal medicine at the Strong Memorial Hospital of the University of Rochester, NY. Dr. Clark continued his training at the National Institutes of Health, NIAID, in Bethesda, MD, where he was a Clinical and Research Associate. Dr. Clark has earned the Searle Scholars Award, The Patrick and Catherine Weldon Donaghue Medical Research Foundation Award, and the Mary Osborn Teaching Award (from the University of Connecticut).

**Susan Gauthier, DO, MPH**, is Director of Clinical Research at the Judith Jaffe Multiple Sclerosis Center, Weill Cornell Medical College - New York Presbyterian Hospital in New York, and also Assistant Professor of Neurology and Neurosciences there. She received her DO from the Philadelphia College of Osteopathic Medicine and her MPH from the Harvard School of Public Health. She completed an internship in internal medicine at St. Elizabeth's Hospital, Boston, and a residency in neurology at Boston University Medical Center, where she served as Chief Resident. Dr. Gauthier was the recipient of a National MS Society Sylvia Lawry Physician Fellowship, training and

later taking a faculty position at Harvard before moving to Weill Cornell.

**Steven A. Goldman, MD, PhD**, is an eminent neuroscientist who is among the leaders focusing on the potential of cell therapy to treat MS and other diseases of myelin and nerves. He began his career by earning a B.A. with Honors from the University of Pennsylvania, a PhD in neurobiology from Rockefeller University, and a medical degree from Cornell University Medical College. After doing his neurology residency at Cornell, in 1988 he took a position as Assistant Professor in neurology and neuroscience there, going on to become full professor in 1997. In 2003 he became Dean Zutes Chair in Biology of the Aging Brain at the University of Rochester Medical Center, where he is also Professor and Chairman of the Department of Neurology, Professor of neurosurgery and pediatrics, as well as Attending Neurologist. He is also Neurologist-in-Chief at Strong Memorial and Highland Hospitals. Dr. Goldman is a physician-scientist who has received many awards and honors. He was also a member of the Society-supported Promise: 2010 Nervous System Repair team led by Professor Charles ffrench-Constant.

**Alexander Gow, PhD**, is Professor and Charles H. Gershenson distinguished fellow at the Center for Molecular Medicine and Genetics/ Carman and Ann Adams Department of Pediatrics/ Department of Neurology at Wayne State University in Detroit, Michigan. He earned his PhD in Biochemistry at the University of Queensland in Australia, and received postdoctoral training at Mount Sinai School of Medicine in New York, going on to his first

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faculty position there. He moved to Detroit in 2000 as Assistant Professor, pursuing many research interests including understanding nerve degeneration. He has generously shared his expertise to peer review committees worldwide, from the MS societies of the U.S., Canada and Great Britain/Northern Ireland to the Italian Ministry for University and Research.

**Robyn Klein, MD, PhD**, is Associate Professor of Medicine at Washington University School of Medicine in St. Louis. Dr. Klein received her MD and PhD from Albert Einstein College of Medicine in New York. She then completed her internship and residency in Internal Medicine at Harvard's Brigham & Women's Hospital, and her fellowship in infectious diseases and post-doctoral training in immunology at the Massachusetts General Hospital. She joined the Washington University School of Medicine in 2003. She serves as a peer reviewer for the National MS Society's research programs. Her long-term research goal is to understand the molecular basis of damage in the central nervous system that results from the immune attack, and to identify potential therapeutic targets for the treatment of immune-mediated diseases such as MS.

**Jianrong Li, PhD**, is an Assistant Professor in the Department of Veterinary Integrative Biosciences at the College of Veterinary Medicine and Biomedical Sciences, Texas A&M University. Dr. Li earned her PhD in Biochemistry at the University of Hawaii and completed postdoctoral studies in the Department of Surgery at the University of Pittsburgh School of Medicine. She was an Instructor in the Division of Neuroscience at

Children's Hospital in Boston and Harvard Medical School before moving to Texas A&M. Dr. Li currently serves on the editorial board of the *International Journal of Physiology, Pathophysiology and Pharmacology* and reviews grants for the Italian Ministry of Health. Her research focuses on mechanisms involved in the death of myelin-making cells in diseases such as MS.

**Albert Lo, MD, PhD**, is Associate Professor of Neurology and Public Health, Brown University; Director of the MS Clinic and Associate Director of the Center of Excellence for Restorative and Regenerative Medicine at the Providence VA Medical Center. He is also the Director for Neuroscience Research at the Mandell MS Center, Saint Francis Hospital, Hartford CT. He earned his MD and PhD in neuroscience at Wake Forest University School of Medicine, Winston-Salem, NC. He completed his neurology residency at Yale University, and trained in neurorehabilitation at the National Hospital of Neurology & Neurosurgery, Queen Square, London. He was a faculty member at Yale and Director of the MS clinic at the West Haven VA until 2007. Dr. Lo is widely published and is a member of the American Academy of Neurology's Writing Panel for MS Clinical Practice Guideline Parameters, and is member of the Research Advisory Panel for the VA Multiple Sclerosis Centers of Excellence.

**M. Edward Medof, MD, PhD**, is Professor of Pathology, Medicine, Ophthalmology, and Cancer Center at Case Western Reserve University. He began his career with a medical degree and PhD in immunology from the University of Southern California in Los Angeles. He did his residency at

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Columbia-Presbyterian Medical Center in New York and also at the Wadsworth Veterans/UCLA Medical Center. Dr. Medof trained in rheumatology and immunology at Harvard and at the University of Chicago's Pritzker School of Medicine. He took his first faculty position there as Assistant Professor of Medicine, and stayed at Pritzker for 7 years before becoming Research Assistant Professor of Pathology at New York University Medical Center. He moved to Case Western in 1986 as Associate Professor in Pathology and Medicine. He has made significant contributions to the understanding of immune aspects of autoimmune diseases.

**Sarah Minden, MD**, is a psychiatrist at Brigham and Women's Hospital and an Assistant Professor of Psychiatry at Harvard Medical School. She earned a medical degree at McMaster University Medical School in Hamilton, Ontario, and was Chief Resident in Psychiatry at Harvard's Brigham and Women's Hospital, and also a fellow there. Dr. Minden has served as principal investigator of the National MS Society's Sonya Slifka Longitudinal MS Study and has led several other MS studies; she has also conducted research on mental health policy.

**Akiko Nishiyama, MD, PhD**, is a highly accomplished Professor of Physiology and Neurobiology at the University of Connecticut, Storrs. Dr. Nishiyama received her medical degree at the Nippon Medical School in Tokyo, Japan and doctorate in Neuropathology and Molecular Neurobiology at Niigata University in Niigata, Japan. She then moved to the U.S. and completed postdoctoral studies in Developmental Neurobiology at La Jolla

Cancer Research Foundation (currently Burnham Institute). She learned about MS while spending 3 years in the Department of Neuroscience at the Cleveland Clinic's Lerner Research Institute before moving to Connecticut. The goal of her research is to develop strategies to promote myelin repair from stem cells in diseases such as MS.

**Pablo Paez, PhD**, is Assistant Research Neurobiologist at the Semel Institute for Neuroscience and Human Behavior in the Department of Psychiatry and Biobehavioral Sciences in the Neuropsychiatric Institute, University of California, Los Angeles. He received his PhD in Neurochemistry at the University of Buenos Aires, Argentina and completed a postdoctoral fellowship funded by the National MS Society in developmental neuroscience at UCLA. Dr. Paez has earned the Young Investigator Educational Enhancement Award and Young Latin American Scholars Award from the American Society for Neurochemistry.

**Matthew Plow, PhD**, is Project Scientist at the Cleveland Clinic in the Departments of Biomedical Engineering and Physical Medicine. He received his PhD in Rehabilitation Science at the University of Minnesota at Minneapolis. He completed a postdoctoral fellowship in health services research at Brown University. Dr. Plow then trained in MS-specific rehabilitation research under the mentorship of Marcia Finlayson, PhD (University of Illinois at Chicago), as part of the Mentor-Based Postdoctoral Fellowship in Rehabilitation Research program funded by the National MS Society.

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**Gabriel Rabinovich, PhD**, is Head of the Division of Immunopathology and Glycoimmunology at the Institute of Biology and Experimental Medicine, Buenos Aires, Argentina, and is also Visiting Scientist at the University of Maryland and the Dana Farber Cancer Institute, Harvard Medical School, Boston. He received his PhD in Immunology at the University of Cordoba, Argentina and did his postdoctoral studies in Immunology/ Glycobiology at the University of Buenos Aires. Dr. Rabinovich has earned several awards including the Bernardo Houssay Award (Ministry of Science and Technology) Best Young Scientist in Argentina, the John Simon Guggenheim Foundation Award, and the 2010 Third World Academy of Science Award to the Best Scientist in Medical Research in Developing Countries. He was designated Chair of the First Keystone Symposium on Glycoimmunology.

**Richard M. Ransohoff, MD**, is a distinguished researcher and Director of the Neuroinflammation Research Center in the Department of Neurosciences of Lerner Research Institute, Cleveland Clinic. He is also Professor of Molecular Medicine at the Cleveland Clinic Lerner College of Medicine at Case Western Reserve University, and Staff Neurologist in the Mellen Center for MS Treatment and Research. Dr. Ransohoff graduated with honors from Bard College, Annandale, NY, with a BA in literature, and received an MD with honors from Case Western. He did residencies in internal medicine at Mt. Sinai Medical Center in Cleveland and in neurology at Cleveland Clinic. Dr. Ransohoff was a Postdoctoral Fellow at Case Western Reserve University School of Medicine. Among other honors and awards, Dr. Ransohoff received a Harry

Weaver Neuroscience Scholarship from the National MS Society and a Clinical Investigator Development Award from the NIH. He has been repeatedly listed in the "Best Doctors in America," and has served as a scientific peer reviewer for the NIH and National MS Society, and on editorial boards of the *Journal of Immunology*, *Trends in Immunology*, the *Journal of Neuroimmunology*, *Nature Reviews Immunology*, and *Neurology*. He has published over 305 papers and edited five books.

**Barbara Ranscht, PhD**, is a noted neuroscientist and Professor at the Sanford-Burnham Medical Research Institute and Adjunct Professor in the Department of Neurosciences, School of Medicine, UC San Diego. She earned a PhD in Neurobiology at the University of Tübingen, Germany, and was a fellow of the European Molecular Biology Organization (EMBO) at King's College London, a Research Associate at Washington University in St. Louis, and a fellow of the Gene Technology Program of the German Ministry of Science and Technology at Massachusetts Institute of Technology, Cambridge, before coming to California. Her laboratory investigates short- and long range signals that regulate in the nervous system development and function.

**Anthony Reder, MD**, is a highly respected neurologist who began his career with an MD degree from the University of Michigan, and he did his residency in Neurology at the University of Minnesota under AB Baker. He completed a fellowship in Neuroimmunology with Jack Antel at the University of Chicago, where he is now a Professor in the Department of Neurology. Dr. Reder has served on the National MS

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Society's National Clinical Advisory Board, its International Advisory Committee for Clinical Trials in MS, and as a Society scientific peer reviewer. Dr. Reder is a well-published researcher who has been repeatedly voted Best Doctor in Chicago by Chicago Magazine. He has a long-standing interest in clinical trials in MS, and basic research on interferons in MS. His co-investigator, **Xuan Feng**, received a PhD in Immunology and Molecular Virology from the Medical College of Georgia, and did post-doctoral training in Neuroimmunology at the University of Chicago and on interferon resistance during virus infections at Washington University, St Louis. She has significant publications on the role of interferon in combating brain viruses, neurodegenerative diseases, and MS.

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**Sheng-Kwei “Victor” Song, PhD**, is Associate Professor in the Department of Radiology at Washington University, St. Louis. Dr. Song received his BS degree in Chemistry at Tamkang University in Taiwan and his MS degree in Physical Chemistry from University of Alabama at Birmingham. He earned his PhD in Physical Chemistry from Washington University, where he also did his postdoctoral work in Biophysics/Cell Biology. He was Research Associate, Senior Scientist and Operations Director at Washington University’s Biomedical MR Lab in the Department of Chemistry, and has worked closely with other MS researchers at Washington University for several years.

**Jack Strominger, MD**, is a respected biochemist, with more than 1,000 published academic papers. He is the Higgins Professor of Biochemistry, Department of Stem Cell and Regenerative Biology, Harvard University, and was formerly the Director of Basic Sciences at the Dana Farber Cancer Center. Dr. Strominger served in the Navy during World War II, and then completed his medical degree at Yale University and an internship and research fellowship at Washington University in St. Louis. He served as an assistant professor at Washington University, and then Professor of Pharmacology & Chemical Microbiology at the University of Wisconsin Medical School, and Chairman of the Department of Pharmacology, before moving to Harvard. Dr. Strominger is the recipient of multiple awards including election to the National Academy of Sciences, the Guggenheim Fellowship, the Albert Lasker Basic Medical Research Award, the Japan Prize, and the American Association of Immunologists Excellence in Mentoring Award.

**Jenny Ting, PhD**, is William Rand Kenan Professor of Microbiology and Immunology at the University of North Carolina at Chapel Hill, where she is the Director of the Center for Translational Immunology as well as the co-Director of the Institute of Inflammatory Diseases. Dr. Ting received her PhD in Microbiology/Immunology at Northwestern University in Chicago, and completed postdoctoral fellowships in microbiology-immunology at the University of Southern California, Los Angeles and Duke University. She took her first faculty appointment at Duke University before moving on to UNC. She is a highly respected scientist and has published in multiple major scientific journals. Dr. Ting has been honored by many organizations and has served as a scientific peer reviewer for the National MS Society, National Institutes of Health and others.

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