



NEW TRAINING FELLOWSHIPS

Newly Funded Research and Clinical Fellowships/2010

New Research and Clinical Training Fellowships

The National MS Society funds different fellowship programs that allow young men and women to train with seasoned MS scientists and physicians in laboratories and MS clinics, and ease their transitions into independent careers. Often these are the hands doing the experiments and providing the first line of care for patients.

Following are brief summaries of the new research projects, grouped according to avenues of MS investigation as they fit into the major goals of stopping MS, restoring function and ending MS forever.

RESEARCH AIMED AT STOPPING MS Therapy/Management

Searching for better treatments to stop all forms of MS is a high priority for the National MS Society. Well-designed clinical trials are crucial to determining the safety and effectiveness of therapies for MS.

The National MS Society has current, multi-year commitments of \$xx million to support some xx research projects focusing on improving therapies for people with MS, including Sylvia Lawry Physician Fellowships that provide training in designing and conducting MS clinical trials.

Enrique Alvarez, MD, PhD

Washington University School of Medicine
Saint Louis, MO

Chapter Area: Gateway Area Chapter

Award: Sylvia Lawry Physician Clinical Fellowship

Term/Amount: 7/1/10-6/30/13; \$195,000

Funded in full by the NMSS Gateway Area Chapter

“Sylvia Lawry Physician Clinical Fellowship”

About the investigator: Dr. Enrique Alvarez completed his MD and PhD (in neurosci-

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ence) at the University of Colorado Health Sciences Center, along with an internship in internal medicine. His doctoral research revealed new genes involved in the development of nerve cells. He then completed a residency in neurology at Washington University in St. Louis. Dr. Alvarez's training prepared him for the field of MS research, with undergraduate work in microbiology and immunology, and graduate work in neurosciences. He wants to devote his career to helping advance the understanding of MS and its treatment.

Project details: The promising young doctors receiving training from a Sylvia Lawry Physician Fellowship learn from top MS experts who mentor their initiation into the complex methods of designing and conducting clinical trials in persons with MS.

Dr. Alvarez's fellowship is a three-year program at the John L. Trotter MS Center at the Washington University in Saint Louis, where his mentor is Anne Cross, MD, a noted expert in MS neuroimmunology clinical care and research. Dr. Alvarez's training plan incorporates a broad range of experiences ranging from patient care to translational and epidemiologic investigation. He is participating as an investigator in several clinical trials ongoing at the center and also is spending a block of time during his training at the Rehabilitation Institute of St. Louis, learning approaches to spasticity management.

By the end of their training, Lawry fellows emerge fully ready to plan and conduct studies of promising new treatments for MS.

Daniel Ontaneda, MD

Cleveland Clinic Foundation
Cleveland, OH

Chapter Area: Ohio Buckeye Chapter

Award: physician fellowship

Term/Amount: 7/1/10-6/30/13; \$ 195,000

"Sylvia Lawry Physician Clinical Fellowship"

About the investigator: Dr. Daniel Ontaneda's dedication to the field of MS and clinical trials started immediately after earning his MD at Pontificia Universidad Catolica del Ecuador, when he left to complete a fellowship in MS at Baylor College of Medicine Houston MS Center under Dr. Victor Rivera. During that year, he became involved in several ongoing MS trials and grew to appreciate the complexities of MS clinical trials. He then completed an internship in internal medicine and residency in neurology at the Cleveland Clinic, in part because of the large MS program at the Clinic's Mellen Center at Cleveland. Dr. Ontaneda has been studying the natural history of lesions using advanced imaging techniques. Ontaneda's Sylvia Lawry Physician Fellowship is being done under the mentorship of Dr. Jeffrey Cohen, who has an extensive background in the design and execution of MS trials.

Project details: The promising young doctors receiving training from a Sylvia Lawry Physician Fellowship learn from top MS experts who mentor their initiation into the complex methods of designing and conducting clinical trials in persons with MS.

Dr. Ontaneda's fellowship is funding a Clinical Neuroimmunology Fellowship within the Mellen Center Experimental Therapeutics Program at the Cleveland Clinic Foundation.

New Clinical Fellowships

The National MS Society's clinical fellowship program is an "intellectual pipeline" for the next generation of MS physicians and physician-investigators. Clinical fellowships provide one year of post-residency training in specialized MS clinical care to board eligible/certified neurologists or psychiatrists. The fellows perform patient consultations and follow-up evaluations under the supervision of an MS specialist physician, and participate in multidisciplinary team activities and professional meetings, enhancing their ability to provide high quality care for individuals with MS.

These new fellowships are funded through generous gifts from: Allene and Weyman Johnson, Sr. Fellowship Fund; The New York Community Trust, Diane Goldman Fund through a generous gift from Mrs. Diane Goldman Kemper and Ms. Robin Kemper; National MS Society Greater New England, Lone Star and Wisconsin chapters, and unrestricted grants from Acorda Therapeutics, Bayer HealthCare, and Teva Neuroscience.

Jonathan Cahill, MD

University of Massachusetts
Memorial Medical Center
Worcester, MA
Mentor: Peter Riskind, MD, PhD

Patricia DeJesus, MD

(See profile, page 6)
Baylor College of Medicine
Houston, TX
Mentor: Victor Rivera, MD

Zulma Hernandez, MD

Northwestern University
Chicago, IL
Mentor: Joy Derwenskus, DO

Don Mahad, MD

Cleveland Clinic
Cleveland, OH
Mentor: Jeffrey Cohen, MD

Corey McGraw, MD

Mount Sinai Medical Center
New York, NY
Mentor: Fred Lublin, MD

Mac McLaughlin, MD

University of Massachusetts
Memorial Medical Center
Worcester, MA
Mentor: Peter Riskind, MD, PhD

John Scagenli, MD

University of Virginia
Charlottesville, VA
Mentor: Myla Goldman, MD

Timothy West, MD

University of California, San Francisco
Mentor: Bruce Cree, MD

This is a three-year program designed to provide the skills needed to diagnose and treat people with MS, as well as function as a clinical researcher focusing on clinical trials.

This is accomplished through direct patient care, participation in clinical trials, and formal course work in clinical research. Dr. Ontaneda will be involved in ongoing trials, including phase 3 studies of oral MS treatments, and also will design, carry out, analyze, and report an independent clinical research project.

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

RESEARCH AIMED AT 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 \$41 million to support research projects focusing on stopping the immune system attack in MS.

Laura Piccio, MD, PhD

Washington University
Saint Louis, MO

Chapter Area: Gateway Area Chapter

Award: Harry Weaver Neuroscience Award

Term/Amount: 7/1/10-6/30/15; \$566,393

Funded in full by the NMSS Gateway Area Chapter

“Role of TREM-2 in multiple sclerosis and its animal model”

About the investigator: Dr. Laura Piccio received her medical degree and completed a residency in neurology at the University of Milano, Italy. She then obtained a PhD in neurological sciences at the University of Milano and a Society-funded fellowship in neurology at Washington University. She is currently a Research Instructor in Neuroimmunology there. Dr. Piccio already is an award-winning MS researcher, having earned the Whitaker prize for the best research presentation at the 22nd annual Consortium of Multiple Sclerosis Centers meeting, and the 2007 Wexler Prize for MS Research. The Harry Weaver Neuroscience Scholar Award is the National MS Society’s most prestigious award for young investigators, and it will enable Dr. Piccio to launch her career as an independent MS researcher.

Project details: Multiple sclerosis involves immune-system attacks and damage to the brain and spinal cord. Dr. Piccio has obtained results indicating that a molecule found on some immune cells called TREM-2 plays a role in mice that have EAE, an MS-like disease. Importantly, treating these mice with an antibody that blocks TREM-2 worsened EAE, suggesting that it might be involved in inhibiting the immune attack.

Now, Dr. Piccio is examining the effects of TREM-2 further in mice that lack this molecule. She also is looking at TREM-2 activity in cells obtained from people with MS, and is then treating these cells with an anti-TREM-2 antibody to observe changes in immune activity.

These studies may show that TREM-2 activity is a target for new therapeutic strategies for MS.

Xiaohu Wang, PhD

MD Anderson Cancer Center

Houston, TX

Chapter Area: South Central

Award: postdoctoral fellowship

Mentor: Chen Dong, PhD

Term/Amount: 7/1/10-6/30/13; \$ 150,800

Funded in part by the NMSS Lone Star Chapter

“Transcriptional regulation of IL-17/IL-17F expression in a mouse model of multiple sclerosis”

About the investigator: Dr. Xiaohu Wang received his PhD from Baylor College of Medicine in Houston. His research led to a major finding regarding the genes that instruct bacteria in response to environmental stimuli. He also developed novel high-throughput technology. After that, Dr. Wang moved to the University of Texas MD Anderson Cancer Center in Houston for postdoctoral training in immunology. He is working with Dr. Chen Dong, whose lab has described a novel subset of immune T cells – Th17 cells. After his training, Dr. Wang hopes to join the ranks of leading immunologists who focus on immune-mediated diseases such as MS.

We especially need to know more about the molecules that the immune system uses to attack the nervous system, because each of these is a potential therapeutic target.

Project details: Multiple sclerosis occurs when the immune system attacks the brain and spinal cord. In the immune system, Th17 (T helper 17) cells play an important role in eliminating certain disease-causing microorganisms that cannot be adequately handled by other T-helper cells. However, excessive Th17 cell responses often cause serious tissue and organ inflammation and damage. Th17 cells are major players in the immune attack launched in MS.

Up Close: Clinical Fellow Patricia DeJesus, MD

Patricia De Jesus, MD (Baylor College of Medicine, Houston) learned about MS in high school: Her brother moved up his wedding date so that his mother-in-law, who had the disease, could walk her daughter down the aisle before her MS progressed. This woman's courage and faith inspired Dr. De Jesus to pursue a career in treating people with MS and conducting clinical research. "She has hope for a discovery that will help stop MS progression," says Dr. De Jesus. "Someday I want to be an active part of this discovery."



Dr. De Jesus comes to Baylor from the University of Puerto Rico, and she is well on her way to an active career in MS, having earned a MASTER MS fellowship from the Medical College of Georgia and an MS Awareness Scholarship to attend the 2009 meeting of the Consortium of MS Centers. She also attended the Update in MS and Parkinsons Disease course given by the Medical College of Georgia in 2008. Dr. De Jesus has now earned a clinical fellowship from the National MS Society, designed to train neurologists in specialized MS clinical care. Her mentor is Victor Rivera, MD, Medical Director of the Maxine Mesinger MS Comprehensive Care Center at Baylor, and a noted physician in the field of MS.

Dr. Rivera believes that Dr. De Jesus has the enthusiasm and dedication to become an MS clinician, noting that clinical fellows play an important role in the management of people with MS at the center, and in conducting clinical research. "Our MS Center has exposed me to people with different types of MS, at different stages of the disease," says Dr. De Jesus. "This experience has helped me to understand that people with MS need to work with a team of people from different disciplines to help manage and improve their quality of life."

Dr. De Jesus has developed a research protocol to study the neuropsychological manifestations and quality of life in people with relapsing-remitting MS. "With this fellowship, I hope I can acquire the knowledge and tools to make a difference in the lives of people with MS," she says. Read about other clinical fellows on page 3.

Dr. Wang is investigating the genetic factors that regulate Th17 cell development and its production of immune messenger proteins. His team is deleting genes in mouse models to determine how Th17 activity is affected, and also is studying the development of MS-like disease in these mice to clarify the role of Th17 cells in disease development.

The results from these studies may reveal new details about a major player in the MS immune attack, and may provide novel drug targets for treating MS.

RESTORING FUNCTION

Rehabilitation

New Mentor-Based Rehabilitation Research Fellowship!

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 about \$6.1 million to support investigations focusing on rehabilitation in MS.

Susan Forwell, PhD, FCAOT

University of British Columbia
Vancouver, BC, Canada

Award: Mentor-Based Rehabilitation Research Fellowship

Term/Amount: 7/1/10-6/30/13; \$ 212,978
"UBC MS Rehabilitation Fellowship"

About the investigator: Dr. Susan Forwell completed her PhD in Occupational Science at the University of Southern California, Los Angeles. She is an Associate Professor at the University of British Columbia (UBC) Department of Occupational Science and Occupational Therapy, a Research Associate at the UBC MS Clinic, an Affiliate Investigator at BC Children and Women's Hospital and at the Vancouver Coastal Health Research Institute. Dr. Forwell is on the Board of the Consortium of MS Centers and is a member of the health care advisory council of the MS Association of America. She is an associate editor of the *International Journal of MS Care*, on the edi-

torial board of the *Journal of Occupational Science*, and the past president of the Canadian Association of Occupational Therapists (CAOT). Dr. Forwell has earned several awards and recognitions, including the UBC Faculty of Medicine Distinguished Service award, the CAOT Dr. Helen P. Levesconte Prize and is a fellow of CAOT.

Project details: The goal of the National MS Society's mentor-based postdoctoral fellowship program in MS rehabilitation research is to recruit and train talented clinician-scientists in rehabilitation research specific to MS. The ultimate goal is to get more hands and minds working on the best ways to help people with MS maximize their abilities.

At the University of British Columbia, in partnership with the Vancouver Hospital, there is a large infrastructure that focuses specifically on clinical care and research in MS. Part of this infrastructure is the British Columbia Multiple Sclerosis Clinic Network, with a database of more than 5,900 cases of MS in British Columbia and up to 25 years of natural history data, offering tremendous possibilities to engage in population and comparative studies. The mentoring team collectively has over 150 years of experience in MS research. The fellows trained by the program will have opportunities to engage in several projects, including the topics of fatigue, tremor, community re-integration, depression, spasticity, pain, mobility, cognitive function, Asian-Canadian MS, and aerobic exercise.

The goal of this unique fellowship program is to increase the number of MS rehabilitation researchers targeting psychosocial, occupational, and behavioral issues in people with 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 \$17.8 million to support research on myelin biology in MS.

Sharyl Fyffe-Maricich, PhD

Case Western Reserve University
Cleveland, OH

Chapter Area: Ohio Buckeye Chapter

Award: postdoctoral fellowship

Mentor: Robert H. Miller, PhD

Term/Amount: 7/1/10-6/30/13; \$ 150,800

"MAP kinase regulation of oligodendrocyte differentiation: The role of Erk2"

About the investigator: Dr. Sharyl L. Fyffe-Maricich enters her postdoctoral studies with an outstanding academic background, having received her PhD under the guidance of Dr. Huda Zoghbi, a leader in the field of nerve cell degeneration research at Baylor College of Medicine. During this training, she focused on understanding the neural basis of a range of behaviors including aggression in response to stress, and has reported findings at the annual meeting of the Society of Neuroscience and in several publications. Now Dr. Fyffe-Maricich is training with expert neuroscientist Dr. Robert Miller at Case Western Reserve University in Cleveland. She is seeking a better understanding of the basic biology of myelin, and intends to use this information to develop

novel therapeutic strategies that will augment myelin repair in people with MS.

Project details: Myelin, the substance that ensheathes nerve fibers, is a main target of the immune attack that damages the brain and spinal cord in multiple sclerosis. Oligodendrocytes are cells of the brain and spinal cord that make myelin. In the healthy central nervous system, oligodendrocyte precursor cells (OPCs) can sometimes repair damaged myelin, but in people with MS, OPCs ultimately fail to develop into myelinating cells. Understanding the precise mechanisms that regulate the transition of OPCs to myelinating oligodendrocytes can allow the development of new therapies that promote functional recovery in people with MS.

Dr. Fyffe-Maricich is examining the role that one enzyme, extracellular signal-regulated kinase 2 (ERK2), plays in the development of OPCs. She is using sophisticated techniques to assess the development of myelin sheaths in mice after the Erk2 gene has been deleted and/or increased during development. Based on preliminary data, she predicts that OPCs lacking ERK2 will have a defective or delayed capacity to generate myelin, and that increasing the activity of ERK2 in the mouse brain will result in the myelin formation during brain development. She also is probing the role of ERK2 during the repair process and determining whether removal of the ERK2 protein from OPCs will result in the delay or inhibition of myelin repair. Conversely, she is assessing whether addition of the ERK2 protein can enhance the repair process.

Understanding the role of ERK2 may lead to the design of new therapies that enhance myelin repair in people with MS.

Jia Liu, PhD

Mount Sinai School of Medicine

New York, NY

Chapter Area: New York City-Southern New York Chapter

Award: Postdoctoral research fellowship

Mentor: Patrizia Casaccia, MD, PhD

Term/Amount Required: 7/1/10-6/30/13; \$150,800

Title: "Role of histone methylation in oligodendrocyte differentiation in development and remyelination in MS"

About the investigator: Dr. Jia Liu completed her PhD in neuroscience at Wesleyan University, providing new information about the role of DNA repair genes in nerve cell protection. She has now joined the lab of noted MS researcher Dr. Patrizia Casaccia at Mount Sinai School of Medicine to complete her postdoctoral training. This team is exploring the genetic regulation of myelin formation. This promising young scientist already has presented findings at annual meetings of the Society for Neuroscience. Dr. Liu also is benefiting from her exposure to the MS experts at the Corinne Goldsmith Dickinson Center for MS at Mount Sinai. She is dedicated to becoming an independent researcher investigating the mechanisms underlying the cause of MS and repair, with the ultimate goal of finding new strategies to restore function in people with MS.

Project details: Multiple sclerosis involves immune system attacks that damage the brain and spinal cord, with a major target being the myelin substance that ensheathes nerve fibers. Failed or inadequate myelin repair is a common feature in people with MS, but the reasons are poorly understood.

Oligodendrocyte precursors (OPCs, the

Understanding the role of

this molecule may lead

to the design of new

therapies that enhance

myelin repair in

people with MS.

cells that mature into myelin-making oligodendrocytes) exist within areas of myelin damage in people with MS but fail to specialize into mature oligodendrocytes to produce myelin. Studies from Dr. Casaccia's laboratory and others have noted that the genes inhibiting OPC differentiation may be unusually active in areas of myelin damage.

The level of gene activity is determined by methylation – a natural regulatory process in the cell that controls gene activity. In particular, methylation on the gene H3K9 is found to be decreased in areas of myelin damage in people with MS and MS models. Now Dr. Liu is examining the role of this modification more closely in OPCs isolated in the laboratory. She is also exploring myelin repair in mouse models in which the genes responsible for histone methylation have been genetically manipulated to decrease activity.

The proposed studies should provide insights on whether manipulating histone methylation could be a potential therapeutic strategy for inducing myelin repair in people with MS.

Up Close: Research Fellow Angela Hahn, PhD

Angela Hahn, PhD (University of California at San Francisco) is going after myelin – a major target of the immune attack in MS – and it's personal. While in graduate school, Dr. Hahn was diagnosed with multiple sclerosis. "At the time, my knowledge of neurobiology was limited to what I had learned in a few courses," she says. "What was a topic of interest became a topic of utmost importance." Dr. Hahn is now completing her training through a postdoctoral research fellowship from the National MS Society. Her project focuses on finding a way to rebuild myelin at sites of damage by stimulating oligodendrocytes (myelin-making cells).



Dr. Hahn's emotions about having MS fuel her studies. "As a patient, MS frustrates me," she says. "After decades of research there is no cure, just a handful of treatment options; no drug to repair the damage already inflicted; and no way of knowing what the progression of my illness will be. "As a scientist, MS intrigues me because I can logically separate myself from the "no's" that frustrate me to see the fascinating biological problems behind them."

Jonah Chan, PhD – Dr. Hahn's mentor – says that her emotion will serve her well in these experiments. "Angela possesses great dreams for the future," he says. "She has a vision for the 'big picture' concerning MS research and – more importantly – her life. While most researchers and scientists focus on the details of the experiments, Angela has the unique ability to bring a touch of humanity into scientific research." Dr. Chan is a former fellow himself, whose independent research career was launched with funding from a Harry Weaver Neuroscience Award.

Dr. Hahn will spend the majority of her fellowship in the laboratory conducting and designing experiments, learning new techniques of studying brain cells and new microscope technologies. In the short-term, she is learning the ropes of neurobiology, but her long-term goal is to better the lives of people with MS – like herself. "By understanding the mechanisms involved in how oligodendrocytes make myelin, I want to help discover a treatment to repair the damage, and also the physical and emotional stress caused by MS."

Jennifer Welser, PhD

The Scripps Research Institute
La Jolla, CA

Chapter Area: Pacific South Coast Chapter

Award: postdoctoral fellowship

Mentor: Richard Milner, MD, PhD

Term/Amount: 7/1/10-6/30/13; \$ 150,800

"Role of the alpha6 beta4 integrin in astrocyte activation"

About the investigator: Dr. Jennifer Welser completed her PhD in Cellular and Molecular Pharmacology and Physiology at the University of Reno, Nevada. She has completed a postdoctoral fellowship there as well, focusing on molecules known as integrins and their role in muscular dystrophy. Her highly productive doctoral training included three publications in which she was the first au-

thor. Dr. Welser also received the university's George C. Bierkamper Outstanding Graduate Student Award in Pharmacology, which is presented to the student who demonstrates the highest level of excellence in academics and research. Dr. Welser is now studying the role of integrins in MS at The Scripps Research Institute in La Jolla with Dr. Richard Milner, a noted expert in integrins and MS. Her ultimate goal is to reveal new information about the underlying mechanisms that lead to MS.

Project details: Multiple sclerosis occurs when immune cells attack the brain and spinal cord, damaging the nerve fiber sheaths (myelin) and nerve fibers in the brain. Normally, the blood-brain barrier (BBB) acts as a shield to protect the brain from potentially harmful constituents of the blood. Astrocytes are the most abundant cells in the brain. They are involved in the formation and maintenance of the BBB and provide protective effects during injury to the brain by becoming activated in a process known as reactive gliosis. Recent studies however suggest that reactive gliosis may prevent repair of the brain and may contribute to MS progression.

Dr. Welser is testing the idea that alpha6 beta4 integrin (an adhesion molecule expressed by astrocytes) may contribute to reactive gliosis. She is studying the function of this molecule both during mouse development and in a mouse disease model of MS called EAE.

As astrocytes are the only cell type in the brain that express the alpha6 beta4 integrin, this integrin may represent a promising therapeutic target for stopping MS.

RESTORING FUNCTION

The Nervous System in Health and Injury

The immune attack in MS unleashes a cascade of events that damage the wire-like arms of nerve cells (axons) and the protective tissue (myelin) that wraps around axons, disrupting nerve signal transmission. Understanding these processes is crucial to efforts to protect and repair the nervous system. The National MS Society has current, multi-year commitments of \$7.7 million to support investigators focusing on neuropathology and neurophysiology.

Cheng Fang, PhD

Oregon Health & Science University
Portland, OR

Chapter Area: Oregon Chapter
Award: postdoctoral fellowship
Mentor: Gary Banker, PhD

Term/Amount: 7/1/10-6/30/13; \$ 156,515
"Effects of inflammatory mediators on axonal transport in cultured neurons and in intact optic nerves"

About the investigator: After completing predoctoral education in Nanjing, China, Dr. Cheng Fang came to the United States to pursue her passion for biology. She completed a PhD at Penn State University. Fascinated by the complexity of the brain and driven to understand more about neuropathological diseases, she joined Dr. Gary Banker's lab for postdoctoral training. Dr. Banker is an expert in nerve cell structure and development, and Dr. Fang is taking advantage of this expertise to study nerve fiber damage in MS.

Project details: Multiple sclerosis occurs when the body's own immune response attacks the central nervous system. Evidence suggests that this misdirected immune response destroys nerve cells (neurons), nerve fibers (axons), and their myelin coating, leading to disability in people with MS. Neurons are complex: Proteins are produced in the cell bodies, and proper and timely transportation of proteins to their proper locations are extremely critical for normal neuronal function. Dr. Fang is studying whether the degeneration of neurons and axons associated with MS is caused by some defect in protein transport within these cells.

In order to determine this, she is observing in real time how inflammation affects neurons and axons. First, she is investigating neuron cultures isolated in the laboratory and treated with messenger chemicals involved in stimulating inflammation. She is also using a new tool to examine how inflammation affects nerve cells and fibers in live tissue. About 50% of MS patients will develop optic neuritis (inflammation of the optic nerve) at some point. Her system uses a transplanted optic nerve from a mouse model of MS to investigate protein transport in living cells.

This study may provide a novel method for testing potentially neuroprotective drugs in people with MS.

Angela Hahn, PhD

University of California at San Francisco
San Francisco, CA

Chapter Area: Northern California Chapter

Award: postdoctoral fellowship

Mentor: Jonah R. Chan, PhD

Term/Amount: 7/1/10-6/30/13; \$150,800

“Controlling the number and length of myelin segments formed by oligodendrocytes”

About the investigator (See profile, page 10):

Dr. Hahn received her PhD in Molecular and Cellular Physiology from the Stanford University School of Medicine under the mentorship of Dr. Tobias Meyer. During graduate school, she was diagnosed with MS. As a person with MS, she is frustrated by the disease – there is no cure, no drug to repair the damage, no test to predict the occurrence or severity of a relapse or disease progression. As a scientist, she is intrigued by the fascinating biological problems presented by MS and the complex hypotheses behind them. During her training, Dr. Hahn utilized novel methods of microscopy and genetics screening to study cells. Now she is applying her skills to study myelin-making cells in the lab of neurobiology expert Dr. Jonah Chan. This training is providing her with the tools, knowledge and creative freedom to advance MS research.

Project details: Many of the delicate tissues in the central nervous system are ensheathed by a mixture of fat and protein known as myelin. In MS, damage to the myelin coating is caused by an attack of the immune system.

Dr. Hahn is searching for a way to rebuild the myelin at sites of damage by coaxing oligodendrocytes (myelin-making cells). Her team is using cells isolated from mice to de-

termine which components of the environment surrounding the oligodendrocytes affect their potential to produce myelin. They are focusing on proteins located in the oligodendrocyte lining. Proteins identified in cell studies are being studied further in mouse models where the proteins can be genetically manipulated to increase or decrease in activity.

By understanding mechanisms involved in the oligodendrocyte production of myelin, this team hopes to contribute to development of a treatment to repair damage in MS.

ENDING MS FOREVER

Epidemiology: Studying People Who Get MS

Farren Briggs, PhD

University of California, Berkeley
Berkeley, CA

Chapter Area: Northern California Chapter

Award: postdoctoral fellowship

Mentor: Lisa F. Barcellos, PhD

Term/Amount: 7/1/10-6/30/13; \$ 135,448

“Detecting complex genetic environment interactions in multiple sclerosis”

About the investigator: Dr. Farren Briggs earned his PhD at the University of California, Berkeley, under the mentorship of MS genetics expert Dr. Lisa Barcellos, and proposes to continue his training in the same lab. Dr. Briggs is dedicated to investigating the contribution of genetics, environmental exposures, and psychosocial experiences, including their intersections, to MS risk and progression. His global and inclusive outlook is reflected in his extracurricular activities: Dr. Briggs has been a team leader for the School of Public Health Volunteer Mobilization Day, a Graduate Recruitment and Diversity Services Student Ambassador, an International

Student mentor, the School of Public Health Graduate Assembly Representative, and currently serves on the Executive Board of the Graduate Assembly.

Project details: Multiple sclerosis is a complex disease, with both genetic and environmental factors contributing to its onset. Despite recent successes in scientific research, the cause of MS remains unknown. Research indicates that exposure to tobacco smoke and stressful life experiences may contribute to disease activity, though the biological mechanisms they act through is unclear.

Dr. Briggs is investigating interactions that influence MS risk, particularly interactions between tobacco smoke exposure and genetic variation, and stressful life experiences and genetic variation. This project is applying a novel statistical strategy to investigate a large data set of 1,500 people with MS and 1,500 healthy individuals, for whom detailed clinical, genetic, and environmental exposure information is available.

This project may identify biological mechanisms that contribute to the onset of MS.

ENDING MS FOREVER

Searching for MS Genes

Research suggests that MS occurs in individuals and in families whose genes make them susceptible to developing the disease, and that many genes contribute to MS susceptibility. In addition, individuals who are genetically at risk must encounter some other triggering factor in the environment to actually develop MS. Pinpointing the exact location of these "MS genes" could help determine who is at risk for developing the disease, and may provide clues to its cause, prevention and better treatment.

The National MS Society has current, multi-year commitments of \$8.6 million to support research focusing on MS genetics.

Zongqi Xia, MD, PhD

Brigham and Women's Hospital &
Massachusetts General Hospital
Harvard Medical School
Boston, MA

Chapter Area: Greater New England Chapter

Award: NMSS/AAN Clinician Scientist Development Award

Mentor: Philip De Jager, MD

Term/Amount: 7/1/10-6/30/13; \$ 248,517

"Exploring the function of the TNFRSF1A allele associated with multiple sclerosis"

About the investigator: Dr. Zongqi Xia envisions a research career that will benefit humanity, and thus is a perfect fit for the National MS Society/AAN Clinician Scientist Development Award, which enables talented young clinicians to address problems in MS with the most current scientific tools.

Dr. Xia pursued the combined MD/PhD program at Case Western Reserve University in Cleveland. He completed an internship in internal medicine at Case Western, followed by a residency in neurology at Harvard Medical School-affiliated Brigham and Women's Hospital and Massachusetts General Hospital. During this residency, he developed an interest in neuroinflammatory disorders, and thus is completing postdoctoral training under the mentorship of Dr. Philip De Jager, a Harry Weaver Neuroscience Scholar who has forged a successful career in MS research.

Project details: Research suggests that MS occurs in individuals and in families whose genes make them susceptible to develop the disease, and that many genes contribute to MS susceptibility. A previous study associated TNFRSF1A (the gene that instructs the immune messenger protein TNF-alpha receptor 1) with MS.

Dr. Xia is seeking to understand how a genetic variation in the TNFRSF1A gene may alter the immune system to increase an individual's risk of developing MS. His team is selecting 200 variations in this gene, and is studying them in 5000 people with MS and 5000 healthy controls.

This large-scale study could provide insights and lead to an early clinical impact, since several existing FDA-approved drugs modulate the effects of TNF-alpha.

Fellowship Program Reports on Success

In 2008, the National MS Society conducted a survey of our past postdoctoral fellows to assess current involvement in the MS field and the impact of the fellowships on their careers. The results presented here are based on feedback from 300 past fellows who responded to this survey.

Employment Status

More than 50% of the survey respondents are employed in academic (medical/graduate school or college/university) settings. Of the most recent fellows (1996-2005) who have gone into academia, only 2 out of 85 were still in postdoctoral positions at the time of this survey. More than 80% have obtained faculty appointments. Starting in the 1980s, a significant proportion of individuals have obtained employment in the biotechnology/pharmaceutical industry.

Commitment to MS-Related Research

Overall, 56% (167/300) of survey respondents are currently involved in basic and/or clinical MS-related research. Looking only at the former fellows in academia, 69% are working in the MS field. Other activities show the continued commitment of former fellows to the field of MS. A majority of them have written more than 10 research articles on MS and 78% have trained at least one fellow in MS research or clinical care. Nearly half of the survey respondents have volunteered for the Society in many different capacities, from participating in an MS Walk to serving on a national peer review committee. In addition, over 20 survey respondents have played a role in establishing a start-up or biotech company. A number of these companies currently have potential treatments for MS in clinical trials or in their product pipeline.

Funding Success

Past fellows have been very successful in securing funds to support their MS-related research. The initial NMSS investment, which is currently about \$150,000 for a 3-year fellowship, has leveraged significant funding for the MS-related research programs of the former fellows throughout their careers. The estimated total amount of funding, for MS-related research, obtained through NMSS, federal agencies, private foundations, industry, universities, and other sources is nearly 370 million dollars.

Preparation for Career Advancement: Recent Fellows (1996-2005)

These former fellows had success in advancing following their postdoctoral training, but felt that additional training in specific career skills such as grant writing and networking would have had a positive impact. The Society responded to this need, convening the Tykeson fellows conference was convened by the Society and launched by a generous contribution from Mr. Donald Tykeson, active volunteer and Honorary Life Director of the Society's National Board of Directors. Read more about the 2010 Tykeson Conference on our Web site at: nationalmssociety.org/news/news-detail/index.aspx?nid=3440.

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Lists of all Society-supported research projects are available on our Website at the following link: <http://www.nationalmssociety.org/research/research-we-fund/index.aspx>

“New Training Fellowships” is produced by the National Multiple Sclerosis Society, Research Programs, 733 Third Avenue, NY, NY 10017-3288. For more information about multiple sclerosis research, call **1-800-344-4867** or visit our World Wide Web site: **<http://www.nationalMSsociety.org>**.