INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Intrathecal monoclonal antibody therapy and cerebral microdialysis in progressive multiple sclerosis

Principal Investigator: Anders Svenningsson, M.D., Ph.D.

Institution: Umeå University

Country: Sweden

Amount Awarded: €74,800

Summary: Small clusters of immune cells called B cells are commonly found within the brains of people with progressive MS, which points to the presence of hidden and potentially damaging immune activity. Rituximab is an agent that eliminates B cells. Trials using rituximab in progressive MS so far have not been successful, possibly because rituximab is unable to access these particular B cell clusters. This team is administering rituximab directly into the spinal fluid (intrathecally). In an ongoing trial they have been treating people with progressive MS with this method, with some success. Now, while continuing to test this treatment, the team will sample immune messenger chemicals inside the brain using a device called a microdialysis catheter. They plan to insert this device in 20 people to better determine outcomes of the treatment and, for the first time, attempt to monitor immune activity inside the brains of people with progressive MS.

What does this mean for people living with progressive MS? This study can answer the question of whether there is ongoing inflammation in the brains of people with progressive MS, and whether rituximab has potential as a treatment for progression.

Anders Svenningsson, MD, PhD

Head of Neuroimmunology Unit and Associate Professor of Neurology, Department of Neurology and Clinical Neuroscience, Umeå University, Sweden

Anders Svenningsson, MD, PhD, earned his medical degree at the University of Gothenburg in Sweden and his doctoral degree at the same University on the subject of immunological changes in the cerebrospinal fluid in MS. He completed postdoctoral training at the Karolinska Institute in the group of Professor Tomas Olsson with further focus on the immunopathology of MS. He became a board certified Neurologist 1998 and is one of the leading persons in the field of MS treatment in Sweden, holding regular teaching courses on the topic for Swedish neurology residents. Dr. Svenningsson was chair of the Swedish MS Association 2011 – 2013 and is presently chair of the Swedish Association of Neurology. The main focus of Dr. Svenningsson's research today is to develop new efficient treatment protocols in MS in both the inflammatory phase and the progressive phase of the disease.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Discovery of biomarkers reflecting progression pathophysiology for primary progressive MS subtype by applying next generation sequencing and novel multiplex aptamer approach

Principal Investigator: Charlotte Teunissen, Ph.D.

Institution: University Hospital Vrije Universisteit-VUMC

Country: The Netherlands

Amount Awarded: €74,250

Summary: MS, whether relapsing-remitting or primary progressive, progresses differently in different people, suggesting that disease progression occurs for different reasons in different people. Early in the disease it is difficult to predict the course that any individual will experience, which makes it difficult to determine optimal treatment approaches. This group proposes to investigate blood samples from people with different subtypes of MS to identify disease activity and potential biomarkers – or molecular signatures -- that will differentiate relapsing-remitting from primary-progressive MS. They also aim to find ways to discriminate between people who have slow versus rapid progression. Identifying biomarkers that identify the underlying disease activity responsible for a person's disease course will allow prediction of the response to therapy and new targets for novel therapies.

What does this mean for people living with progressive MS? Having reliable biomarkers would greatly increase the ability to determine the best therapy for an individual, and offer clues to the underlying causes of MS progression.

Charlotte Teunissen, PhD
Head, Neurochemistry Laboratory and Biobank,
Department of Clinical Chemistry
VU University Medical Center Amsterdam, The Netherlands

Charlotte Teunissen, PhD, has focused on body fluid biomarkers for neurodegenerative disease and other neurological diseases since the start of her PhD thesis in 1997 at Maastricht University in The Netherlands. Her subsequent postdoctoral research fellowship was at the MS Center at the VU University Medical Center Amsterdam, and since 2009 she has been the head of the Neurochemistry Laboratory and Biobank at the VU University Medical Center. She is the initiator and general manager of the NeuroUnit Biomarkers (NUBIN) at VUMC and the BioMS-EU network. She led the development of several international consensus guidelines for spinal fluid biobanking (which served as templates for similar initiatives), and recent criteria and definitions for control group selection for spinal fluid biomarker studies. Her research group focuses on identifying novel biomarkers, primarily by proteomics, and developing and validating tests for these biomarkers for their ultimate use in clinical practice.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: T-cell activation molecules and progressive MS

Principal Investigator: David Haegert, M.D.

Institution: McGill University

Country: Canada

Amount Awarded: €74,739

Summary: Early in the course of MS it is difficult to know whose disease will progress and whose will not. This team proposes to identify and test potential biomarkers – molecular signatures – in the blood to determine if they can be used to predict whether someone with MS will show rapid or slow disease progression. They will test blood samples from people with MS who participated in clinical trials in the past, and whose course of disease progression is known. If the biomarker is indeed increased in people with rapidly progressing MS and not in those whose MS is more benign, this biomarker could be developed as a test to predict disease progression and identify people who need more aggressive treatment.

What does this mean for people living with progressive MS? Finding a biomarker that can be tested in blood samples of people with MS could help predict the rate of disease progression and help determine the most appropriate therapy.

David G. Haegert, MD, FRCPC

Professor, Department of Pathology, McGill University,
Montreal, Quebec, Canada

Dr. David G. Haegert earned his undergraduate degree from the University of Victoria, British Columbia, Canada, and his medical degree from the University of British Columbia. He completed his internship at the Royal Victoria Hospital, Montreal, and his residency training in Anatomic Pathology in the McGill University teaching hospitals. He received post-doctoral training in Immunology at the University of Cambridge, Cambridge, England. Dr. Haegert is a Fellow of the Royal College of Physicians and Surgeons of Canada in Anatomic Pathology. He now conducts research focusing on multiple sclerosis and possible biomarkers that predict rates of disease progression in multiple sclerosis and responses to therapy.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Using patient-specific, iPSC-derived neurons to model neurodegeneration in multiple sclerosis

Principal Investigator: David Pitt, M.D.

Institution: Yale University School of Medicine

Country: United States

Amount Awarded: €75,000

Summary: Disease progression varies greatly among people with MS. The reason for this is unknown, but may be related to genetic differences in the susceptibility of nerve cells to injury. Glutamate is a compound that is normally found in the brain that can cause injury to neurons when it is present in excessive amounts. This team proposes to use neuron stem cells that have been derived from skin cells from individuals with MS to test if there are genetic differences in their neurons' sensitivity to injury from glutamate. Several medications have been developed that modulate glutamate, and these could be potential new therapies for people with MS if it can be determined who may have glutamate sensitivity.

What does this mean for people living with progressive MS? If some people are genetically predisposed to sensitivity to glutamate, this subset of individuals may benefit from therapies that address excessive glutamate to slow or stop disease progression.

David Pitt, MD

Assistant Professor of Neurology, Department of Neurology, Division of Neuroimmunology, Yale School of Medicine, New Haven, Connecticut, USA

David Pitt, MD, earned his medical degree from the University of Marburg, Germany in 1998. Subsequently, he received postdoctoral research training at the Albert Einstein College of Medicine, NY, where he later completed a neurology residency and served as a chief resident. Dr. Pitt went on to complete a three-year fellowship in Multiple Sclerosis and Neuroimmunology at Washington University in St. Louis. At Yale, he conducts basic and translational research focusing on neurodegenerative aspects of multiple sclerosis. Dr. Pitt is funded by the National Multiple Sclerosis Society (USA) and the NIH and collaborates with several companies on various research projects.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Cause and consequences of mitochondrial injury in progressive multiple sclerosis

Principal Investigator: Don Mahad, M.D., Ph.D.

Institution: University of Edinburgh

Country: United Kingdom

Amount Awarded: €74,868

Summary: In MS, myelin, the fatty substance that surrounds and protects nerve fibers, is destroyed. This loss of myelin can affect the function and survival of nerve cells. Some research suggests that nerve cells may die due to damage to tiny energy-producing factories inside the cells, called mitochondria. The DNA that is found in degenerating mitochondria in nerve cells in MS often contains mutations. This team proposes to develop a test to determine the susceptibility to mitochondrial DNA mutations in MS, and will investigate the features of the abnormal mitochondria that result from the loss of myelin. The results from this study may identify ways to protect the nerve fibers and their mitochondria in people with progressive MS.

What does this mean for people living with progressive MS? If this research verifies a crucial role for damaged mitochondria in MS progression, it may identify new approaches to protecting nerve cells from harm to stop or prevent progression.

Don Mahad, MD, PhD, MRCP

Scottish Senior Clinical Fellow, Department for Clinical Neuroscience, University of Edinburgh, United Kingdom

Don Mahad, MD, PhD, MRCP, graduated from the University of Sheffield, UK, and undertook post-doctoral training at the Cleveland Clinic Foundation sponsored by Dr. Richard Ransohoff before returning to do neurology residency and a Wellcome Trust Intermediate Clinical Fellowship in Newcastle upon Tyne, UK. He then returned to Cleveland Clinic as a Multiple Sclerosis Clinical Care Physician Fellow at the Mellen Center for Multiple Sclerosis, sponsored by the National MS Society. Dr Mahad is currently a Scottish Senior Clinical Fellow based in Edinburgh, UK. He has a 20% clinical commitment seeing patients with MS at the Anne Rowling Clinic and 80% research focusing on the role of mitochondria in progressive MS.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Miglustat as a therapy for secondary-progressive multiple sclerosis

Principal Investigator: Francisco Quintana, Ph.D.

Institution: Brigham and Women's Hospital

Country: United States

Amount Awarded: €75,000

Summary: Astrocytes are cells in the brain that may play a destructive role in MS since among other activities, they are known to create scar tissue that may interfere with tissue repair. In the search for leads to new approaches to treating progressive MS, this team proposes to use an experimental mouse model that resembles several features of secondary-progressive MS to investigate the potential of a drug called miglustat. This drug is approved to treat other diseases, and it has been found to inhibit a protein, called "B4GALT6," which the team found to be involved in the activation of astrocytes. The investigator proposes to test whether miglustat can inhibit astrocytes to stop disease progression. The team will also test its impact on human and mouse nerve cells isolated in the laboratory.

What does this mean for people living with progressive MS? This study may point to a new strategy for stopping a key contributor to MS progression. Since miglustat is already is FDA-approved for other disorders, this would expedite its application to MS if it indeed proves safe and effective.

Francisco J. Quintana, PhD

Associate Professor of Neurology, Center for Neurologic Diseases, Department of Neurology, Brigham and Women's Hospital, Harvard Medical School
Boston, Massachusetts, USA

Francisco J. Quintana, PhD, earned his Diploma in Biology from the University of Buenos Aires and his doctoral degree in Immunology from the Weizmann Institute of Science in Rehovot, Israel. He completed postdoctoral training with a focus on Neuroimmunology at Brigham and Women's Hospital, Harvard Medical School. He now conducts research focusing on the regulation of the adaptive and the innate immune response and biomarkers in Multiple Sclerosis and other immune-mediated diseases. His work in the field of Immunology has earned Dr. Quintana recognition from The Weizmann Institute of Science, the National MS Society, Nature Biotechnology, the Harvard Catalyst and the Tecan Group Ltd.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Inflammation drives mitochondrial dysfunction and associated neurodegeneration in MS

Principal Investigator: Jack van Horssen, Ph.D.

Institution: University Hospital Vrije Universisteit-VUMC

Country: The Netherlands

Amount Awarded: €75,000

Summary: One of the main reasons that there are no specific therapies for progressive MS is that we know little about the processes underlying worsening disability. It has become increasingly clear that injury and loss of nervous tissue, also known as neurodegeneration, largely drives progressive MS. This team and others have shown that mitochondria, the tiny energy factories within cells, are dysfunctional in nerve cells of people with progressive MS and this may contribute to neurodegeneration. Nerve cells rely heavily on an adequate supply of energy to facilitate conduction of signals and therefore proper mitochondrial function is crucial. Eventually, impaired mitochondrial function will lead to severe nerve cell injury and loss. Now this team is unraveling which immune cells and associated inflammatory products may be responsible for mitochondrial dysfunction in nerve cells of mice and in cells isolated from people with MS.

What does this mean for people living with progressive MS? This project will significantly contribute to our understanding of mechanisms underlying progressive MS, and provide a potential basis for the development of new therapeutics to stop neurodegeneration and progression.

Jack van Horssen, PhD

Associate Professor, Department of Molecular Cell Biology and Immunology, VU University Medical Center Amsterdam, MS Center Amsterdam, The Netherlands

Jack van Horssen, PhD, received his PhD from the Radboud University Nijmegen, The Netherlands, where he was involved in Alzheimer's disease research. Thereafter, he moved to Amsterdam working in the field of MS neurobiology and neuropathology at the MS Center Amsterdam. His research focuses on the involvement of mitochondrial dysfunction and free radicals in MS pathology and how these processes contribute to inflammation-driven neurodegeneration. In 2010 he received the Dutch MS Fellowship and he is currently appointed as a visiting professor at the University of Hasselt in Belgium.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: The effects of oculomotor retraining on upper and lower limb function in progressive MS: A proof of concept study

Principal Investigator: Jonathan Marsden, M.Sc., Ph.D.

Institution: Plymouth University

Country: United Kingdom

Amount Awarded: €74,895

Summary: Balance problems typically result in a swaying and "drunken" type of gait known as ataxia. People with MS who have ataxia find it difficult to perform tasks such as manipulating tools, balancing, and avoiding obstacles. One reason for this is that they often move their eyes involuntarily from side-to-side and have inaccurate eye movement. In people who don't have MS but have ataxia for other reasons, this team has shown that inaccurate eye movements directly lead to uncoordinated arm and leg movements, and, importantly, that eye movements can be retrained, leading to improved walking and balancing. Now they are proposing to measure eye movements in 30 people with progressive MS who have symptoms of ataxia, and to also explore whether a 4-week program of eye movement retraining can improve their mobility.

What does this mean for people living with progressive MS? This study could lead to the further testing of a strategy to reduce ataxia in people with MS, potentially providing a solution that improves their daily lives.

Jon Marsden BSc (hons), MSc, PhD

Professor of Rehabilitation, School of Health Professions,
Faculty of Health and Human Sciences Plymouth
University, United Kingdom

Dr. Jon Marsden earned a degree in physiotherapy from Manchester University, UK, and an MSc in Neurological Science and PhD in Clinical Medicine from University College London, UK. He worked as a Medical Research Council postdoctoral scientist and clinical fellow at the Human Movement and Balance Unit, Institute of Neurology in London, prior to taking up his current position at Plymouth University. His research focuses on the pathophysiology and rehabilitation of balance and movement in adult and paediatric acquired and hereditary neurological conditions.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Longitudinal multicenter cervical spinal tract diffusion MRI for progressive MS

Principal Investigator: Junqian Xu, Ph.D.

Institution: Mount Sinai School of Medicine

Country: United States

Amount Awarded: €74,841

Summary: Axons, also commonly known as nerve fibers, are the primary transmission lines of our nervous system. Destruction of axons during the course of MS has been found to be critically linked with long-term disability in people with progressive MS. Finding a way to accurately assess the stage and rate of axonal loss over time is key to developing new therapies that can protect or even regenerate axons to improve function. This team proposes to develop the infrastructure needed to facilitate clinical trials that track cervical spinal cord MRI measurements as a way of measuring the impact of potential therapies on MS damage and progression. The team proposes to use very high resolution cervical spinal cord MRI to study groups of people with progressive MS and controls without MS. This method will be used at two different sites and multiple times to ensure the quality of the findings.

What does this mean for people living with progressive MS? Developing methods for tracking nervous system damage that occurs during MS progression is crucial for clinical trials that set out to determine the effectiveness of strategies at stopping or reversing this progression.

Junqian Xu, PhD

Assistant Professor of Radiology, Translational and Molecular Imaging Institute, Icahn School of Medicine at Mount Sinai, New York, USA

Junqian (Gordon) Xu, PhD, earned his BS from Peking University and his PhD in physical chemistry from Washington University in Saint Louis. He completed his National MS Society postdoctoral fellowship with a focus on spinal cord diffusion MRI at the John L. Trotter MS center, Washington University School of Medicine. He now conducts research in establishing highly reliable quantitative MRI biomarkers through an integrated technical development approach. His work in the field of in vivo diffusion MRI methods and applications has earned his recognition from Radiological Society of North America (RSNA) and International Society for Magnetic Resonance in Medicine (ISMRM).

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Can the degree of meningeal inflammation and cortical pathology be used to stratify early progressive MS patients?

Principal Investigator: Massimiliano Calabrese, M.D., Ph.D.

Institution: University of Verona

Country: Italy

Amount Awarded: €68,673

Summary: This team has previously shown that the amount of damage to the grey matter on the surface of the brain in early stages of MS associates with an increased chance that the future disease course will be more severe. Now they are analyzing the cerebrospinal fluid that surrounds the brain and using MRI brain scanning to examine brain tissue from people with progressive MS obtained via autopsy. They are examining types and quantities of messenger proteins and molecules that may be associated with damage seen by MRI scanning. This combined approach may identify both the molecules and brain imaging signals that predict a more severe disease, so that neurologists can recognize and address a more severe course of MS before quality of life is severely affected.

What does this mean for people living with progressive MS? Being able to address and vigorously treat a severe course of MS as early as possible is crucial to stopping progression in its tracks.

Massimiliano Calabrese, MD

Head of the Advanced Neuroimaging Lab, Neurology Section,
Department of Neurological and Movement Sciences,
University Hospital of Verona

Massimiliano Calabrese is a neurologist who leads the Advanced Neuroimaging Lab of the Neurology Section, University Hospital of Verona. After graduating in Medicine and Surgery at Padua's University, Dr. Calabrese completed his residency in Neurology with honors at the first Neurology Clinic of the same University (specialization thesis focused on "Regional Cortical Atrophy in Multiple Sclerosis"). He also completed a fellowship at the Neuroimmunology Branch of National Institute of Health in Bethesda (Chairman Prof. Henry McFarland and Dr. Roland Martin). In January 2013 he moved to the University of Verona to develop and expand his research focused on neurodegeneration and neuroprotection in Multiple Sclerosis, with the ultimate aim of predicting and of slowing down the accumulation and progression of irreversible disability. His work on grey matter inflammation and neurodegeneration in Multiple Sclerosis has earned more than 60 highly cited publications in international peer reviewed journals and several international awards.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Treating new learning and memory deficits in Progressive MS: the modified Story Memory Technique

Principal Investigator: Nancy Chiaravalloti, Ph.D.

Institution: Kessler Foundation Research Center

Country: United States

Amount Awarded: €74,976

Summary: Cognitive function, especially learning and memory, impacts a substantial proportion of people with MS. This team has demonstrated that the modified "Story Memory Technique" (mSMT) – which helps people to learn new information and remember older information using imagery and context – improves learning, as well as laboratory measures of memory and activities of everyday life. However, this treatment has not yet been adequately tested in people with progressive MS. Now the team proposes to test the mSMT in persons with progressive MS, measuring post-treatment changes on both laboratory measures of memory abilities and on daily life memory abilities, self-efficacy, quality of life, and occupational functioning.

What does this mean for people living with progressive MS? The results may have a significant impact on addressing the troubling symptom of cognitive dysfunction and improving quality of life for people with progressive MS

Nancy D. Chiaravalloti, PhD

Director of Neuropsychology and Neuroscience and TBI Research, Kessler Foundation, West Orange, New Jersey and Associate Professor, Department of Physical Medicine and Rehabilitation, Rutgers University-NJ Medical School, USA

Nancy D. Chiaravalloti, PhD, 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 populations. She has over 85 peer-reviewed publications. She focuses her work on cognitive rehabilitation in persons with MS and traumatic brain injury.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Novel enabling infrastructure for outcomes monitoring: dynamic remote performance capture to assess disability in progressive multiple sclerosis

Principal Investigator: Paul Matthews, M.D., Ph.D.

Institution: Imperial College London

Country: United Kingdom

Amount Awarded: €74,995

Summary: Development of new medicines for progressive MS is difficult in part because measures of disability are insensitive to the smaller changes that may be meaningful to a person with MS. People with MS also appreciate changes in their symptoms on a day-to-day basis that are not well captured in periodic, single tests done as part of clinic visits. The popularity of small movement sensing devices called “actigraphs” that allow activity to be continuously tracked, stored and then downloaded onto a computer provides an illustration of one of the kinds of technology that might help. This team proposes to conduct a pilot study to determine if actigraphs can provide a useful tool to measure and track disability in people with progressive MS. If these devices could be adapted for use for people with MS, doctors and researchers would be able to understand how people are performing in their homes, offices and communities and get a real-time sense of outcomes from treatments.

What does this mean for people living with progressive MS? Providing real-time information about symptoms and disability progression can help to track the course of MS and determine the effectiveness of treatments designed to stop progression.

Paul M. Matthews, MD, DPhil, FMedSci

Edmund J and Lily Safra Chair of Translational Neuroscience and Therapeutics and Head, Division of Brain Sciences, Department of Medicine, Imperial College London, United Kingdom

Paul M. Matthews, MD, DPhil, FMedSci, earned his BA (Hon) and his DPhil in Biochemistry from the University of Oxford. He completed medical school and an internship in Medicine at Stanford University, followed by a residency in neurology at the Montreal Neurological Institute and McGill University. He subsequently undertook post-doctoral and further clinical training in Oxford, before academic positions at McGill and Oxford. He now conducts research focusing on therapeutics development and optimization of medicine use in multiple sclerosis. His work in translational neuroimaging has led to honors including being made an Officer of the Most Excellent Order of the British Empire and to election as a Fellow of the Academy of Medical Sciences.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: A phase 1 open-label trial of intrathecal rituximab for progressive multiple sclerosis patients with magnetic resonance imaging evidence of leptomeningeal enhancement

Principal Investigator: Peter Calabresi, M.D.

Institution: Johns Hopkins University

Country: United States

Amount Awarded: €74,998

Summary: Multiple sclerosis involves an immune system attack on the brain and spinal cord. Within the tissues covering the brain and spinal cord (meninges), abnormal clusters of immune B cells have been described in progressive, and to a lesser extent, relapsing MS. These clusters are associated with increased damage to the adjoining surface of the brain and may play a role in MS progression. Rituximab is an agent that can eliminate B cells. This team proposes to use a special MRI technique to identify these cell clusters in 12 people with secondary- or primary-progressive MS. In people who have them, the team will then conduct a pilot test of rituximab delivered directly into the spinal fluid (intrathecally), and will evaluate the safety and potential effectiveness of this method for reducing the immune cell clusters.

What does this mean for people living with progressive MS? This study may point to a new treatment approach for stopping MS progression in some people with MS, and also provide a new biomarker for tracking the success of this treatment.

Peter A. Calabresi, MD

Professor of Neurology, Johns Hopkins School of Medicine and Director, Johns Hopkins Multiple Sclerosis Center, Baltimore, Maryland, USA

Peter A. Calabresi, MD, earned his undergraduate degree from Yale College and medical degree from Brown University. He completed residency training at Strong Memorial Hospital in Rochester, NY, and a research fellowship at the National Institutes of Health, Neuroimmunology Branch. He serves as Chair of a grant review committee of the National MS Society and on the board of trustees of the Society's Maryland Chapter. Dr. Calabresi is the principal investigator on several clinical trials and also oversees translational laboratory research projects. Dr. Calabresi has published over 200 research papers including numerous articles on imaging and the immunopathogenesis of MS. He is the recipient of a five-year National MS Society Collaborative Center grant from the National MS Society to study remyelination in MS, and the Jacob Javits Neuroscience Investigator award from the National Institutes of Health.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Towards a shared data repository to enhance the standards of rehabilitation in MS: Feasibility, capacity building and proof-of-concept on exercise therapy & mobility measures

Principal Investigator: Peter Feys, Ph.D.

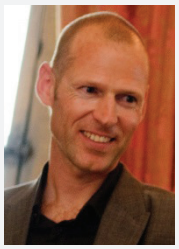
Institution: University Hasselt

Country: Belgium

Amount Awarded: €74,985

Summary: Exercise therapy is a potentially effective treatment for people with MS. However, despite an explosion of research on physical rehabilitation and exercise, it is not yet clear whether beneficial effects are equally present in progressive compared to relapsing-remitting type of MS. One issue has been the small size of studies. This project proposes to prepare the construction of a large, shared data repository that would be established by retrieving data from published studies and new data entered by clinical and research centers. This would enable researchers to investigate questions on the effects of specific exercise interventions and settings, or on the appropriateness of different outcome measures. Ultimately, this will lead to improved standards in MS rehabilitation practice.

What does this mean for people living with progressive MS? This endeavor could enhance the ability to determine the best rehabilitation and exercise interventions for people with progressive MS, and provide the data needed to advocate for its widespread use to improve lives.



Peter Feys, PhD

Associate Professor in Rehabilitation Sciences and Physiotherapy,
University of Hasselt, Limburg, Belgium

Peter Feys, PhD, received a Master's degree in physiotherapy and PhD in rehabilitation services and physiotherapy from Catholic University Leuven. He worked as clinical therapist in Bürgerspital Solothurn (CH), the University Hospitals Leuven and the National MS Centre in Melsbroek. He has been conducting MS research since 1998, funded by European projects, WOMS (affiliated to the Flemish MS Society) and the Fund for Scientific Research, Flanders. He is part of the REVAL rehabilitation research institute within BIOMED. Internationally, he is president of R.I.M.S. (stands for Rehabilitation in MS, an European network of best practice and research, www.euRIMS.org), after being chairman of the Special Interest Group on Mobility from 2008 till 2011, and serves on many other collaborative committees. He has published over 60 peer reviewed articles in international neurological and rehabilitation journals.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Azetidine-induced oligodendrogliopathy

Principal Investigator: Raymond Sobel, M.D.

Institution: Stanford University

Country: United States

Amount Awarded: €75,000

Summary: In MS, myelin, the fatty substance that surrounds and protects nerve fibers, is destroyed. Myelin is made by cells in the brain called oligodendrocytes. This team proposes to investigate one way that oligodendrocytes may be rendered susceptible to MS early in life. They are focusing on the effects of a compound found in sugar beets called Azetidine-2-carboxylic acid (Aze). Sugar beets are used in meat and dairy products and their geographical use resembles that of MS incidence. Aze resembles an amino acid called proline. Amino acids are the building blocks of proteins, and if Aze is mistakenly incorporated into proteins instead of proline, the resulting protein may be unstable. Previous studies have shown that when Aze is incorporated into proteins made by oligodendrocytes, the cells do not function normally. The team will investigate the possibility that when fed to rodents early in life, Aze is a dietary contributor to susceptibility to MS pathology. If Aze is shown to be harmful to oligodendrocytes, the results will establish a new, highly relevant rodent model of MS and suggest new research to explore this possible clue to an MS trigger.

What does this mean for people living with progressive MS? If susceptibility to MS is due at least in part to exposure to a dietary component early in life, this will suggest ways to prevent and perhaps treat MS.

Raymond A. Sobel, MD

Professor, Department of Pathology (Neuropathology), Stanford University and neuropathologist at the VA Health Care System, Palo Alto, California, USA

Raymond Sobel, MD, received a BS (Chemistry and Biology) from Stanford and medical degree from the University of California, San Francisco (UCSF). He trained in Pathology and Neuropathology at UCSF, University of California, Davis and Stanford University, and did a fellowship in Immunopathology at the Massachusetts General Hospital in Boston. Dr. Sobel has performed research on pathogenetic mechanisms in MS and EAE since 1981, and has authored or co-authored over 200 papers and book chapters on these subjects. He was President of the American Association of Neuropathologists in 2012 and is the Editor-in-Chief of the *Journal of Neuropathology and Experimental Neurology*. Current research projects address autoimmune mechanisms of reparative failure and oligodendrogliopathy, which lead to lesion and hence clinical progression in MS patients.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: New mouse model of repeated demyelination that results in a progressive neurological decline

Principal Investigator: Robin Avila, Ph.D

Institution: Renovo Neural, Inc.

Country: United States

Amount Awarded: €75,000

Summary: Multiple sclerosis involves repeated immune system attacks on the brain and spinal cord. Most people begin with a relapsing-remitting disease course of MS, which eventually develops into a progressive neurological disease course called secondary-progressive MS. Most treatments are approved for the people who are still experiencing relapses. One of the obstacles to developing treatments is the lack of animal models that mimic non-relapsing secondary-progressive MS. The purpose of this proposal is to develop a mouse model that will serve as a platform for testing new experimental strategies for stopping MS progression. The investigators propose to replicate some of the repeated injury that occurs over time and determine and document the longer-term consequences of that injury.

What does this mean for people living with progressive MS? Developing a model for testing whether therapies can stop MS progression is a critical step in bringing these strategies from the laboratory to the clinic where they can end progression in people with MS.

Robin Avila, PhD

Scientist II, Renovo Neural Inc., Cleveland, Ohio, USA

Robin Avila, PhD, earned her BS from the University of Vermont and her PhD in Biology/Structural Biochemistry from Boston College, where she studied myelin structural defects in rodent models of MS using X-ray diffraction. She completed her postdoctoral training focusing on gene regulation of the growth and specialization of myelin-making cells (oligodendrocytes) and myelination at University of Chicago. Dr. Avila now conducts research at Renovo Neural Inc. focusing on the development of pre-clinical models of multiple sclerosis.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Immune-primed microglia: a factor underlying progressive multiple sclerosis

Principal Investigator: Sandra Amor, Ph.D.

Institution: University Hospital Vrije Universisteit-VUMC

Country: The Netherlands

Amount Awarded: €74,999

Summary: This team aims to investigate the specific role of brain cells called "microglia" on MS progression. Both primary and secondary progressive MS start around 35 years, irrespective of relapses, suggesting that age may be a factor. Microglia help to activate the immune system (which attacks the brain and spinal cord in MS), but also dampen inflammation, producing substances that promote repair. A subtle balance exists between these two opposing functions. With increasing age, this balance shifts, and microglia become less effective in their protective functions, and more active stimulating damage, possibly explaining why progression increases with age. This team proposes to examine microglia from people with different types of MS, and people without neurological disease, taking into account their ages. This may reveal differences between "young" and "old" microglia, and differences between people with and without MS. They are extending these experiments in mice with relapsing-remitting MS-like disease that later becomes progressive.

What does this mean for people living with progressive MS? Understanding the impact of age on inflammation and repair may help to identify new avenues to counteract age-induced changes and prevent them from causing MS to progress.

Sandra Amor, PhD

Professor, Department of Pathology, VU University Medical Center Amsterdam, The Netherlands, and Queen Mary University of London, United Kingdom

Sandra Amor, PhD, earned her BSc and her PhD from the University of London, England. She completed her postdoctoral training with a focus on viral infections and autoimmunity in the central nervous system at St Thomas' Hospital, London. She now conducts research at the VU University Medical Center Amsterdam, focusing on understanding the first steps in the formation of MS brain lesions (damaged areas) and the impact of aging and the immune response in progressive MS. Her work in the field has earned her recognition from the Dutch MS society (Stichting MS Research) for which she was awarded a Senior fellowship. She was also awarded a "Best Information" Award by the UK MS Society for establishing "Meet the Scientist," a forum to explain scientific research to people with MS.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Genetic analysis of high-resolution imaging endophenotypes in MS progression

Principal Investigator: Sergio Baranzini, Ph.D.

Institution: University of California, San Francisco

Country: United States

Amount Awarded: €75,000

Summary: Screenings of the entire complement of common genes (genome) have identified more than 100 genes associated with a person's susceptibility to MS. Yet a significant proportion of the genetic risk to MS remains to be explained, and to date gene links to disease course have been weak. This team has evidence suggesting that the varied courses of MS seen across people is in part instructed by genes, and the team is studying specific gene regions that associate with certain hallmarks of progression, such as the total area of nervous tissue damage, brain volume loss, and decline in the visual system. In this study, the team proposes to integrate gene profiling, brain MRI, optical coherence tomography (which captures images of nerve structures behind the eye), together with sophisticated bioinformatics, to uncover genetic "signatures" that are associated with different types of disease course among hundreds of people.

What does this mean for people living with progressive MS? If this project successfully enables better understanding of how and why MS progresses in certain people, it would enable doctors to give more accurate prognoses to individuals, inform treatment decisions, and help stop progression in its tracks.

Sergio E. Baranzini, PhD

Professor In-Residence, Department of Neurology, University of California, San Francisco, and member of the Graduate Program in Bioinformatics, and of the California Institute for Quantitative Biology, USA

Dr. Baranzini holds the Heidrich Friends and Family endowed chair in Neurology. He earned a degree in clinical biochemistry and PhD in human molecular genetics from the University of Buenos Aires, Argentina. Dr. Baranzini then moved to UCSF to specialize in the analysis of complex hereditary diseases, and focused his efforts on multiple sclerosis. His current research involves characterizing the activity of genes during different stages of MS, differential response to treatment, and disease progression. He collaborates with several interdisciplinary teams worldwide to integrate all the available knowledge obtained in different research domains in an approach known as systems biology. Dr. Baranzini has published his research on MS in several top-tier journals like Science, Nature, PNAS, J Immunol, and PLos Biol.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Establishing the resource for a genetic analysis of progression

Principal Investigator: Stephen Sawcer, Ch.B., F.R.C.P., M.B., Ph.D.

Institution: University of Cambridge

Country: United Kingdom

Amount Awarded: €72,778

Summary: By bringing together dedicated researchers from 15 different countries, the International Multiple Sclerosis Genetics Consortium (IMSGC) has already successfully used genome-wide association studies to identify over 100 genetic variations influencing the risk of developing MS. The team now proposes to leverage the compiled DNA samples from 50,000 people with MS to compare gene profiles among 1000 people with the most severe course against 1000 people having the most benign course. The collecting together and collating of these samples should provide the first resource with sufficient power to identify gene variants that influence progression in MS.

What does this mean for people living with progressive MS? This resource could provide a means to identify the key biological processes determining progression in MS, and point the way to selecting rational targets for therapy development.

Stephen Sawcer, MB, ChB, PhD, FRCP

Professor of Neurological Genetics,
University of Cambridge, United Kingdom

Dr. Stephen Sawcer received his MB, ChB degrees in medicine at Birmingham University and earned a PhD in Medicine from the University of Cambridge. He has been deeply involved in the International Multiple Sclerosis Genetics Consortium (IMSGC), formed to leverage new technologies emerging through the human genome project. Bringing together researchers from Australasia, Europe and North America, the group achieved critical mass in terms of sample size and has been highly successful in pushing forward our understanding of the genetic basis of susceptibility to MS. Among its achievements were the largest MS genome-wide association study (GWAS) (Nature 2011), the largest GWAS follow up study (Nat Genet 2013) and other papers. The consortium has identified over 100 genetic variants influencing the risk of developing MS, and is now focusing on identifying the genetic factors shaping progression in the disease.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Limiting axonal degeneration in a model of multiple sclerosis

Principal Investigator: Steven Petratos, Ph.D.

Institution: Monash University

Country: Australia

Amount Awarded: €74,326

Summary: Nerve fiber damage is thought to underlie progressive disability in MS. This team has been working to understand the biological processes that lead to nerve degeneration. They have found evidence that one protein, Nogo-A, may play a role in this damage, and they have also found a possible strategy for protecting against it. They are now proposing to investigate this further by deleting this protein from nerve cells in mouse models, and then observing the effects starting at the onset of MS-like disease. Then will then attempt to block Nogo-A using novel strategies for delivering agents to the brain and spinal cord.

What does this mean for people living with progressive MS? This study may yield a new strategy for developing a therapy that limits damage to nerve cells and stops the progression of MS.

Steven Petratos, PhD

Senior Lecturer (Pathology), Department of Medicine,
Central Clinical School, Monash University,
Melbourne, Australia

Steven Petratos, PhD, earned his Bachelor of Science with Honours from the University of Melbourne and his PhD in Pathology from the University of Melbourne. He completed postdoctoral training at the Walter and Eliza Hall Institute, the Howard Florey Institute both at the University of Melbourne, as well as the Department of Biochemistry and Molecular Biology at Monash University, with a focus on the neurobiology of demyelination and remyelination. He now conducts research focusing on axonal degeneration in multiple sclerosis as well as the differentiation of oligodendrocytes. His work in the field of demyelination has earned him recognition from Commonwealth AIDS Research Grants Scholarship, Multiple Sclerosis Research Australia Project Grants Faculty of Medicine Monash University Postdoctoral and Senior Research Fellowships, National Multiple Sclerosis Society Research Grants.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: MS genetic and environmental factors for severity/progression through studies of complications including spasticity, pain, depression, urogenital complications, sick leave/pension/income using Swedish registries for comparisons/interaction analysis

Principal Investigator: Tomas Olsson, M.D., F.R.C.P.(C), Ph.D.

Institution: Karolinska Institute

Country: Sweden

Amount Awarded: €74,250

Summary: MS is unpredictable; this team is looking for a way to change that. They are studying risk genes, and lifestyle/environmental factors (such as smoking and previous infections), and their potential interactions, in a large Swedish, nationwide database. They have collected blood samples for 10 years from 8000 persons with MS and 6500 matched controls without MS, collecting data on disease development. Genetic information and the most critical lifestyle/environmental factors will be assessed for their association with MS complications such as spasticity, as well as MS severity and time to progression. The team hopes to identify genes and lifestyle factors related to outcomes and quality of life.

What does this mean for people living with progressive MS? This study could pave the way for new therapeutic strategies, and help define lifestyle and environmental factors that may provide clues to preventing or stopping MS.

Tomas Olsson, MD, PhD

Professor of Neurology, Professor of Neurosurgery and
Head of the Neuroimmunology Unit, Karolinska Institute,
Stockholm, Sweden

Tomas Olsson, MD, PhD, earned his MD and his doctoral degree in neuropathology from the University of Linköping. He completed internship, residency or postdoctoral training with a focus on Neurology and Multiple Sclerosis at the Karolinska Institute. He now conducts research focusing on neuroinflammation in general but with a strong focus on multiple sclerosis. His work in the field of neuroimmunology has earned recognition from several granting agencies (Swedish Research Council, EU, Wallenberg Foundation). He was past president of the International Society of Neuroimmunology, and is currently a member of the ECTRIMS (European Committee for Treatment and Research in MS) Executive Committee. He has received research prizes from the Fernström Foundation, The Johansen foundation in Denmark, and Umeå University for the most distinguished neuroscientist in Sweden this year. He has also been a member of the Nobel assembly for 14 years.

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Title: Search of biomarkers in patients with progressive multiple sclerosis

Principal Investigator: Xavier Montalban, M.D, Ph.D.

Institution: Institut de Recerca Vall d'Hebron (VHIR)

Country: Spain

Amount Awarded: €74,250

Summary: Ending progressive MS is an urgent and unmet need that must be overcome so that people can live their lives without the uncertainty of what tomorrow will bring. Long-term follow-up of people with progressive MS is crucial to reducing this uncertainty and establishing a disease prognosis based on how the disease course evolves. This research team has followed a group of individuals with progressive MS for more than 10 years, and has carefully collected all the necessary clinical, radiological, and biological information to propose "biomarkers" that might be used as flags to predict individuals' prognosis of progressive MS. Now they are using innovative technologies to mine this information for the identification of these predictive biomarkers.

What does this mean for people living with progressive MS? It is crucial to have ways to predict an individual's course of MS early on to help make rational treatment decisions. This project may not only reveal useful biomarkers, but also help to identify the molecular mechanisms that operate during progressive phases of MS and which might be blocked by therapies to stop progression.

Xavier Montalban, MD, PhD

Professor of Neurology and Chairman of the Department of Neurology-Neuroimmunology and Director of the Multiple Sclerosis Centre of Catalonia Vall d'Hebron University Hospital in Barcelona, Spain

Professor Montalban gained his medical license, trained as a Neurology specialist and completed his PhD in Neuroimmunology at the Universitat Autornoma de Barcelona. He then undertook a postdoctoral fellowship at the Lupus Research Institute, St.Thomas Hospital and additional clinical training at the National Hospital for Neurology and Neurosurgery, Queen Square in London, UK. He is Vice President of Fundació Esclerosi Múltiple (MS Foundation), Vice President of the Executive Committee of the European Committee for the Treatment and Research in Multiple Sclerosis (ECTRIMS), and Vice President for Institutional Relations of the Spanish Neurological Society (SEN). He serves on the medical board and committee of the Multiple Sclerosis International Federation (MSIF), the European Charcot Foundation, and many other organizations, and is a committee member of the European Magnetic Resonance Research Group (MAGNIMS). He has authored over 200 publications, and recently directed the first Spanish (second worldwide) Multiple Sclerosis Clinical Practice Guidelines.