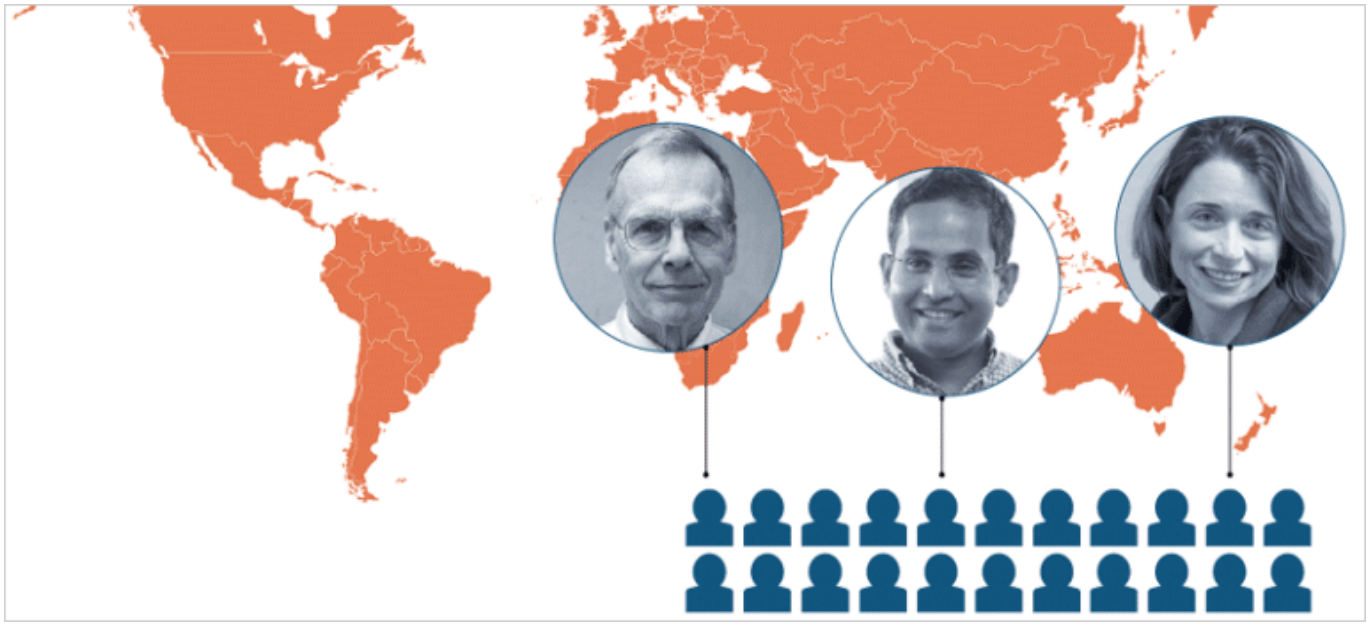
Progressive MS research sees funding boost



Worldwide effort spurs new insights into disease progression.

by Mary E. King, PhD

The more than one million people worldwide who have progressive multiple sclerosis desperately need treatment options. While there are 12 FDA-approved disease-modifying treatments for relapsing MS, these agents work primarily by reducing inflammation in the central nervous system and don't work as well in progressive MS, whose hallmark is nerve degeneration rather than inflammation. There are few FDA-approved therapies for secondary-progressive MS and none for people with primary-progressive MS.

This urgent need is driving the members of the Progressive MS Alliance, a worldwide collaborative established in 2012, to uncover the solutions that will end progressive MS. The Alliance comprises several MS organizations from around the globe, including the U.S.-based National MS Society. The Alliance's overarching, ambitious goal is to change the world for people with progressive MS.

The Alliance's founders began by identifying four major barriers to progress: a lack of understanding of the disease, the absence of markers to test for disease progression, slow and costly trials, and the lack of clear evidence to guide decisions about rehabilitation and symptom management.

Next, the group prioritized several research areas in progressive MS and then sponsored an

awards program to galvanize potential investigators and to jumpstart progress. The organization received 195 research proposals from nearly two dozen countries. From those, the Alliance awarded grants to 22 projects from researchers in nine countries, whose work will focus on six targeted areas:

- Clinical trials of new therapies, including some that will attempt to “repurpose” existing medications, and better ways to measure the effectiveness of therapies
- Identification of markers for disease progress
- Genetic studies
- Trials of rehabilitation programs
- Studies of the underlying pathways of progressive MS
- Development of new disease models for future research

This first round of funding launches an ambitious program that will cumulatively invest nearly $30 million over the next six years and will forge international collaborative research networks—leveraging research already underway and stimulating new research through the Alliance’s significant funding programs.

Here’s a look at just three of the selected studies, which demonstrate the potential for these awards to quickly change the face of research in progressive MS. (To see the full list of all 22 projects, visit nationalMSsociety.org/ProgressiveAllianceGrants.)

Identifying biomarkers of progression

Two pressing questions for people with MS are “Will my disease progress in the near future?” and “Will my disease progress quickly or slowly?” Knowing the likely course of their disease can help them make important life decisions. And once new treatments become available, doctors would want to identify the people with rapidly advancing progressive disease who might benefit most from early aggressive treatment.

Dr. David Haegert and his team are studying

“biomarkers” that may forecast disease progression. Photo courtesy of Dr. David Haegert

Dr. David Haegert, a professor in the department of pathology at McGill University in Montreal, and his team are looking closely at “biomarkers” that may forecast disease progression—in this case, proteins that are present on the surface of T cells, a type of immune cell found in the blood. Dr. Haegert’s team will look specifically for these biomarkers in blood samples from people with MS who participated in past clinical trials, and whose rate of disease progression
is already known.

“We hope to identify a biomarker that is indeed increased in people with rapidly progressing MS but not in those whose MS is more benign,” explains Dr. Haegert. “If we can do this, then we want to develop a clinical test [using the biomarker] to predict disease progression.” He also hopes that a clinical test arising from this work using biomarkers on immune cells may help identify people with progressive MS who will respond well to treatments that target those immune cells.

Understanding progressive MS

Nerve cell damage is a hallmark of progressive MS, and one of the underlying reasons may be damage to nerve cell mitochondria, those tiny energy-producing factories found inside all cells. Mitochondria contain a small amount of special genetic material, called mitochondrial DNA (mtDNA), which program mitochondrial function and energy production.

Dr. Don Mahad wants to know how easily mutations develop in

cells of people with progressive MS. Photo courtesy of Dr. Don Mahad

Dr. Don Mahad, a Scottish Senior Clinical Fellow in the department for clinical neuroscience at the University of Edinburgh, explains, “The mtDNA found in nerve cells from people with progressive MS often contains mutations.” He and his team want to determine how easily these mutations develop in mitochondria from people with progressive MS. They will also investigate a potential relationship between the loss of myelin and changes to mitochondria.

Dr. Mahad continues, “The study may show a crucial role for damaged mitochondria in the progression of MS. If that is true, our results may identify ways to protect the nerve fibers and their mitochondria in people with progressive MS.” He points out that one possible limiting factor in this project is that the nerve cells used in the study will be derived from volunteers with MS, using skin biopsy, and because the cells are peripheral nerve cells, they “may not fully reflect the properties of those that are housed in the brain.”

ID’ing effective rehabilitation programs

“Approximately 45 to 65 percent of people with MS develop memory deficits, primarily due to inefficient new learning,” says Nancy Chiaravalloti, PhD, director of neuropsychology and neuroscience and traumatic brain injury research at the Kessler Foundation Research Center in West Orange, New Jersey. “These changes are very disruptive to everyday life activities.”

Nancy Chiaravalloti, PhD, is studying whether the modified “Story Memory Technique” helps improve recall in people with progressive MS. Photo courtesy of Dr. Nancy

Chiaravalloti

Dr. Chiaravalloti and her team previously demonstrated that the modified “Story Memory Technique” (mSMT)—a practice that helps people to learn new information using imagery and context—improves learning and memory in people with MS. “The volunteers [in the earlier study] were mostly people with relapsing-remitting MS, however,” explains Dr. Chiaravalloti. The Alliance grant will allow her team to test whether mSMT will be helpful to people with progressive MS.

In the earlier research, participants received training in mSMT twice each week for five weeks, with each session lasting approximately one hour. After the training, participants demonstrated 10 percent or greater improvement in memory tests administered by the researchers. Just as importantly, the people with MS and their family members also reported significant improvement in the participants’ memory in everyday life activities. The trial included a control group that met with therapists but did not receive the same special training, and this group showed no improvement.

The investigators also saw increased brain activation in a subgroup of the study subjects when they were examined using a special type of brain imaging called “functional MRI,” additional evidence that mSMT changes brain activity.

The improvements in memory lasted for at least six months of follow-up, a very encouraging result. “The new study may help us address the troubling symptom of cognitive dysfunction and improve quality of life for people with progressive MS,” says Dr. Chiaravalloti.

Such research could not be undertaken without the support of the Progressive MS Alliance, she notes. “The Alliance is instrumental in providing resources to tackle critical problems in progressive MS, and, at the same time, developing new collaborations among top international scientists to develop additional research goals.”

Mary E. King, PhD, is a freelance medical writer in Boulder, Colorado.

For more information on progressive MS, read “New heights for progressive MS research.” The Serial Unified Multicenter MS InvesTigation (SUMMIT) study is generating excitement in its quest to unravel the mystery of MS progression.

For more information on the Alliance, visit progressivemsalliance.org.