

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.

by Donna Shryer

Why do some people experience aggressive worsening of their multiple sclerosis and others experience a mild course? Right now, no one knows the answer to this critical question. In its quest to unravel the mystery of MS progression, the Serial Unified Multicenter MS InvesTigation (SUMMIT) is generating much excitement. This international consortium, a special initiative launched by the National MS Society, began in 2010 and, as its moniker suggests, aims to propel MS research to new heights.

The SUMMIT involves a tightly coordinated international team of researchers working at four leading MS centers located in Boston; San Francisco; Basel, Switzerland; and Amsterdam. Collectively, the consortium is following 1,500 people with MS. The goal is to distinguish what causes the disease to progress more rapidly in some people versus others. To answer this question, the team is looking at potential risk factors or disease triggers as well as biological indicators (biomarkers) that can help predict progression or point to a biological pathway that's driving it.

Scientists need to understand these still-unknown disease mechanisms in order to lay a foundation for discovery and development of new therapies that can slow, halt, reverse and perhaps someday even prevent degenerating progressive attacks on the central nervous system.

This work addresses an urgent need in the field of MS research. Virtually every disease-modifying therapy approved for relapsing-remitting MS—which is characterized by periodic exacerbations of symptoms, followed by partial or complete recovery—has been tried, or is currently undergoing clinical trials, for MS progression. Unfortunately the results so far indicate that they aren't effective in people who do not experience relapses.

“The big unanswered question is why MS sometimes progresses and sometimes does not. We're going to find those answers, and it will mark an important step toward understanding how to approach a cure,” says SUMMIT consortium leader Dr. Howard L. Weiner (Harvard Medical School), an expert on MS research and clinical care, and recipient of the 2007 National MS Society/American Academy of Neurology's [John Dystel Prize for MS Research](#).

Joining Dr. Weiner in the SUMMIT consortium are three global leaders in MS clinical research: Dr. Stephen Hauser (University of California, San Francisco), an MS genetics expert and also a Dystel prizewinner; and MS clinical trials experts Drs. Ludwig Kappos (University Hospital, Basel, Switzerland) and Chris Polman (VU University Medical Center, Amsterdam).

At all four centers, the researchers are collecting data from patient examinations, MRI scans, blood tests, genetic analyses and other epidemiological reviews from the participants, and compiling them into one standardized data set to identify factors that may affect disease progression. Suspected factors that may affect disease progression include family history, smoking, sun exposure, and gender hormones.

The SUMMIT consortium marks the first joint study between worldwide centers funded by the Society. The study targets MS progression and the factors associated with it. With all the data merged into one central location, great minds from these and other research centers can coordinate their efforts—and perhaps quicken the process—to isolate prognostic factors that define MS progression patterns.

Patterned for success

SUMMIT leaders expect that in time, patterns will emerge. Any one factor—or a combination of biological, environmental and lifestyle factors—may unite people whose MS progresses, and differentiate them from those whose MS does not progress. With that information, scientists might have new leads on developing more effective treatments for MS progression. And physicians might one day be able to proactively begin treatment of those predisposed to MS progression.

That's the storyline that's unfolded in other diseases, such as when scientists discovered a mutated gene pattern among women who face a higher risk of developing breast and ovarian cancer. Testing for this gene now gives women and their physicians an opportunity to take proactive cancer prevention steps under certain circumstances.

“When we can predict why, when and how MS progresses over time, we'll be in a strong position to develop highly targeted MS treatments, make better use of existing treatments and move closer to a cure that stops MS disease progression and restores function,” Dr.

Weiner explains.

Breaking new ground

One point that sets the SUMMIT team apart is its long-term approach to the problem. This would be a significant step forward, says Dr. Hauser. “In the past, we’ve examined how MS progression behaves through clinical trials, and typically with only a two- or three-year window. But because meaningful changes in MS progression happen more slowly, we need a longer time frame to assess how our theories and therapies are working. We need studies like the SUMMIT to find those kinds of answers.”

A second distinguishing SUMMIT feature is its international perspective. “We’ve learned through other multinational trials that what happens in Eastern Europe may not necessarily happen in North America,” Dr. Hauser points out. “Genetic ancestry is different. People tend to take more medications in the Western world, so there could be interaction effects. People may have different levels of sun exposure, smoking histories and exposure to the Epstein-Barr virus. These are just some of the things that may influence the onset and behavior of progressive MS—and they’re all things we’re looking at. But before we can identify patterns, we have to know if our conclusions for patients in San Francisco are transportable to Amsterdam.”

Looking forward

Though SUMMIT is still in its infancy, Dr. Weiner believes that the study is on the right trajectory. During the initial two-year pilot study phase just completed, SUMMIT researchers established a seamless process to pool patient data across all four hospital centers. And with a trusted data sharing process in place, there may be opportunities to expand the SUMMIT, bringing other interested research groups into the study.

As for SUMMIT’s future, the team leaders are ready to move forward with a few clues they’ve already uncovered. So far, merged data indicates that certain changes in MRI scans, such as brain atrophy (shrinkage), may link to MS progression, although it’s too soon to say for certain. Specific MRI changes may also tie back to patterns of genetic inheritance.

“One thing people sometimes forget is that everyone who has MS, even at its earliest phases, faces the probability of disease progression, whether they have relapsing-remitting, primary-progressive, or other forms of MS,” notes National MS Society Chief Research Officer Dr. Timothy Coetzee. “Knowing what’s driving this is critical to stopping MS in its tracks,” he adds.

SUMMIT’s objectives address key aspects of the [Society’s Strategic Response to MS](#), and also to priorities established by the International Progressive MS Collaborative. Now the SUMMIT team is working with Society leadership to develop a plan for the feasibility of sustaining this project on a long-term basis.

When asked to predict what the world will someday say about SUMMIT, Dr. Weiner is quick

with a response: “I hope scientists say that the SUMMIT inspired them to develop better treatments that led us to a cure.”

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