

Bigger, better, faster, more—high-tech research in MS

We have big goals for MS research—stop the disease, restore function and end the disease forever. These days, big goals in biomedical research demand the best that high technology has to offer. Here are just a few examples of how investigators funded by the National MS Society and others are reaching to the cutting edge and beyond.

A marriage of data and biology

Sergio E. Baranzini, PhD (University of California, San Francisco), was chosen for the Society's prestigious Harry Weaver Neuroscience award this year because he is a young investigator with potential to make great contributions to MS research. He is a world-class expert in "systems biology" and is now applying this approach to MS.

Systems biology has only recently become possible. Using a combination of new techniques including rapid genome analysis (the entire collection of an individual's genes), data banks of information about gene and protein sequences and sophisticated computer programs to analyze massive amounts of information, Dr. Baranzini and his team can evaluate how networks of many factors interact.

As part of his project, Dr. Baranzini is conducting a full genome analysis of a pair of

identical twins. One twin has MS, while the other does not. Because identical twins start life with identical sets of genes, this analysis should reveal the alterations in gene structure related to the development of MS that may have been influenced by the environment.

The results could improve our understanding of MS and reveal new targets for the development of treatments.

Imaging the genetics of MS

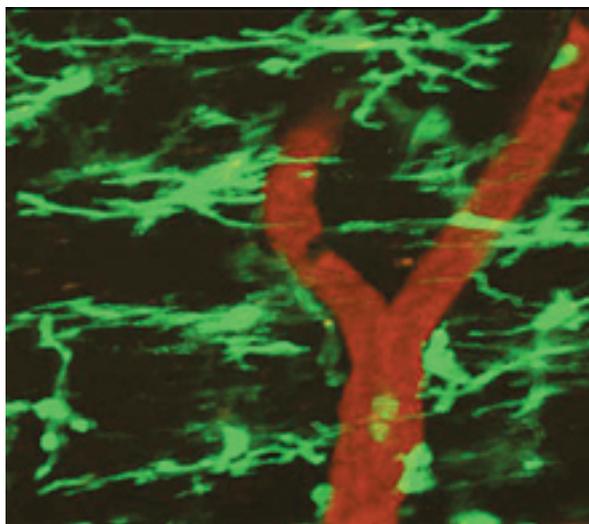
Heather A. Wishart, PhD (Dartmouth Medical School), started her career as an award-winning scholar who studied psychology. Now she is launching a unique study where genetics and imaging information will be linked with participants' levels of physical and cognitive impairment. This groundbreaking study is geared

to understanding why MS varies so greatly among individuals.

With support from the Department of Defense, Dr. Wishart is using advanced magnetic resonance imaging techniques—including high-resolution scans and diffusion imaging (which measures the flow of water particles) to map details of nerve tissue damage. Next, her team will screen the entire genome of these individuals, looking for differences and focusing on genes involved in nerve growth factors that may facilitate nervous system repair.

Piggy-backing on these high-tech approaches with the help of Society funding, she will then search for linkages to the results from series of tests measuring the physical and cognitive impairment of her study participants.

This ambitious study should enable Dr. Wishart's team to determine how the extent and location of nerve damage (revealed by imaging), and genetic



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Nervous system immune cells (green) extend processes towards the blood vessels (red) in myelin-covered areas in the spinal cord; such images are possible using two-photon microscopy, a technique that uses fluorescence to image living tissue.

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variations (revealed by the whole genome studies) relate to physical impairments and cognitive disability. This new knowledge could form the basis for methods to predict the course of MS and tailor treatments for individuals.

Seeking clarity in the spinal cord

Katerina Akassoglou, PhD (University of California at San Francisco) is a pioneer in nervous system research known for her efforts to understand the effects of blood proteins such as fibrinogen. She reported that blocking a segment of the fibrinogen protein reduced MS-like disease in mice. She received the Presidential Early Career Award for Scientists and Engineers for her research, the highest honor bestowed by the United States government on scientists and engineers beginning independent careers.

Dr. Akassoglou also integrates novel technology into her studies. She uses two-photon microscopy, a technique that uses fluorescence to image living tissue. Until now, two-photon microscopy has been applied highly successfully to studies of the brain, but not the spinal cord. For one thing, says Dr. Akassoglou, the proximity of the heart to the spinal column results in interference caused by the heartbeat and breathing movements.

With Society funding, Dr. Akassoglou's team, which

includes Dimitrios Davalos, PhD, a postdoctoral fellow funded by the Society, has developed a way to adapt two-photon microscopy to get live images of myelinated areas by exposing only a very small area of the spinal cord of an anesthetized mouse. The technique allowed them to see cells in action. They were able to watch immune cells interacting with nervous system cells and blood cells. This technique should allow researchers to visualize the immune attack launched on the spinal cord in MS. **Journal of Neuroscience Methods** 2008;169:1-7

Capturing a viral culprit

John Kriesel, MD (University of Utah), uses genetics to "capture" viruses that cause disease. His team reported on findings linking a gene to cold sores in 2008. Now, with funding from a Society Pilot Research Award, Dr. Kriesel is using genetics technology to identify a possible viral trigger of MS.

MS is thought to occur when people whose genes make them susceptible encounter something in their environment that triggers an immune attack. But no single viral or bacterial trigger has yet been identified.

Dr. Kriesel's team is applying "subtractive sequencing" to brain specimens taken from 12 people who had MS in their lifetimes and

12 controls who did not have MS. Subtractive sequencing allows detection of millions of different RNA molecules in a single specimen. RNA, or ribonucleic acid, is the chemical that delivers the instructions from a gene to a cell. All living things, including viruses, make RNA. In subtractive sequencing, human RNA is "subtracted" out from the millions of RNAs in a human tissue specimen, detected, leaving thousands of non-human, possibly disease-causing RNAs. This pilot study will help determine whether this technique will be fruitful for identifying infectious triggers of MS.

The men and women who are exploring the underpinnings of MS continue to apply the best of new technology to move us closer to the great goal of ending this disease forever.

In the Fall 2009 issue, we ran a story called "Dangerous foe or tiny protector? Understanding microglia" and failed to cite pioneering work by Society-funded researcher Dr. Ian D. Duncan and team, who in a series of papers showed the impacts of the antibiotic minocycline on microglia and its potential promise as a therapeutic approach for MS. We regret the inadvertent omission.