

Fostering teamwork: Progress from the first MS Collaborative Centers

The first Collaborative MS Research Centers launched by the National MS Society in 2003 have completed their projects, and the results vouch for the potential of this award to speed us toward a world free of MS. These \$825,000 grants create teams where seasoned MS researchers work with experts from other fields, and basic scientists join clinical investigators, addressing tough issues in MS research.

New window on MS activity

Anne Cross, MD, assembled an interdisciplinary team at Washington University in St. Louis to determine whether a novel MRI technology—“diffusion tensor imaging,” or DTI, could do a better job than conventional MRI at differentiating the extent and types of tissue damage and repair in MS. DTI reveals how many protons in water molecules are moving in tissue, and in what direction. If fatty myelin is intact, then water should be repelled, but if it is damaged, water will infiltrate the tissue.

With funding from the Center Award, Dr. Cross, Sheng-Kwei Song, PhD, and a team of neurologists, radiologists, biophysicists, biomedical engineers and pharmacologists used DTI to extensively study models of MS-like disease. Their results

show great potential for using this technology as a noninvasive method of detecting damage to nerve fibers in MS and differentiating this damage from injury to the myelin that insulates nerve fibers.

In one study, the team showed that nerve fiber injury detected by DTI actually correlated with symptoms in mice with an MS-

Teams work! Society-funded collaborations are bringing new insights and new talents to the search for better answers.

like disease. (**NMR Biomedicine** 2007 Nov 28 [Epub ahead of print]) Such findings help to confirm the link between nerve fiber injury and the progression of disability in MS. Dr. Cross and colleagues also reported that DTI revealed abnormalities that were not apparent under a microscope. (**Magnetic Resonance Medicine** 2007 Apr;57(4):688–95)

Aside from scientific progress, Dr. Cross has used this award to establish a vibrant team of scientists dedicated to MS at her university. The group meets twice monthly to discuss progress. They have attracted new talent to the field, including Junqian Xu, PhD, who switched from cancer

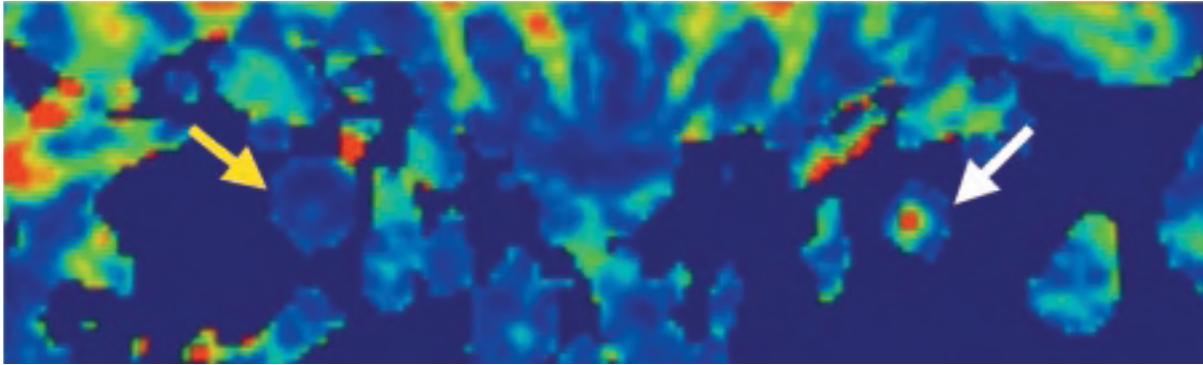
research to MS, and now has a postdoctoral fellowship from the National MS Society.

Going for genetic gold

In 2003, David A. Hafler, MD (Harvard Medical School and Brigham and Women’s Hospital) created an MS genetics “dream team” by joining with MS genetics pioneer Stephen L. Hauser, MD, (see p. 67), Eric Lander (Broad Institute of MIT and Harvard), who spearheaded the mapping of the human genome, and Alastair Compston, PhD, FRCP (University of Cambridge). The group received the Palmer Collaborative MS Research Center Award: MS Targeted Haplotype Project from the National MS Society to speed work toward discovering MS genes. (Funded by a generous gift from Barbara Palmer.)

Mission accomplished! This award propelled the formation of the IMSGC, an international group of investigators with expertise in genetics, database design/construction, and clinical assessment and immunology of MS. Members have established a shared DNA repository, which enables them to gather the large amounts of data necessary to conduct genetics studies.

In 2007, the IMSGC completed the largest replicated whole genome scan (scan of all the genes in the body) for MS to date, identifying two new genetic variations associated with MS. The findings



Collaboration among researchers at Washington University in St. Louis yielded new information on how diffusion tensor imaging (DTI) might enhance the ability to track nerve tissue damage in MS. This DTI image shows damage in the optic nerve in a person with chronic optic neuritis, an inflammation of the optic nerve that can be the first symptom of MS. Increased water content in the chronically affected eye (the yellow arrow) is seen with less organized structures (the blue color), indicating nerve tissue damage. The unaffected eye (white arrow) is seen with normal-appearing structures (red and green color).

point to potential mechanisms underlying the disease and present possible new targets for designing better therapies to stop the immune attack in MS. (*The New England Journal of Medicine* 2007 Aug 30;357[9]:851–62) The next steps for the IMSGC are even more exciting—the consortium launched by Dr. Hafler’s Center Award is now engaged in an even larger study of over 10,000 patients in which they expect to identify all of the common MS susceptibility genes.

Closer to repairing myelin

Charles Stiles, PhD (Dana Farber Cancer Institute, Boston) and David Rowitch, MD, PhD (now at University of California, San Francisco) were investigating the foundation of brain cancer when they joined forces to identify “Olig” genes, which instruct

immature cells to become myelin-making oligodendrocytes. They showed that these genes are tremendously important in the early development of cells in the brain and spinal cord, and could hold the key to repairing myelin, the nerve insulator considered the main target in MS.

Although these scientists are experts in molecular genetics and brain development, they were relatively new to the field of MS, so they joined with an expert MS research team at Albert Einstein College of Medicine, including Cedric S. Raine, PhD, DSc, winner of the Society’s 1996 John Dystel Prize for MS Research.

It didn’t take long for this group to break new scientific ground. They studied Olig genes during development of the mouse brain and spinal cord, and in tissue samples from persons

with MS obtained by Dr. Raine’s group. The results show that Olig 1 is **required** for repairing myelin damage. (*Science* 2004 Dec 17;306[5704]:2111–5)

Based on these results, the work continues, as the group focuses on developing methods of enhancing Olig 1 activity and stimulating repair. Dr. Rowitch—who was doing mostly cancer research in 2003—is sticking with MS-related research, studying myelin-damaging diseases in children.

Fourteen Collaborative MS Research Centers are currently funded by the National MS Society to focus on many aspects of MS, including central nervous system repair, the search for MS therapies, and understanding MS damage and how to stop it. Read more about them on our Web site at nationalmssociety.org/CenterAwards.