

VA Rehabilitation Research and Development

**Center of Excellence for Restoration of
Nervous System Function**

West Haven, CT

Stephen G. Waxman, MD, PhD, Director
Jeffery D. Kocsis, PhD, Associate Director

About the Center

The goal of West Haven VA Rehabilitation Research and Development Center of Excellence is to advance rehabilitation through novel molecular and cellular approaches that will provide neuroprotection and neural repair, to preserve and restore function in people with nervous system disorders. Our initial focus on multiple sclerosis (MS) and spinal cord injury (SCI) has now expanded to include neuropathic pain, stroke and traumatic brain injury (TBI). These disorders affect the lives of many thousands of veterans. Our recent progress and plans include:

- Demonstration that human bone marrow-derived stem cells improve functional outcome in stroke models. These preclinical studies are aimed at providing the basis for human clinical studies in stroke, and then, if appropriate, TBI.
- Demonstration that bone marrow-derived stem cells, delivered intravenously, support remyelination within injured spinal cord in experimental models. This study brings us closer to novel stem cell-based therapies for people with MS and SCI.
- Demonstration of sodium channel plasticity in MS. We have translated our observations from experimental models to human MS, and have demonstrated enhanced expression of sodium channels and established their molecular identities in demyelinated spinal cord axons from MS patients. We have delineated the channel that drives Ca²⁺-importing Na⁺/Ca²⁺ exchange in degenerating axons in MS, thus identifying it as a therapeutic target.
- Human genetic model of neuropathic pain. We have demonstrated a critical role for a specific ion channel in human pain. We have begun to identify human polymorphisms that may confer resistance, or susceptibility, to acquired pain, and increased/decreased responsiveness to pharmacotherapy. We plan to build upon these observations, to provide a basis for genomically-based, personalized therapies for chronic pain.
- Painful human neuromas. We have begun to identify specific sodium channel isoforms, and protein kinases, as targets in painful human neuromas.

The Center has to its credit, over 400 articles in peer-reviewed journals including *Nature Medicine*, *Nature Reviews Neuroscience*, *Annals of Neurology*, *PNAS*, and *Journal of Neuroscience*. These articles have been cited over 18,000 times according to Citation Index. In addition, Center staff have authored or edited more than half a dozen books including *Spinal Cord Compression*, the definitive work on the subject; *Diseases of the Spine and Spinal Cord*, and *The Axon*. The Center is currently engaged in major collaborations with investigators in England, Germany, China, and Japan.

The multidisciplinary team of scientists at the Center includes molecular cell biologists, physiologists, pharmacologists, stem cell biologists, computational neuroscientists, and clinicians that move back and forth between the laboratory and clinic as they conduct rigorous investigations in experimental models and human disease. Most have joint appointments with Yale University, and include PhD and MD-PhD students that are training to become the next-generation researchers of CNS plasticity and recovery of function in SCI, MS and related disorders. Center scientists have received a number of prestigious awards and honors; continue to organize and chair scientific

symposia and workshops, and deliver numerous lectures both nationally and internationally, as listed below.

Major Awards and Honors

Wartenberg Award, American Academy of Neurology
Reingold Award, National MS Society
Dystel Prize, National MS Society, and American Academy of Neurology
Institute of Medicine, National Academy of Science
Presidential Early Investigator Award
C.P Symonds Award, British Association of Neurologists
Caroline Suden/Hellebrandt Award, American Physiological Society
CNS Section Young Investigator Award, American Physiological Society
Bridget Marie Flaherty Professorship, Yale University School of Medicine
William S. Middleton Award, Department of Veterans Affairs

Major Lectures

JZ Young Memorial Lecture, University College, London
Denny-Brown Lecture, Harvard University
Tuve Memorial Lecture, National Institutes of Health
Aird Lecture, University of California, San Francisco
Charcot Memorial Lecture, Washington, DC
Norman Geschwind Lecture, Harvard University
RS Allison Lecture, British Neurological Association
K. Casey Lecture, University of Michigan
Donald Munro Lecture, American Paraplegia Society

Contact Information

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Stephen Waxman, MD, PhD, is the Center Director who exemplifies the bridge between basic research and clinical medicine. He is the Bridget Marie Flaherty Professor of Neurology, Neurobiology, and Pharmacology at Yale University. He has served as Chairman of Neurology at Yale since 1986 and is also the Director of the Yale Center for Neuroscience and Regeneration Research at the West Haven VA.

Dr. Waxman received his BA from Harvard and his MD and PhD degrees (1970, 1972) from Albert Einstein College of Medicine. Following Neurology Residency at Boston City Hospital/Harvard Medical School (1972-75), he held faculty appointments at Harvard Medical School, MIT, and Stanford University, prior to moving to Yale in 1986. Dr. Waxman's research has the goal of delineating the roles of sodium channels both in normal neuronal function, and in neuronal pathophysiology, and is aimed at developing new therapies for neurological disorders such as spinal cord injury, nerve injury, multiple sclerosis, and neuropathic pain.

Dr. Waxman has published more than 500 scientific papers, has authored the clinical text *Spinal Cord Compression*, and has edited seven books. He has served on the editorial boards of many journals including *Brain*, *Annals of Neurology*, *Trends in Neurosciences*, *Nature Clinical Neurology*, and *Trends in Molecular Medicine*, and he serves as Editor of *The Journal of Physiology* and as Editor-in-Chief of *Neuroscience Letters*. Dr. Waxman has trained more than one hundred and fifty academic neurologists and neuroscientists who work at institutions around the world.

A member of the Institute of Medicine of the National Academy of Sciences, Dr. Waxman is an Established Investigator of the National MS Society. His many awards include the Tuve Award from NIH, the Distinguished Alumnus Award from Albert Einstein College of Medicine, the Reingold Award from the National MS Society, the Dystel Prize and the Wartenberg Award from the American Academy of Neurology, and the William S. Middleton Award from the Department of Veterans Affairs.

Jeffery D. Kocsis, PhD is the Associate Director of the Center for Neuroscience and Regeneration Research in West Haven, Connecticut. He is also a Senior VA Medical Research Scientist, and Professor in the Departments of Neurology and Neurobiology at Yale University School of Medicine. Dr. Kocsis is an expert in the field of axonal regeneration and remyelination, and on cell-based approaches to nerve injury repair. His research focuses on axonal pathophysiology in diseases and injuries of the central nervous system (CNS) and on transplantation based mechanisms to repair and protect the damaged CNS. Dr. Kocsis is the Chairman of the Scientific Advisory Board for the Paralyzed Veterans of America Spinal Cord Research Foundation, and serves on numerous committees for the VA and NIH. Dr. Kocsis has authored more than 200 publications pertaining to his work. He received his Ph.D. from Wayne State University School of Medicine and carried out post-doctoral work in the Department of Neurology at the Harvard Medical School and the Department of Biology at the Massachusetts Institute of Technology.