

Fast ForwardSM

Accelerating Innovation Fund

This project is funded through a collaboration between Fast Forward, LLC, established by the National MS Society to speed potential therapies into drug development and clinical trials, and EMD Serono, Inc., an affiliate of Merck KGaA, Darmstadt, Germany. Fast Forward and EMD Serono committed \$3 million in 2009 to support innovative early-stage projects directed towards the development of therapies to prevent, treat, or reverse nervous system damage in MS. This was the first "Request for Proposals" (RFP) issued under the auspices of a multi-year collaboration between Fast Forward and EMD Serono to accelerate innovation and commercial development of MS therapies. Merck KGaA, the parent corporation of EMD Serono, Inc., will provide up to \$19 million in total funding for the collaboration.

<i>Primary Investigator</i> Lawrence Sherman, PhD Division of Neuroscience Oregon Health & Science University Beaverton, OR	<i>Project Title</i> Novel hyaluronidase inhibitors for the promotion of remyelination	<i>Amount to be Committed</i> \$275,000 Term – 12 months
---	---	--

About the Investigator

Dr. Larry Sherman is Senior Scientist in the Division of Neuroscience and a Professor in the Department of Cell and Developmental Biology, in the Neuroscience Graduate Program and the Program in Molecular and Cellular Biology at the Oregon Health & Science University School of Medicine. He received a Ph.D. in Cell Biology and Anatomy from OHSU. Dr. Sherman conducted post-doctoral research at the Institut für Genetik at the Forschungszentrum in Karlsruhe, Germany, then became an Assistant Professor in the Department of Cell Biology, Neurobiology & Anatomy at the University of Cincinnati School of Medicine. He joined the OHSU faculty in 2002. Dr. Sherman serves on a number of national grant review boards, is on the editorial board of the journal GLIA, and is the President of the Oregon Chapter of the Society for Neuroscience.



FastForwardSM

Accelerating Innovation Fund

Project Background & Goals

Multiple sclerosis occurs when the immune system attacks the myelin insulation on nerve fibers. Nerve fibers themselves are also destroyed. Some spontaneous repair occurs via populations of immature myelin-making cells – also known as OPCs, or oligodendrocyte precursors – resident in the brain, but this repair is not sufficient to completely reverse the damage. Researchers are searching for ways to stimulate these natural repair resources as one of several strategies being tested for restoring function in people with MS.

Dr. Sherman has found that a form of a complex sugar molecule, called hyaluronan, accumulates in myelin-damaged areas in the brains of people with MS. In models of MS-like disease, hyaluronan prevented myelin repair by inhibiting OPCs from maturing. (Nature Medicine 2005 Sep;11(9):966-72)

Dr. Sherman's team postulates that by-products of hyaluronan inhibit myelin repair. In this project they will test whether blocking of the enzymes which produce these by-products, known as hyaluronidases, will overcome the myelin repair blockage. They aim to accomplish this by identifying molecules that inhibit hyaluronidase activity and promote the maturation of OPCs in laboratory cultures. In this aim, the team is collaborating with Dr. Joachim Jose from the Institute for Pharmacology and Medicinal Chemistry at the Heinrich-Heine University in Düsseldorf, Germany, who has identified a number of hyaluronidase inhibitors.

In a series of further steps, Dr. Sherman and colleagues will take the most promising compounds and evaluate their ability to promote myelin repair in animal models that have myelin damage or have diseases that mimic aspects of MS, as a prelude to early testing in people.

If successful, this project could lead to a new therapeutic strategy to stimulate repair in people with MS and restore function. These experiments may identify a novel group of agents that promote myelin repair and set the stage for testing the safety and efficacy of these agents in a clinical trial in people with MS.