Fast Forward℠

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 Request for Proposals (RFP) was 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.

Primary Investigator	*Project Title*	*Amount to be Committed*
Bevyn Jarrott, PhD, BPharm Florey Neuroscience Institutes University of Melbourne Melbourne, Australia	Development of novel sodium channel blocking drugs for treating multiple sclerosis	$275,000 Term – 12 months

About the Investigator

Professor Bevyn Jarrott PhD, BPharm, is a Professorial Fellow at Florey Neuroscience Institutes and Honorary Professor of Pharmacology at The University of Melbourne. Dr. Jarrott graduated from the University Of Queensland School Of Pharmacy, where he was awarded the Parke Davis Award and Eleanor Chalmers Prize. He went on to complete a PhD in pharmacology at the University of Cambridge (UK). Dr. Jarrott has been closely involved in the design and assessment of synthetic compounds for use as cardioprotective drugs. These compounds have been patented and a start-up company, NeuProtect Pty Ltd was formed by the Howard Florey Institute and the University of Melbourne to develop candidates through to clinical trials. Professor Jarrott is an Advising Editor in Pharmacology for the journal *Clinical & Experimental Pharmacology and Physiology*. He is the author of 220 original scientific publications.

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Project Background & Goals

The immune attack underlying MS destroys the myelin insulation around nerve fibers and disrupts normal nerve signaling, but the nerve cells and fibers themselves are also damaged, which can lead to progressive disability.

Damage to nerve fibers may be the result of several aspects of the MS disease process. Nerve signaling depends on the function of tiny pores – called sodium channels – on the surface of nerve fibers. A massive influx of calcium is the final step in nerve fiber destruction, and sodium channels seem to play a role in this process. In particular, abnormalities in the sodium channel Nav 1.6 have been linked to excessive calcium influx. In fact, phenytoin, a sodium channel blocker, has a neuroprotective effect in rodent models of MS, and is now being tested in a small study of people with optic nerve damage that is being funded by the National MS Society.

Another aspect of MS that may contribute to nerve cell and fiber damage is the activity of “free radicals.” These are normal byproducts of bodily processes that may be able to turn on immune attacks in MS. Research indicates that these molecules also may cause nerve cell damage by impairing cells’ ability to produce energy.

Bevyn Jarrott, PhD, BPharm, and Spencer Williams, PhD, BSc, at the University of Melbourne have begun to develop novel compounds that are both potent sodium channel blockers and free radical quenchers. The lead compound is called mexiletine. They are now synthesizing a large “library” or collection of these compounds and are screening them for their ability to accomplish both tasks using novel laboratory techniques.

The compounds that show the most promise will be tested to determine their safety and neuroprotective capabilities in mice with EAE, an MS-like disease. If they appear to be safe and effective, clinical trials can then commence in people with MS.

This study may help to accelerate the development of therapies that stop the progression of nerve fiber damage in people with MS.