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## RESEARCH/CLINICAL UPDATE

cc: Chapter President, Programs, Development

December 7, 2012

### **Researchers co-funded by the National MS Society discover possible mechanism for multiple sclerosis damage to nerve tissue in mice**

Researchers funded in part by the National MS Society found evidence that a blood-clotting protein called fibrinogen may play an early role in damage to axons (nerve fibers) in a model of MS-like disease in mice. Axonal damage underlies the progressive disability experienced by people with MS. If confirmed, the findings reveal early events that may trigger nervous system damage in a mouse model of MS, and point to possible new targets for new therapies to protect against that damage in people with MS. Drs. Dimitrios Davalos, Katerina Akassoglou (University of California, San Francisco) and colleagues report their findings in *Nature* (advanced online publication, November 27, 2012, <http://www.nature.com/ncomms/journal/v3/n11/full/ncomms2230.html>).

**Background:** In a healthy immune system, brain cells called “microglia” help to keep the brain and spinal cord safe from infectious agents. For reasons that are not yet clear, microglia switch to the offense in the immune attack in MS, serving up triggering molecules to immune T cells and spurring on the attack. Early in the development of MS and in the MS-like disease EAE, there is disruption in the blood-brain barrier (a system of blood vessels that controls what can enter the brain from the bloodstream).

In previous studies, Dr. Akassoglou and colleagues have shown that fibrinogen, a blood-clotting factor, leaks into the brain during the immune attack, and directly activates microglia. By inhibiting fibrinogen after the first attack in mice with the MS-like disease EAE, they were able to decrease the activation of microglia, and subsequent damage to nerve fiber-ensheathing myelin (a main target of the MS attack) diminished dramatically.

The team integrates novel technology, for example, two-photon microscopy, a technique that uses fluorescence to provide vivid, real-time detail of living tissue in action. Dr. Akassoglou’s

team, which includes current and former National MS Society postdoctoral research fellows Drs. Dimitrios Davalos, Jae Kyu Ryu, and Natacha Le Moan, developed a way to adapt two-photon microscopy to watch immune cells interacting with nervous system cells and blood cells.

The Study: The team traced early events involved in myelin and axon damage in mice with EAE, and the contributions of fibrinogen in these events. They reported evidence that leakage of fibrinogen through the blood-brain barrier early in the course of EAE correlated with sites of axon damage, and that, when stimulated with fibrinogen, microglia cluster near where the blood-brain barrier is disrupted and where myelin and axon damage are located. The team also showed evidence that fibrinogen is required for the damage to occur.

Fibrinogen is the first protein, among many that leak across the disrupted blood-brain barrier during the course of EAE, shown to stimulate microglia. The authors also noted that fibrinogen induced the release by microglia of “reactive oxygen species,” which are molecules that are active in the immune attack and have been found to directly damage axons. Finally, they identified a surface docking site on microglia, called “CD11b/CD18,” which appears to be how fibrinogen interacts with microglia to exert its nerve-damaging effects.

Comment: Taken together, the team’s studies reveal early events that may trigger nervous system damage in a mouse model of MS, and point to a crucial role for the blood clotting protein fibrinogen in stimulating inflammation that leads to that damage. If these early studies are confirmed, targeting the interaction of fibrinogen and CD11b/CD18 may prove to be a novel strategy for stopping MS damage in its tracks.

Read more (<http://www.nationalmssociety.org/research/stop/index.aspx>) about efforts to stop MS.



## VOLUNTEER MANAGEMENT

December 7, 2012

CC: All

**Leader in the Movement: Duane Haverty**

Duane Haverty is a **Leader in the Movement!** For twenty-nine years he has been a passionate volunteer, leading others to join the MS movement! He leads by example, with a sense of purpose and a sense of humor!

Click [here](#) to read the story!

We invite all to share your **Leaders in the Movement** with us, and with your colleagues across the country. Do you have volunteers leading and training other volunteers? Are your volunteers empowered to use their skills and make a difference in the lives of people living with MS? Do you engage a volunteer who has unleashed their creativity to inspire others to join the movement?

Send stories to:

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