

Inhibiting blood to save the brain

March 22 2007

A fibrous protein called fibrinogen, found in circulating blood and important in blood clotting, can promote multiple sclerosis (MS) when it leaks from the blood into the brain, triggering inflammation that leads to MS-related nerve damage. Researchers at the University of California, San Diego (UCSD) School of Medicine have identified a fibrin-derived peptide that inhibits this specific inflammation process in mouse models of MS, reducing MS symptoms.

"Current strategies to develop therapies to fight MS primarily target T cells," said Katerina Akassoglou, Ph.D., assistant professor in UCSD's Department of Pharmacology, whose study was published in the March 19 issue of *Journal of Experimental Medicine*. "Blood proteins have been neglected as a therapeutic target, but this research shows that a blood clotting factor is an important player in MS."

MS is an inflammatory disease that affects the central nervous system, causing symptoms such as loss of balance and muscle coordination, and changes in cognitive function. The disease is marked by loss of myelin, a material that coats nerve fibers. Past studies showed that the destruction of the myelin sheath is associated with the accumulation of fibrinogen deposits in the brain of human MS patients. In this study, Akassoglou and colleagues showed that fibrinogen is not merely associated with the damage in MS, but an active participant. Fibrinogen activates macrophage cells in the brain called microglia, causing inflammation which damages myelin.

The scientists sought to design a therapeutic strategy that would block

the damaging effects of fibrinogen without affecting its beneficial blood coagulation. Studying a mouse model, the researchers identified a specific receptor called Mac-1 that is expressed by microglial cells and binds to fibrinogen. Mice expressing a mutant form of fibrinogen that failed to bind Mac-1 had fewer inflammatory lesions and less severe MS symptoms. Blocking the interaction between Mac-1 and fibrinogen after the first episode of paralysis using the fibrin peptide prevented subsequent relapses. It also prevented further microglia activation and damage to myelin in the diseased mice, allowing them to survive with improved motor function.

"Importantly, this approach blocks fibrin's interaction with microglia, but not with platelets, so clotting wouldn't be impacted," said Akassoglou, adding that this potential MS therapy might also have applications to other blood-brain barrier diseases where blood leakage and microglia activation is present such as spinal cord injury, Alzheimer's disease or stroke.

Source: University of California - San Diego

Citation: Inhibiting blood to save the brain (2007, March 22) retrieved 23 April 2024 from <https://medicalxpress.com/news/2007-03-inhibiting-blood-brain.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--