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Study leads to better understanding of multiple sclerosis
by Lisa Spellman, UNMC public affairs

It is commonly known that more women than men suffer from multiple sclerosis, lupus and thyroiditis, but researchers didn't understand why - until now.

A UNMC study appearing Friday (Sept. 23) in The Journal of Biological Chemistry reveals that the way female T cells interact with brain immune cells causes more inflammatory neurotoxic molecules capable of destroying brain myelin.

Myelin is a fatty tissue that surrounds and protects the nerve fibers of the central nervous system. Myelin also helps nerve fibers to conduct electrical impulses. When myelin or the nerve fiber is destroyed or damaged, the ability of the nerves to conduct electrical impulses to and from the brain is disrupted producing symptoms of multiple sclerosis.

The study was conducted by Kalipada Pahan, Ph.D., associate professor of biochemistry, oral biology, pharmacology, and neurological sciences at the UNMC College of Dentistry in Lincoln.

Drs. Subhajit Dasgupta, Malabendu Jana and Xiaojuan Liu have beer working on this project with Dr. Pahan since 2003 using mice to delineate the molecular mechanism behind the gender difference in multiple sclerosis.

Among their findings, the researchers discovered that T cells from female, but not male, mice cause excessive production of nitric oxide and pro-inflammatory cytokines by brain immune cells.

They also discovered that T cells isolated from castrated male mice produce the same results suggesting that the male sex hormone has role in disabling male T cells from activating brain immune cells.

"Interestingly, after castration, male T cells behave like female T cells suggesting that males are protected against autoimmune disorders probably due to the high levels of testosterone," Dr. Pahan said.

Myelin, said Dr. Pahan, is synthesized by oligodendrocytes, a

particular cell type in the central nervous system, which is very vulnerable to inflammation.

It is believed that excessive nitric oxide and the pro-inflammatory cytokines produced within the central nervous system kill oligodendrocytes and destroy myelin in multiple sclerosis patients, he said.

"Our next step is to find out how testosterone disables the T cells preventing the stimulation of brain immune cells, production of nitric oxide and pro-inflammatory cytokines," Dr. Pahan said. "Once we find the underlying mechanism, we would like to screen several drugs that are capable of mimicking the effect of testosterone on T cells."

Dr. Pahan said the finding of their research also indicates that testosterone supplementation may ameliorate symptoms of multiple sclerosis in females. "However, this is risky as it may lead to adverse side effects in young female multiple sclerosis patients," Dr. Pahan said.

Female multiple sclerosis patients may be treated with other agents that mimic the effect of testosterone on T cells, but do not exhibit the masculinizing and muscle-building effects of testosterone, he said. "Testosterone supplementation could be used to treat male multiple sclerosis patients if the rationale behind such treatment is proved," Dr Pahan said.

Multiple sclerosis is almost rare among young males, he said. Most who do develop the disease are not diagnosed until their late 30s or early 40s.

"So it is possible that some males in their late to middle age become susceptible to multiple sclerosis due to a drop in testosterone level," Dr. Pahan said. "If this is true, testosterone supplementation in male multiple sclerosis patients could be beneficial."

Date Published: Thursday, September 22, 2005

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