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April 20, 2001

UNMC Researchers Receive \$1 Million Grant to Study Multiple Sclerosis

Researchers at the University of Nebraska Medical Center College of Dentistry in Lincoln have received a \$1 million grant to study whether a protein present in large amounts in mice with multiple sclerosis affects the disease process. If they are right, their discovery may lead to prevention and better drug treatments for multiple sclerosis in humans.

Kalipada Pahan, Ph.D., assistant professor, department of oral biology and a neuroimmunologist, is principal investigator of the four-year grant from the U.S. Department of Health and Human Services.

Dr. Pahan and his colleagues are studying NF-kB, a protein naturally found in the body. Researchers have found when multiple sclerosis is present in animals, the amount of NF-kB markedly increases in the brain and spinal cord.

Multiple sclerosis is a disease of the white matter of the brain and spinal cord that affects the central nervous system. In multiple sclerosis, a complex inflammatory process destroys myelin which enables nerves to carry out their function. When myelin is destroyed, the brain and spinal cord lose the ability to transmit signals.

Although the disease is not fatal, it causes weakness, tremors, loss of vision, cognitive changes, depression and other problems. About half of patients become wheelchair bound within 15 years of disease onset and during the last stages of the disease, patients are bedridden. In Nebraska, about 110 to 140 cases per 100,000 people will occur, according to the National Multiple Sclerosis Society. An estimated 1,600 to 1,800 Nebraskans have MS.

UNMC researchers are studying NF-kBs potential role in the multiple sclerosis disease process through laboratory mice models called experimental allergic encephalomyelitis, or EAE, which allow studying of the immunology and treatment of MS. They are trying to understand how the disease process originates.

Dr. Pahan said too much NF-kB stimulates the production of cytokines and nitric oxide within the brain and spinal cord. Once they are produced in excessive amounts, they become toxic and kill myelin, a protector of nerve cells.

We find huge amounts of NF-kB in the spinal cord and the brain when the mouse gets MS, Dr. Pahan said. Further, if we give a drug called pyrrolidine dithiocarbamate, which prevents the production of NF-kB, the disease process of multiple sclerosis is stopped in animals. This tells us that NF-kB is involved in the disease process.

Currently, there is no effective treatment for multiple sclerosis, said Dr. Pahan. Basteron, one of several

available treatments, must be injected two to four times a day. The painful injections often cause a rash at the injection site. Flu-like symptoms are common, as well as some depression and other side effects.

The ultimate goal of Dr. Pahan's team is to find a more effective drug that can stop the multiple sclerosis disease process in humans and cause fewer side effects.

Recently, Dr. Pahan found that lovastatin, a non-toxic, well-established drug that controls cholesterol, and sodium phenylacetate, another non-toxic compound being tested for cancer treatment, stop NF- κ B in brain cells. He is trying to determine if the two compounds can stop the disease process in laboratory animals, as well as in humans.

This disease affects young people's lives, their family, their productivity, just when they're beginning their life, their career, their family, Dr. Pahan said. I hope we can pinpoint the cause of the disease and develop better drugs that will stop the progress of MS or prevent it entirely.

Life expectancy for people with MS has steadily improved. In 1890, the disease was treated with herbs and bedrest, and life expectancy was five years, according to the NMSS. By 1970, life expectancy rose to about 32 years, and today, people have a normal life expectancy.

Nationwide, it is estimated 250,000 to 350,000 people have multiple sclerosis, which is often diagnosed between age 20 and 40. It is more common among Caucasians, particularly those of northern European ancestry, and is more common in women than in men. Some of the potential causes of the disease are believed to be viruses, as well as environmental, genetic, and immune system factors.