

## **Genetic Link Found for Pesticides, ADHD, Gulf War Syndrome**

**LA JOLLA, California**, March 17, 2003 (ENS) - Supported by a \$1.5 million grant from the U.S. Department of Defense, research at the Salk Institute have identified a gene that may link certain pesticides and chemical weapons to a number of neurological disorders, including the Gulf War syndrome and attention deficit/hyperactivity disorder (ADHD).

The finding, published in the March 17 online version of "Nature Genetics," is the first to demonstrate a clear genetic link between neurological disorders and exposure to organophosphate chemicals.

The gene is one that scientists had not studied in previous efforts to find connections between these chemicals and disease. Organophosphates include household pesticides as well as deadly nerve gases like sarin.

The Gulf War syndrome is a "loosely defined collection of symptoms," the researchers said, "ranging from headache and fever to severe forgetfulness and movement disorders." It was first noted after Operations Desert Storm and Desert Shield in 1991, when U.S., Canadian and British military veterans reported more symptoms than soldiers who were not deployed. Its cause is unknown.

Dr. Carrolee Barlow, who led the work at the Salk Institute and is now at Merck and Co., Inc., and her team, headed by Christopher Winrow, found in mice that organophosphate exposure inhibited the activity of a gene called neuropathy target esterase, or NTE. The gene is active in parts of the brain controlling movement - the hippocampus, the cerebellum and the spinal cord.

This inhibition either killed the mice before birth, or led to a range of behaviors very similar to ADHD. Some of the neurological problems were similar to symptoms seen in Gulf War syndrome.

"This study shows that there may indeed be a genetic connection that explains how organophosphates can cause these reactions; it's just not what we assumed it would be," Barlow said.

"There have been anecdotal links made between rises in attention deficit/hyperactivity disorder, Parkinson's disease and other disorders and exposure to pesticides," she said. "There also has been suspicion of a link to Gulf War syndrome. But scientists have been focusing on enzymes that act on acetylcholine neurotransmitters.

Barlow's group had originally been looking at how environmental factors immediately affect the nervous system. They found that mice bred to lack the NTE gene died before birth.

But the group also found that mice with only one copy of the NTE gene, when exposed to experimental organophosphates and examined over a prolonged period, exhibited behavior similar to attention deficit/hyperactivity disorder.

"NTE is a large gene," said Barlow. "It's possible that we all have slightly different forms of the NTE enzyme, which may explain why some may get ADHD when they're exposed at young ages, and why some may get Gulf War syndrome at a later age, or why some of us have no symptoms at all. It appears to be a case of delayed toxicity, inhibiting the function of NTE."

The Salk Institute for Biological Studies is an independent nonprofit organization dedicated to fundamental discoveries in the life sciences, the improvement of human health and conditions, and the training of future generations of researchers. The institute was founded in 1960 by polio vaccine discoverer Jonas Salk, M.D., with a gift of land from the City of San Diego and the financial support of the March of Dimes Birth Defects Foundation