SOUTHWESTERN NEWS

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SCIENTISTS IDENTIFY LINK BETWEEN NEURONAL CALCIUM CHANNEL, MUTATED GENE THAT CAUSES HUNTINGTON'S DISEASE

DALLAS – July 17, 2003 – Abnormally high calcium levels spurred on by a mutated gene may lead to the death of neurons associated with Huntington's disease, an inherited genetic disorder, characterized by mental and physical deterioration, for which there is no known cure.

This discovery by researchers at UT Southwestern Medical Center at Dallas, published in the current issue of *Neuron,* sheds new light on the process that causes the selective death of neurons in the region of the brain called the striatum. Neurons in this area control emotions, body movements and several other neurological processes, including addiction.

Since the discovery of the *huntingtin* gene (*Htt*) in 1993, researchers have been searching for what actually causes certain neurons to die in the striatum, leading to the disease.

"It had not been clear why in Huntington's only neurons in the striatum are affected," said Dr. Ilya Bezprozvanny, associate professor of physiology and senior author of the study. "We found that the mutant form of the huntingtin protein causes abnormally high calcium levels in neurons, which likely cause them to die.

"This is the first time that we have some idea about what the mutant *huntingtin* gene does to kill striatum neurons and opens potentially new areas for treatment of the disease."

Calcium triggers the release of neurotransmitter signals, a process that initiates communication between neurons in the brain. But too much calcium, Dr. Bezprozvanny said, kills neurons.

Researchers hope the discovery leads to the development of drugs to block the activation of a receptor linked to calcium signaling in striatal neurons, thus potentially slowing the progression of Huntington's, Dr. Bezprozvanny said. Currently, transgenic mouse models that express the human mutant form of the *Htt* are being studied.

"We are going to move from biochemical and cellular studies to studies in transgenic mice to test our hypothesis," he said.

(MORE)

Other UT Southwestern researchers involved in the study include Dr. Anton Maximov, instructor in the Center for Basic Neuroscience; Dr. Tie-Shan Tang, a postdoctoral researcher in physiology and lead author of the study; Dr. Huiping Tu, a postdoctoral researcher in physiology; and Dr. Zhengnan Wang, research associate in physiology. Researchers at the University of British Columbia also contributed.

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