SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS IDENTIFY KEY PROTEIN THAT ESTABLISHES COMMUNICATION WITHIN CENTRAL NERVOUS SYSTEM

DALLAS – Aug. 30, 2002 – Researchers at UT Southwestern Medical Center at Dallas have identified one of the key proteins involved in the establishment of the central nervous system.

The researchers found that the protein, SynCAM, plays a major role in the formation of synapses, which are specialized junctions at which a neuron communicates with a target nerve cell. Neurons receive and send electrical signals over long distances within the body. The process of synaptic transmission drives communication between neurons in the brain and underlies all brain function.

This is only the second study that cites the initial events leading to the formation of synapses in the central nervous system, said Dr. Thomas Biederer, a postdoctoral researcher in the Center for Basic Neuroscience and lead author of the study, reported in today's issue of *Science*.

"Until this discovery very little was known about how neurons form synapses with each other," Biederer said. "We defined how the initial contact points are being developed and from there we can figure out how the young nervous system grows into an active network."

Synaptic formation is important in both newborns and adults. In newborns, synapses are formed rapidly and abundantly. The central nervous system, which encompasses the brain and spinal cord, establishes a stable network by keeping those that are functionally important and eliminating those that are not important. In adults, there is constant remodeling of neurons and synapses that relates to ongoing processes like learning and memory.

In neurological diseases such as Alzheimer's and Parkinson's, there is a loss of neurons and synapses, Biederer said. A better understanding of the ingredients of trans-synaptic signaling could lead to new disease treatments.

"One can speculate that the detrimental effects of these diseases can be balanced by a molecule such as SynCAM that can induce new synapses," Biederer said. "Other possible applications could include therapies for spinal cord injuries."

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The researchers identified the protein by searching the mouse genome for a candidate molecule that could form a bridge between neurons and recruit synaptic components. A model for synaptic transmission was created by artificially inducing synapses and performing a functional characterization using cultured neurons from laboratory mice. This is the first study in which a model was designed to artificially induce synaptic transmission, Biederer said.

When SynCAM was overexpressed the researchers reported an increase in spontaneous synaptic structures and spontaneous synaptic activity by as much as three-fold. When this function of SynCAM was interrupted, there was a decrease in the number of synapses and activity.

"We are now at the very core of what creates active neuronal networks and a functional central nervous system," Biederer said.

The researchers are currently studying other proteins that may be involved in this process.

Other researchers involved in the study included Dr. Thomas C. Südhof, senior author of the study, director of the Center for Basic Neuroscience and an investigator in UT Southwestern's Howard Hughes Medical Institute; Deniz Atasoy, a student research assistant in cell and molecular biology; Drs. Ege Kavalali and Xinran Liu, both assistant professors in the Center for Basic Neuroscience; and Drs. Marina Mozhayeva and Yildirim Sara, both postdoctoral researchers in the Center for Basic Neuroscience.

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