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Mitochondria In Spinal Cords Is ALS Target According To UCSD Medical Researchers

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The selective killing of spinal cord neurons in amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, occurs when tiny cellular components called mitochondria actively recruit a mutant disease-causing protein into specific neuron cells, according to new research by University of California, San Diego (UCSD) School of Medicine investigators.

Published in the July 8, 2004 issue of the journal *Neuron*, the findings identify mitochondria as the focus of ALS toxicity and provide the first explanation of how a mutant protein called SOD1 that occurs in all cells in the body is damaging only to specific neuron cells. The result is ALS, a progressive degeneration of motor nerve cells in the spinal cord that leads to wasted muscles and premature death in middle-aged adults.

Found in all cells, mitochondria provide cellular energy in their role as the body's power generators. In addition, mitochondria are intricately involved in a process called apoptosis, or programmed cell death, which is the body's normal method of disposing of damaged, unwanted or unneeded cells.

"We believe that when the mutant SOD1 binds to mitochondria, it affects the ability of these components to generate cell energy," said the study's senior author, Don Cleveland, Ph.D., a UCSD professor of medicine, neurosciences, and cellular and molecular medicine, and a faculty member of the Ludwig Institute for Cancer Research.

He added that "the SOD1 may also tip the balance and induce mitochondria to send a cell death signal to the motor neurons."

In laboratory studies with tissue from animals and humans, the UCSD team determined that the mutant SOD1 ignores all other mitochondria in cells and tissue outside of the spinal cord, and binds only to the mitochondria in the large motor neurons that begin in the spinal cord and extend down the arms and legs. They found SOD1 both inside the mitochondria and coated on the mitochondria's outer components.

"However, we don't know yet which is the most damaging, the mutant protein inside the mitochondria or coated on the outside," Cleveland said. "This is part of our continuing work as we seek components to block the toxicity of SOD1 and find ways to slow the damage that occurs in ALS."

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