SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS FIND PROTEIN TRANSFORMS SEDENTARY MUSCLES TO RESEMBLE EXERCISED MUSCLES

DALLAS – April 12, 2002 – A calcium-signaling protein transforms sedentary, easily fatigued muscles into energy-producing, fatigue-resistant muscles, UT Southwestern Medical Center at Dallas researchers report.

In a study published in today's issue of *Science*, the researchers found that by genetically expressing the protein in skeletal muscles of laboratory mice, easily fatigued, or type II, muscle fibers were transformed into fatigue-resistant and mitochondria-rich, or energy-producing, type I muscle fibers, which resemble muscles that have been exercised.

This research could lead to novel measures to stimulate muscles in patients with chronic diseases such as congestive heart failure or respiratory insufficiency, or individuals confined to bed rest.

"The muscles of individuals who are on bed rest resemble type II muscle fibers; they fatigue quickly and the muscles are tired," said Dr. Rhonda Bassel-Duby, associate professor of internal medicine and co-author of the study. "If we have a way of mimicking this protein, we can convert the muscle with a drug to a more fatigue-resistant, mitochondria-rich muscle."

Researchers expressed the active form of the calcium signaling protein called calcium/calmodulin-dependent protein kinase (CaMK) in the skeletal muscles of transgenic mice. CaMK controls production of mitochondria – structures in cells that are responsible for energy production – in mammalian muscle tissue.

"Calcium signaling plays an essential role in muscle remodeling," said Dr. Hai Wu, lead author of the study and a postdoctoral research fellow in molecular biology.

"CaMK has been intensely studied in neurons, where it is responsible for neuron plasticity and involved in learning and memory. Both neurons and muscle cells are excitable,

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and they share a lot of common signaling pathways in response to either brain activity or exercise," he said.

Further studies will be conducted to determine the specific properties of CaMK responsible for these effects.

"Greater understanding of the molecular-signaling pathways by which skeletal muscles sense and respond to changing activity patterns by altering gene expression ultimately may promote the development of novel measures to enhance the oxidative state of muscle, producing fatigue-resistant muscle," Bassel-Duby said. "This could enhance muscle performance of patients overcoming muscle immobility or recovering from illnesses producing muscle fatigue such as heart failure."

Other researchers involved in the study were Dr. Eiji Isotani, a visiting assistant professor in physiology; Dr. Shane Kanatous, a postdoctoral research fellow in internal medicine; Teresa Gallardo, a research scientist in cardiology; Dr. Frederick Thurmond, a postdoctoral research fellow in internal medicine; Dr. R. Sanders Williams, formerly chief of cardiology at UT Southwestern and presently dean of Duke University School of Medicine.

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