SOUTHWESTERN NEWS

Media Contact: Amy Shields
214-648-3404
amy.shields@utsouthwestern.edu

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PROTEIN TRANSFORMS SEDENTARY MUSCLES INTO EXERCISED MUSCLES, RESEARCHERS REPORT

DALLAS – Aug. 15, 2002 – Researchers have discovered a second protein found in skeletal muscle that can transform sedentary muscles into energy-producing, exercised muscles.

Researchers from UT Southwestern Medical Center at Dallas and Harvard Medical School reported in a study in today's issue of *Nature* that when the protein PGC-1α is genetically introduced in mice, easily fatigued type II muscle fibers are transformed into fatigue-resistant, mitochondria-rich, or energy-producing, type I muscle fibers that mimic highly exercised muscles.

"When you exercise, your muscles change fiber type specificity, switching from type II fibers to type I fibers," said Dr. Rhonda Bassel-Duby, associate professor of internal medicine at UT Southwestern and a co-author of the study. "When we expressed this protein in the mouse model, we found that the muscle switched from a type II muscle to a type I muscle. It visibly looked like a type I muscle. The presence of this protein alone switched the muscle type."

The protein PGC-1α, identified by a Harvard Medical School researcher, activates energy production and oxidative metabolism. PGC-1α is the second protein identified this year that's involved in muscle fiber-type switching. In an April study, reported in *Science*, UT Southwestern scientists reported that a protein called calcium/calmodulin-dependent protein kinase (CaMK) transformed type II muscle fibers into type I muscle fibers.

"The significance of this finding is that a nuclear cofactor alone was found to be sufficient to drive easily fatigued muscles into fatigue-resistant muscles," said Dr. Hai Wu, second author of the study and a postdoctoral researcher in molecular biology at UT Southwestern.

UT Southwestern researchers performed fatigue resistance measurements in the mice

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by stimulating the muscles and evaluating the response. The muscles were subjected to continuous electrical stimulation, which mimics muscle contraction during exercise.

"After evaluating the measurements we found that the muscles looked like and functioned as a type I muscle," Bassel-Duby said.

UT Southwestern scientists also performed the muscle-fiber type analysis for today's study and are continuing their own research into the signal transduction pathways that are involved in muscle fiber-type switching.

"The long-term goal of this research is to provide insight and treatment therapy to patients who have muscle fatigue, or are confined to bed rest, to enable them to have stronger, exercised muscles," Bassel-Duby said.

Other UT Southwestern researchers involved in the *Nature* study were Dr. Eric Olson, chairman of molecular biology, and Dr. Eiji Isotani, a former visiting assistant professor in physiology.

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