SOUTHWESTERN NEWS

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OXYGEN-CARRYING MYOGLOBIN NOT NECESSARY FOR SURVIVAL

DALLAS – October 29, 1998 – Myoglobin, the protein long thought to be the sole carrier of oxygen to heart and certain skeletal muscle, is not necessary for survival, UT Southwestern Medical Center at Dallas scientists reported in today's issue of the journal *Nature*.

Because of this discovery, investigators will be able to delve further into causes, prevention and cures for heart failure. The researchers made their breakthrough by developing a strain of mice lacking the gene to produce myoglobin, which transports oxygen from capillaries to mitochondria in heart and endurance muscle cells. Mitochondria are the structures within cells that transform oxygen and other molecules into energy for all cellular functions.

"Myoglobin is found in the heart and the slow-twitch, or endurance, skeletal muscles in a number of species. So because of its prevalence and the energy required for contraction of the heart, we predicted that mice could not live without this protein," said Dr. Dan Garry, assistant professor of internal medicine and first author of the report. "We were surprised that not only did they survive without it, they were born, developed, reproduced, nurtured and exercised normally."

The mice were exercised on treadmills along with littermates that had myoglobin. All the animals were exposed to conditions simulating different altitudes at which the body would normally experience some lack of oxygen. Neither group showed any differences in their behavior or their ability to handle the different conditions.

The only alteration researchers found in the rodents lacking myoglobin was that the heart and endurance muscles were nonpigmented or almost white rather than a rich pink because most of the red color actually comes from the myoglobin.

"Our research suggests that the system transferring the oxygen necessary to fuel the contraction of heart and slow-twitch muscles is much more complicated than the long-held

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paradigm," Garry said.

Now, the researchers will look for other genes that are expressed at a higher level in the genetically altered mice during times when they are exposed to conditions where their hearts and endurance muscles need more oxygen. In studying these genes, the investigators may be able to discover the system that enables the heart and skeletal muscles to get the energy they need to continue functioning.

"We still believe that myoglobin is important, but something else is also important; there are some cellular adaptations that we have not yet defined," Garry said. "By understanding and identifying these adaptations, we will increase our knowledge of what happens when people get chest pains. This will impact our treatment of patients who suffer from coronary-artery disease."

The other researchers on the study were: Dr. George Ordway, associate professor of physiology; Dr. Nina Radford, assistant professor of internal medicine; Dr. Eva Chin, postdoctoral fellow in internal medicine; Dr. Robert Grange, assistant instructor of physiology; Dr. Rhonda Bassel-Duby, associate professor of internal medicine; Dr. R. Sanders Williams, chief of cardiology, director of the Frank M. Ryburn Jr. Cardiac center and holder of the James T. Willerson, M.D., Distinguished Chair in Cardiovascular Diseases; and Dr. John Lorenz, Department of Molecular and Cellular Physiology, University of Cincinnati.

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