SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS DISCOVER PROTEIN ESSENTIAL TO DEVELOPMENT OF HEART

DALLAS – June 29, 2001 – UT Southwestern Medical Center at Dallas researchers have found a protein that controls the development of the heart – a discovery that could contribute to novel methods of creating heart cells which could be used in the treatment of various cardiac conditions.

In today's issue of *Cell*, the researchers – led by Dr. Eric Olson, chairman of molecular biology – report that the protein myocardin is expressed in cardiac muscle cells and turns on cardiac genes. Without this protein, formation of the heart is eliminated in frog embryos.

"Very little is known about the regulatory proteins that control formation of the heart. We discovered a protein called myocardin, which specifically turns on cardiac genes that are expressed from the embryo stage throughout the life of the organism," Olson said.

The scientists studied the function of myocardin by injecting frog embryos with a mutant form of the myocardin protein. As a result, the development of the heart was completely eliminated. The growth of other organs was not affected.

"This protein appears to be essential for heart formation in the embryo," Olson said.

Their findings could lead to the conversion of other types of cells into heart cells, Olson said, which could impact the treatment of heart patients of all ages, from babies born with heart defects to victims of heart failure.

"If the gene responsible for myocardin is a 'master gene,' it could possibly be used in heart repair," said Olson, who directs the Nancy B. and Jack L. Hamon Center for Basic Research in Cancer and the Nearburg Family Center for Basic Research in Pediatric Oncology. "The Holy Grail in the heart field is finding the gene or genes that can convert noncardiac cells into cardiac cells. Myocardin is necessary for heart formation, and we are now determining if it is sufficient."

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The method of discovery also was novel, said Olson.

"We found this using a bioinformatics screen, searching for sequences present only in the heart. This was enabled by the vast amount of DNA sequence being deposited into public databases. Only a few years ago, this wouldn't have been possible," he said.

The next step is to study genes related to myocardin.

"It looks like this is one in a family of related genes. We'll next study this in the mouse by targeted gene inactivation," Olson said. "We'll see whether it can be used to convert non-cardiac cells to cardiac fate, either by itself or with other factors."

Other researchers involved in the study from UT Southwestern are Dr. Da-Zhi Wang, instructor of molecular biology; Priscilla S. Chang and Zhigao Wang, both research assistants in molecular biology; Lillian Sutherland, senior research associate in molecular biology, and Dr. James A. Richardson, professor of pathology. Eric Small and Paul A. Krieg, from the Department of Cell Biology and Anatomy at the University of Arizona College of Medicine, participated in the research.

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