SOUTHWESTERN NEWS

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Heart protein could be used to repair damage caused by a heart attack

DALLAS – Nov. 25, 2004 – A protein that the heart produces during its development could be redeployed after a heart attack to help the organ repair itself, researchers at UT Southwestern Medical Center at Dallas have found.

The mouse-study findings could eventually lead to new treatments for heart disease in humans and could even change the way healthcare providers respond to people suffering from heart attacks. The research appears today's edition of *Nature* and is available online.

"If the protein has a similar effect in humans as it does in mice, the impact by sheer volume is great – nearly 1 million people have heart attacks every year just in the United States," said Dr. Deepak Srivastava, professor of molecular biology and pediatrics and the study's senior author. "The delivery is very simple and avoids many of the problems of using stem cells."

While more common in adults, heart disease is the leading noninfectious cause of death in children younger than one year. Heart disease in children is usually caused by developmental abnormalities.

The protein, Thymosin beta-4, is expressed by embryos during the heart's development. It encourages the migration of heart cells and affects those cells' survivability. The new findings show that the protein prevents cell death after an experimentally-induced heart attack and limits the degree of scar tissue formation.

Thymosin beta-4 is already used in clinical trials to promote wound healing on the skin. As a result, the protein could enter clinical trials for treating the heart in the very near future, said Dr. Srivastava, who holds the Pogue Distinguished Chair in Research on Cardiac Birth Defects and the Joel B. Steinberg, M.D., Chair in Pediatrics. He also co-directs the March of Dimes Birth Defects Center at UT Southwestern.

During their study, UT Southwestern researchers discovered that Thymosin beta-4 works in conjunction with two other proteins to promote survival and migration of heart muscle cells by

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activating the protein Akt/Protein Kinase B. Akt/PKB, when active, promotes cell survival.

After studying the activity of cells in culture, researchers created a mouse model by tying off the coronary artery of 58 adult mice, simulating a heart attack. Half of the mice were given Thymosin beta-4 systemically, directly into the heart, or through both routes immediately after the ligation. The other half were given control injections of saline immediately after the artery was tied off.

Researchers found that Thymosin beta-4 caused fewer cells in the affected part of the heart to die, resulting in improved function even several weeks after the heart attack. Researchers now believe that Thymosin beta-4 changes cell metabolism to create stronger heart muscle cells that can resist the low oxygen conditions after a heart attack.

The next step, Dr. Srivastava said, is to determine the most effective dose, the optimal time to administer Thymosin beta-4 and how long after an attack the protein can be given to be effective.

Other UT Southwestern researchers involved were Dr. Ildiko Bock-Marquette, a postdoctoral researcher in pediatrics and co-lead author; Ankur Saxena, graduate student research assistant in the genetics and development program and co-lead author; Dr. J. Michael DiMaio, assistant professor of cardiovascular and thoracic surgery; Michael White, a research assistant in cardiovascular and thoracic surgery; and Glenn Adams IV, a research technician in cardiovascular and thoracic surgery.

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