UT SOUTHWESTERN MEDICAL CENTER NEWS

Media Contact: Aline McKenzie
214-648-3404
aline.mckenzie@utsouthwestern.edu

# Tiny molecule helps control blood-vessel development, UT Southwestern researchers find

DALLAS – Aug. 12, 2008 – The development and repair of heart tissue and blood vessels is intimately tied to a tiny piece of ribonucleic acid (RNA) that is found nowhere else in the body, researchers at UT Southwestern Medical Center have found.

Because of its specificity to the cardiovascular system, this "microRNA" is an attractive potential target for therapeutic treatment, the researchers said.

"Manipulating this microRNA provides a completely new way of addressing cardiovascular disorders," said Dr. Eric Olson, chairman of molecular biology and senior author of a study appearing in today's issue of *Developmental Cell*.

MicroRNAs are tiny snippets of genetic material, naturally produced by the body, that help fine-tune the production of proteins by DNA. More than 500 have already been identified.

In the current study, the researchers focused on a specific microRNA called miR-126, which was already known to be associated with blood vessels. They found that miR-126 is found only in a class of cells called endothelial cells, which line the inside surfaces of blood vessels.

Endothelial cells control the development of new blood vessels in developing embryos; the repair of injured blood vessels; and the creation of blood vessels to support developing tumors.

The researchers genetically engineered mice to lack miR-126, and found that about 40 percent of them died before or just after birth. These mice showed cardiovascular abnormalities such as fragile, leaking blood vessels.

The surviving mice, however, appeared normal and lived to adulthood. The researchers concluded that miR-126 is important in creating new vessels, but once the cardiovascular system is established, it is not needed to maintain the system.

However, the surviving mice were less able to recover from a simulated heart attack. Almost all mice lacking miR-126 died within three weeks, while 70 percent of normal mice survived for at least three weeks.

The researchers also tested the role of miR-126 in the branching of blood vessels using cut sections of mouse aortas in culture. When cultured with growth factors that stimulate branching, aortal sections from normal mice displayed branching of their endothelial cells.

(MORE)

Aortal sections from mice lacking miR-126, however, showed much less branching.

"MicroRNA research represents a new frontier in understanding and treating human disease. This is just a hint of what can come," said Dr. Olson, director of the Nancy B. and Jake L. Hamon Center for Basic Research in Cancer and the Nearburg Family Center for Basic Research in Pediatric Oncology.

The researchers have filed several patents related to miR-126, and plan to license it for development as a therapeutic agent through Miragen Therapeutics, a Boulder-based company co-founded by Dr. Olson, which UT Southwestern owns equity in.

Other UT Southwestern researchers involved in the study were lead author Dr. Shusheng Wang, postdoctoral researcher in molecular biology; Dr. Arin Aurora, postdoctoral researcher in molecular biology; graduate student Brett Johnson; Xiaoxia Qi, research scientist in molecular biology; John McAnally, research associate in molecular biology; Dr. Joseph Hill, professor of internal medicine; Dr. James Richardson, professor of pathology; and Dr. Rhonda Bassel-Duby, professor of molecular biology.

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