SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCH SHOWS GENE THERAPY MAY BE TOOL TO LOWER RISK OF CARDIOVASCULAR DISEASE

DALLAS — September 13, 1994 — Research conducted at The University of Texas Southwestern Medical Center at Dallas suggests gene therapy may be a useful tool in reducing the risk of atherosclerosis — the clogging of arteries with fatty plaque.

Using a gene coding for a major protein component of high-density lipoprotein cholesterol particles, scientists at UT Southwestern were able to temporarily raise the level of high-density lipoprotein (HDL) or "good" cholesterol between 30 percent and 50 percent in animal models. Individuals with high levels of HDL have a lower risk for developing cardiovascular disease, the No. 1 killer of Americans.

The findings were published in the September issue of *Circulation*, a journal of the American Heart Association. Dr. Robert S. Meidell, assistant professor of internal medicine/cardiology division, is principal investigator of the study. Other researchers involved are Dr. William P. Kopfler, a fellow in internal medicine; Maureen Nolan-Willard, a research associate; Dr. Timothy Betz, a former fellow in internal medicine; Dr. John E. Willard, assistant professor of internal medicine/cardiology division; and Dr. Robert D. Gerard, assistant professor of biochemistry and internal medicine.

In the study, genes responsible for the production of HDL were

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transferred into laboratory animals, significantly raising their HDL levels.

"We used a virus carrying the gene that contains the major protein component of the 'good' cholesterol particle, a gene coding for a protein called apolipoprotein A-1, and infected mice with it," Meidell said. "It raised the HDL cholesterol fairly dramatically — 30 to 50 percent."

Because cholesterol is an important risk factor in the development of heart disease, making genetic changes in the level of either HDL or LDL (low-density lipoprotein, the "bad" cholesterol) would be expected to have a profound effect on the propensity to develop atherosclerosis, Meidell said. Similarly, it may also be useful in slowing the progression of established atherosclerosis.

Atherosclerosis results from deposits of cholesterol and other fatty substances in the lining of an artery. This plaque buildup can lead to the partial or total blockage of an artery.

One drawback to the study was the limited duration of the increased level of "good" cholesterol. It lasted for just a week.

"To be effective as therapy, it would have to last a very long time," Meidell said.

Despite the limitations of the current study, these experiments demonstrate the potential for gene transfer to augment HDL levels and exert a protective effect in both experimental animals and, potentially, in humans, according to the study.

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