CEDARS-SINAI MEDICAL CENTER NEWS

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***EMBARGOED AS PER JAMA***

**HIGHLIGHTS:**
The mutant form of a cholesterol-related gene has been shown in animal studies to protect against vascular plaque buildup that can lead to heart attacks and strokes. Now the first report of a Phase II human trial of recombinant apo A-1 Milano therapy will be published in the Nov. 5 *Journal of the American Medical Association*. P.K. Shah, M.D., director of the Division of Cardiology at Cedars-Sinai and one of the key researchers who studied the gene and the protein (product of the gene) and developed the therapy, is available to provide history, background and details.

**PIONEER OF ARTERIAL PLAQUE-FIGHTING GENE THERAPY AVAILABLE AS HUMAN RESULTS ARE ANNOUNCED**

**LOS ANGELES (Nov. 3, 2003 – STORY EMBARGOED AS PER JAMA)** – In its Nov. 5 issue, the *Journal of the American Medical Association* (*JAMA*) will publish results of a significant Phase II human trial of recombinant apolipoprotein A-1 Milano, a mutant gene product that appears to have protective effects against the development of plaque buildup in coronary arteries.

Many developments in this potential therapy, including the animal studies that preceded and provided the basis for human trials, have been carried out in the laboratories of atherosclerosis researchers at Cedars-Sinai Medical Center in Los Angeles and led by P.K. Shah, M.D., Director of the medical center's Division of Cardiology.

The therapy is based on the effects of a mutant gene identified by researchers at the University of Milan in the 1980s in several individuals living in Limone sul Garda, Italy. Instead of causing disease, this gene mutation appeared to be beneficial. In fact, members of the family carrying the gene have been virtually immune to cholesterol-related heart problems and strokes, regardless of lifestyle practices that normally increase risk.

The normal gene and the protein it produces are apolipoprotein A-1, often referred to as apo A-1. The protein is a component of "good" cholesterol called high-density lipoprotein or HDL. In 1992, Dr. Shah and his colleagues began studying the mutant apo A-1 Milano protein, and in the mid-90s they launched long-term animal studies that showed apo A-1 Milano to be extremely potent in reducing and reversing plaque buildup.

(more)

Apo A-1 Milano protein appeared to actually remove bad cholesterol, even from sites on arteries where plaque had accumulated. If such results are confirmed in future trials, the need for such invasive procedures as angioplasty and bypass surgery could someday be eliminated or drastically reduced. And because apo A-1 Milano treats the entire circulatory system, it may be useful in repairing diseased vessels that cannot be reached by invasive techniques.

Dr. Shah and his research team have been among the leading investigators working with the biopharmaceutical industry to create and test therapeutic approaches using the gene and its protein product. Several years ago, for example, Dr. Shah and scientists at the City of Hope National Medical Center received a grant from the National Institutes of Health to conduct a five-year study inserting the gene itself – not just the protein – into animals to try to stimulate tissues to produce the protein and provide a constant supply. This and other studies are continuing.

Small-scale human trials using the apo A-1 Milano protein began about three years ago. The *JAMA* article, authored by researchers at the Cleveland Clinic, is believed to be the first major report on apo A-1 Milano therapy in a Phase II human clinical trial.

Dr. Shah is available to provide additional history, background and details on apo A-1 Milano gene intervention. In addition to serving as director of the Division of Cardiology and the Atherosclerosis Research Center, Dr. Shah holds the Shapell and Webb Family Endowed Chair in Cardiology at Cedars-Sinai. He is professor of medicine at the University of California, Los Angeles School of Medicine.

Cedars-Sinai is one of the largest nonprofit academic medical centers in the Western United States. For the fifth straight two-year period, it has been named Southern California's gold standard in health care in an independent survey. Cedars-Sinai is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthroughs in biomedical research and superlative medical education. The Medical Center ranks among the top 10 non-university hospitals in the nation for its research activities.

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