SOUTHWESTERN NEWS

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SCIENTISTS CLOSER TO LOCATING GENE THAT MAY EXPLAIN CHOLESTEROL ABSORPTION

DALLAS – September 1, 1998 – In a discovery that may shed light on why people absorb cholesterol at different rates, scientists from UT Southwestern Medical Center at Dallas and the National Institutes of Health have narrowed their search for a gene responsible for abnormal cholesterol absorption in individuals with a rare hereditary disease.

While cholesterol metabolism has been well-documented, scientists understand little about how cholesterol is absorbed from our diet and excreted by the body.

"Only a fraction of the cholesterol we consume is actually absorbed by the body," said Dr. Shailendra Patel, assistant professor of clinical nutrition and a scholar in the Center for Human Nutrition at UT Southwestern. "Different people absorb different amounts. Some might eat a cholesterol-laden meal and absorb 30 percent of it; someone else might eat a low-cholesterol meal but absorb 60 percent of it."

The researchers studied 10 families with sistosterolemia, a rare, recessively inherited disease characterized by the accumulation of plant sterols, premature heart disease and fatty deposits on the skin and tendons. Plant sterol is akin to cholesterol in animal products but normally is not absorbed by the body.

"In normal individuals, the body has the ability to selectively absorb cholesterol and exclude plant sterols,"said Patel, lead author of the study published in the Sept. 1 issue of the *Journal of Clinical Investigation.* "Individuals with sistosterolemia hyperabsorb cholesterol, but

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also absorb plant and shellfish sterols that are not normally absorbed. Hence, the gene that is disrupted may regulate selective absorption of dietary cholesterol.

"If we wanted to change someone's cholesterol absorption, this gene would be the target of treatment," Patel said. "We hope this is the key gene that will allow us to target cholesterol absorption as a whole new form of drug therapy."

"Our studies of sitosterolemia may help explain the mechanisms responsible for cholesterol uptake from the diet and on mechanisms that protects us from absorbing and retaining substances in food that are potentially harmful," said co-author Dr. Michael Brownstein, chief of the NIH's Section on Genetics: People Investigating Genes.

The researchers examined the genes of families from India, Finland, the Netherlands, Japan and the United States and mapped the genetic defect to chromosome 2p21.

Other researchers participating in the study included Dr. Scott Grundy, professor of internal medicine and director of the Center for Human Nutrition at UT Southwestern; Mi-Hye Lee, a fellow in the nutrition center; Dr. Gerald Salen of UMDNJ-New Jersey Medical School; and researchers from Shiga University of Medical Science (Japan), Johns Hopkins Hospital, University Hospital Jijmegen (The Netherlands) and University Hospital Helsinki (Finland).

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