UT SOUTHWESTERN MEDICAL CENTER NEWS

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EMBARGOED UNTIL 11 A.M. CST WEDNESDAY, DEC. 1, 2010

UT Southwestern researchers identify gene tied to extremely rare disorder that causes inflammation and loss of fat

DALLAS – Dec. 1, 2010 – UT Southwestern Medical Center researchers have identified a gene responsible for a rare disease that results in severe joint stiffness, muscle loss, anemia and panniculitis-induced lipodystrophy, or JMP syndrome.

The researchers identified a blip in the gene – *proteasome subunit, beta-type, 8* (*PSMB8*) – in three patients from two distinct families who were suffering from progressive loss of fat and muscles as well as joint contractures that particularly affected the hands and feet. The fat loss was due to recurrent inflammatory lesions under the skin called panniculitis. Lipodystrophies are disorders characterized by the selective loss of fat tissues and complications of insulin resistance.

Dr. Abhimanyu Garg, chief of nutrition and metabolic diseases and senior author of the study appearing online and in the Dec. 2 issue of *The American Journal of Human Genetics*, said that in addition to providing a clue to the cause of JMP syndrome, the findings also tell researchers more about the role proteasomes play in an individual's immune response. Although researchers identified proteasomes many years ago, their precise contribution to immunity in humans has eluded scientists.

"Our findings show that if this gene is mutated, it can lead to the development of an auto-inflammatory syndrome," Dr. Garg said. "How the mutation triggers lipodystrophy is not entirely clear, but this does suggest new therapeutic targets for individuals with the condition."

The researchers used gene mapping technology on DNA samples of the study participants and their family members to find the *PSMB8* gene. Two of the patients hailed from Monterrey, Mexico, and the third from Portugal.

They found that the mutation reduces activity of the PSMB8 enzyme within the immune cells and affects normal processing of antigens, resulting in inflammation.

The next step, Dr. Garg said, is to determine the best type of therapy and whether it is possible to prevent the disease or lessen the severity of some of its symptoms.

"This is a good start," Dr. Garg said. "There's more to be learned from the patients about the function of this immune-response gene."

(MORE)

Other UT Southwestern researchers involved in the study include Dr. Anil Agarwal, associate professor of internal medicine; Dr. Chao Xing, assistant professor of clinical sciences; Dr. George DeMartino, professor of physiology; and Dr. Dario Mizrachi, instructor of internal medicine. Researchers from the Universidad Autonoma de Nuevo Leon in Mexico and the Hospital de Santa Maria in Portugal also contributed to the study.

The National Institutes of Health supported the work.

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