

Liver Protein Associated with Type 2 Diabetes in Older Adults

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S *tudy may indicate novel targets for prevention or treatment*

The presence of a protein expressed by the liver which inhibits insulin action may identify individuals more likely to develop type 2 diabetes, according to a new study led by a researcher from the University of California, San Diego School of Medicine, to be published July 9 in the *Journal of the American Medical Association (JAMA)*.

Researchers led by Joachim H. Ix, M.D., M.A.S., assistant professor in the Division of Nephrology and Hypertension and the Division of Preventive Medicine at UC San Diego and at the San Diego Veterans Affairs Healthcare System, found that higher serum levels of a protein called fetuin-A, produced by liver cells, was associated with type 2 diabetes in humans, independent of other risk factors.

“Higher fetuin-A was associated with a 1.7-fold increased risk of diabetes, when adjusted for other factors,” said Ix. Despite compelling laboratory and animal data of the protein’s role in insulin resistance, until now the association of fetuin-A with new development of type 2 diabetes had not been evaluated in humans, according to Ix. “On the basis of this study, fetuin-A might be considered as a novel therapeutic target for prevention or treatment of insulin resistance,” he said.

Type 2 diabetes is a metabolic disorder characterized by insulin resistance that has become a global epidemic. The increased prevalence of obesity is a major contributing factor; however diabetes does not develop in all obese individuals, and reasons why one individual develops type 2 diabetes while another does not are largely unknown.

Recent research shows that proteins from fat tissue called adipocytokines regulate the metabolism of blood sugar or glucose, and may ultimately prove to be a target for new diabetes therapies. In contrast, fetuin-A is produced in liver cells, and is secreted into blood. In laboratory studies, fetuin-A binds to the insulin receptor found in muscle and fat, resulting in insulin resistance – the hallmark of diabetes. Preliminary data from a separate study of participants without diabetes had shown an association between fetuin-A and insulin resistance.

In this study, the researchers measured levels of fetuin-A in 519 diabetes-free individuals aged 70 to 79 years, and followed them for development of diabetes for six years. Participants with the highest levels of fetuin-A showed a higher risk of developing diabetes, when compared to those with low levels. The association was not affected by levels of adipocytokines.

“The associations we demonstrate are independent of an individual’s level of physical activity, the presence of inflammation or other common measures of insulin resistance,” said Ix. “The results were also similar in participants, regardless of gender, race or obesity status.”

The researchers also state that further studies should evaluate whether the results prove true in middle-aged individuals in whom the incidence rate of type 2 diabetes is highest.

Additional contributors to this study include Christina L. Wassel, M.S., University of Minnesota and University of California, San Francisco; Alka M. Kanaya, M.D. and Eric Vittinghoff, Ph.D., UC San Francisco; Steven R. Cummings, M.D., UC San Francisco and California Pacific Medical Center; Michael G. Shlipak, M.D., MPH, UC San Francisco and San Francisco Veterans Affairs Healthcare System; Karen C. Johnson, M.D., MPH, University of Tennessee Health Science Center; Annemarie Koster, Ph.D., and Tamara B. Harris, M.D., National Institute on Aging; and Jane A. Cauley, Dr.Ph., University of Pittsburgh.

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