Study identifies target for diabetes drug

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New research from the University of Cincinnati (UC) points to the naturally produced protein apolipoprotein A-IV (apoA-IV) as a potential target for a new diabetes therapeutic.

Patrick Tso, PhD, professor in the UC Department of Pathology and Laboratory Medicine, has published research on the ability of apoA-IV to reduce blood sugar levels and enhance insulin secretion.

The results appear the week of May 21, 2012, in the online early edition of Proceedings of the National Academy of Sciences.

ApoA-IV is secreted by the small intestine in response to fat absorption. Previous studies have shown apoA-IV to be elevated in humans following gastric bypass—coinciding with improvement in symptoms for diabetes.

The Tso team found that mice deficient in apoA-IV had impaired glucose tolerance (insulin was not secreted to move glucose from the blood stream). These mice also developed diabetes when continuously fed a high-fat diet. When injected with apoA-IV, these same mice showed improved insulin response to glucose, despite a diet high in fat.

Tso's team also tested the response to injected apoA-IV in diabetic mice and found it reduced glucose levels among that group as well.

Tso says their research shows apoA-IV to behave similar to an incretin—a gastrointestinal hormone causing an increased release of

insulin after eating to combat the onset of elevated blood glucose. Two well-known incretins that have been used in the development of existing diabetes medications include gastric inhibitory peptide (GIP) and glucagon-like peptide-1 (GLP-1).

"The problem with both of these incretins is that they are short-lived—lasting only for minutes—and are quickly inactivated by an enzyme," says Tso. "They have also been linked to hypoglycemia, or low blood sugar, when administered when the body has a low glucose concentration. The challenge is to find something safer with a longer half-life."

Tso says apoA-IV has a long half-life (between seven and eight hours) and that tests in his lab showed it to have no effect on glucose levels when administered at low glucose concentrations. Instead, he says, it seems to function to normalize glucose.

The University of Cincinnati has licensed this research finding to a startup biotech company, Apofore Corporation, formed by HealthCare Ventures of Cambridge, Mass. Apofore will further study apoA-IV in humans in an effort to develop a novel diabetes therapeutic.

Provided by University of Cincinnati Academic Health Center

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