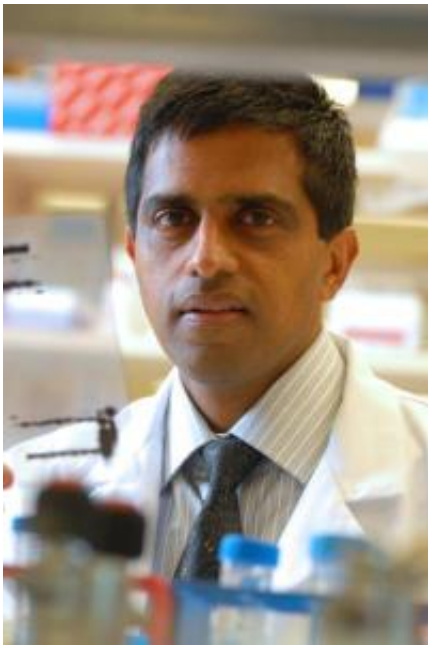


Research points to two promising proteins for preventing diabetes

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A research team led by Raghu Mirmira, M.D., Ph.D., at Indiana University School of Medicine has identified two new potential protein targets for preventing diabetes. Credit: Indiana University School of Medicine

Two human proteins that evolutionary processes have conserved from ancient single-celled organisms appear to provide new targets of opportunity for scientists hoping to thwart the development of diabetes.

In experiments using diabetes-prone mice, blocking the actions of the proteins significantly reduced the development of [diabetes](#) in the mice.

The findings were reported by a multi-institutional research team led by Raghu Mirmira, M.D., Ph.D., associate professor of pediatrics at the Indiana University School of Medicine, and were published online May 24 and will appear in the June 2010 issue of the [Journal of Clinical Investigation](#).

More than 23 million Americans have been diagnosed with diabetes, which is one of the leading causes of the death in the United States. Diabetes can occur when the body is unable to produce enough insulin, or when it loses its ability to respond properly to the production of insulin, a hormone the body uses to convert food into energy. No matter the cause, research suggests that inflammatory processes contribute to the development of diabetes.

One of the proteins targeted in the research, eIF5A, is believed to be involved with inflammation processes, but its activities had not been studied in the pancreas islet cells that produce insulin. The research team looked at eIF5A because its corresponding gene sits near other inflammation-related genes in both the mouse and human genomes, said Dr. Mirmira, director of the Pediatric Diabetes Research Group at the Herman B Wells Center for Pediatric Research, on the campus of Indiana University-Purdue University, Indianapolis.

"Because it sat in a hotbed of inflammatory genes, and because many of these inflammatory genes are known to be important in the progression of diabetes, we thought eIF5A might also have role in the progression of diabetes," Dr. Mirmira said.

But eIF5A doesn't act on its own. Instead, another protein, an enzyme called DHS, is necessary to activate eIF5A - in fact it appears that the sole role of DHS is to activate eIF5A.

"So our underlying premise was that if eIF5A is crucial in inflammation,

and DHS is crucial in activating eIF5A, then inhibiting DHS should block eIF5A," Dr. Mirmira said.

The researchers used two different approaches to block the activity of eIF5A. In one, they constructed a special genetic molecule called a small interfering RNA - siRNA - designed to disrupt the production of eIF5A in the islet cells within a living mouse. The second approach used a compound, GC7, that inhibits the production of DHS. Both approaches gave similar results—that the development of diabetes can be blocked in a mouse—but the DHS approach seems to offer a more promising route to possible treatments because no therapies have yet been approved using siRNA technologies.

"What this study has done is identify what we believe is a new target that could be amenable to a drug therapy," said Dr. Mirmira. A next step would be to further illuminate the role of eIF5A in the normal development of diabetes, in contrast to the experimental models used in this research, he said.

Provided by Indiana University School of Medicine

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