New study finds possible source of beta cell destruction that leads to Type 1 diabetes

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Doctors at Eastern Virginia Medical School's Strelitz Diabetes Center have been stalking the culprit responsible for Type 1 diabetes. Now, they are one step closer.

Members of a research team at the center, led by Jerry Nadler, MD, professor and chair of internal medicine and director of the center, have been studying the role of the enzyme 12-Lipoxygenase (12-LO) in the development of Type 1 diabetes. They hope that targeting this enzyme will hold the key to a cure.

Dr. Nadler and several research colleagues in the EVMS Department of Internal Medicine, including Kaiwen Ma, PhD, research instructor; Swarup K. Chakrabarti, PhD, research assistant professor; and David A. Taylor-Fishwick, PhD, associate professor, recently published their findings in the February issue of *The* Journal of Clinical Endocrinology and Metabolism.

Type 1 diabetes is a chronic condition that develops when the pancreas stops generating enough insulin to maintain normal levels of glucose (sugar) in the blood. Insulin moves sugar from the bloodstream to cells so that it can be used to generate energy. In Type 1 diabetes, a person's immune system attacks the insulin-producing beta cells, found only in the pancreas. When the beta cells die, the body no longer can produce enough insulin to regulate blood-glucose levels, and this can lead to serious health complications, even death, without treatment.

It is generally understood that inflammation plays a vital role in beta-cell destruction. But the precise factors are not well known. A protein-based enzyme found in beta cells, 12-LO produces specific lipids that cause inflammation and can lead to the death of beta cells in laboratory models. In fact, EVMS researchers have demonstrated that deleting the gene that produces 12-LO prevents the development of Type 1 diabetes in mice.

The challenge has been to validate that 12-LO and its pro-inflammatory lipid products have a role in human diabetes. Gaining access to human beta cells can be difficult, but EVMS is among a limited number of research groups that can receive human islets — the region of the pancreas that contains beta cells — from individuals who have donated their bodies to science through the Juvenile Diabetes Research Foundation Islet Resource Center Consortium Dr. Nadler explains.

Thanks to that resource, the EVMS team has confirmed that 12-LO is indeed found in human islets, and in humans, like in mice, its pro-inflammatory lipid products can lead to lower insulin production and beta cell death.

"We've now confirmed that 12-LO is a relevant target in humans, particularly in the pancreas, and will help lead to new therapies," Dr. Ma says.

"That's why these new findings are so important," Dr. Chakrabarti says. "The next step will be to develop a drug that targets 12-LO and combine that with cell regeneration."

"We are currently working with investigators in California and the National Institutes of Health to identify ideal medications that would target 12-LO as a new treatment to halt immune damage to human insulin-producing cells," Dr. Taylor-Fishwick says.

Provided by Eastern Virginia Medical School