

## Researchers find clue to cause of type 1 diabetes

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By Martin F. Downs

NEW YORK (Reuters Health) - In a new study, scientists found a protein that appears to play a key part in the development of type 1, or early-onset diabetes.

The finding may lead to new diabetes treatments, and it may be useful in diagnosing the disease, said study author Dr. Teresa DiLorenzo, a researcher at the Albert Einstein College of Medicine, in the Bronx, New York.

Type 1 diabetes is typically diagnosed in children or young adults, and requires life-long insulin injections for survival. The disease is much less common than type 2 diabetes, which is often diagnosed in older people and can be linked to lifestyle and diet.

In type 1 diabetes, the immune system's T cells destroy insulin-producing beta cells in the pancreas. T cells react to a molecular "red flag," or antigen, which tells them they should attack a cell that has the antigen.

Scientists don't know which specific antigens prompt T cells to attack beta cells in people, but this study offers a compelling clue.

In the online early edition of the Proceedings of the National Academy of Sciences, DiLorenzo and colleagues report that T cells in diabetes-prone mice, known as NOD mice, target a protein called IGRP.

"There certainly is reason to believe that if IGRP is the antigen in the NOD mice, it may also be an antigen in humans," DiLorenzo told Reuters Health.

It's standard practice for researchers to study type 1 diabetes in this kind of mouse. What they find in these mice, they often find in humans later, DiLorenzo said.

To identify the protein, the researchers began by breaking down beta cells from the test mice into various molecular components, until they had separated out the peptides -- molecules that are building blocks of proteins.

They found peptides that T cells recognized, and then screened them against a database of known protein sequences to find out which protein they came from.

"When that was done, there was an exact hit with this protein called IGRP," DiLorenzo said.

The researchers also found that T cells in the blood and pancreatic tissue of test mice reacted to IGRP.

What's more, the gene for IGRP is found at a site in the human genome that other researchers have identified as one that may make people prone to type 1 diabetes.

"It's long been clear that there's a genetic component to type 1 diabetes," DiLorenzo said. "Several groups for many years have been searching for the genes responsible for that susceptibility."

People with a close relative who has type 1 diabetes have a greater risk for developing the disease. So far, researchers have found 18 sites in the genome that may play a role, DiLorenzo said.

"These are, in general, huge chunks of DNA. It's not a single gene," she said. "We have more work to do to find out whether IGRP is indeed one of the responsible genes contributing to susceptibility."

She said it's an "intriguing" coincidence that IGRP corresponds to a site suspected in diabetes susceptibility. But it is too early to draw any conclusions beyond what the study shows -- that T cells target the IGRP protein in mice.

The next step will be to find out if the same is true in humans.

"This is generating a fair amount of excitement in the field, so we're not going to be alone in these human studies," DiLorenzo said. "We should know, hopefully within the next year, whether this is a relevant target in humans."

If it is, researchers could try to develop treatments for type 1 diabetes based on IGRP. Doctors could also identify people at risk for the disease based on whether their T cells react to IGRP.

"If you could identify at-risk individuals you could potentially come up with earlier diagnoses," DiLorenzo said.

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