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Scientists identify factor that may trigger type 1 diabetes

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A team of researchers, led by investigators at the University of Colorado School of Medicine, have identified a new class of antigens that may be a contributing factor to type 1 diabetes, according to an article published in the current issue of the journal *Science*.

In autoimmune disease, the key question is why the immune system attacks the body's own tissues. Type 1 diabetes is the autoimmune form of diabetes, in which insulin-producing beta cells in the pancreas are destroyed by immune cells, especially those known as T cells. Insulin is the hormone that regulates levels of glucose in the blood and without insulin, a life-threatening disease results. Currently, there is no cure for type 1 diabetes.

"Our lab studies the type of T cell known as a CD4 T cell," said Kathryn Haskins, PhD, professor of immunology and microbiology and corresponding author of the article. "We have focused on autoreactive CD4 T cells using a mouse model of autoimmune diabetes. We have been especially interested in identifying the antigens that activate these T cells."

Antigens for T cells are pieces of proteins, or protein fragments (peptides) that have to be taken up and presented to the T cells by antigen-presenting cells. Normally, a CD4 T cell is supposed to respond to "foreign" antigens, like a viral peptide. But in autoimmune disease the T cells respond to antigens that are generated in the body. Such proteins and peptides are called autoantigens.

When an autoreactive T cell sees its antigen, it becomes activated and can initiate disease. By identifying those antigens, scientists may be able to use that information to detect autoreactive T cells early in disease, or better yet, in at-risk individuals. If they are able to use the antigens to turn off destructive T cells, they may be able to prevent the disease.

Haskins and others, including fellow corresponding author Thomas Delong, PhD, assistant professor of immunology and microbiology, conducted experiments to analyze the fractions of beta cells that contain antigen for autoreactive CD4 T cells in order to identify autoantigens in type 1 diabetes. They discovered a new class of antigens that consist of insulin fragments fused to peptides of other proteins present in beta cells. That fusion leads to generation of hybrid insulin peptides that are not encoded in an individual's genome.

If peptides in the body are modified from their original form, they essentially become "foreign" to the immune system and this may explain why they become targets for the autoreactive T cells. The discovery of hybrid peptides as targets of the immune system provides a plausible explanation of how the immune system is tricked into destroying the body's own beta cells. The discovery may also lead to a better understanding of other autoimmune diseases.

More information: "Pathogenic CD4 T cells in type 1 diabetes recognize epitopes formed by peptide fusion," by T. Delong et al. science.sciencemag.org/cgi/doi … 1126/science.aad2791

Provided by University of Colorado Denver

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