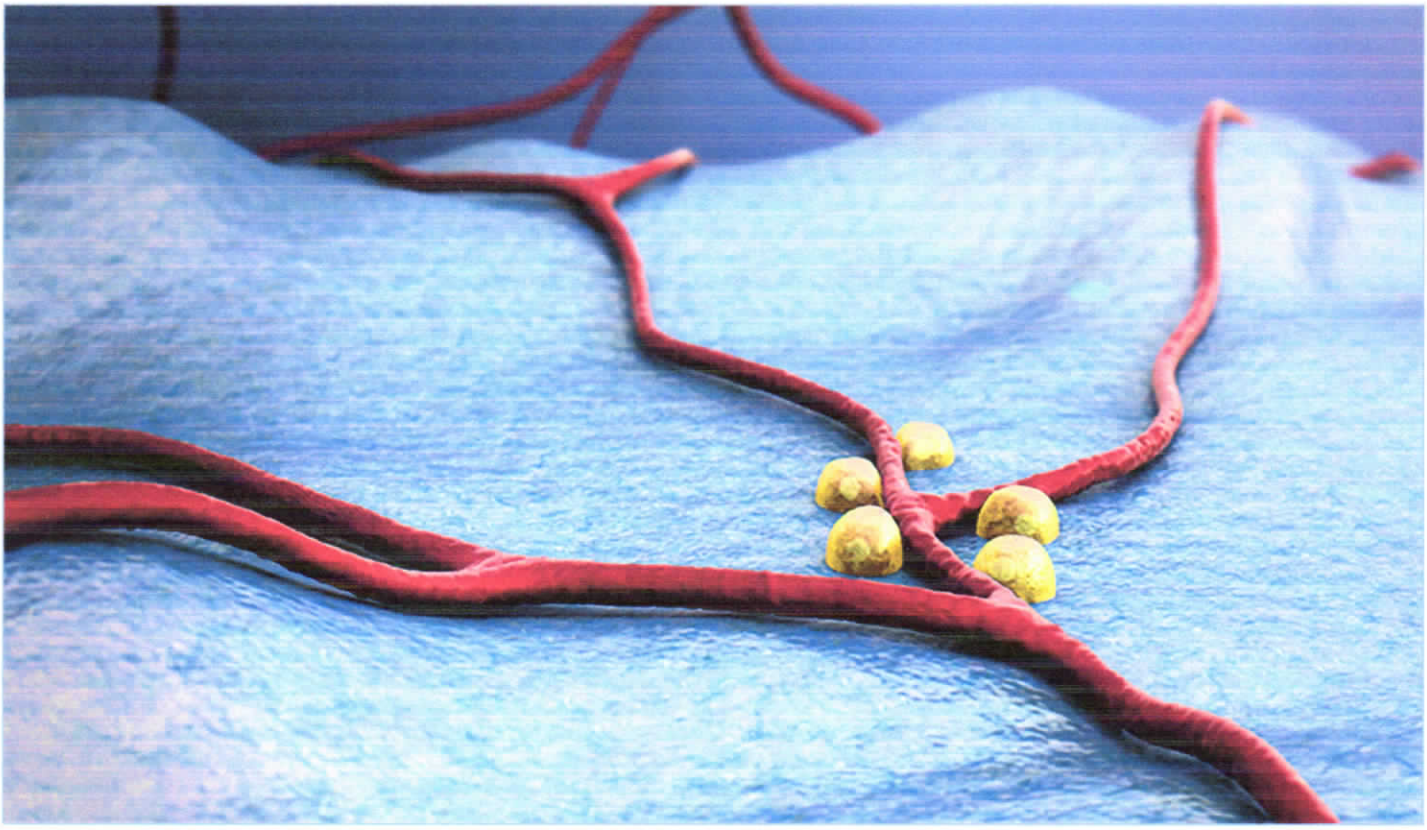
YaleNEWS

Yale scientists study how some insulin-producing cells survive in type 1 diabetes

By Ziba Kashef February 9, 2017



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A Yale-led research team identified how insulin-producing cells that are typically destroyed in type 1 diabetes can change in order to survive immune attack. The finding may lead to strategies for recovering these cells in diabetic patients, said the researchers.

The study was published on Feb. 9 in Cell Metabolism.

In patients with type 1 diabetes, an autoimmune disease, the immune system destroys beta cells — the cells that produce insulin in the pancreas. But some beta cells survive in diabetic patients even years after the onset of disease.

A team of researchers at Yale and the Broad Institute of MIT and Harvard studied the changes in beta cells that occur during immune attack that may lead to their persistence in both mouse models of type 1 diabetes and in human cells in culture.

The researchers identified a subpopulation of beta cells that resists immune attack. "During the development of diabetes, there are changes in beta cells so you end up with two populations of beta cells," said professor of immunobiology and senior author Dr. Kevan Herold. "One population is killed by

the immune response. The other population seems to acquire features that render it less susceptible to killing."

This subpopulation survives by using a "duck and cover" approach, Herold noted. The cells express molecules that inhibit the immune response. They also acquire "stemness," or a stem-cell-like ability to revert to an earlier stage of development in which they can persist and proliferate despite immune attack.

The discovery will lead to further investigation of strategies that could benefit diabetic patients. "The next question is, can we recover these cells so that there is insulin production in someone in type 1 diabetes?" said Herold. He and his colleagues plan to test drugs to see if they can modify the beta cell subpopulation and turn it into insulin-producing cells.

Other authors are Jinxiu Rui, Songyan Deng, Arnon Arazi, Ana Luisa Perdigoto, and Zongzhi Liu.

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β Cells that Resist Immunological Attack Develop during Progression of Autoimmune Diabetes in NOD Mice

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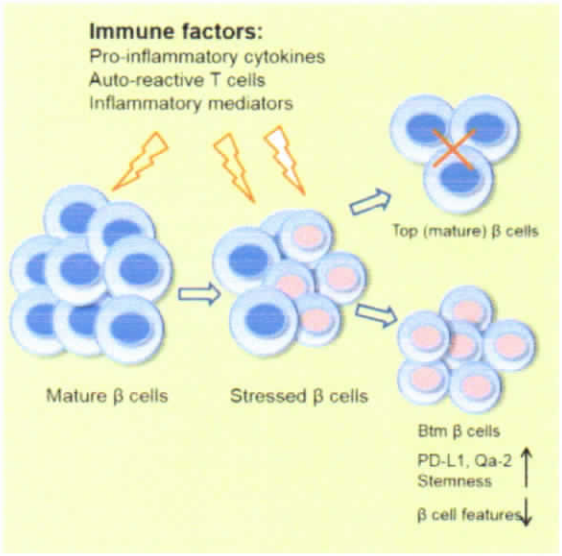
Highlights

- Novel β cells with lower granularity develop during progression of T1D in NOD mice
- The novel β cells show decreased expression of markers of mature β cells
- The novel β cells are protected from immune killing
- The novel β cells are less differentiated and show stem-like features

Summary

Type 1 diabetes (T1D) is a chronic autoimmune disease that involves immune-mediated destruction of β cells. How β cells respond to immune attack is unknown. We identified a population of β cells during the progression of T1D in non-obese diabetic (NOD) mice that survives immune attack. This population develops from normal β cells confronted with islet infiltrates. Pathways involving cell movement, growth and proliferation, immune responses, and cell death and survival are activated in these cells. There is reduced expression of β cell identity genes and diabetes antigens and increased immune inhibitory markers and stemness genes. This new subpopulation is resistant to killing when diabetes is precipitated with cyclophosphamide. Human β cells show similar changes when cultured with immune cells. These changes may account for the chronicity of the disease and the long-term survival of β cells in some patients.



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β cell, autoimmunity, immune regulation, stem cell