Study identifies immune cells that promote growth of beta cells in type 1 diabetes

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Joslin researchers have identified immune cells that promote growth of beta cells in type 1 diabetes. This study provides further evidence of a changed role for immune cells in type 1 diabetes pathology. The study appears online today and will also appear in the January issue of *Diabetes*.

In type 1 diabetes, the immune system infiltrates pancreatic islets and destroys insulin-producing beta cells. However, previous studies in non-obese diabetic (NOD) mice have suggested that immune cells can also contribute to preserving beta cells. This notion is strengthened by the observation by Joslin researchers who reported that members of the Center's 50-Year Medalist Study, who have lived with type 1 diabetes for 50 years or more, retain some beta cells and produce insulin.

"The traditional view of type 1 diabetes was that immune cells killed all beta cells and people with the disease would have to take insulin for life. But we know that some beta cells do survive and secrete insulin even when the patients have had type 1 diabetes for 50 years," says senior author Rohit N. Kulkarni, M.D., Ph.D., a Senior Investigator in the Section on Islet Cell and Regenerative Biology at Joslin and Associate Professor of Medicine at Harvard Medical School.

In this study, Joslin researchers were interested in learning exactly how immune cells could promote beta cell growth and identifying the type of cell and the mechanisms underlying this effect.

In a series of experiments, the researchers injected NOD mice with immune cells from the pancreatic islets of donor NOD mice and assessed their effects on beta cells. The immune cells tested included subtypes of B or T immune cells.

The researchers found that it is T cells not B cells that are associated with beta cell proliferation. Mice that received B cells showed no difference in beta cell growth. Mice that received the T cell subtypes CD4+ and CD8+ showed an elevation in all markers of beta cell proliferation compared to mice that did not receive them. The researchers also found that beta cell growth happens after islets are infiltrated by immune cells and is independent of the effects of glucose and insulin.

Further experiments with cell cultures showed that CD4+ and CD8+ cells secrete inflammatory cytokines and chemokines (Interleukin 2, Interleukin 6, Interleukin 10, MIP-1? and RANTES), which together enhanced beta cell proliferation. This is the first study to report that this group of "soluble factors" is involved in promoting beta cell growth.

"This gives us new insights into what is happening in the pathology of type 1 diabetes. The immune cells we identified send signals which appear to protect and promote growth of beta cells. This opens up an exciting new area that scientists have thought about; now we have the hard data to substantiate it," says Dr. Kulkarni.

The next step is to investigate the effects of immune cells on human beta cell growth. The factors secreted from CD4+ and CD8+ cells are potential therapeutic candidates to enhance beta cell growth to prevent or delay the onset of type 1 diabetes.

"We need to learn more about the relationship of beta cell death and proliferation to determine if we can harness these soluble substances to encourage beta cell proliferation rather than destruction," says Dr. Kulkarni.

Provided by Joslin Diabetes Center