MedicalXpress

Cancer and arthritis therapy may be promising treatment for diabetes

December 18 2007

An antibody used to treat certain cancers and rheumatoid arthritis appears to greatly delay type 1 diabetes in mice, Yale School of Medicine researchers report in the *Journal of Clinical Investigation*.

“Even better, the beneficial effects of the antibody continue to be observed long after the antibody is no longer administered,” the researchers said.

The antibody, rituximab (anti-CD20), depletes B cells. Experimental evidence in mutant mice indicates that B cells play a role in autoimmune diseases by interacting with T cells of the immune system. It is T cells that destroy insulin-producing cells directly in the pancreas, leading to type 1 diabetes.

“Our paper shows, for the first time, that after successful B cell depletion, regulatory cells emerge that can continue to suppress the inflammatory and autoimmune response even after the B cells return,” said Li Wen, senior research scientist in the division of endocrinology. “Even more strikingly, we found that these regulatory cells include both B and T cells.”

To determine if B cell depletion would work as a therapy for type 1 diabetes, Wen and her colleague at Yale, Mark Shlomchik, M.D., professor of laboratory medicine and immunobiology, developed a mouse model. They engineered mice that were predisposed to diabetes and had the human version of CD20, the molecule rituximab targets, on

the surface of their B cells.

The researchers tested a mouse version of the drug to deplete B cells in mice either before diabetes onset, or within days of diagnosis with diabetes. The drug treatment significantly delayed diabetes onset in pre-diabetic mice. This translated to a 10- to 15-week delay in developing diabetes compared to mice given a “sham” treatment. The equivalent period for humans would be approximately 10 to 15 years. Of the 14 mice that already had diabetes, five stopped needing insulin for two to five months while all the sham-treated mice remained diabetic.

“These studies suggest that B cells can have dual roles in diabetes and possibly other autoimmune diseases. The B cells might promote disease initially, but after being reconstituted following initial depletion with rituximab, they actually block further disease,” Shlomchik added. “This means that multiple rounds of medication to deplete the B cells might not be necessary or even advisable.”

Source: Yale University