Researchers find genetic variation associated with Type 1 diabetes

Findings could lead to more efficient treatment, earlier detection of diabetes

Diabetes is the seventh leading cause of death in the United States, and some 215,000 Americans younger than age 20 have diabetes, according to the Centers for Disease Control and Prevention. Most cases of diabetes among children and adolescents are type 1, which develops when the body can no longer make insulin, a hormone that controls the amount of blood glucose. It has become clear over the last decade that the inability to make insulin is caused by an abnormal immune by the affected patient to his/her own insulin producing cells.

Now, researchers from Seattle Children’s Research Institute and Benaroya Research Institute at Virginia Mason have identified new clues as to how a common genetic change in a gene called PTPN22 may pre-dispose children and adults to develop auto-immune conditions including type 1 diabetes, rheumatoid arthritis and systemic lupus. The related study, “Altered B Cell Homeostasis is Associated with Type 1 Diabetes and Carriers of the PTPN22 Allelic Variant,” was published in January 2012 in The Journal of Immunology.

“Five to 15 percent of Caucasians in the U.S. carry the specific genetic change we studied,” said David Rawlings, MD, and director of the Center for Immunity and Immunotherapies at Seattle Children’s Research Institute. “Our research focuses on how this change impacts the immune system.”

When you think about immune conditions like the Human Immunodeficiency Virus, or HIV, you typically hear about T cells. In this study, however, Dr. Rawlings, Dr. Buckner and their colleagues looked at how B cells may promote auto-immune disease. B cells make antibodies, proteins that are required by the body to control many harmful agents including most viruses and bacteria.

“People can be healthy, meaning they are not diagnosed with diabetes or other conditions, and still have the genetic change in PTPN22” said Dr. Rawlings. “Identifying associated changes in the function of immune cells, however, can help us learn more about people who are at risk for auto-immune conditions. In this new study we identified altered features in the B cells in both unaffected people as well as in diabetics who carried this change in PTPN22. Based on the study, these abnormalities may help to explain how this genetic change promotes diabetes or other auto-immune conditions.”

Dr. Rawlings said that researchers have long suspected that abnormal T cells lead to diabetes. But prior to this study, there was “less compelling evidence that abnormal B cells promote diabetes,” he said.

Researchers involved in a recent worldwide clinical trial at 15 medical centers found that injections of the drug rituximab (also known as Rituxin) which is used eliminate B cells, can slow the destruction of insulin-producing cells in some patients with type 1 diabetes. Rawlings and Buckner and their teams will now follow up on that study, investigating what happened with the children treated in that clinical trial and whether the changes they have identified may predict a better response. They will also look into whether the same immune abnormalities can be observed before children develop diabetes.

“Nobody really knows precisely how changes in the PTPN22 gene or in the growing number of other genetic traits now known to be linked to auto-immune diseases actually work together to promote disease,” said Dr. Rawlings. As part of the continued research, he and the team have begun to generate a series of new animal models where the identical genetic changes found in humans have been introduced in mice. In parallel, they will study samples from patients and controls in repositories at the Benaroya Research Institute at Virginia Mason. “This combined approach will allow us to learn much more about the human immune system and how it is regulated,” he said. “We aim to determine what we can do to reduce the risk for auto-immune conditions or to be better at treating or, ideally eliminating these conditions when they are initially diagnosed.”