Reversing Autoimmunity: Can the DRI Do It?

Meet Alberto Pugliese, M.D., a Research Associate Professor of Medicine, Immunology and Microbiology, and Head of the Immunogenetics Program at the Diabetes Research Institute in Miami, FL. He was scheduled to host a chat on "Reversing Autoimmunity" on the DiabetesTalkFest site on Feb. 8, but some technical difficulties prevented him from logging on. So he was kind enough to talk with us all via the DiabetesMine.com community here.

Since joining the DRI in 1994, Dr. Pugliese's main research focus has been studying and characterizing the natural mechanisms of genetic resistance to insulin-dependent diabetes. His important findings in the field of immunogenetics involve the body's regulation of the self-antigens in thymus and other lymphoid organs which are thought to be important mechanisms of predisposition to type 1 diabetes.

All that science talk sound a little over your head? No worries. That's why I asked Dr. P to explain it to us in plain English (to the extent that a top-notch researcher can :)

DM) In very lay terms, can you explain what dendritic cells are and why they have the potential to thwart diabetes?

Dr. P) Dendritic cells are key regulators of the immune system. This class of immune cells can both stimulate or suppress immune responses and therefore, researchers are studying their potential to treat many immune-mediated diseases. With respect to diabetes, the approach is to develop dendritic cells that control unwanted immune responses against the insulin-producing cells.

DM) Where exactly do these cells reside? And what is their relationship to the beta cells we normally associate with
curing diabetes?

Dr. P) Dendritic cells are found in many tissues, including but not limited to organs of the immune system (thymus, spleen, lymph nodes). They may circulate in the pancreas and can also be involved in the stimulation of the autoimmune process that leads to diabetes.

DM) What was the biggest revelation of your latest research? Discovering the dendritic cells themselves, or learning that they can potentially produce insulin?

Dr. P) We have discovered that certain dendritic cells can produce insulin. This insulin is not released and does not affect blood sugars. Dendritic cells are not like beta cells. Instead of secreting insulin, these cells "expose" this insulin on their surface. We believe that the dendritic cells that make insulin do so to educate the immune system and control unwanted immune responses against insulin-producing cells. We have devised a method to purify these insulin-positive dendritic cells to further study their function, as well as for developing potential therapeutic applications to prevent and cure diabetes.

DM) Your survival technique theory says that some cells may compensate for the loss of others by taking on new functions, like pancreatic ductal cells that start to produce insulin. If this is possible, why don’t we see it happening more often?

Dr. P) We are studying some pancreatic organs in which beta cells were destroyed by autoimmune. By studying biopsy samples, we have found insulin expression in ductal cells (cells in the pancreatic ducts), which normally do not make insulin.

These findings, along with other research, suggest that the pancreas may have the ability to remodel and generate new beta cells. It is possible that some remodeling may occur in patients, but the remodeling potential may be limited by the ongoing autoimmune response that likely destroys beta cells as they form. The pancreatic organs we studied were obtained from immunosuppressed patients who had received pancreas transplants. Thus, the immunosuppression may have slowed the immune system enough to have allowed for the development of these new cells, giving the ability to observe these phenomena.

DM) If it is viable, do researchers have an idea yet how to prompt this cell transdifferentiation in humans?

Dr. P) In general, research is helping us to understand pancreatic development and what factors are critical for the generation of beta cells. Many studies are underway to understand the process of transdifferentiation. We hope that this knowledge will help us devise treatments that stimulate regeneration or transdifferentiation. However, we also need...
DM) In your opinion, what is the most promising approach to islet cell transplants currently being studied at the DRI? By promising, I mean closest to actually being available to mainstream patients within the next 5 to 10 years?

Dr. P) We hope that all of our research contributes to improved therapies for people living with diabetes. However, we cannot responsibly predict how long or what precise therapy may offer “the” answer. That is what makes the DRI unique. We are working in many different areas of research to restore insulin production, not only with colleagues within the institute, but also those within the University of Miami and throughout the world. There are many novel approaches being studied that are aimed at manipulating the immune system to prevent both foreign tissue rejection and autoimmunity. I think it is critical that we aim at developing and testing approaches that address both problems.

Thank you, Dr. Pugliese. You can’t imagine a more dedicated cheering squad than the folks reading you here!

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