Study shows roles of beta cells and the immune system in Type 1 diabetes

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A new JDRF-funded study shows that many of the genes known to play a role in type 1 diabetes (T1D) are expressed in pancreatic beta cells, suggesting that the cell responsible for producing insulin may be playing a part in its own destruction to lead to T1D. Published in the March issue of *PLoS Genetics*, researchers in Belgium suggest this interpretation after producing an extensive catalogue of more than 15,000 genes expressed in human islets, forming the most extensive characterization of human islets reported to date.

The researchers, led by Decio Eizirik, M.D., Ph.D., professor and director of the Laboratory of Experimental Medicine at Universite Libre de Bruxelles in Brussels, Belgium, used a technique called RNA sequencing-a method that identifies all forms of transcribed RNAs in a cell-to assemble a catalog that showed that more than 15,000 genes are expressed in healthy human islets. Transcribed RNA (ribonucleic acid) molecules serve as the vehicles through which a cell's genetic information is expressed. The data has been made available to other researchers to be used for future studies of beta cell function.

In the study, the researchers found many of the previously known genes associated with T1D among the genes expressed in human islets. When the researchers exposed the human islets to agents (cytokines) released by immune cells that may trigger T1D, they noted changes in the expression patterns of these genes. This finding suggested that the islets may be contributing to the recruitment of immune cells as T1D starts to develop.

While conventional wisdom was that these genes played a role in T1D by affecting the function of the immune system, their expression in human islets led the scientists to consider the possibility that the beta cells-once seen as merely victims in T1D-might actually assist in their own attack by the immune system.

"Based on our research, our understanding now is that type 1 diabetes in its early stages, is characterized by a dialog between beta cells and the immune system, instead of the previous view of beta cells as purely passive victims of the immune attack," said Dr. Eizirik. "We can now open our eyes a bit wider to the possible ways that type 1 diabetes can develop. As we expand our focus on beta cells, we could start to unearth more answers in the mystery of this disease."

"What we're seeing is that beta cells may in fact be playing a larger role in triggering type 1 diabetes than we previously thought, and exploring this concept more deeply could lead to a better understanding of the what causes the autoimmune attack," said Julia Greenstein, Ph.D., JDRF's assistant vice president for cure therapies. "Dr. Eizirik's work is important to JDRF because it shows us that there is a need for more research on beta cell survival and health and its role as a potentially key part of the early disease process. Furthermore, the catalog of genes from this study will continue to support progress in many more areas of diabetes research."

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