

Examination of Human Pancreatic Tissue and Isolated Pancreatic Islets from Organ Donors with Diabetes-associated Autoantibodies

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Purpose: The notion that development of type 1 diabetes is a slow process progressing over several years is supported by the appearance of auto-antibodies against islet antigens years before clinical presentation. It is not known what triggers this humoral response, nor whether it is a cause or a consequence of the disease. In this study we had the opportunity to examine the pancreas from ten auto-antibody positive, and ten control multiorgan donors.

Methods: Insulin, immune cell marker, and enterovirus stainings were performed on formalin-fixed paraffin-embedded samples from the pancreas head. Insulin/DNA ratio, glucose-stimulated insulin release, and chemokine secretion were measured in isolated islets. PCR was used to detect enteroviral nucleic acid.

Summary of Results: Islets from pre-diabetic donors did not differ significantly from control donors in respect to immunopositivity to insulin, glucose-stimulated insulin release, or insulin/DNA ratio (3.7 ± 2.9 in pre-diabetic and 4.9 ± 2.0 in controls). Islet content of chemokines IL-6, IL-8, and MCP-1 was not altered in autoantibody positive donors. T cells and macrophages infiltrated the pancreatic tissue in all donors to a various extent, but no increased infiltration or accumulation in or around islets could be seen in auto-antibody positive donors compared to controls. Islets from one donor with auto-antibodies against GAD65 stained positive for enterovirus structural protein VP1 and the presence of enterovirus genome was confirmed with PCR. Inoculation of culture media from these islets on green monkey kidney cells induced cytopathic effect in these cells for up to four passages.

Conclusions: No ongoing pathogenic processes were found in pre-diabetic pancreata, but it cannot be excluded that beta-cell destruction has occurred or is ongoing in a sub-fraction of pancreatic lobules. The presence of enterovirus in pancreatic islets, at least in one of these autoantibody-positive individuals, suggests that infection can contribute to triggering the appearance of autoantibodies. This is one of very few cases in the world where the presence of enteroviral genome in islets has been proven by PCR and virus isolation.