Pancreatic islet transplantation to treat diabetes – defining molecular tools to select suitable islets

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A complete understanding of pancreatic islet biology is essential to the development of preventive or curative interventions for diabetes. It has been known that subpopulations of islets of different sizes exist; however, whether they are biologically and functionally unique has not been investigated. As an example, our work comparing the biology of large versus small islets isolated from rats showed that small islets were superior to large islets in in vitro function and in transplantation outcomes. These results provided the stimulus for an improved approach to islet transplantation in humans. The work also led to new questions regarding the basic physiology of healthy islets. Through collaboration between our University of Kansas Medical Center and Children's Mercy Hospital teams, we determined that small islets secrete higher amount of insulin in vitro when compared to the large islets. We sought to identify whether the islet subpopulations showed differences at the molecular level and thus we investigated their protein expression profiles using two-dimensional polyacrylamide gel electrophoresis (2D PAGE). We found that the protein repertoire in the small and large islets differed significantly. Specifically, some proteins were found only in one type of islets, small or large, while they were missing or their expression levels were different in the other subpopulation. We identified some of the proteins by liquid chromatography – mass spectrometry. Immunofluorescence performed on small and large islets in pancreatic sections, with antibodies against identified proteins, confirmed that the proteins were present in one subpopulation of islets. Of these proteins, at least one was unique to large islets and can potentially be used as a marker to distinguish in vivo between islets that are high-insulin producers and those that fail to secrete significant amounts in insulin. Our long-term goal is to monitor the fate of the different islet populations during diabetes development. In addition, markers like this can be used to determine the best islet subpopulation for transplantation. The data support our hypothesis that integral differences exist between small and large islets that might determine the islets' unique properties under normal conditions and during the development of diabetes. These differences may also influence islet subpopulation behavior in transplantation affecting the outcome.