Pancreatic Islet Composition Affects Hormone Secretion in Isolated Alpha and Beta cells

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Background/Objective:
The Integrated Islet Distribution Program (IIDP) distributes islets from five isolation Centers and serves as the main source of human islets for research in the U.S. In 2016, the IIDP initiated the Human Islet Phenotyping Program (HIPP), which provides standardized post-shipment assessment of islet hormone secretion and endocrine cell composition for each IIDP-supported islet isolation. To date, islets from 276 non-diabetic donors have been analyzed. We hypothesized that analysis of this unique resource will provide novel insights into how demographic and clinical features impact islet health.

Methods:
Relationships between insulin and glucagon secretion assessed by perifusion and islet composition (% of β- and α-cells) were analyzed using SAS Version 9.4. For each analysis, the isolation center was used as a covariate.

Results:
Of the 276 donors, 60% were male; 59% of donors were Caucasian, 28% were Hispanic, 9% were African-American; 4% were Asian; and 0.36% were American Indian. The % of β-cells was moderately correlated with insulin responses to 16.7 mM glucose ($r=0.2785$; $p<0.0001$) and 20 mM KCL ($r=0.3109$, $p<0.0001$). Similarly, the α-cell% was moderately correlated with total glucagon content ($r=0.3362$, $p<0.0001$) and glucagon responses to 1.7 mM glucose + 1mM epinephrine ($r=0.2015$, $p=0.0001$). The % of β -cells was negatively correlated with glucagon total content ($r=-.243$,$p=.0001$), while the α-cell% was negatively correlated with insulin stimulation index to KCL ($r=-0.2573$, $p<0.0001$). Notably, Asian donors exhibited a significantly higher β-cell% compared to other groups ($p<0.05$). Consistent with this, glucose-stimulated insulin secretion was higher in Asian donors compared to responses observed in islets from African American donors ($p<0.01$).

Conclusion:
These data indicate that islet cell composition influences insulin and glucagon secretory responses and suggests that race may impact islet composition and hormone secretion. Continued analysis of the HIPP dataset may aid in our understanding of risk factors for the development islet dysfunction in diabetes.