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A personalized approach for assessing pancreatic function in diabetes using novel islet biomarkers

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Pancreatic islets play a critical role in diabetes disease development. Their status is currently approximated through measurements of basal and stimulated blood glucose, C-peptide, and insulin levels. Glycated hemoglobin (HbA1c) levels are used to estimate disease progression and response to therapy. These tests are either insufficient, or impractical to perform in a clinical setting. Therefore, an important unmet need remains for biomarkers that can accurately monitor the function and health of pancreatic islets. Such biomarkers may help predict disease progression, guide drug selection, monitor therapeutic efficacy and accelerate the development of disease-modifying therapies that aim at improving the function of -cells. We have identified candidate blood biomarkers associated with pancreatic islet function by proteomic analysis of secretory vesicles isolated from primary human pancreatic islets under steady state and following induced dysfunction. Candidate specificity was evaluated by comparing the pancreatic islet datasets to a library of secreted proteins produced by multiple major organs and selecting the proteins uniquely present in pancreatic islets. The performance of the biomarkers was assessed using targeted multiple reaction monitoring mass spectrometry (MRM-MS) or ELISA in plasma from patients that were either normoglycemic (n=47), had impaired glucose tolerance (n=17), or were Type 2 diabetics diagnosed for less than 1.5 years (n=19) or for over 5 years (n=28). A pool of 14 candidates was able to accurately classify patients into the disease progression groups when used in small combinations of 3-5 biomarkers. This performance was independent of and superior to the standard of care (SOC; glycated hemoglobin and fasting plasma glucose). This performance improvement was especially important for pre-diabetic patients where about 50% can be currently be correctly identified by the SOC. Most candidate biomarkers had functions related to metabolic homeostasis or regulation of islet secretion, tissue remodeling, and inflammation. We have thus identified candidate biomarkers derived from human pancreatic islets that appear able to distinguish between disease progression groups. Independent confirmatory studies are underway using cross-sectional groups from a different clinical site as well as longitudinal cohorts of patients with gestational diabetes or who underwent bariatric surgery.

Biography

Eustache Paramithiotis completed a PhD in Immunology from McGill University and Post-doctoral research at the Howard Hughes Medical Institute at the University of Alabama at Birmingham with an award from the Irvington Institute for Immunological Research. He has extensive experience in large scale biology and translational medicine, in particular biomarker discovery and validation, and has led several privately or publically funded multi-year projects. He is currently the Caprion's Vice President of Biomarker discovery and Diagnostics, responsible for the advancement of Caprion's diagnostics development pipeline and for discovery of biomarkers with diagnostic application potential.

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