OBJECTIVES

- Our long-term goals are:
  - To discover more accurate biomarkers (i.e. "diagnostic tests") for early prediction of T2D in diverse human populations.
  - To understand the molecular mechanisms that underlie the development of T2D in diverse human populations.

ABSTRACT

• Type 2 diabetes mellitus (T2D) is a globally prevalent disease with substantial morbidity and mortality.
• Early prediction of the pathological processes that lead to T2D is important because it will facilitate novel interventions aimed at delaying or preventing the disease.
• Several risk prediction models that combine clinical information with conventional biomarkers exist, but most do not account for the large variability in biological and environmental factors and tend to overestimate risk.
• Here we use a precision medicine approach to discover novel and more accurate biomarkers of T2D development in diverse Caribbean Populations.

METHODS

Metabolomic analysis of plasma and urine
Targeted and quantitative metabolomics approaches by ultra performance liquid chromatography (UPLC) combined with tandem mass spectrometry (MS/MS).
Several chromatographic and preparative approaches will be used to facilitate separation of polar compounds (hydrophilic interaction liquid chromatography, (HILIC)) and chiral compounds (chiral columns and chiral derivatizing agents).
The different techniques are expected to detect and quantify amino acids (D- and L-forms), organic acids, fatty acids, carbohydrates and acylcarnitines.
Statistical analysis
Preliminary data was analyzed using various statistical approaches, including orthogonal partial least squares discriminant analysis, multiple t-tests, ANOVA and area under the curve for biomarker prediction.
Pathway and Network analysis tools (e.g. Ingenuity, Qlucore) will be used as well.

PRELIMINARY RESULTS

• We are able to detect and quantify numerous metabolites in minute plasma samples (<10 microL) and have discovered significant metabolic changes in a First wave collection of T2D patients.
• Numerous metabolites have been observed to be significantly different (p<0.05, FDR=0.05) between patients of T2D and normal individuals.
• We demonstrate that metabolites such as Aminoadipic acid (AUC 0.85), Isoleucine (AUC 0.72), metabolite ratios and pairwise metabolite ratios can be used as potential biomarkers for T2D.
• Subsequently, we have identified predictive clinical markers that can be useful in assessing the risk of T2D among the Caribbean population.
• Continued method validation with analysis of larger cohorts of subjects will take place over the next years.

CONCLUSIONS