A beta pancreatic methylation biosignature for the diagnosis & prediction of type 2 diabetes mellitus.

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Abstract

Background

The need for minimally invasive biomarkers of early diagnosis of type 2 diabetes (T2DM) and beta-pancreatic cell loss monitoring is emerging for timely and effective interventions to preserve significant beta-cell mass.

Objective

In the present study, we focus on studying the methylation fingerprint of circulating cell-free DNA (cfDNA) from liquid biopsies, to build accurate diagnostic/monitoring biosignatures for clinical application in diabetes.

Methods

The study group consisted of 353 T2DM patients, 164 individuals with prediabetes, and 279 healthy individuals. Plasma cfDNA levels were quantified directly via fluorometry and after extraction of ccfDNA, methylation analysis of INS (Insulin), IAPP (Islet Amyloid Polypeptide-Amylin) and GCK (Glucokinase) was performed by qMSP. Automated Machine Learning was used to build classifying biosignatures.

Results

cfDNA levels were found to be elevated in diabetes ($p<0.001$) and in prediabetes ($p=0.002$) as compared to health. A biosignature via Classification Random Forests algorithm, accurately discriminated diabetes from health (AUC 0.899, average precision: 0.919). External validation in two independent datasets exhibited high sensitivity but low specificity in both datasets. Moreover, the model could predict development of T2D in the prediabetic group with high PPV (0.810).

Conclusion

Our approach exploiting methylation, liquid biopsy and ad-hoc autoML, can lead to an effective minimally invasive solution for diabetes management and prevention.

Do you have any conflicts of interest?

Yes, I have a conflict of interest.

Th. Theodosiou and E. Chatzaki are co-founders of ABCureD PC.