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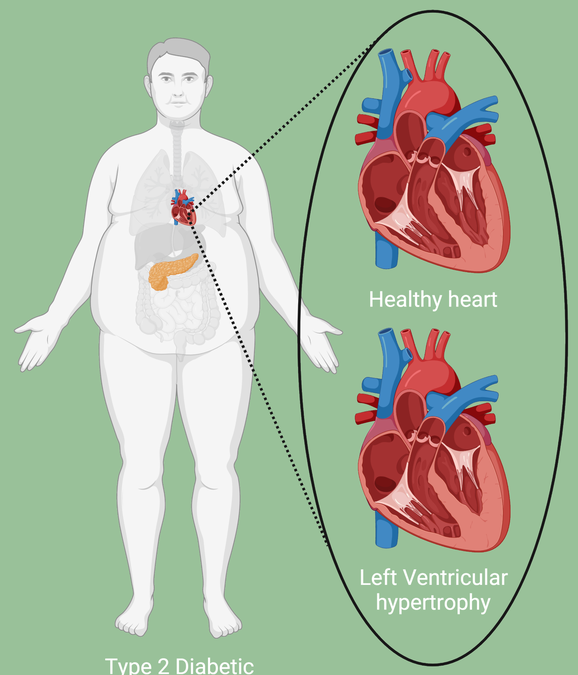
27 proteins to predict heart failure in otherwise healthy type 2 diabetics.



BACKGROUND

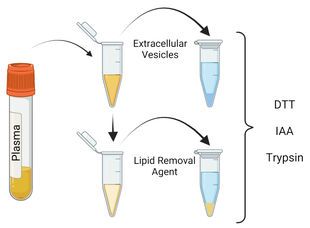
The prevalence of type 2 diabetes (T2D) is increasing rapidly. It currently effects 537 million adults worldwide. This is expected to increase to 643 million adults by 2030. It is estimated that 50 % of T2D patients have subclinical heart failure (HF). This is due to T2D patients having 2 - 5 fold increased risk of developing HF.

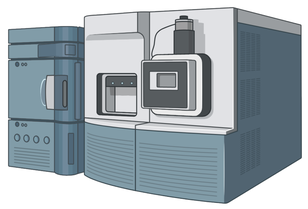
Aims

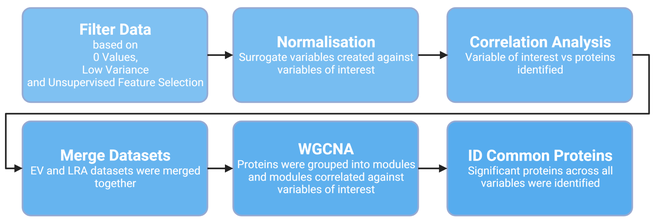
Identify plasma proteins that are associated with subclinical HF in asymptomatic T2D that can be additive to or replace a clinical risk score for this population.

METHODS

Proteins were isolated from plasma (n=92) using a novel method to isolate EV and lipid associated proteins which were then subjected to MS analysis. Raw data were filtered, normalised and subjected to statistical analysis to determine which proteins were associated with subclinical HF in T2D. HF was assessed via the clinical variables GLS, ECV, E/e' and Peak VO2.







RESULTS

Table of 27 proteins identified to be significantly correlated with subclinical HF in asymptomatic T2D.

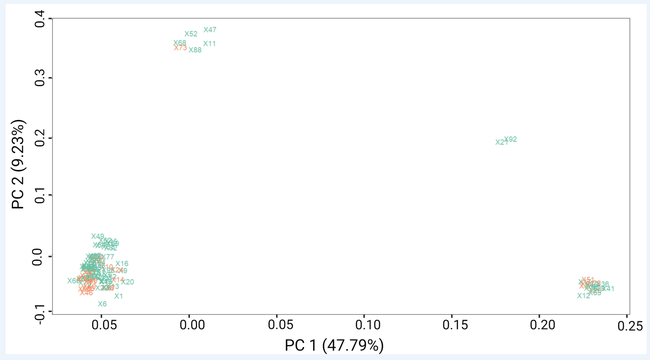
UQCRC2	PSMA6	RACK1	PRPF40B	RPL5
SARS1	RAB7A	WARS1	DOCK4	SFPQ
PDIA3	TTN	MYH11	LMNA	GC
SMARCAD1	RPS2	ATP6V1A	CS	
AHSG	DDX46	DHX9	CLASP2	
KNG1	CFB	CP	FGG	

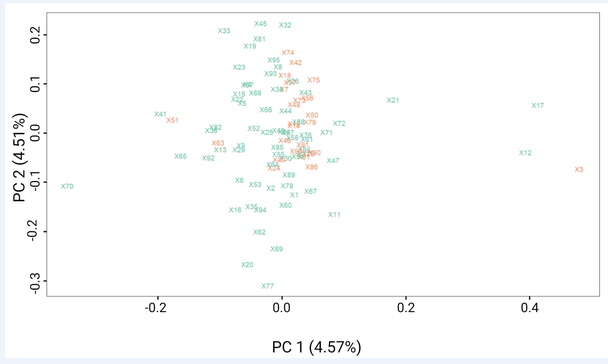
DISCUSSION

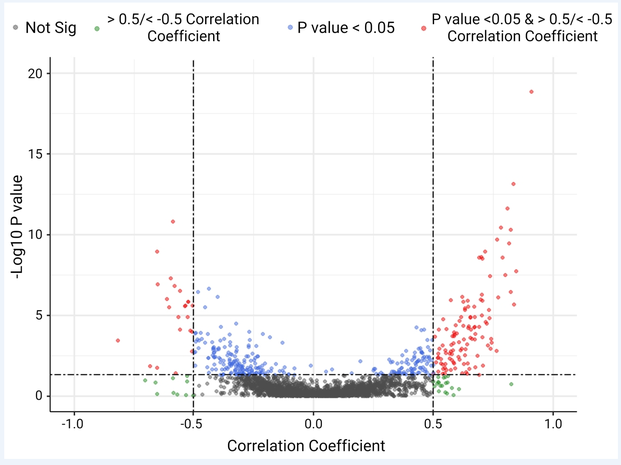
The aim of this study was to identify if plasma proteins were associated with subclinical HF in asymptomatic T2D. **27 candidate biomarkers have been identified in a discovery cohort**. These proteins will be verified in a larger internal cohort (n=500) before moving onto validation following ICH guidelines in an external cohort (n=300).
This forms part of a wider study conducted by Professor McCann who is investigating HF in T2D. Using cardiac MRI, Echocardiography and cardiopulmonary exercise testing a clinical risk score is being created to predict the likelihood of HF in T2D. The fully validated panel of biomarkers will either add to or replace the clinical risk score depending on the predictive performance.

RESULTS

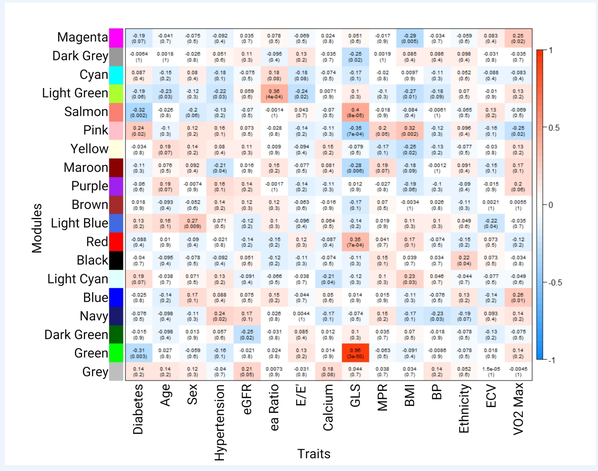
Data were normalised using surrogate variables, which preserved one variable of interest at a time. Plot A is a PCA plot that shows non-normalised EV data. Plot B is a PCA plot that shows EV data after normalising against the variable global longitudinal strain (GLS).







Volcano plot of correlation coefficient and -Log10 P value for proteins plotted against the variable GLS. A volcano plot was produced for each variable of interest in each dataset.



Heatmap showing proteins grouped into modules (y-axis) and correlated against patient variables (x-axis) after normalising for the variable GLS. A heatmap was produced for each variable of interest and common proteins between each significant module were identified.

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