Postprandial changes in plasma metabolome of non-diabetic men are related to genetic susceptibility to type 2 diabetes

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INTRODUCTION

Type 2 diabetes (T2DM) is a group of metabolic disordes. The predisposition to T2DM and impaired β cell function are associated with single nucleotide polymorphism (SNP) in the prospero homeobox 1 (PROX1). However, the exact role of PROX1 gene in T2DM development still remains unclear. For this reason we conducted metabolomics studies to better understand the contribution of this gene in progression of T2DM.

AIM

The aim of this study was to use gas chromatography-mass spectrometry (GC-MS) (Fig. 1) based metabolomics to evaluate postprandial changes in plasma metabolites after the high-carbohydrate (HC) and normo-carbohydrate (NC) meal-challenge-tests in non-diabetic men with different PROX1 genotypes.

Figure 1. Workflow of plasma sample preparation.

Parameters	HR genotypes	LR genotypes	p-value
Age, y	35.3± 9.5	36.3±7.0	0.75
BMI, kg/m²	29.1±8.1	27.3±4.2	0.74
Body fat content, %	23.8±10.1	23.2±7.8	0.87
Fat free mass, %	69.6±11.0	67.6±8.3	0.60
WHR	0.9±0.1	1.0±0.1	0.81
HbA1c	5.2±0.5	5.2±0.2	0.90
HOMA-IR	2.2±2.0	1.9±1.3	0.81
HOMA-B	188.2±163.3	143.7±88.9	0.85
Fat, % energy	34±0.07	27±0.008	0.17
Fasting glucose concentartion, mg/dL	86.2±8.0	86.7±6.4	0.85
Fasting insulin concentration, IU/mL	10.4±9.1	8.9±5.4	0.84
Carbohydrates, % energy	43±0.08	44±0.06	0.88

*HOMA-IR = Homeostatic Model Assessment of Insulin Resistance; HOMA-B = Homeostatic Model Assessment of β-cell function; HbA1c = glycated hemoglobin; WHR = waist-hip ratio

Table 1. The baseline characteristics of study group by the rs340874 PROX1 genotypes

Metabolite	Time	B-H corrected p-value	Fold change	Percenage change
(R)-3-Hydroxybutyric acid	0′ – 120′	0.027510857	0.13	-87%
Galactosamine	0′ – 30′	0.027510857	1.61	61%
	0′ – 60′	0.038717111	1.91	91%
5-Keto-D-Gluconic Acid	0′ – 30′	0.027510857	1.67	67%
	0′ – 60′	0.02750875	2.02	102%
D(+)galactose	0′ – 30′	0.027510857	1.61	61%
D-Allose (anti)	0′ – 30′	0.027510857	1.61	61%
	0′ – 60′	0.027510857	1.88	88%
D-Allose (syn)	0′ – 30′	0.027510857	2.89	189%
	0′ – 60′	0.027510857	2.04	104%
Gulonic acid γ-lactone	0′ – 30′	0.027510857	1.64	64%
	0′ – 60′	0.038717111	1.98	98%
Tyramine	0′ – 30′	0.0275058	1.66	66%
	0′ – 60′	0.0275058	2.97	197%

Table 2. Differences in postprondial plasma metabolites level in HR genotype carriers after intake of HC-meal

MATERIALS AND METHODS

Thirteen contestants from the 1000PLUS cohort study of Polish origin Caucasian population (5 with high risk (HR) and 8 with low risk (LR) genotype) participated in HC and NC meal-challenge-tests. The characteristic of study group is presented in Table 1. None of the participants suffered from T2DM, prediabetes, or other disorders, nor did they report any treatment that might have affected the tests results. Fasting (0′ min.) and postprandial (30′, 60′, and 120′ min. after meal intake) plasma samples were fingerprinted with GC-MS.

RESULTS

After data pretreatment, identification and quality assurance protocol, 52 metabolites were forwarded for statistical analysis. The Wilcoxon signed-rank test was performed using the R software environment (version 4.0.0, https://www.R-project.org/). Multiple comparisons were corrected using the Benjamini-Hochberg procedure. GC-MS based metabolomics revealed that LR genotype carriers did not demonstrate any alterations between fasting and postprandial metabolites level (neither after LC, nor HC meal). However, HR genotype carriers exhibited changes between fasting and postprandial level of 7 metabolites but only after HC meal (Table 2). Altered metabolites were associated with carbohydrates metabolism.

CONCLUSION

The results of our study led to the conclusion that HC meal challenge test provoked changes in plasma metabolites in HR-, but not LR-genotype carriers. More detailed studies and pathways analyses are required to determine the exact mechanism of this process and its role in T2DM development.