

Figure S1. PLSDA score scatter plot between CG and T2DM-NC

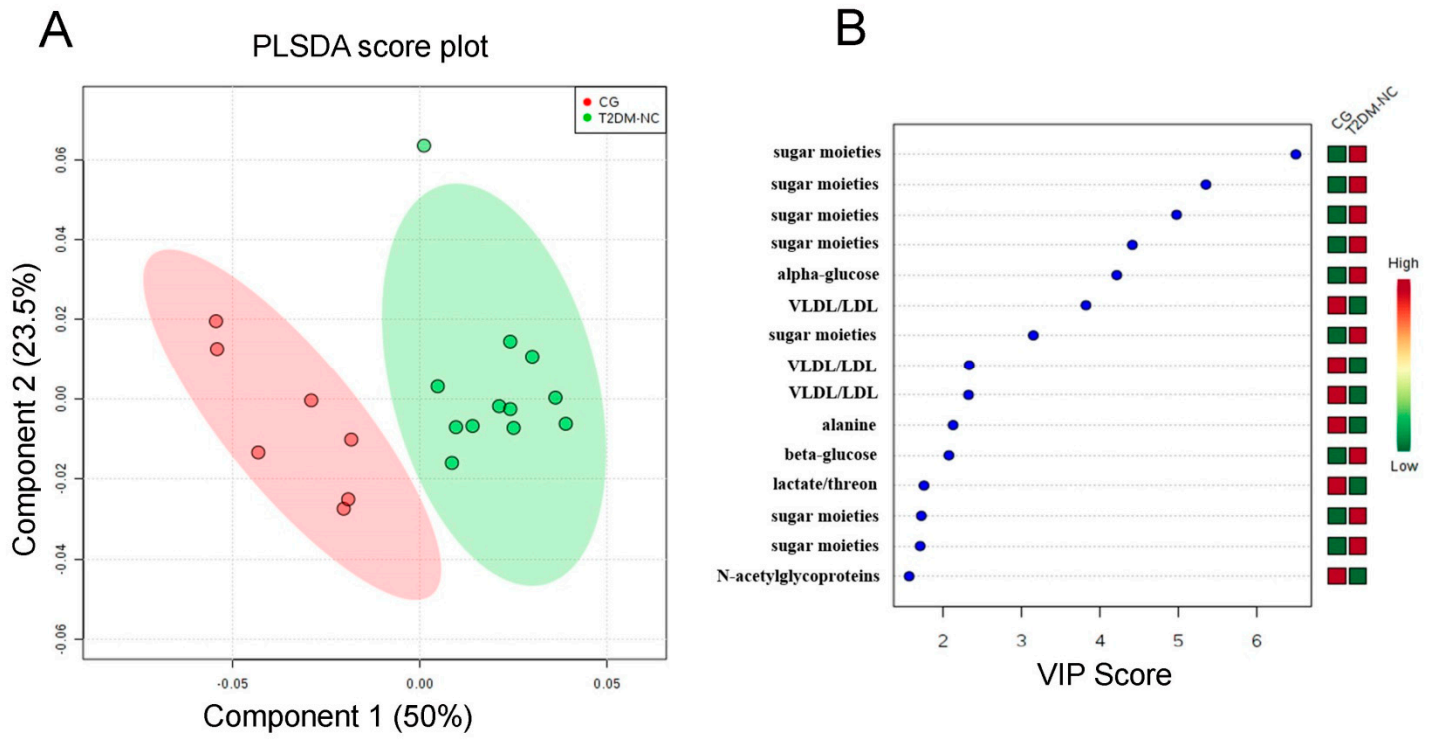


Figure S2. PLSDA score scatter plot between CG and T2DM-C

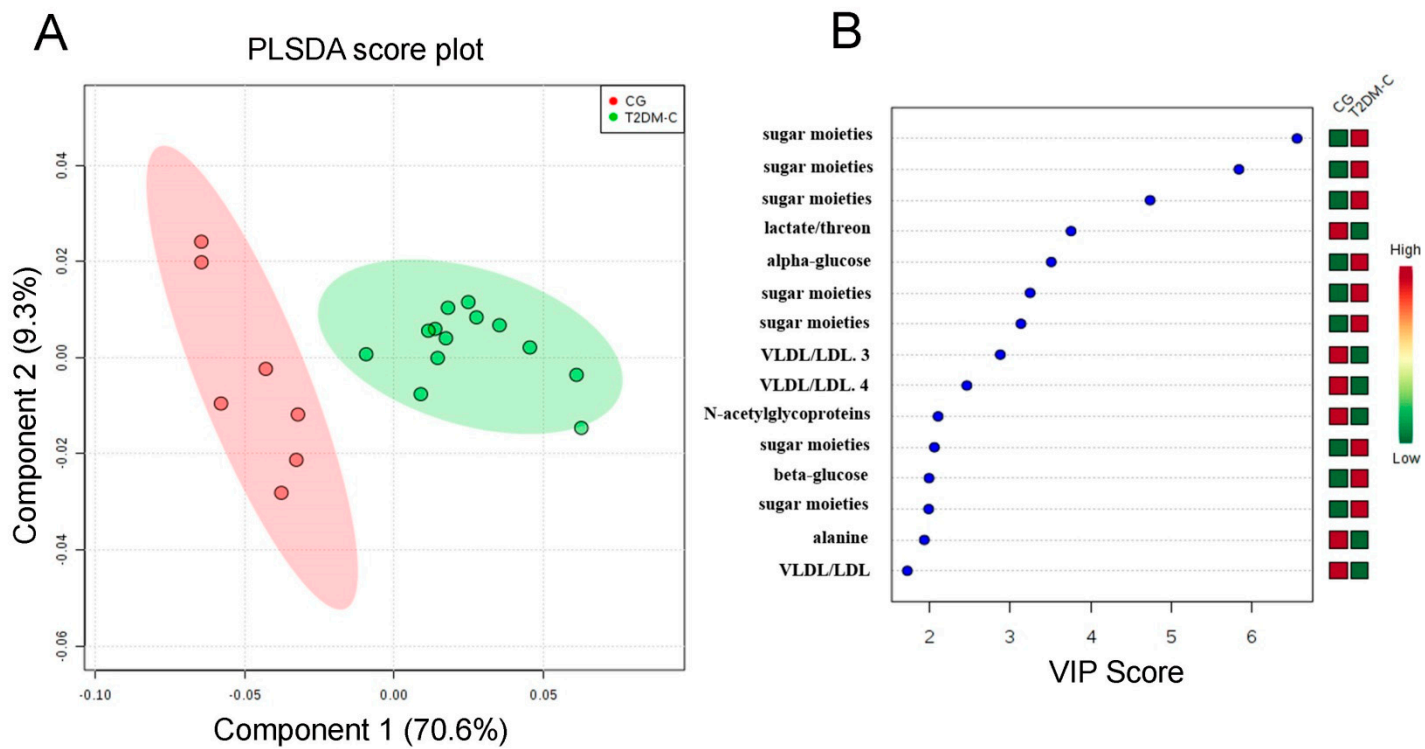
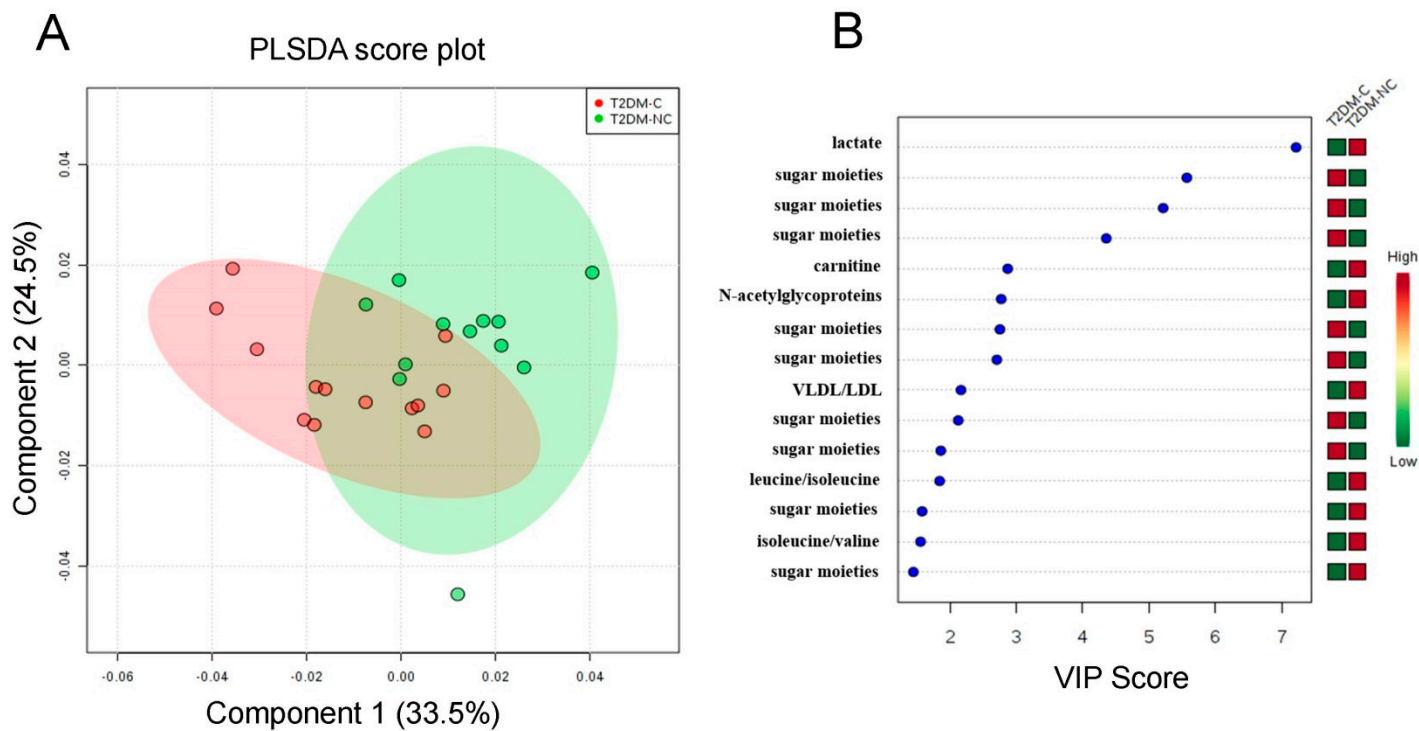


Figure S3. PLSDA score scatter plot between T2DM-C and T2DM-NC



**Table S1. Results from Pathway Analysis with MetPA for serum samples of CG vs T2DM-NC patients.**

Pathway Name	Matched metabolites	p-value	impact
Alanine, aspartate and glutamate metabolism	Alanine, Glutamine, Glutamate (3/24)	$1.055 \times 10^{-4}$	0.44065
Aminoacyl-tRNA biosynthesis	Phenylalanine; Glutamate; Glutamine; Methionine; Valine; Alanine; Lysine; Isoleucine; Leucine; Tyrosine (10/75)	$3.472 \times 10^{-4}$	0.11268
Lysine degradation	Lysine (1/47)	$5.174 \times 10^{-4}$	0.14675
D-Glutamine and D-glutamate metabolism	Glutamate; Glutamine (2/11)	$6.9113 \times 10^{-4}$	0.13904
Starch and sucrose metabolism	$\alpha$ -, $\beta$ -glucose (2/50)	$3.1103 \times 10^{-8}$	0.03195
Glycolysis or gluconeogenesis	$\alpha$ -, $\beta$ -glucose; lactate (3/31)	$3.0189 \times 10^{-8}$	0.01094

Total number of compounds involved in each pathway and metabolites actually matched from the uploaded data; p is the original p-value calculated from the enrichment analysis; the impact is the pathway impact value calculated from pathway topology analysis.

**Table S2. Results from Pathway Analysis with MetPA for serum samples of CG vs T2DM-C patients.**

<b>Pathway Name</b>	<b>Matched metabolites</b>	<b>p-value</b>	<b>impact</b>
Alanine, aspartate and glutamate metabolism	Alanine, Glutamine, Glutamate (3/24)	$1.2835 \times 10^{-7}$	0.44065
Aminoacyl-tRNA biosynthesis	Phenylalanine; Glutamate; Glutamine; Methionine; Valine; Alanine; Lysine; Isoleucine; Leucine; Tyrosine (10/75)	$3.9568 \times 10^{-8}$	0.11268
Lysine degradation	Lysine (1/47)	$8.3129 \times 10^{-7}$	0.14675
D-Glutamine and D-glutamate metabolism	Glutamate; Glutamine (2/11)	$4.6644 \times 10^{-6}$	0.13904

Total number of compounds involved in each pathway and metabolites actually matched from the uploaded data; p is the original p-value calculated from the enrichment analysis; the impact is the pathway impact value calculated from pathway topology analysis.

**Table S3. Results from Pathway Analysis with MetPA for serum samples of T2DM-C vs T2DM-NC patients.**

Pathway Name	Matched metabolites	p-value	impact
Alanine, aspartate and glutamate metabolism	Alanine, Glutamine, Glutamate (3/24)	0.13152	0.44065
D-Glutamine and D-glutamate metabolism	Glutamate; Glutamine (2/11)	0.016616	0.13904
Lysine degradation	Lysine (1/47)	0.008533	0.14675
Phenylalanine metabolism	Phenylalanine; tyrosine (2/45)	0.006458	0.11906
Aminoacyl-tRNA biosynthesis	Phenylalanine; Glutamate; Glutamine; Methionine; Valine; Alanine; Lysine; Isoleucine; Leucine; Tyrosine (10/75)	0.00438	0.11268
Valine, leucine and isoleucine biosynthesis	Valine; Isoleucine; Leucine (3/27)	$5.1516 \cdot 10^{-4}$	0.03975
Valine, leucine and isoleucine degradation	Valine; Isoleucine; Leucine (3/40)	$5.1516 \cdot 10^{-4}$	0.02232

Total number of compounds involved in each pathway and metabolites actually matched from the uploaded data; p is the original p-value calculated from the enrichment analysis; the impact is the pathway impact value calculated from pathway topology analysis.