

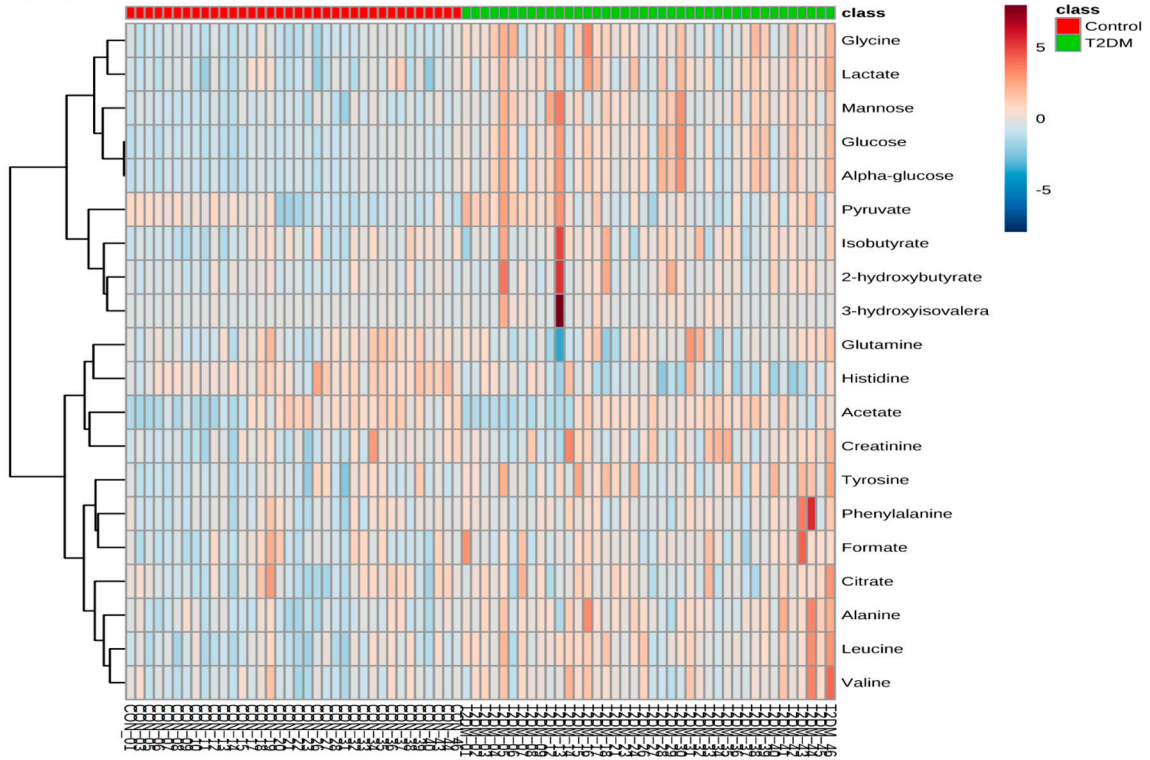
Supplementary Materials:

Table S1. Association of altered metabolites in CSF and plasma samples with the presence of T2DM.

Comparison	T2DM vs. control			
	Crude OR	<i>p</i>	Adjusted OR ^a	<i>p</i>
Significantly changed metabolites in CSF				
CSF glucose	1.062	<0.001*	1.061	0.002*
Alanine	1.009	<0.001*	1.009	0.002*
Glycine	1.023	<0.001*	1.001	0.001*
Histidine	0.906	<0.001*	0.871	0.001*
Mannose	1.035	<0.001*	1.040	0.002*
2-hydroxybutyrate	1.005	0.003*	1.004	0.036*
Lactate	1.000	<0.001*	1.001	0.001*
Tyrosine	1.021	0.002*	1.029	0.003*
Leucine	1.000	<.0001*	1.039	0.004*
Phenylalanine	1.000	0.007*	1.033	0.033*
Pyruvate	1.000	0.006*	1.003	0.049*
Valine	1.012	0.003*	1.008	0.037*
Alanine, Glycine, Histidine, Mannose, Pyruvate	2.618	0.003*	4.364	0.005*
Significantly changed metabolites in plasma	Crude OR	<i>p</i>	Adjusted OR ^a	<i>p</i>
Plasma glucose	1.070	<0.001*	1.092	0.003*
Plasma HbA1c	1.207	0.002*	1.288	0.019*
Plasma HOMA-IR	1.732	0.002*	1.712	0.027*
Alanine	0.999	0.015*	0.998	0.004*
Citrate	0.991	0.002*	0.988	0.003*
Histidine	0.977	0.002*	0.974	0.003*
Lipid (CH ₂ -CH=CH)	1.000	0.005*	1.000	0.043*
N-acetyl glycoprotein	1.000	<0.001*	1.000	0.003*
Phenylalanine	1.024	<0.001*	1.024	0.001*
Glutamine	1.000	0.001*	0.997	0.001*
Acetate	1.004	0.099	1.006	0.028*
Leucine	1.000	0.002*	1.004	0.036*
Acetate, Citrate, Histidine, Leucine, N-acetyl-glycoprotein	2.718	<.0001*	5.355	<0.001*

Abbreviation: T2DM, type 2 diabetes mellitus; OR, odds ratio; HbA1c, glycated hemoglobin A1c; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance ^aAdjusted for age, sex, body mass index (BMI), and medications for chronic diseases (hypertension, hyperlipidemia) * *p* < 0.05.

(A) CSF



(B) Plasma

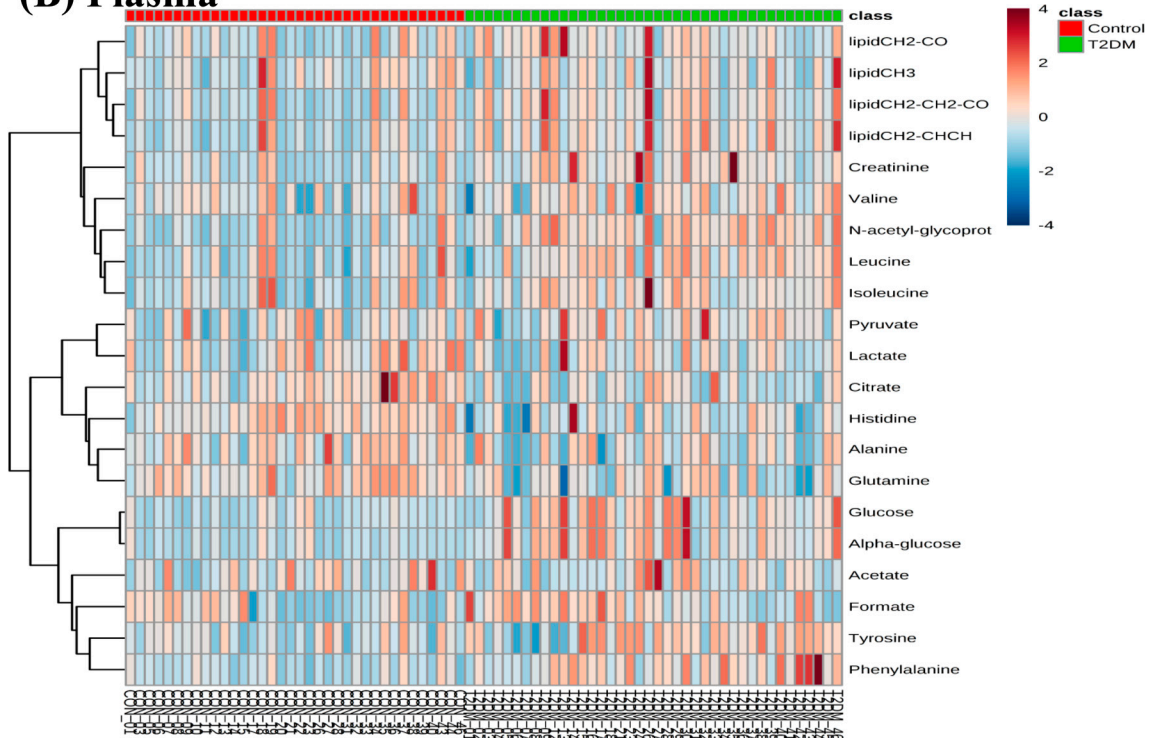


Figure S1. Metabolite heatmaps in (A) CSF and (B) plasma samples from T2DM patients and control subjects.

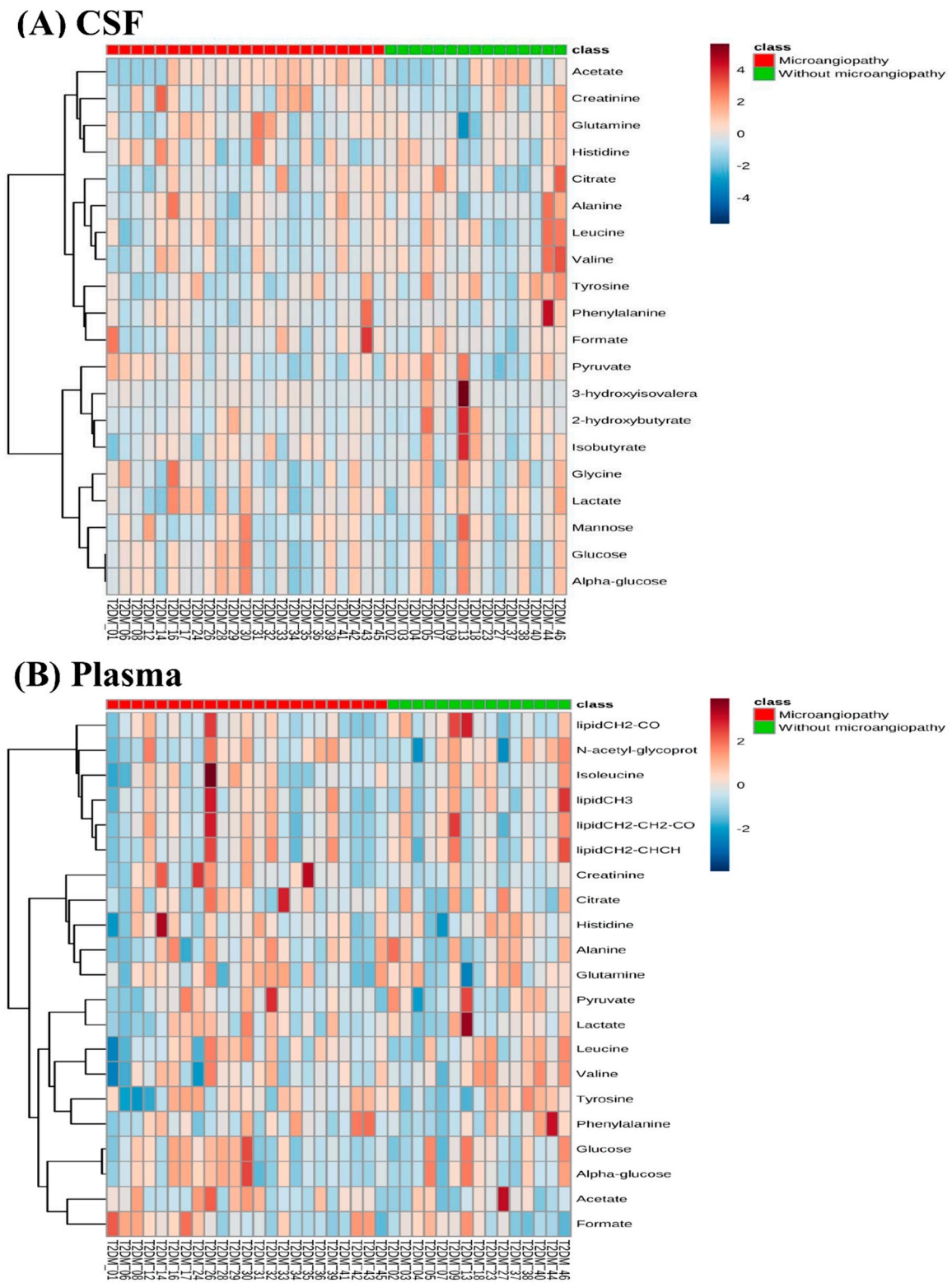
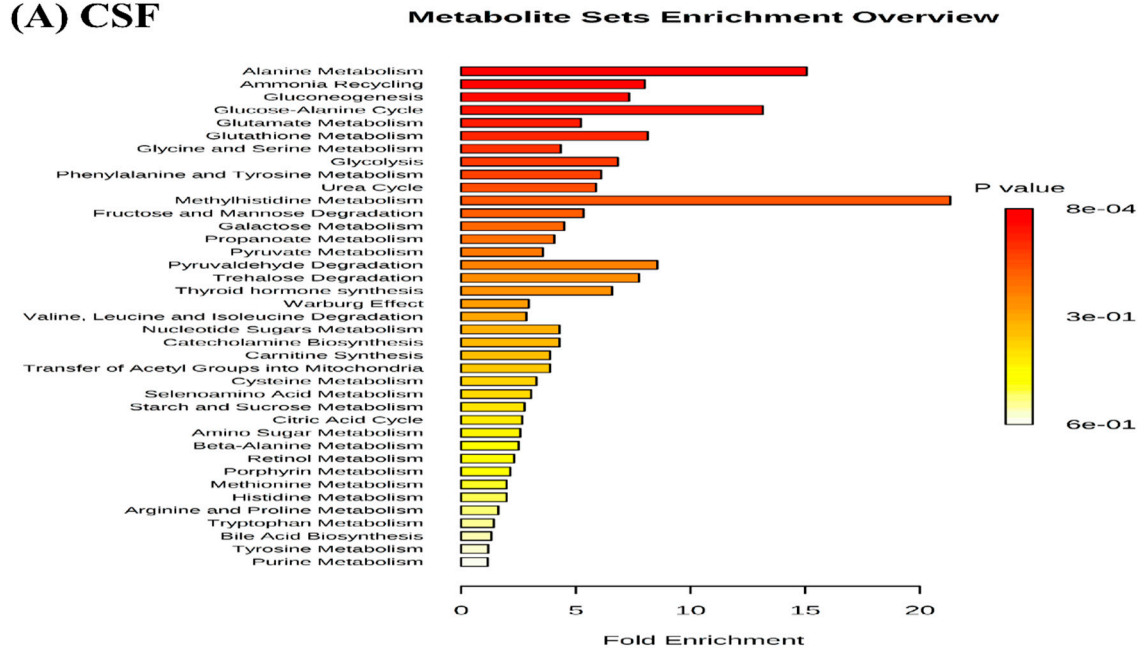


Figure S2. Metabolite heatmaps in (A) CSF and (B) plasma samples from T2DM patients with microangiopathy versus T2DM patients without microangiopathy.

(A) CSF



(B) plasma

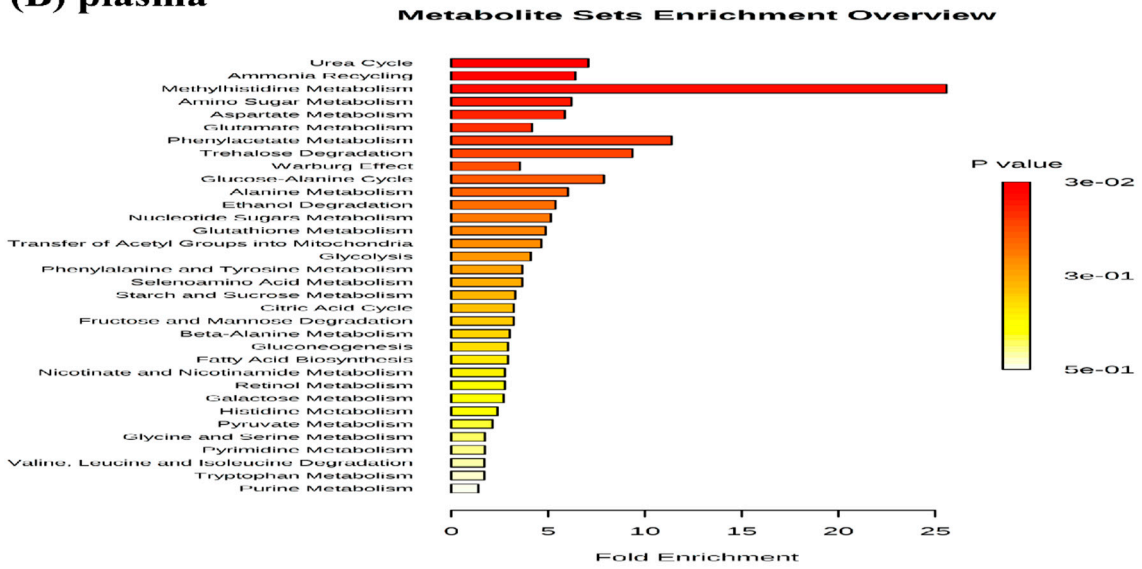


Figure S3. Enrichment analysis of involved metabolic pathways for significant metabolites in (A) CSF (B) plasma samples from T2DM patients.