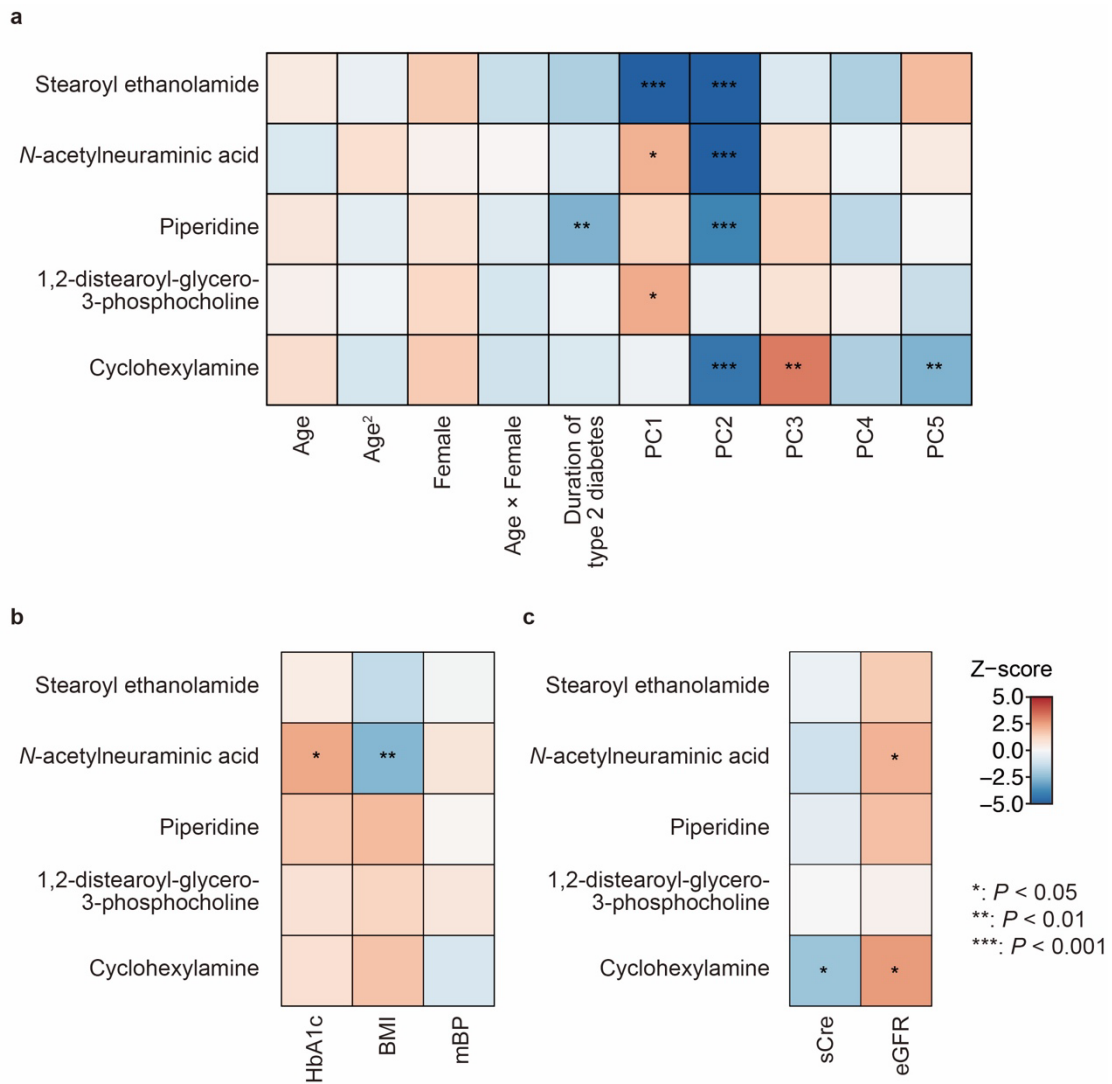# Supplementary information

Identification of serum metabolome signatures associated with retinal and renal complications of type 2 diabetes

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Supplementary Fig. 1 | Results of the linear regression analysis to obtain the covariates-adjusted metabolite abundances.

Heatmaps represent the Z-score of the covariates in the linear regression to obtain the covariate-adjusted metabolite abundances. (a), (b), and (c) correspond to **Fig. 1**, **Fig. 2a**, and **Fig. 2b**, respectively. The x-axis indicates the covariates and the y-axis indicates the metabolites. The color of the tile indicates the Z-score (effect size / standard error) in the linear regression. The asterisk indicates the significance of Wald's tests. Number of samples used for the analyses are following; **a**, $N_{DR + DKD}$ = 141 and $N_{control}$ = 159 for all the covariates; **b**, $N_{DR + DKD}$ = 109 and $N_{control}$ = 112 for HbA1c, $N_{DR + DKD}$ = 131 and $N_{control}$ = 132 for mBP, and $N_{DR + DKD}$ = 135 and $N_{control}$ = 147 for BMI; **c**, $N_{DR + DKD}$ = 139, $N_{control}$ = 157 for sCre and eGFR.

BMI, body mass index; DKD, diabetic kidney disease; DR diabetic retinopathy; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; mBP, mean blood pressure; PC, principal component; sCre, serum creatinine.
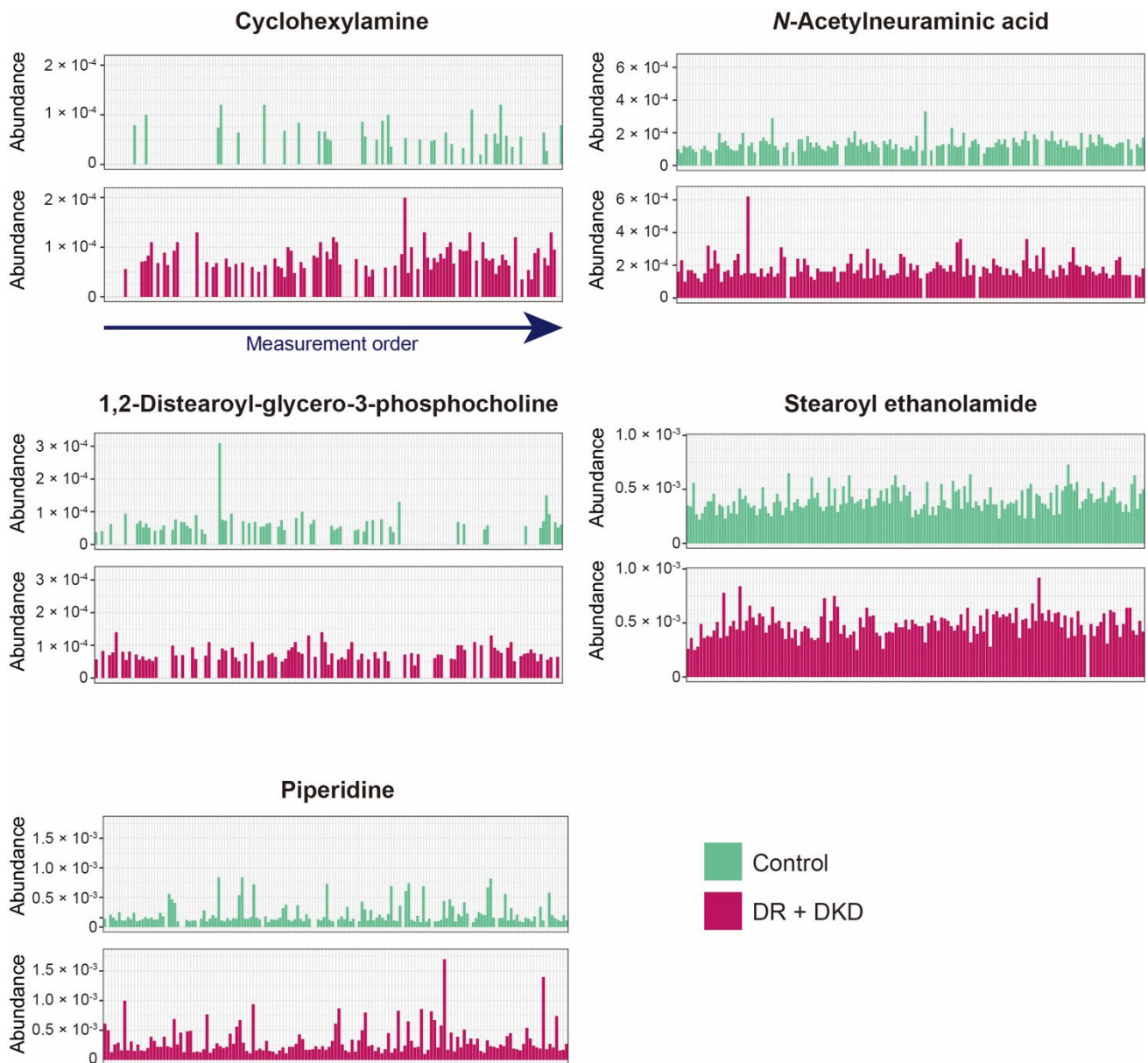
Supplementary Fig. 2 | Raw abundances of the metabolites associated with the complications of the T2D.

Bar plots represent the raw abundances of the metabolites associated with the complications of T2D. The x-axis indicates the order of the measurements and the y-axis indicates the raw abundances of the metabolites. The number of samples used for the analysis is $N_{DR + DKD}$ = 141 and $N_{control}$ = 159. DKD, diabetic kidney disease; DR diabetic retinopathy; T2D, type 2 diabetes.

Supplementary Table 1 | Wilcoxon rank sum test for the metabolites associated with the complications of T2D.

Metabolite	Control				DR + DKD				P
	Median	1st Q.	3rd Q.	N	Median	1st Q.	3rd Q.	N	
Cyclohexylamine	0.0	0.0	0.0	159	5.6×10^{-5}	0.0	7.7×10^{-5}	141	6.1×10^{-12}
1,2-Distearoyl-glycero-3-phosphocholine	0.0	0.0	5.5×10^{-5}	159	5.7×10^{-5}	0.0	7.6×10^{-5}	141	7.1×10^{-8}
Piperidine	1.4×10^{-4}	1.1×10^{-4}	2.2×10^{-4}	159	2.3×10^{-4}	1.7×10^{-4}	3.6×10^{-4}	141	1.4×10^{-13}
N-Acetylneuraminic acid	1.2×10^{-4}	9.5×10^{-5}	1.5×10^{-4}	159	1.6×10^{-4}	1.4×10^{-4}	2.0×10^{-4}	141	1.8×10^{-19}
Stearoyl ethanolamide	3.8×10^{-4}	3.3×10^{-4}	4.8×10^{-4}	159	4.8×10^{-4}	4.1×10^{-4}	5.6×10^{-4}	141	3.7×10^{-10}

1st Q., first quantile; 3rd Q., third quantile; DKD, diabetic kidney disease; DR diabetic retinopathy; T2D, type 2 diabetes.