**Supplementary information**

**Selecting the tuning parameter λ in LASSO models**

The selection of parameter λ is based on the evaluation of classification performance (reflected by the area under the curve (AUC) in the current study) at each value of λ. Normally a ten-fold cross-validation is used, where 90% of all the samples are randomly selected to form a training set for parameter estimation and the other 10% of the samples are kept for model validation. Since the folds are selected at random, the determination of λ will be different from time to time, which further leads to diverse metabolite profile compositions accordingly. One of the solutions to reduce the randomness is to repeat the cross-validation for multiple times. In our analysis, we repeated the ten-fold cross-validation for ten times, and chose the metabolite profile with the smallest number of metabolites (Fig. S1). The reasons for choosing the most parsimonious set of metabolites lie in two aspects: 1). The metabolites comprised of the most parsimonious set were also selected nearly 10/10 times, which were deemed as the most robust makers; 2). The redundant or irrelevant metabolites might be no harm for a model from the classification point of view, but they are not economical for practical use.

Commonly a “one-standard error” rule is adopted to determine the optimal parameters within cross-validation, in which the most parsimonious model is chosen with the AUC no more than one standard error above the AUC of the “best” model (AUC achieved the maximum by the parameter) (Hastie et al. 2009). By this rule, the most regularized model is determined, which reduces the chance of overfitting. Fig. S2 shows the AUCs achieved along with varying cut-off values on λ as well as the corresponding number of metabolites selected in the most parsimonious models highlighted in Fig. S1. On the basis of the “one-standard error” rule, the determination of λ was right shift (towards larger λ values and less number of metabolites) from the maximum of AUCs. Under the fasting state, twelve metabolites were obtained with the median AUC of 0.93 (range: [0.91, 0.94]) within ten-fold cross-validation. A similar pattern was observed for the four metabolites identified under the postprandial state, with a median AUC of 0.93 (range: [0.91, 0.94]). The sixteen metabolites selected under the response achieved a markedly lower separation between the NGT and T2D groups, with a median AUC of 0.81 (range: [0.77, 0.84]).

**References**

Hastie, T., Tibshirani, R., & Friedman, J. (2009). *The Elements of Statistical Learning: Data Mining, Inference, and Prediction.* : Springer-Verlag.



**Fig. S1** The procedure of performing LASSO regularised logistic regression. All the samples from the NGT and T2D group were used as the input for the LASSO model selection. Ten-fold cross validation was repeated by ten times, and the most parsimonious metabolite profile was highlighted in red square.



**Fig. S2** Parameter λ and the optimal number of metabolites were determined by optimizing area under the curve (AUC). The number of metabolites selected for the most parsimonious metabolite profile was indicated by the dashed line (within one standard error of the AUC maximum). The red dot represented the average value of AUC within the ten-fold cross validation, and the largest and smallest AUCs by a certain number of metabolites were labelled by the grey bar across the red dot.

**Table S1** List of metabolites measured in Biocrates platform, with the short names and biochemical names.

| **Short\_name** | **Biochemical\_name** | **HMDB\_ID** | **KEGG\_ID** |
| --- | --- | --- | --- |
| **Acylcarnitines** |
| C0 | DL-Carnitine | HMDB00062 | C15025 |
| C10 | Decanoyl-L-carnitine | HMDB00651 |  |
| C10:1 | Decenoyl-L-carnitine | HMDB13205 |  |
| C10:2 | Decadienyl-L-carnitine |  |  |
| C12 | Dodecanoyl-L-carnitine | HMDB02250 |  |
| C12:1 | Dodecenoyl-L-carnitine |  |  |
| C12-DC | Dodecanedioyl-L-carnitine | HMDB13327 |  |
| C14 | Tetradecanoyl-L-carnitine | HMDB05066 |  |
| C14:1 | Tetradecenoyl-L-carnitine | HMDB02014 |  |
| C14:1-OH | Hydroxytetradecenoyl-L-carnitine | HMDB13330 |  |
| C14:2 | Tetradecadienyl-L-carnitine | HMDB13331 |  |
| C14:2-OH | Hydroxytetradecadienyl-L-carnitine |  |  |
| C16 | Hexadecanoyl-L-carnitine | HMDB00222 | C02990 |
| C16:1 | Hexadecenoyl-L-carnitine | HMDB06317 |  |
| C16:1-OH | Hydroxyhexadecenoyl-L-carnitine | HMDB13333 |  |
| C16:2 | Hexadecadienyl-L-carnitine | HMDB13334 |  |
| C16:2-OH | Hydroxyhexadecadienyl-L-carnitine | HMDB13335 |  |
| C16-OH | Hydroxyhexadecanoyl-L-carnitine |  |  |
| C18 | Octadecanoyl-L-carnitine | HMDB00848 |  |
| C18:1 | Octadecenoyl-L-carnitine | HMDB05065HMDB06464 |  |
| C18:1-OH | Hydroxyoctadecenoyl-L-carnitine | HMDB13339 |  |
| C18:2 | Octadecadienyl-L-carnitine | HMDB06461 |  |
| C2 | Acetyl-L-carnitine | HMDB00201 | C02571 |
| C3 | Propionyl-L-carnitine | HMDB00824 | C03017 |
| C3:1 | Propenyl-L-carnitine | HMDB13124 |  |
| C3-DC / C4-OH | Malonyl-L-carnitine/Hydroxybutyryl-L-carnitine | HMDB02095HMDB13127 |  |
| C3-DC-M / C5-OH | Methylmalonyl-L-carnitine/Hydroxyvaleryl-L-carnitine | HMDB13132 |  |
| C3-OH | Hydroxypropionyl-L-carnitine | HMDB13125 |  |
| C4 | Butyryl-L-carnitine | HMDB00736HMDB02013 | C02862 |
| C4:1 | Butenyl-L-carnitine | HMDB13126 |  |
| C4:1-DC / C6 | Fumaryl-L-carnitine/Hexanoyl-L-carnitine | HMDB00705HMDB00756 |  |
| C5 | Valeryl-L-carnitine | HMDB00688HMDB13128HMDB41993HMDB00378 |  |
| C5:1 | Tiglyl-L-carnitine | HMDB02366 |  |
| C5:1-DC | Glutaconyl-L-carnitine | HMDB13129 |  |
| C5-DC / C6-OH | Glutaryl-L-carnitine/Hydroxyhexanoyl-L-carnitine | HMDB13130 |  |
| C5-M-DC | Methylglutaryl-L-carnitine | HMDB00552 |  |
| C6:1 | Hexenoyl-L-carnitine | HMDB13161 |  |
| C7-DC | Pimelyl-L-carnitine | HMDB13328 |  |
| C8 | Octanoyl-L-carnitine | HMDB00791 | C02838 |
| C8:1 | Octenoyl-L-carnitine | HMDB00791 | C02838 |
| C9 | Nonayl-L-carnitine | HMDB06320 |  |
| **Sugars** |
| H1 | Hexose | HMDB00122HMDB00143HMDB00169HMDB00516HMDB00660HMDB01266HMDB03345HMDB03418HMDB03449HMDB12326HMDB33704 | C00031C00984C00159C00221C02336C08356C00267C00795C00962C15923C01825 |
| **Amino acids** |
| Arg | Arginine | HMDB00517HMDB03416 | C00062C00792 |
| Gln | Glutamine | HMDB00641HMDB03423 | C00064C00819 |
| Gly | Glycine | HMDB00123 | C00037 |
| His | Histidine | HMDB00177 | C00135 |
| Met | Methionine | HMDB00696 | C00073 |
| Orn | Ornithine | HMDB00214HMDB03374 | C00515C00077 |
| Phe | Phenylalanine | HMDB00159 | C00079 |
| Pro | Proline | HMDB00162HMDB03411 | C00148C00763 |
| Ser | Serine | HMDB00187HMDB03406 | C00065C00740 |
| Thr | Threonine | HMDB00167HMDB04041 | C00188C05519 |
| Trp | Tryptophan | HMDB00929HMDB13609 | C00078C00525 |
| Tyr | Tyrosine | HMDB00158 | C00082 |
| Val | Valine | HMDB00883 | C00183 |
| xLeu | xLeucine | HMDB00172 | C00407 |
| **Glycerophospholipids** |
| lysoPC a C14:0 | lysoPhosphatidylcholine acyl C14:0 | HMDB10379 | C04230 |
| lysoPC a C16:0 | lysoPhosphatidylcholine acyl C16:0 | HMDB10382 | C04230 |
| lysoPC a C16:1 | lysoPhosphatidylcholine acyl C16:1 | HMDB10383 | C04230 |
| lysoPC a C17:0 | lysoPhosphatidylcholine acyl C17:0 | HMDB12108 | C04230 |
| lysoPC a C18:0 | lysoPhosphatidylcholine acyl C18:0 | HMDB10384HMDB11128 | C04230 |
| lysoPC a C18:1 | lysoPhosphatidylcholine acyl C18:1 | HMDB02815HMDB10385 | C04230 |
| lysoPC a C18:2 | lysoPhosphatidylcholine acyl C18:2 | HMDB10386 | C04230 |
| lysoPC a C20:3 | lysoPhosphatidylcholine acyl C20:3 | HMDB10393HMDB10394 | C04230 |
| lysoPC a C20:4 | lysoPhosphatidylcholine acyl C20:4 | HMDB10395HMDB10396 | C04230 |
| lysoPC a C24:0 | lysoPhosphatidylcholine acyl C24:0 | HMDB10405 | C04230 |
| lysoPC a C26:0 | lysoPhosphatidylcholine acyl C26:0 | HMDB29205 |  |
| lysoPC a C26:1 | lysoPhosphatidylcholine acyl C26:1 | HMDB29220 |  |
| lysoPC a C28:0 | lysoPhosphatidylcholine acyl C28:0 | HMDB29206 |  |
| lysoPC a C28:1 | lysoPhosphatidylcholine acyl C28:1 | HMDB29221 |  |
| lysoPC a C6:0 | lysoPhosphatidylcholine acyl C6:0 | HMDB29207 |  |
| PC aa C24:0 | Phosphatidylcholine diacyl C 24:0 |  |  |
| PC aa C26:0 | Phosphatidylcholine diacyl C 26:0 |  |  |
| PC aa C28:1 | Phosphatidylcholine diacyl C 28:1 |  |  |
| PC aa C30:0 | Phosphatidylcholine diacyl C 30:0 | HMDB07869HMDB07934HMDB07965 | C00157 |
| PC aa C30:2 | Phosphatidylcholine diacyl C 30:2 |  |  |
| PC aa C32:0 | Phosphatidylcholine diacyl C 32:0 | HMDB00564HMDB07871HMDB08031 | C00157 |
| PC aa C32:1 | Phosphatidylcholine diacyl C 32:1 | HMDB07872HMDB07873HMDB07969HMDB08097  | C00157 |
| PC aa C32:2 | Phosphatidylcholine diacyl C 32:2 | HMDB07874HMDB08002 | C00157 |
| PC aa C32:3 | Phosphatidylcholine diacyl C 32:3 | HMDB07876 | C00157 |
| PC aa C34:1 | Phosphatidylcholine diacyl C 34:1 | HMDB07971HMDB07972HMDB08003HMDB08035HMDB08100 | C00157 |
| PC aa C34:2 | Phosphatidylcholine diacyl C 34:2 | HMDB07973HMDB08004HMDB08005HMDB08101HMDB08133 | C00157 |
| PC aa C34:3 | Phosphatidylcholine diacyl C 34:3 | HMDB07974HMDB07975HMDB08006 | C00157 |
| PC aa C34:4 | Phosphatidylcholine diacyl C 34:4 | HMDB07883HMDB07976 | C00157 |
| PC aa C36:0 | Phosphatidylcholine diacyl C 36:0 | HMDB07886HMDB07977HMDB08036HMDB08265HMDB08525 | C00157 |
| PC aa C36:1 | Phosphatidylcholine diacyl C 36:1 | HMDB08037HMDB08038HMDB08069HMDB08102 | C00157 |
| PC aa C36:2 | Phosphatidylcholine diacyl C 36:2 | HMDB08039HMDB08070HMDB08135HMDB00593 | C00157 |
| PC aa C36:3 | Phosphatidylcholine diacyl C 36:3 | HMDB07980HMDB07981HMDB08040HMDB08105 | C00157 |
| PC aa C36:4 | Phosphatidylcholine diacyl C 36:4 | HMDB07982HMDB08042HMDB08106HMDB08107HMDB08138HMDB08170HMDB08203HMDB08429 | C00157 |
| PC aa C36:5 | Phosphatidylcholine diacyl C 36:5 | HMDB07984HMDB08015 | C00157 |
| PC aa C36:6 | Phosphatidylcholine diacyl C 36:6 | HMDB07892HMDB08206 | C00157 |
| PC aa C38:0 | Phosphatidylcholine diacyl C 38:0 | HMDB07893HMDB07985HMDB08043HMDB08267HMDB08528HMDB08755 | C00157 |
| PC aa C38:1 | Phosphatidylcholine diacyl C 38:1 | HMDB07894HMDB07986HMDB08044HMDB08109HMDB08268HMDB08269 | C00157 |
| PC aa C38:3 | Phosphatidylcholine diacyl C 38:3 | HMDB08046HMDB08047 | C00157 |
| PC aa C38:4 | Phosphatidylcholine diacyl C 38:4 | HMDB07988HMDB08048HMDB08112 | C00157 |
| PC aa C38:5 | Phosphatidylcholine diacyl C 38:5 | HMDB07989HMDB07990HMDB08050HMDB08114 | C00157 |
| PC aa C38:6 | Phosphatidylcholine diacyl C 38:6 | HMDB07991HMDB08083HMDB08116HMDB08147HMDB08434HMDB08499HMDB08725 | C00157 |
| PC aa C40:1 | Phosphatidylcholine diacyl C 40:1 | HMDB07993HMDB08052HMDB08084HMDB08117HMDB08275 | C00157 |
| PC aa C40:2 | Phosphatidylcholine diacyl C 40:2 | HMDB08276HMDB08308 | C00157 |
| PC aa C40:3 | Phosphatidylcholine diacyl C 40:3 |  |  |
| PC aa C40:4 | Phosphatidylcholine diacyl C 40:4 | HMDB08054HMDB08279HMDB08628 | C00157 |
| PC aa C40:5 | Phosphatidylcholine diacyl C 40:5 | HMDB08055HMDB08056HMDB08120 | C00157 |
| PC aa C40:6 | Phosphatidylcholine diacyl C 40:6 | HMDB08057HMDB08089HMDB08122 | C00157 |
| PC aa C42:0 | Phosphatidylcholine diacyl C 42:0 | HMDB08058HMDB08282HMDB08537HMDB08760 | C00157 |
| PC aa C42:1 | Phosphatidylcholine diacyl C 42:1 | HMDB08059HMDB08124HMDB08283HMDB08538HMDB08762 | C00157 |
| PC aa C42:2 | Phosphatidylcholine diacyl C 42:2 | HMDB08570 |  |
| PC aa C42:4 | Phosphatidylcholine diacyl C 42:4 | HMDB08572 |  |
| PC aa C42:5 | Phosphatidylcholine diacyl C 42:5 | HMDB08287 | C00157 |
| PC aa C42:6 | Phosphatidylcholine diacyl C 42:6 | HMDB08288 | C00157 |
| PC ae C30:0 | Phosphatidylcholine acyl-alkyl C 30:0 | HMDB13341 |  |
| PC ae C30:1 | Phosphatidylcholine acyl-alkyl C 30:1 | HMDB13402 |  |
| PC ae C30:2 | Phosphatidylcholine acyl-alkyl C 30:2 |  |  |
| PC ae C32:1 | Phosphatidylcholine acyl-alkyl C 32:1 |  |  |
| PC ae C32:2 | Phosphatidylcholine acyl-alkyl C 32:2 |  |  |
| PC ae C34:0 | Phosphatidylcholine acyl-alkyl C 34:0 | HMDB13405 |  |
| PC ae C34:1 | Phosphatidylcholine acyl-alkyl C 34:1 |  |  |
| PC ae C34:2 | Phosphatidylcholine acyl-alkyl C 34:2 | HMDB11151 |  |
| PC ae C34:3 | Phosphatidylcholine acyl-alkyl C 34:3 | HMDB11211 |  |
| PC ae C36:0 | Phosphatidylcholine acyl-alkyl C 36:0 | HMDB13406HMDB13417 |  |
| PC ae C36:1 | Phosphatidylcholine acyl-alkyl C 36:1 | HMDB13427 |  |
| PC ae C36:2 | Phosphatidylcholine acyl-alkyl C 36:2 | HMDB11243 |  |
| PC ae C36:3 | Phosphatidylcholine acyl-alkyl C 36:3 | HMDB13429 |  |
| PC ae C36:4 | Phosphatidylcholine acyl-alkyl C 36:4 | HMDB13435 |  |
| PC ae C36:5 | Phosphatidylcholine acyl-alkyl C 36:5 | HMDB11220 |  |
| PC ae C38:0 | Phosphatidylcholine acyl-alkyl C 38:0 | HMDB13408HMDB13419 |  |
| PC ae C38:1 | Phosphatidylcholine acyl-alkyl C 38:1 | HMDB13430 |  |
| PC ae C38:2 | Phosphatidylcholine acyl-alkyl C 38:2 | HMDB13431 |  |
| PC ae C38:3 | Phosphatidylcholine acyl-alkyl C 38:3 | HMDB13439 |  |
| PC ae C38:4 | Phosphatidylcholine acyl-alkyl C 38:4 | HMDB13420 |  |
| PC ae C38:5 | Phosphatidylcholine acyl-alkyl C 38:5 | HMDB13432 |  |
| PC ae C38:6 | Phosphatidylcholine acyl-alkyl C 38:6 | HMDB13409 |  |
| PC ae C40:0 | Phosphatidylcholine acyl-alkyl C 40:0 | HMDB13421 |  |
| PC ae C40:1 | Phosphatidylcholine acyl-alkyl C 40:1 | HMDB13433 |  |
| PC ae C40:2 | Phosphatidylcholine acyl-alkyl C 40:2 | HMDB13437 |  |
| PC ae C40:3 | Phosphatidylcholine acyl-alkyl C 40:3 | HMDB13445 |  |
| PC ae C40:4 | Phosphatidylcholine acyl-alkyl C 40:4 | HMDB13442 |  |
| PC ae C40:5 | Phosphatidylcholine acyl-alkyl C 40:5 | HMDB13444 |  |
| PC ae C40:6 | Phosphatidylcholine acyl-alkyl C 40:6 | HMDB13422 |  |
| PC ae C42:0 | Phosphatidylcholine acyl-alkyl C 42:0 | HMDB13443 |  |
| PC ae C42:1 | Phosphatidylcholine acyl-alkyl C 42:1 | HMDB13434 |  |
| PC ae C42:2 | Phosphatidylcholine acyl-alkyl C 42:2 | HMDB13438 |  |
| PC ae C42:3 | Phosphatidylcholine acyl-alkyl C 42:3 | HMDB13459 |  |
| PC ae C42:4 | Phosphatidylcholine acyl-alkyl C 42:4 | HMDB13448 |  |
| PC ae C42:5 | Phosphatidylcholine acyl-alkyl C 42:5 | HMDB13451 |  |
| PC ae C44:3 | Phosphatidylcholine acyl-alkyl C 44:3 | HMDB13449 |  |
| PC ae C44:4 | Phosphatidylcholine acyl-alkyl C 44:4 | HMDB13453 |  |
| PC ae C44:5 | Phosphatidylcholine acyl-alkyl C 44:5 | HMDB13456 |  |
| PC ae C44:6 | Phosphatidylcholine acyl-alkyl C 44:6 | HMDB13457 |  |
| **Sphinglipids** |
| SM (OH) C14:1 | Hydroxysphingomyeline C 14:1 |  |  |
| SM (OH) C16:0 | Hydroxysphingomyeline C 16:0 |  |  |
| SM (OH) C22:1 | Hydroxysphingomyeline C 22:1 |  |  |
| SM (OH) C22:2 | Hydroxysphingomyeline C 22:2 |  |  |
| SM (OH) C24:1 | Hydroxysphingomyeline C 24:1 |  |  |
| SM C16:0 | Sphingomyeline C 16:0 | HMDB10169 |  |
| SM C16:1 | Sphingomyeline C 16:1 | HMDB29216 |  |
| SM C18:0 | Sphingomyeline C 18:0 | HMDB01348 |  |
| SM C18:1 | Sphingomyeline C 18:1 | HMDB12100HMDB12101 | C00550 |
| SM C20:2 | Sphingomyeline C 20:2 |  |  |
| SM C22:3 | Sphingomyeline C 22:3 |  |  |
| SM C24:0 | Sphingomyeline C 24:0 |  |  |
| SM C24:1 | Sphingomyeline C 24:1 | HMDB12107 | C00550 |
| SM C26:0 | Sphingomyeline C 26:0 | HMDB11698 |  |
| SM C26:1 | Sphingomyeline C 26:1 | HMDB13461 | C00550 |