

Influence of the microbiome, diet and genetics on inter-individual variation in the human plasma metabolome

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Supplementary information

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Fig. S1 | Comparison of the proportion of variation explained by diet, microbes and genetics between the LASSO and ElasticNet feature selection methods

Each dot represents a metabolite. The x-axis indicates the explained variation at baseline and the y-axis indicates the explained variation at follow-up.

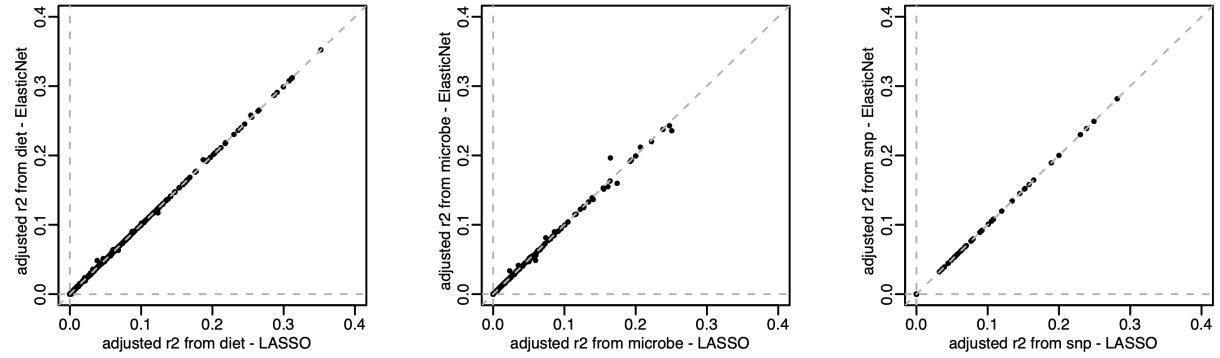


Fig. S2 | Baseline diet, genetics and gut microbiome estimate the inter-individual variation of the whole plasma metabolome in LLD follow-up.

The estimate of explained variation using the PERMANOVA method (two-sided). The x-axis refers to explained variation in metabolic profile at the 2nd timepoint and the y-axis refers to models with different factors.

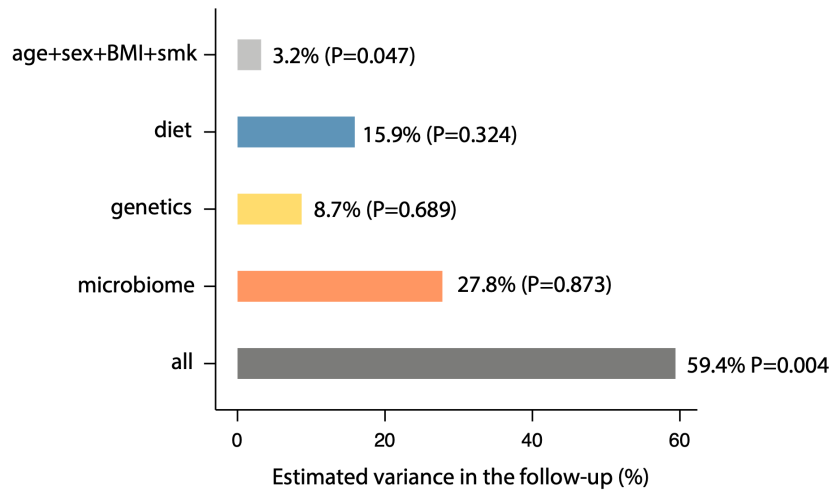


Fig. S3 | Comparison of mQTL effect sizes in different Lifelines cohorts

Dots represent independent mQTLs identified in the Lifelines-DEEP baseline samples. The x-axis indicates the effect size estimated in the LLD₁ cohort and the y-axis indicates the effect size estimated in the LLD₁-follow-up cohort (left), LLD₂ (middle) and GoNL samples (right). mQTLs significant at $P < 0.05$ level (Spearman, two-sided) in the corresponding cohort are shown in black. All others are in gray.

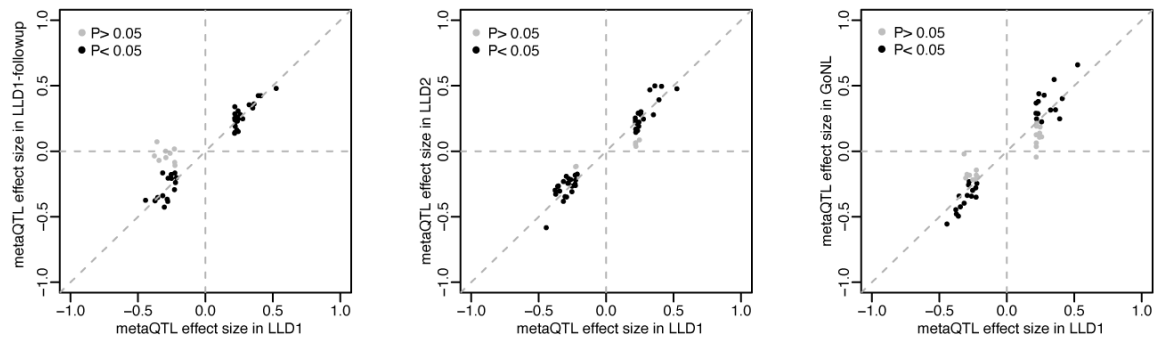


Fig. S4 | Comparison of mQTL effect sizes with and without adjustment for physical activity scores

Dots represent 3,008 study-wide significant mQTLs (from 927 samples) observed in QTL mapping without adjustment of physical activity scores. The x-axis indicates effect size estimated in the LLD₁ cohort (n=927 biologically independent samples) without adjustment for physical activity scores. The y-axis indicates effect size estimated in LLD₁ with adjustment for physical activity scores (n=855 biologically independent samples).

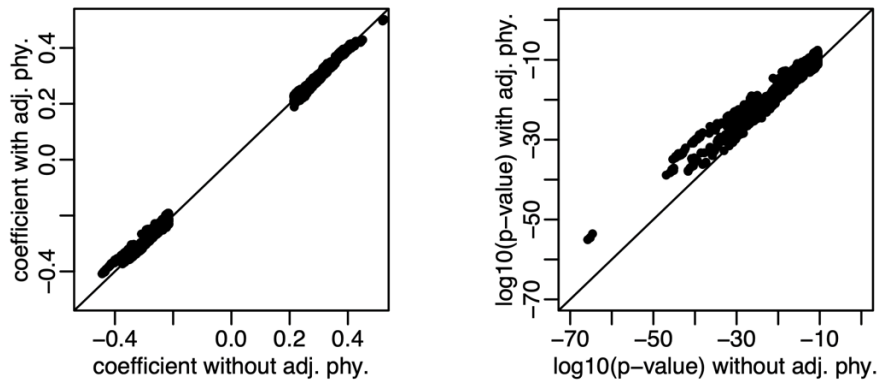


Fig. S5 | Causal relationships between microbiomes and plasma metabolites with Weighted Median and Egger methods

Forest plots show the MR effect size (center dot) and with 95% confidence intervals (CI) for the baseline (blue) and follow-up (green) datasets of the LLD₁ cohort, estimated by Weighted Median and Egger methods. The x-axis indicates effect size of MR. n=927 biological independent samples at baseline and n=311 biologically independent samples at follow-up.

