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Supplemental Information

An Integrated Understanding of the Rapid Metabolic Benefits of a Carbohydrate-Restricted Diet on Hepatic Steatosis in Humans

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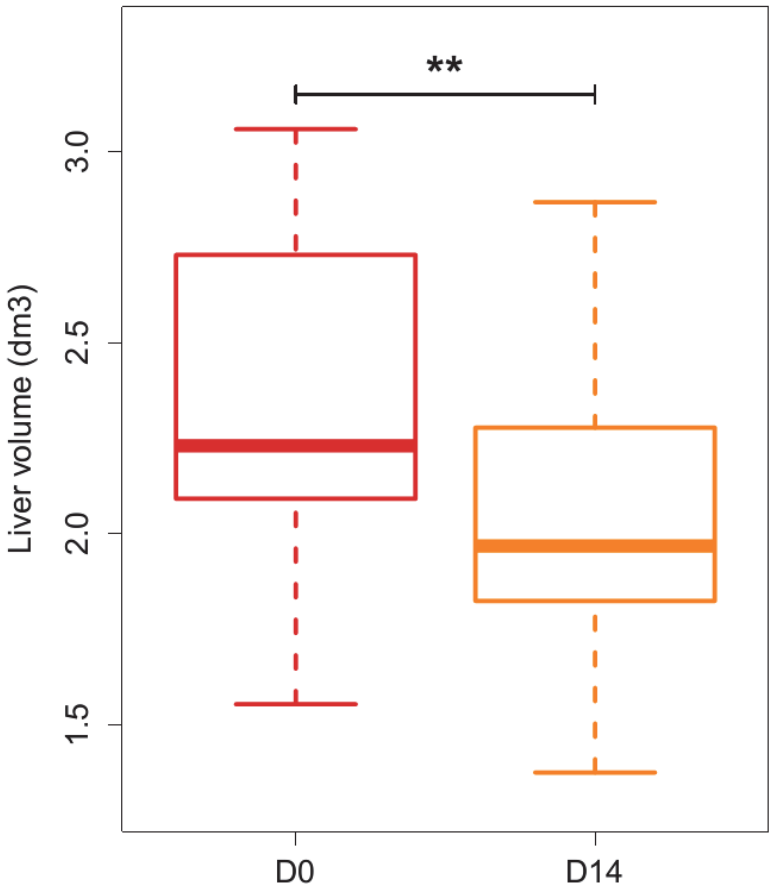

Figure S1. **Box plots (with median) showing liver volume at baseline (D0) and after 14 days of the carbohydrate-restricted diet (D14) in the first cohort (*n* = 10).** Related to Figure 1 and Table S1. $^{**}P < 0.01$ (Wilcox signed-rank test).

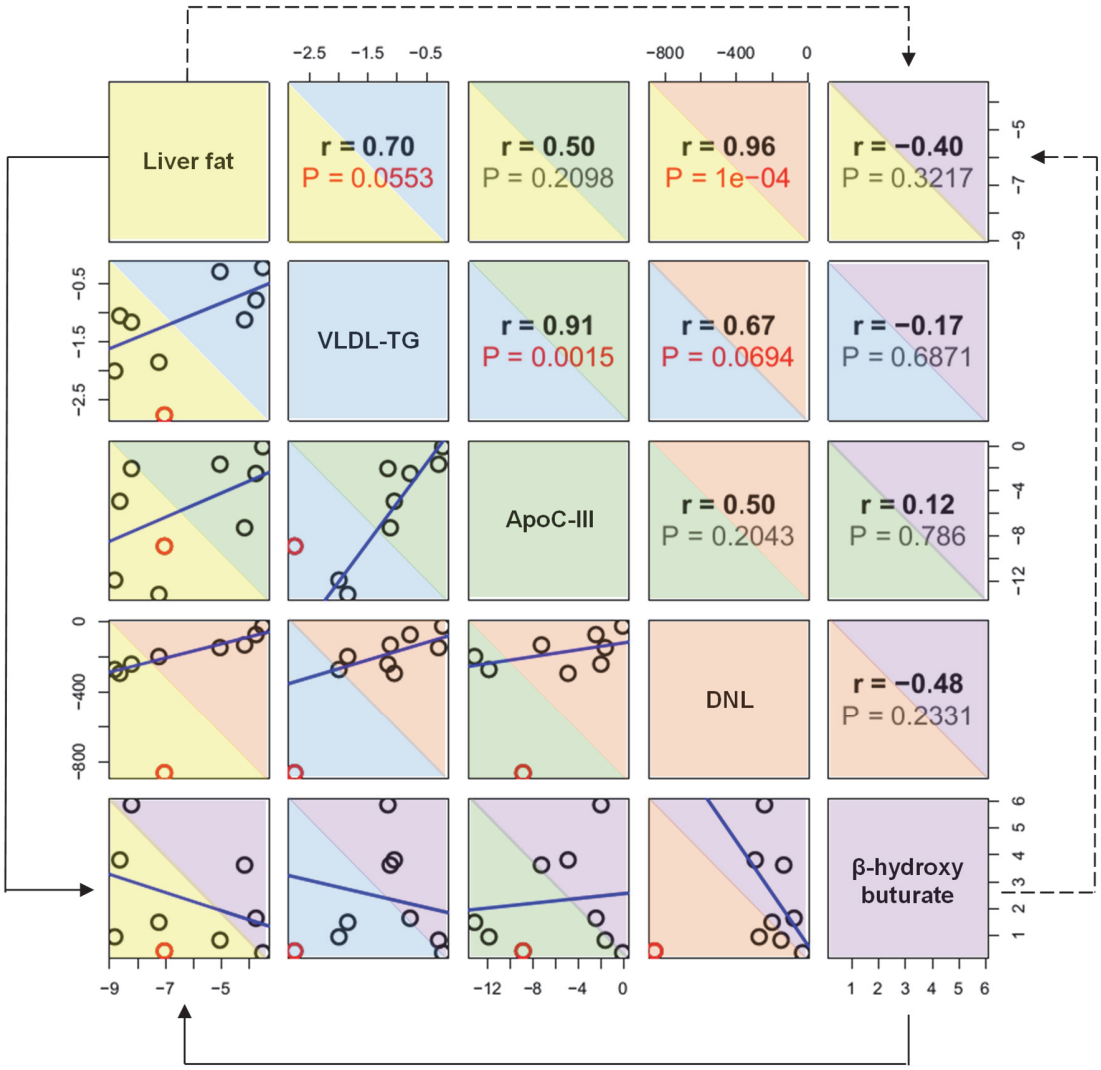

Figure S2. Pairwise Pearson correlations between delta changes (day 14 versus day 0 of the carbohydrate-restricted diet) for liver fat, VLDL-triglycerides (TG), apoCIII, DNL, and β-hydroxybutyrate in the first cohort (*n* = 8). Related to Figure 1 and Table S1. Boxes in the lower triangle (which show correlation plots) are mirrored by boxes in the upper triangles (which present the corresponding correlation coefficient and *P* value). Note the variables are color coded (*e.g.* yellow liver fat, blue border for VLDL-TG). One individual with an extreme DNL value (red circle) and one individual without a DNL measurement were not included in this analysis. Arrows indicate how to read the correlation matrix (in this case the correlation between liver fat and β-hydroxybutyrate). Solid arrows show the plot, and dashed lines the correlation coefficient and *P* value.

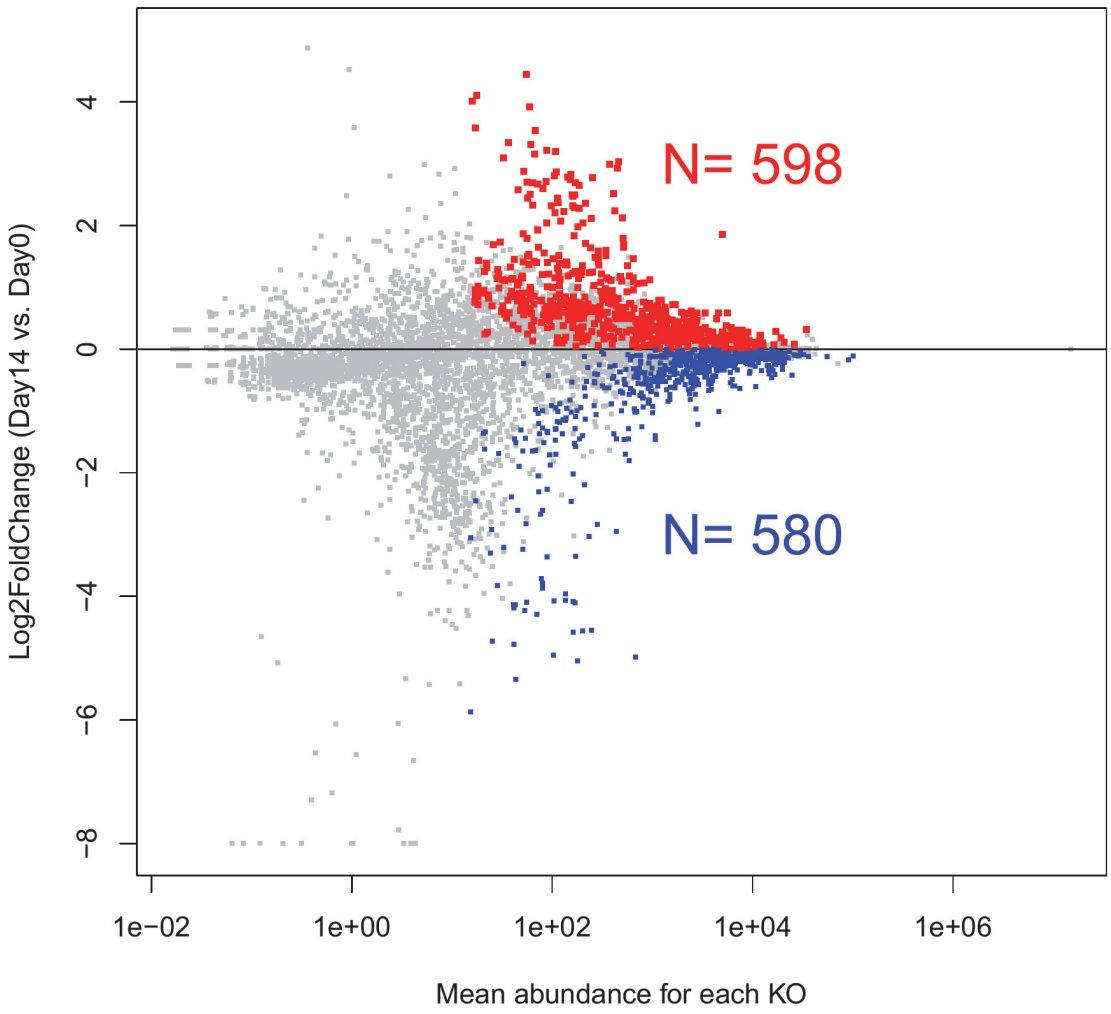

Figure S3. **MA plot for all KOs annotated from metagenomics data in the first cohort at day 14 versus day 0 of the carbohydrate-restricted diet (*n* = 10).** Related to Figure 3 and Table S2. KOs that are significantly upregulated and downregulated at day 14 are shown in red and blue, respectively. FDR < 0.05 (likelihood ratio test).

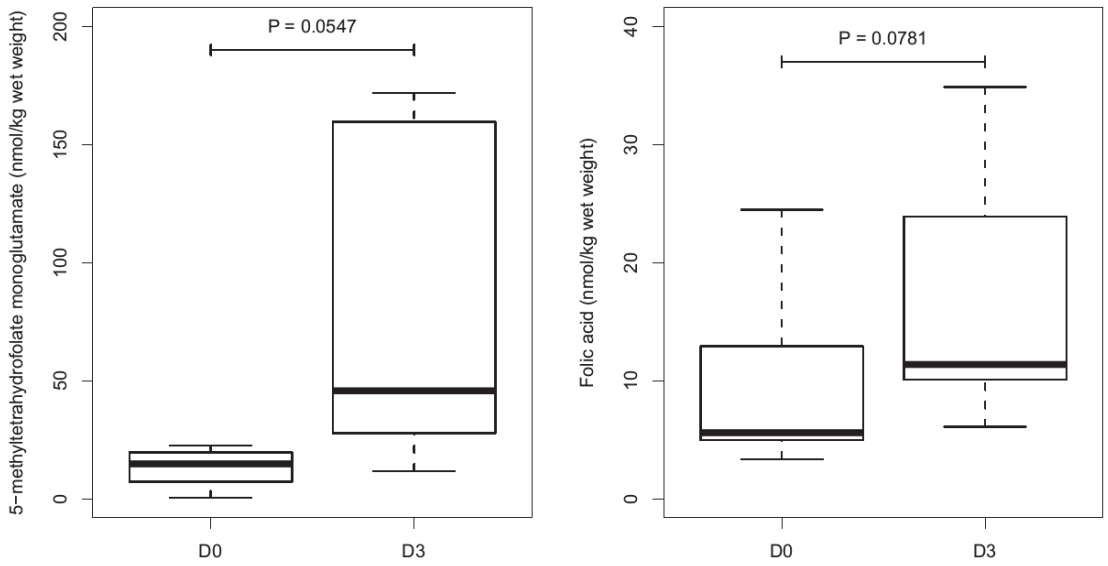

Figure S4. Box plots (with median) showing concentrations of fecal folate at baseline (D0) and after 3 days of the diet (D3) in the first cohort (*n* = 7). Related to Figure 3. Note that only fecal samples obtained at these time points were used here because many fecal samples were missing due to earlier analyses (metagenomics and SCFAs measurements). One-tailed Wilcox signed-rank test.

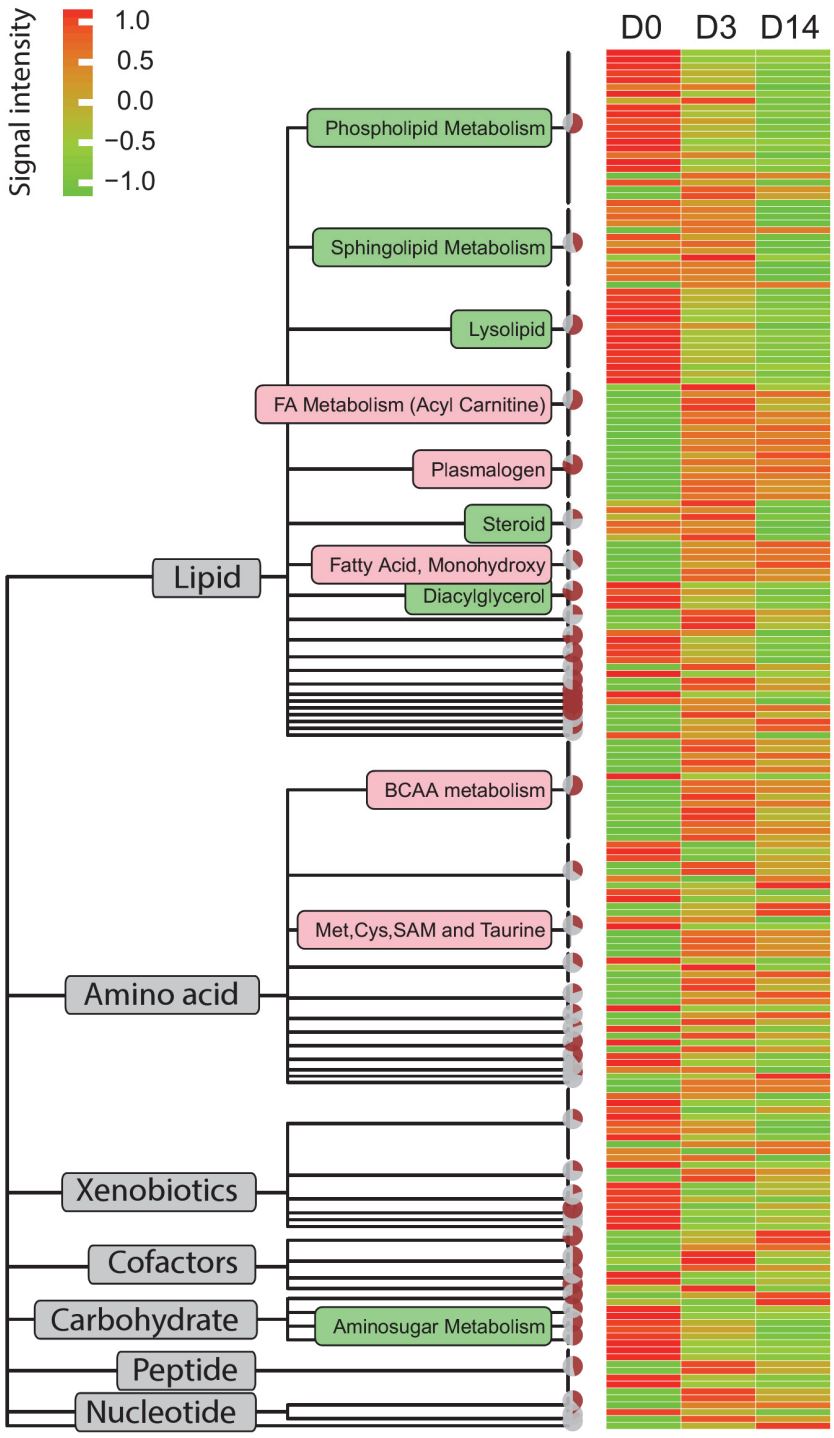

Figure S5. Heatmap plot showing metabolites that significantly changed across the study period in serum from the first cohort (*n* = 10). Related to Figure 4 and Table S3. D, day. Pathways highlighted in pink background are upregulated whereas the ones with green background are downregulated. FDR < 0.05 (one-way ANOVA with repeated measurements).

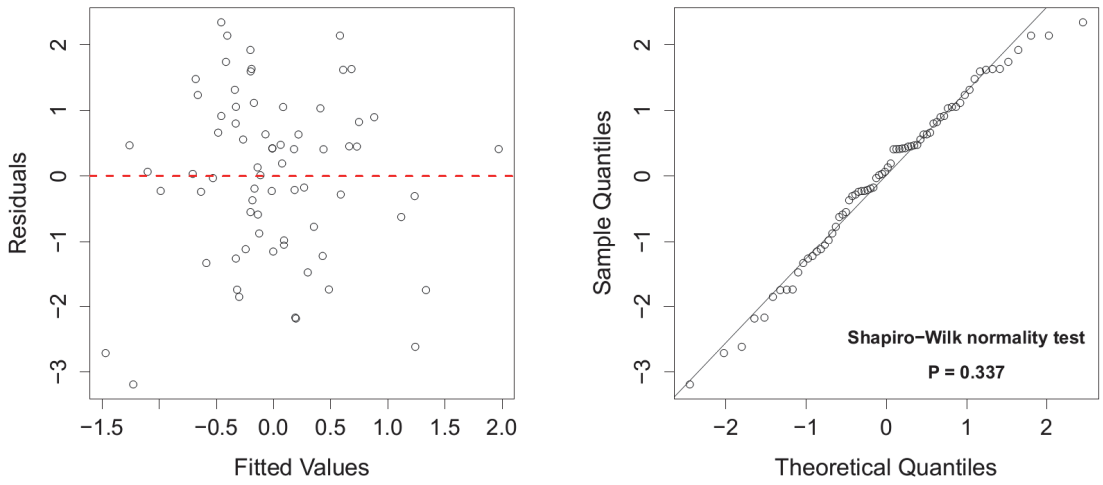

Figure S6. **Residual plot and quantile-quantile (Q-Q) plot for evaluation of the linear mixed-effect model.** Related to Figure 4B.

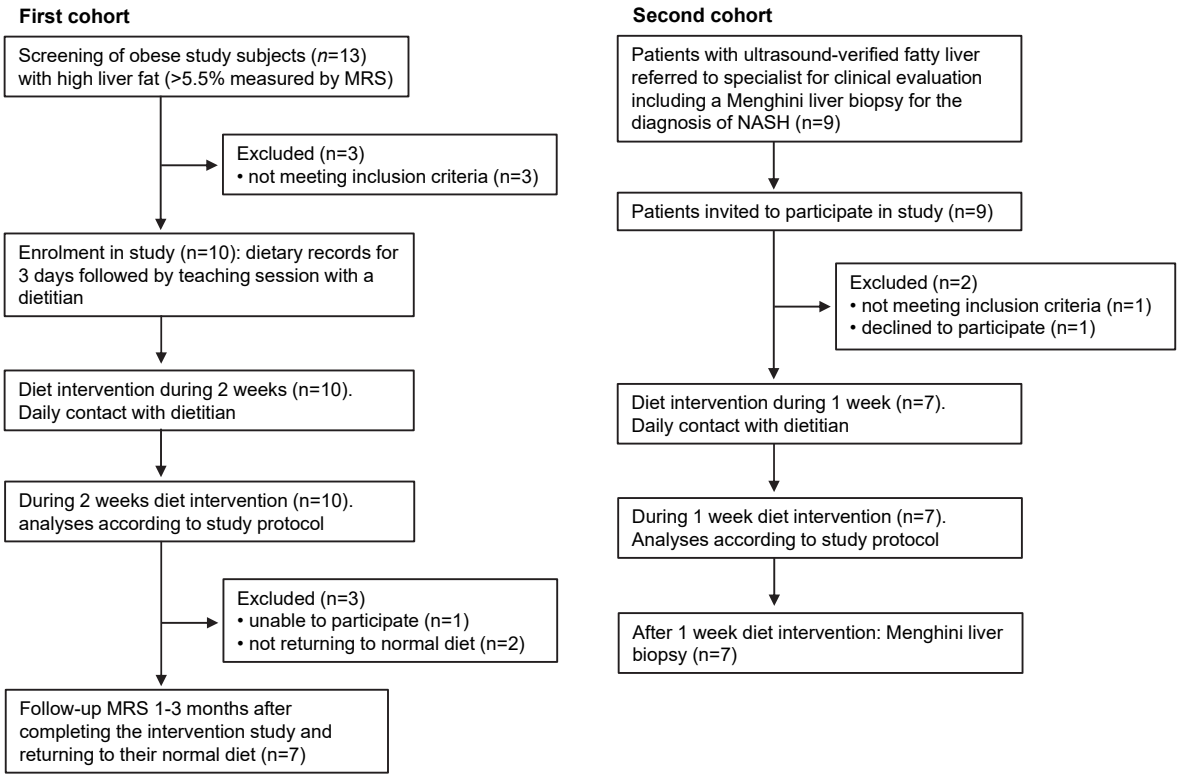

Figure S7. CONSORT flow diagram for the study. Related to Figure 1B.