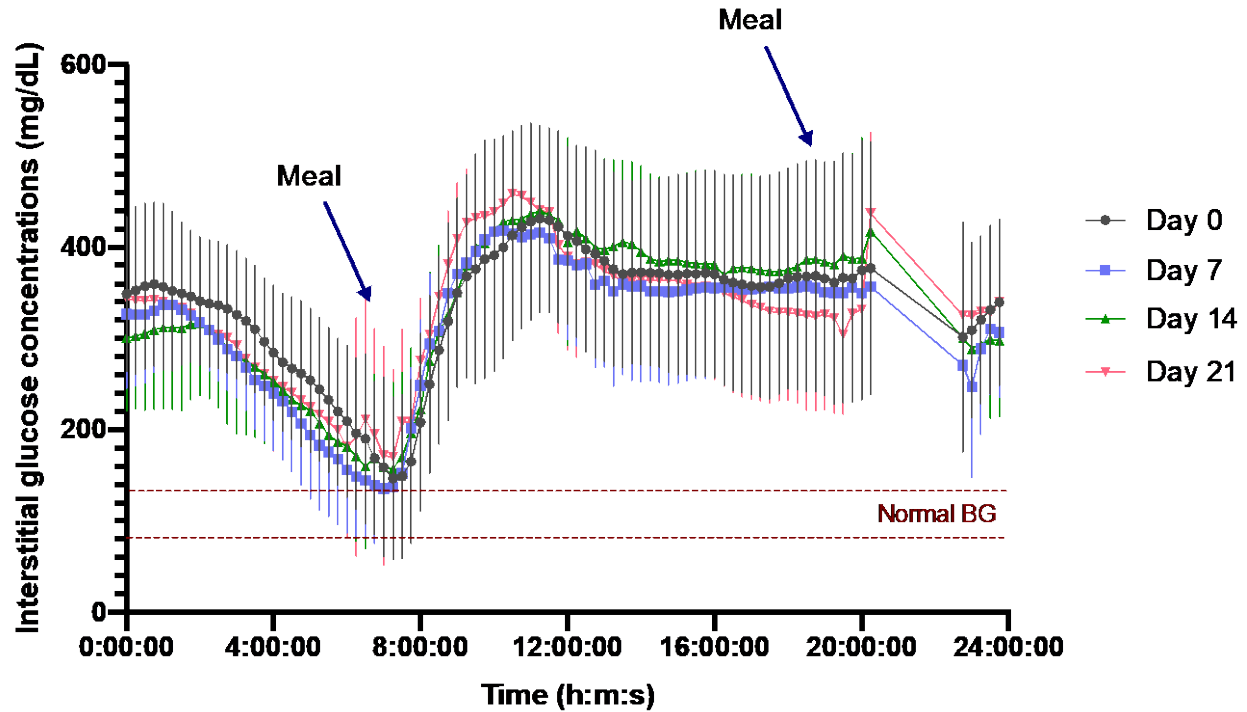
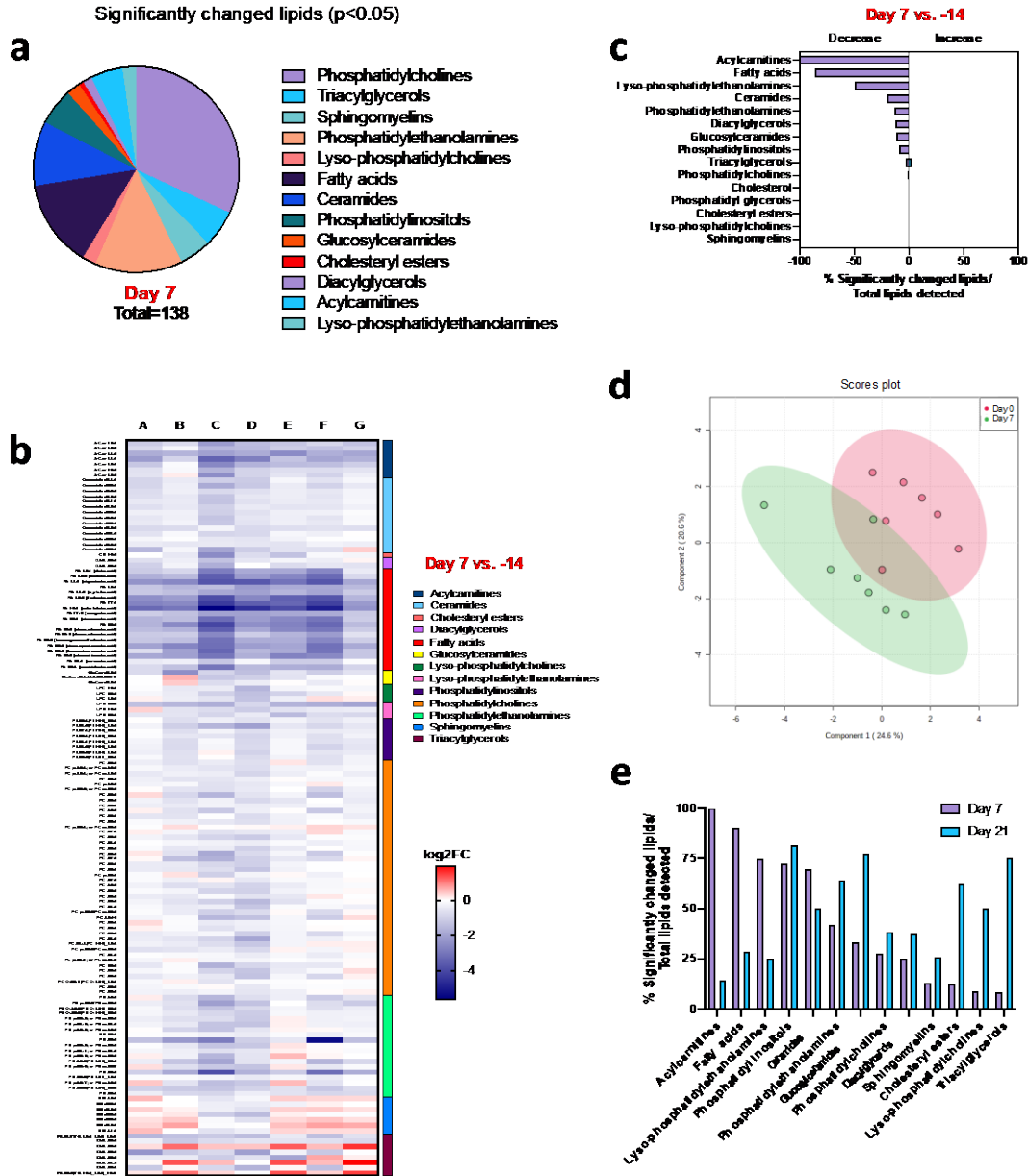


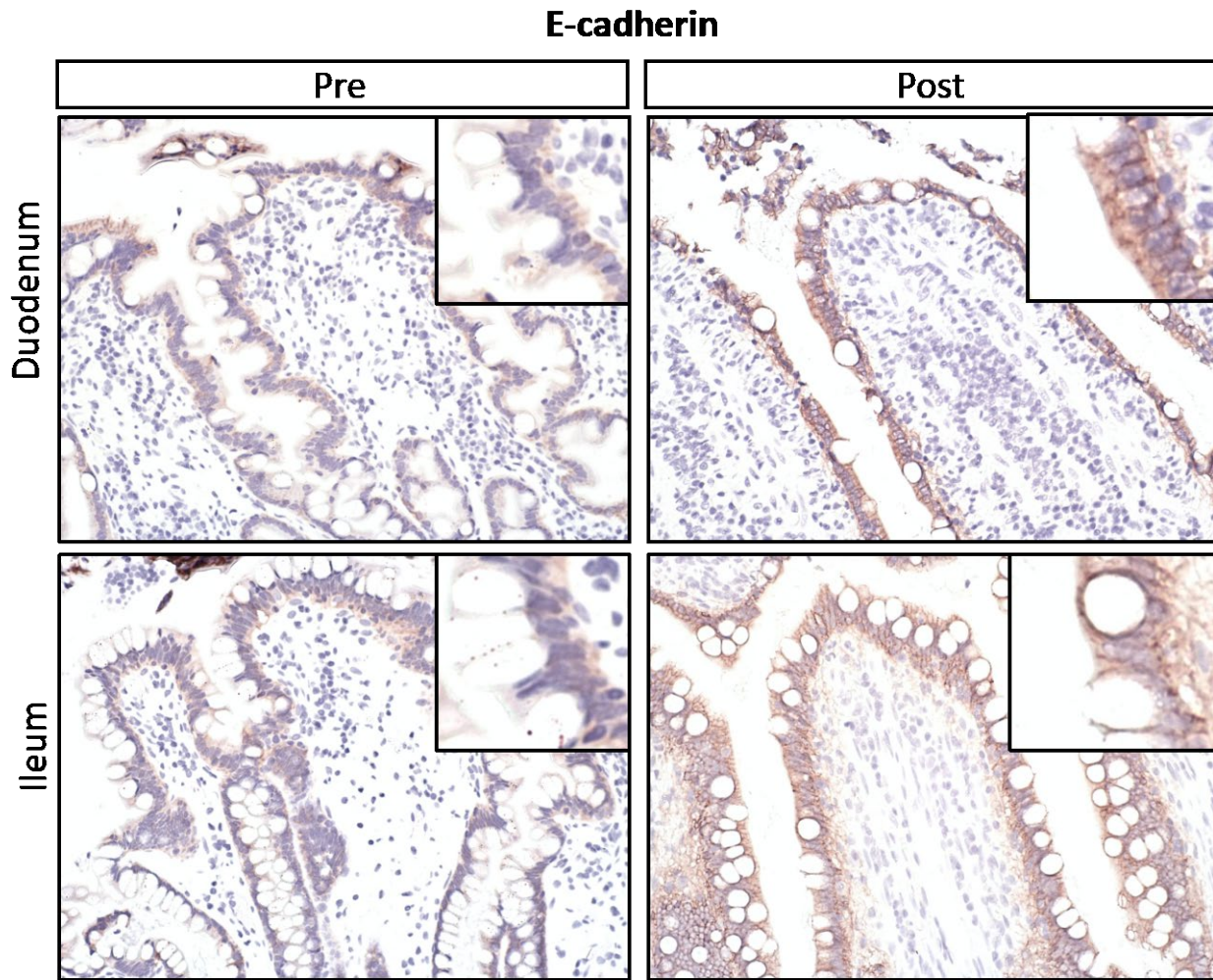
## Supplementary Materials



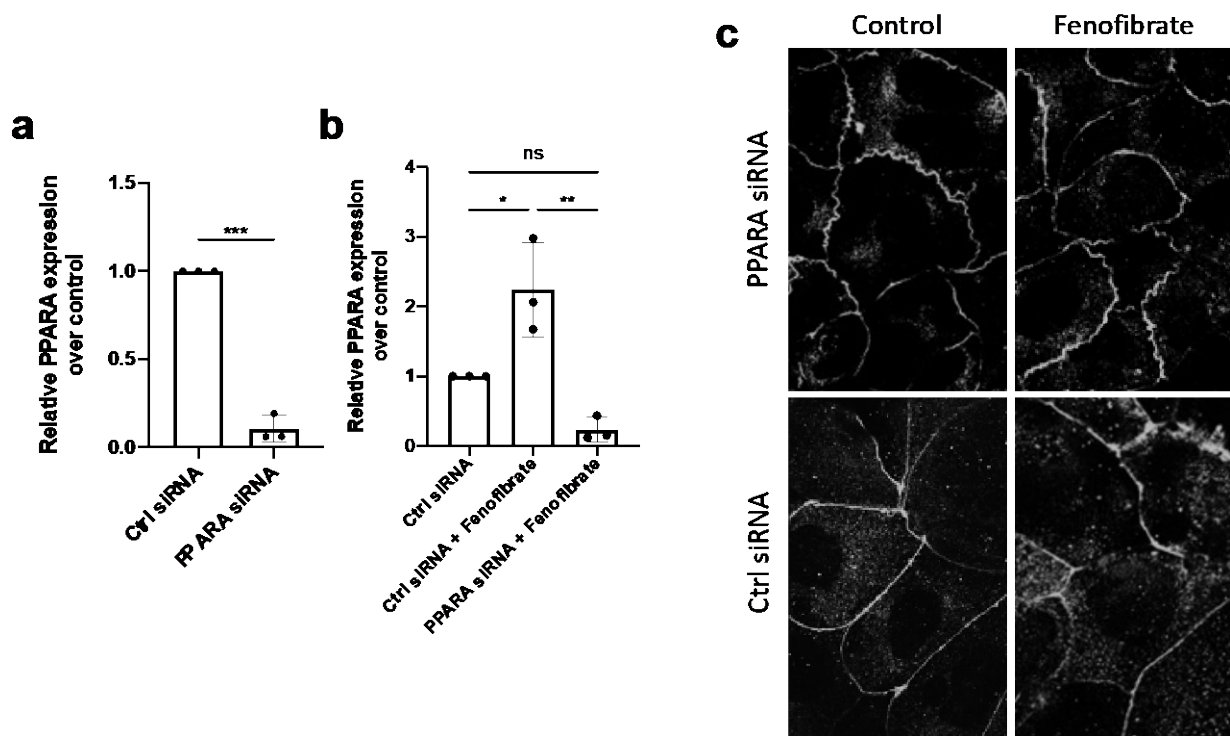
**Fig. S1: Effects of 3 weeks fenofibrate administration on weekly interstitial glucose (IG) concentrations in diabetic dogs.** Mean IG measurements over 24h following fenofibrate administration compared to pre-treatment values. All data represent the average from 7 dogs measured at 15-minute increments. Means  $\pm$  SD are plotted.



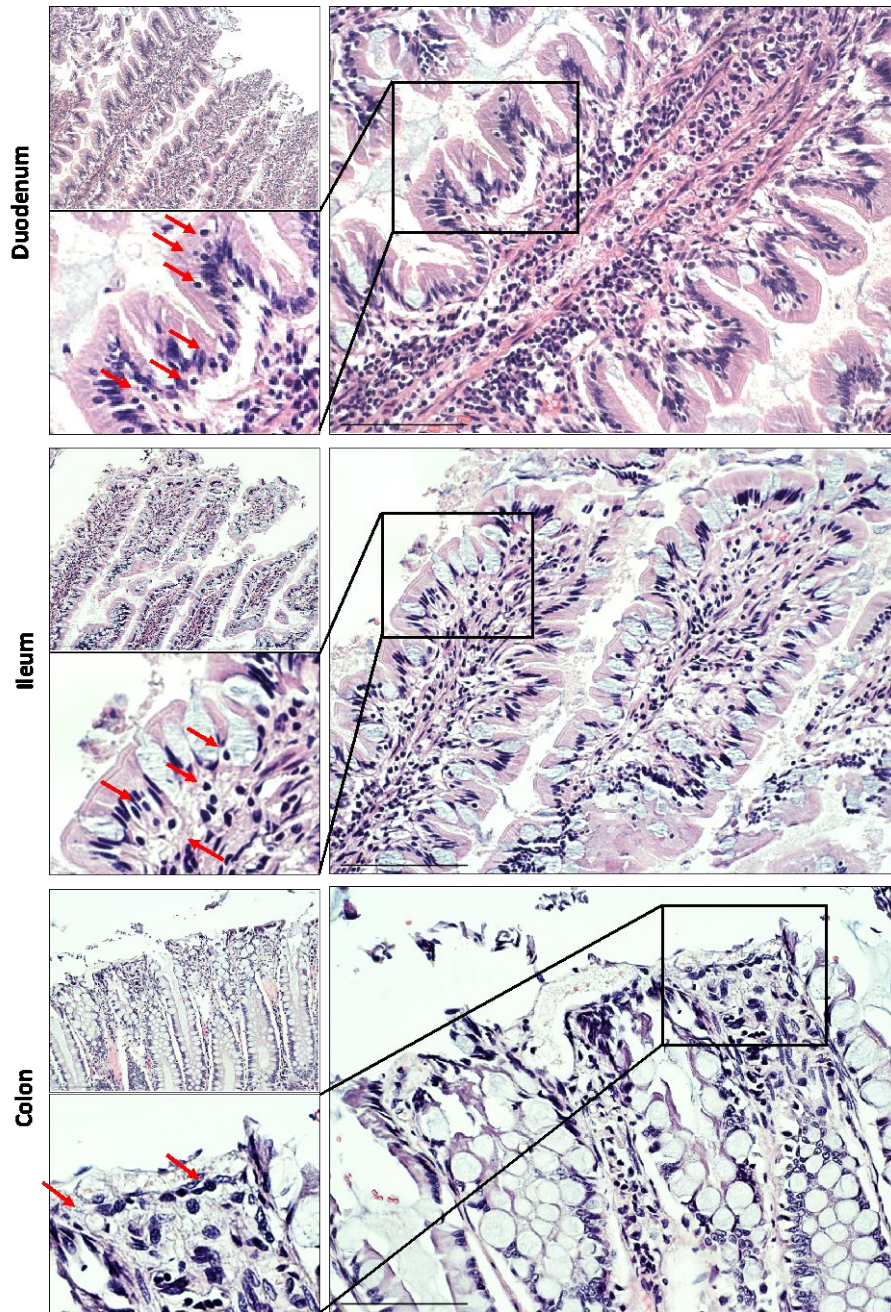
**Fig. S2: Changes in the plasma lipidome after 1 week of fenofibrate treatment.** (a) Composition of lipid groups altered after 1 week of fenofibrate treatment compared to baseline. Significance defined as  $P < 0.05$ . (b) Heatmap of all differentially abundant lipid species in plasma of diabetic dogs pre- and post-fenofibrate treatment. (c) Percentage of lipid groups that were differentially abundant after 1 week of fenofibrate administration. Significance was defined as  $P < 0.05$  and fold-change  $> 1.5$ . (d) Principal component analysis of the plasma lipidome in diabetic dogs at baseline and 1 week after fenofibrate treatment. Circles represent regions of 95% confidence. (e) Comparison of lipid groups altered at 1 week and 3 weeks post-fenofibrate treatment.



**Fig. S3: Fenofibrate upregulates intestinal e-cadherin expression in diabetic dogs.** Immunohistochemical staining of e-cadherin in the duodenum and ileum of diabetic dogs pre- and post-fenofibrate administration. Magnification: 40X



**Fig. S4: PPAR $\alpha$  expression is induced by fenofibrate.** (a) Knockdown of PPAR $\alpha$  in Caco-2 cells. (b) Expression of PPAR $\alpha$  in Caco-2 cells transfected with PPAR $\alpha$  siRNA following treatment with fenofibrate. (c) Presence of tight junction ZO-1 expression following PPAR $\alpha$  knockdown and controls. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$  by one-way ANOVA with Tukey's multiple comparison test. Ns, not significant.



**Fig. S5: Increased intraepithelial lymphocyte density in dogs with spontaneous diabetes.** Lymphocytes (*red arrows*) in the intraepithelial compartments of duodenum, ileum, and colon. (H&E stain: *top left 20X, right 40X, bottom left 100X*)