

Supplementary Figure 1 Effect of western type (WD) diet on body weight (p=0.011) (A) and intestinal permeability measured by serum endotoxin (B), compared to a standard chow (SD) diet (p=0.032, both by Mann-Whitney test). (C) Serum endotoxin levels of SD and WD are increased at 24 hours after pancreatitis induction, compared to untreated SD and WD mice (respectively, p=0.003 and p=0.05 by unpaired t-test). *p<0.05; **p<0.01.



Supplementary Figure 2 Relative abundance of Proteobacteria in cecum tissue (CE-T) (p=0.004) and content (CE-C) (p=0.002, both by Mann-Whitney test). *p<0.05; **p<0.01, ns, not statistically significant.



Supplementary Figure 3 (**A-B**) Radial plot of significant phenotype microarrays using Biolog GENIII plates showing means with bars representing 95% CI (p<0.05 by ANOVA) of aminoacids (**A**) and antimicrobials (**B**) (**D-E**) Univariate metabolomics analyses showing differential abundant metabolites (p<0.1 by DESeq analysis) between experimental groups. *p<0.05; **p<0.01; ***p<0.001.



Supplementary Figure 4 (A) total colony forming units (CFU) of blood in FMT versus SFF group (p>0.05 by Mann-Whitney test). (B) Incidence of Gram(+) and Gram(-) infections of blood in FMT versus SFF group. (C) Incidence of cultured bacterial species in blood. (D) 16S rRNA gene analysis of administered FMT displaying the three most dominant genera found in pancreatic tissue. ns, not statistically significant. FMT, fecal microbiota transplantation; SFF, sterile fecal filtrate.



Supplementary Figure 5 (**A**) Oral butyrate supplementation partially restored cecal butyrate levels compared to untreated WD pancreatitis mice (p=0.016 by Mann-Whitney test). (**B**) 16S rRNA analysis of beta-diversity measured by weighted UniFrac indicates that BUTDW, but not BUTIP significantly influenced cecal microbiota composition (p=0.004 for WD+ANP+BUTDW vs WD+ANP, by PERMANOVA-test). Importantly, the BUTDW treatment partly restored the bacterial composition (p= for WD+VEH vs WD+ANP+BUTDW). (**C**) Relative abundance demonstrating the depletion of Proteobacteria in BUTDW group at the level of WD+VEH (p=0.008 versus WD+ANP in cecum lumen). Depletion of Proteobacteria was also observed in WD+ANP+BUTIP mice but it did not reach statistical significance. (**D**) Microbiota analysis demonstrates effect of butyrate supplementation on genus composition. *p<0.05; **p<0.01, ns, not statistically significant.



Supplementary Figure 6 Survival curves of mice treated with the histone deacetylase inhibitor trichostatin A (TSA) demonstrated no difference in survival compared to vehicle treated control group (p>0.05 by log-rank test). ns, not statistically significant.



Supplementary Figure 7 (**A**) Beta-diversity of fecal microbiota of 35 patients with acute pancreatitis (AP) and 15 healthy volunteers (HV) measured by weighted UniFrac, demonstrates a significant difference in microbial composition (p=0.001 by PERMANOVA-test). (**B**) Alpha diversity of fecal microbiota measured by Shannon index, demonstrates a significant difference between AP and HV. ****p<0.0001