

Supplementary Figure and Table Legends

Figure S1. Antibiotic treatment affects the abundance of the proteins independent from the diet.

Dot/box plots showing the relative abundance of the proteins directly affected by the antibiotics treatment (n=2-3). Data represent mean \pm SEM. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$

Figure S2. Antibiotic treatment affects protease inhibitors and immunity related proteins.

Dot/box plots showing the relative abundance of (A) serine protease inhibitors (serpins) and (B) immune system related proteins identified in the fecal proteome (n=2-3). Data represent mean \pm SEM. * $p \leq 0.05$, student's t-test.

Figure S3. β cell mass and function are not regulated by the gut microbiome.

(A) Quantification of β cell mass and (B) % of β cells for pancreas area (n=6 per group). (C) Glucose-stimulated insulin secretion (GSIS) for HFD fed mice with or without antibiotics (n=5 per group). Data represent mean \pm SEM.

Figure S4. Acinar cell proliferation is not different among groups after 10 weeks of treatment.

Representative images of pancreatic sections co-immunostained for BrdU and amylase. Pancreas were obtained from (A) Chow fed (B) HFD-fed (C) HFD-fed and Vancomycin-treated (D) HFD-fed and Metronidazole-treated mice. DAPI: blue, Amylase: green and BrdU: pink

Figure S5. Acinar cell proliferation is not different among groups after 10 weeks of treatment.

Representative images and quantification of pancreatic sections co-immunostained for Ki67 and amylase. Pancreas were obtained from (A) Chow fed (B) HFD-fed (C) HFD-fed and Vancomycin-treated (D) HFD-fed and Metronidazole-treated mice. Quantification of (E) amylase+ and (F) amylase+ Ki67+ cells. Data represent mean \pm SEM. * $p \leq 0.05$, student's t-test. DAPI: blue, Amylase: green and Ki67: pink

Figure S6. Acinar cell proliferation is not different among germ free mice after the microbiota transfer.

Representative images of pancreatic sections co-immunostained for Ki67 and amylase. Pancreas were obtained from mice colonized with bacteria from mice on (A) Chow fed (B) HFD-fed (C) HFD + vancomycin or (D) HFD + metronidazole. DAPI: blue, Amylase: green and Ki67: pink

Figure S7. Gastrointestinal hormone secretion is altered by gut microbiota.

Plasma levels of tested hormones for donor mice at the end of the treatment (left side) and germ free mice two weeks after the bacterial transfer (right side). Plasma levels of (A-B) Amylin, (C-D) Insulin, (E) Pancreatic peptide (PP) and (F) Ghrelin. Data represent mean \pm SEM. ** $p \leq 0.01$, (n=6-8 for donor mice and n=6 per mice colonized with cecal bacteria from antibiotic treated mice).

Figure S8. (A) Body weight of chow fed C57Bl/6J mice (n=4/group). **(B)** Body weight of HFD fed C57Bl/6J mice (n=4/group). **(C)** Pancreas weight of C57Bl/6J mice on chow diet

(n=4/group). **(D)** Cecum content of 12-week old C57Bl/6J mice after 2 weeks of antibiotic treatment (n=4/group). Data are shown as mean \pm SEM, comparing chow-fed mice to HFD-fed mice $**p < 0.01$ and $***p < 0.001$, Statistical analysis were performed by two-tailed, unpaired Student's t-test. CD = chow diet, HFD = high fat diet, M = metronidazole, V = vancomycin

Table S1. List of host proteins identified in fecal samples.

(A) List of proteins identified in fecal proteomes of four groups. **(B)** 32 proteins that are significantly altered in HFD-fed mice ($FDR \leq 0.25$). **(C)** 8 proteins that are altered with metronidazole treatment ($FDR \leq 0.25$). Gene ID, accession number, annotation, comparative analysis of the abundance among groups were reported for each protein. FDR: False discovery rate, FC: Fold change.

Table S2. Raw data obtained from HMS Proteomics Core Facility.