

Supplementary Figure 1. Food intake, body weight gain, and body composition were unchanged by GP supplementation. Mice (*db/db*) were fed *ad libitum* for 28 days. Diets were LFD (open squares, n= 7) or LFD-GP (closed squares, n= 7) delivering 1% GP (of which 90% were proanthocyanidins). **(A)** Food intake. **(B)** Body weight. **(C)** Fat mass and lean mass. **(D)** Liver weights. **(E)** Cecal weights. Group mean \pm SD is illustrated by horizontal and vertical lines. For panels A – C, difference between groups over time was determined by two-way ANOVA followed by Sidak's post-hoc test (inter-group comparison) or Tukey's post-hoc test (intra-group comparison). Different letters (a, b and c) indicate significant difference within diet groups ($p < 0.05$), while the same letter indicates no difference. For panels D – E, significant difference was determined using unpaired, two-tailed *t*-test followed by Welch's correction: *** $p < 0.001$, **** $p < 0.0001$.

Supplementary Figure 2. GP supplementation rapidly alters gut microbial community.

Microbial β -diversity illustrated as Bray–Curtis principal coordinate analysis (PCoA) of V4 16S rRNA amplicon sequences from fecal and cecal samples from mice fed LFD (open squares) or LFD-GP (closed squares) that were collected at indicated times. Ceca were collected at endpoint, day 29. Samples from GP-supplemented mice separate along PC1, which explains 37% of the variation in sample pool. ADONIS analyses were performed on 15,000 sequences per sample.

Supplementary Figure 3. GP supplementation significantly altered relative abundance of

ASVs clustered at the phyla-level. Change from baseline levels (top row asterisks) and between diet groups comparisons (i.e. GP supplementation effect) at each time point (bottom row asterisks,) were performed for: **(A)** Verrucomicrobia phylum, **(B)** Firmicutes phylum, **(C)** Bacteroidetes phylum, **(D)** Proteobacteria phylum and **(E)** Actinobacteria phylum **(F)** ratio of

Firmicutes to Bacteroidetes. Data are Mean \pm S.D. Two-way repeated-measures ANOVA with Sidak's correction for multiple comparisons was used to test differences between groups (supplementation effect), and Dunnett's multiple comparisons test was employed to detect change from baseline effect: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

Supplementary Figure 4. Intestinal and hepatic gene expression. qPCR analyses showing relative mRNA levels of indicated genes expressed in (A) jejunum, (B) ileum and (C-D) colon and (E) liver tissues of mice fed LFD (open squares) or LFD-GP (closed squares). Target mRNAs were normalized to *HMBS* gene as endogenous control. Group mean \pm SD ($n = 7$ /group) is illustrated by horizontal and vertical lines. Data represent qPCR of technical duplicates analyzed by $2^{-\Delta\text{CT}}$ method. Between-group difference was determined by unpaired, two-tailed t-test with Welch's correction as needed: * $p < 0.05$.

Supplementary Figure 5. GPs reduced taxa associated with production of SBAs

Heatmap of log transformed ASV relative abundance data identified at genera or family level. For genera not identified (N.ID.) family name is provided. Permutation analysis (12,000 x) of ASVs with at least 50% prevalence across samples. Mann-Whitney-Wilcoxon test p-values were adjusted using false discovery rate (FDR) correction (* $q < 0.05$, ** $q < 0.01$, *** $q < 0.001$). ASVs in LFD-GP group that increased are warm/red colored and those that are decreased appear more cold/blue colored. ASVs significantly changed between groups at more than one time-point are presented: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Supplementary Figure 6. Serum BA profiles of *db/db* or WT mice with and without GP

supplementation. (A) Concentrations of individual PBAs and SBAs quantified by LC-MS in serum samples ($n = 6 - 7$ samples/group) collected from *db/db* mice fed LFD (open squares) or LFD-GP (closed squares). (B) Concentration of individual PBAs and SBAs quantified by LC-MS

in serum samples ($n = 5$ samples/group) collected from WT C57BL6/J mice fed HFD (60% kcal fat; open circles) or HFD-GP (black circles). In A and B, group mean \pm SD is illustrated by horizontal and vertical lines. Difference between control and GP-supplemented diet groups was determined by unpaired t -test with Welch's correction as needed: * $p < 0.05$, ** $p < 0.01$.

Supplementary Figure 7. Serum BA profile of WT mice fed HFD or HFD-GP. (A) LC-MS and pure standards were used to determine the mean concentration of individual PBAs and SBAs (mean \pm SD) in serum samples ($n = 5$ samples) collected from individual WT C57BL6/J mice fed HFD (open circles) or HFD-GP (black circles). Group mean \pm SD at each time point are illustrated by horizontal and vertical lines. (B) Total serum BA concentration (mean \pm SD) was determined based on sum of individual PBA and SBA concentrations (shown in panel A) quantified for each mouse fed HFD ($n = 5$, white bars) or HFD-GP ($n = 5$, black bars). (C) Serum PBA and SBA concentrations (mean \pm SD) in HFD (white bar) vs. HFD-GP (black bar) diet groups were calculated by summing the individual PBAs or SBAs shown in panel A. (D) Using data from panels B and C, pie charts illustrate pooled PBAs (green) and pooled SBA (pink) as a percentage of total serum BA concentration quantified for HFD and HFD-GP groups. For panels A – C, significant difference was determined using unpaired, two-tailed t -test followed by Welch's correction: * $p < 0.05$, ** $p < 0.01$.

Supplementary Figure 8. Ileal organoids treated with equimolar concentrations of different BAs present in serum of db/db mice. (A-C) Scatter plot of relative mRNA levels of indicated genes expressed in organoids after 17 h of treatment with: vehicle (5% methanol, open diamonds); 100 μ M CDCA (closed red circles); 200 μ M TMCA (closed black circles); 200 μ M of indicated PBA (open red circles); or 200 μ M of indicated SBA (open blue squares). Data shown was combined from two independent experiments, and for each experiment 3 wells

containing mature organoids were treated with indicated BAs. Data represent qPCR of technical duplicates analyzed by $2^{-\Delta\text{CT}}$ method. Group mean \pm SD (n= 6 wells total per treatment group) is illustrated by horizontal and vertical lines. Difference compared to vehicle was determined by one-way ANOVA followed by Dunnett's test: ***p< 0.001.