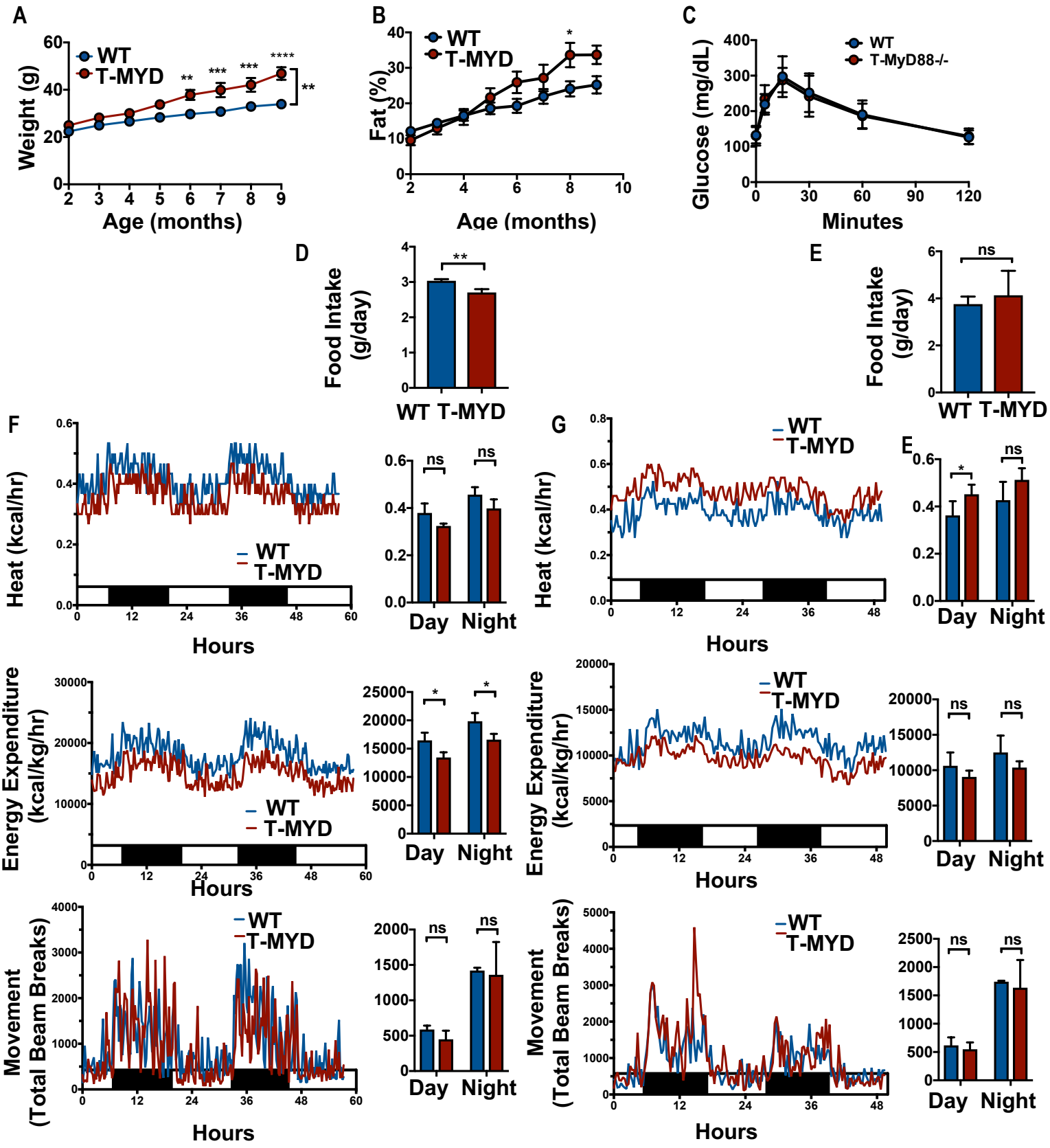

A
Weight (g)
WT
T-MYD
Age (months)
B
Fat (%)
WT
T-MYD
Age (months)
C
Glucose (mg/dL)
WT
T-MyD88-/-
Minutes
D
Food Intake (g/day)
WT T-MYD
E
Food Intake (g/day)
WT T-MYD
F
Heat (kcal/hr)
WT
T-MYD
Hours
Day Night
G
Heat (kcal/hr)
WT
T-MYD
Hours
E
Day Night
Energy Expenditure (kcal/kg/hr)
WT
T-MYD
Hours
Day Night
Energy Expenditure (kcal/kg/hr)
WT
T-MYD
Hours
Day Night
Movement (Total Beam Breaks)
WT
T-MYD
Hours
Day Night
Movement (Total Beam Breaks)
WT
T-MYD
Hours
Day Night

Fig. S1. Mice lacking Myd88 signaling within T cells develop age-associated obesity. (**A**) Weight gained as mice age, starting at 2 months of age (WT, n=8; T-Myd88$^{-/-}$ n=7). (**B**) Percentage of fat gained as mice age, starting at 2 months of age (WT, n=8; T-Myd88$^{-/-}$, n=7). (**C**) Blood levels of glucose (mg/dL) measured over time following i.p. glucose (1 mg/g) injection during glucose tolerance test of 1-year-old WT and T-Myd88$^{-/-}$ mice. (**D)** Grams of food intake per mouse while being fed normal chow at 2 months (n=3 per cohort). (**E**) Grams of food intake per mouse while being fed normal chow 1-year-old mice (n=5 per group. (**F**) Heat, energy expenditure, and total movement of 2-month-old (n=3 per group). (**G**) Heat, energy expenditure, and total movement of 1-year-old mice (n=5 per group). Statistics: p-value<0.05 (*); p-value<0.01 (**); p-value<0.001 (***) using a repeated measures ANOVA with Sidak's correction for multiple comparisons (A, B, C), two-tailed, unpaired *t* test (D-G). Error bars indicate SD.

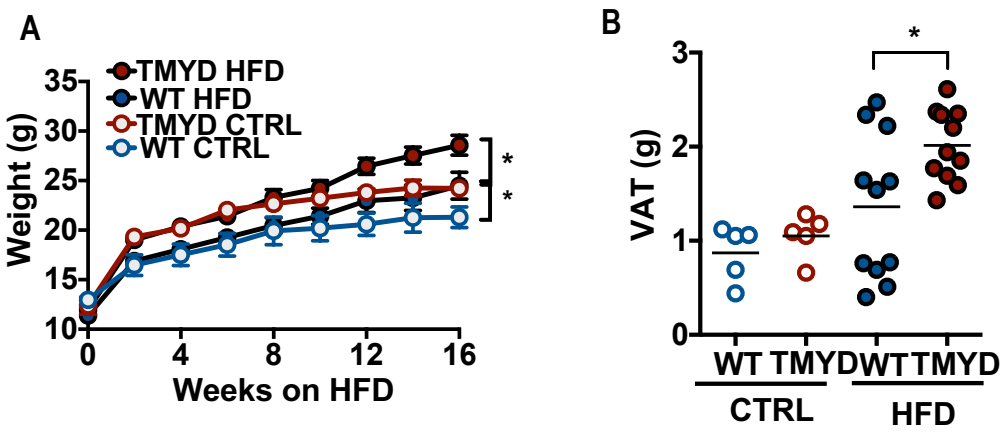
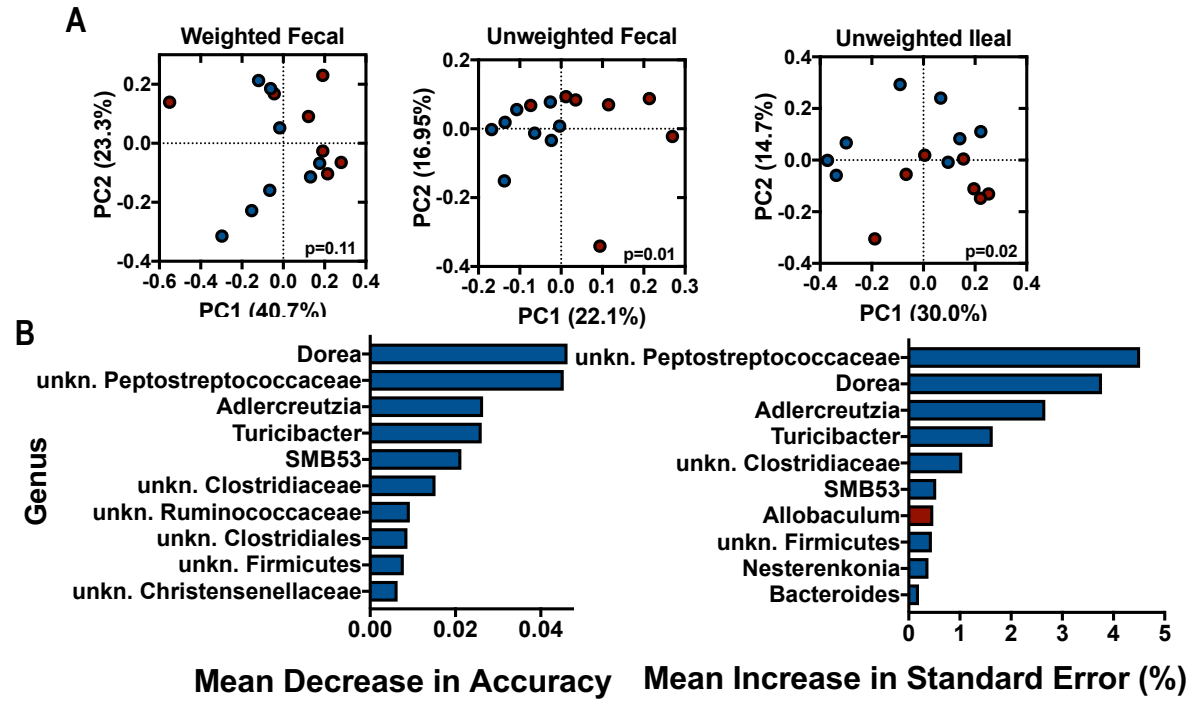


Fig. S2. Obesity in T-Myd88$^{-/-}$ mice is accelerated by increased dietary intake of fat. (**A**) Weight of animals over-time after high fat diet feeding. (**B**) Viceral fat mass in age matched indicated animals on control chow or 16 weeks post HFD feeding. Statistics: P-value<0.05 (*); P-value<0.01 (**); P-value<0.001 (***) using a repeated measures ANOVA (A) and two-tailed, unpaired *t* test (B). Error bars indicate SD.



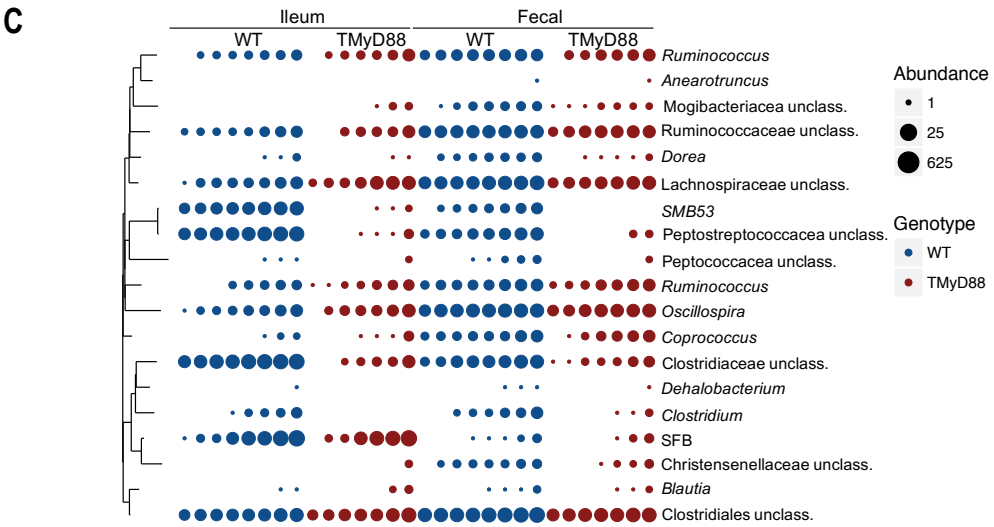


Fig. S3: Changes to microbial composition within T-Myd88$^{-/-}$ mice is associated with spontaneous weight gain. (**A**) Beta-diversity analysis of ileal and fecal 16S sequencing samples from 1-year-old WT and T-Myd88$^{-/-}$ mice, measured by unweighted unifrac and weighted unifrac (WT, n=8; T-Myd88$^{-/-}$, n=7). (**B**) Random forest analysis of microbial communities. (**C**) Number and relative abundance of Clostridia OTUs in fecal and ileal microbiota (WT, n=8; T-Myd88$^{-/-}$ n=7). Statistics: p-value<0.05 (*); p-value<0.01 (**); p-value<0.001 (***) using a PERMANOVA (C).

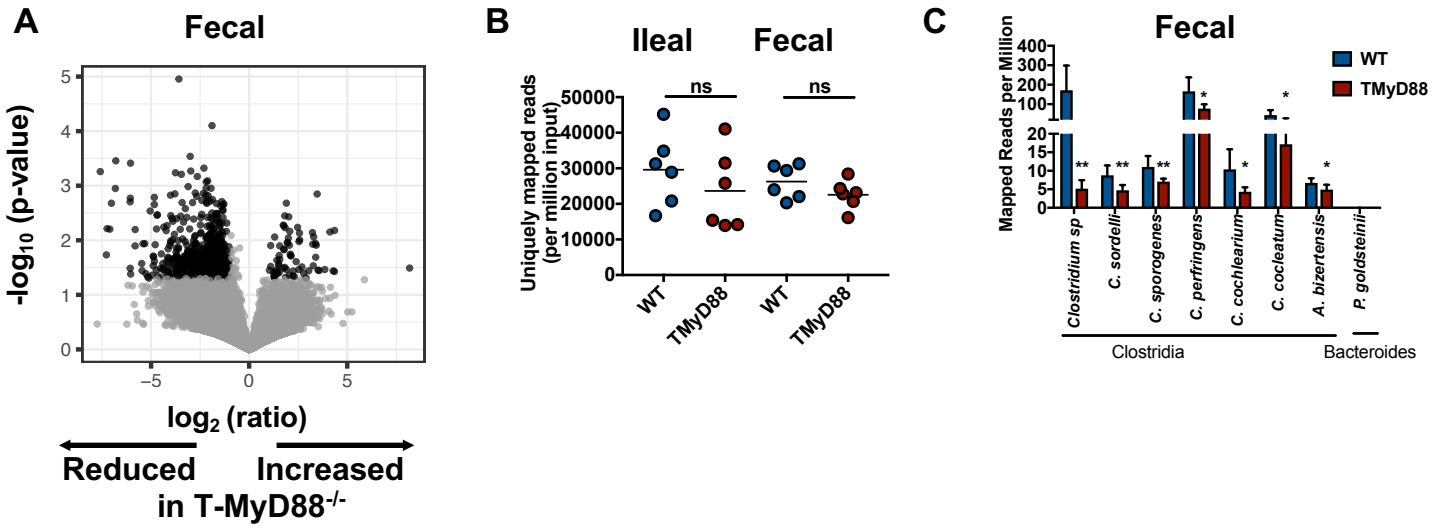


Fig. S4. Transcriptomic data of microbiota from WT or T-Myd88$^{-/-}$ mice. (A) Volcano plot of ratio of bacterial UniRef90 gene family transcript abundances in fecal samples. (**B**) Uniquely mapped reads per million in WT and T-Myd88$^{-/-}$ mice ileum and feces. (**C**) Mapped reads per million of significantly different species from WT and T-Myd88$^{-/-}$ fecal transcripts (n=6 per genotype). Statistics: p-value<0.05 (*); p-value<0.01 (**); p-value<0.001 (***) using a two-tailed, unpaired *t* test. Error bars indicate SD.

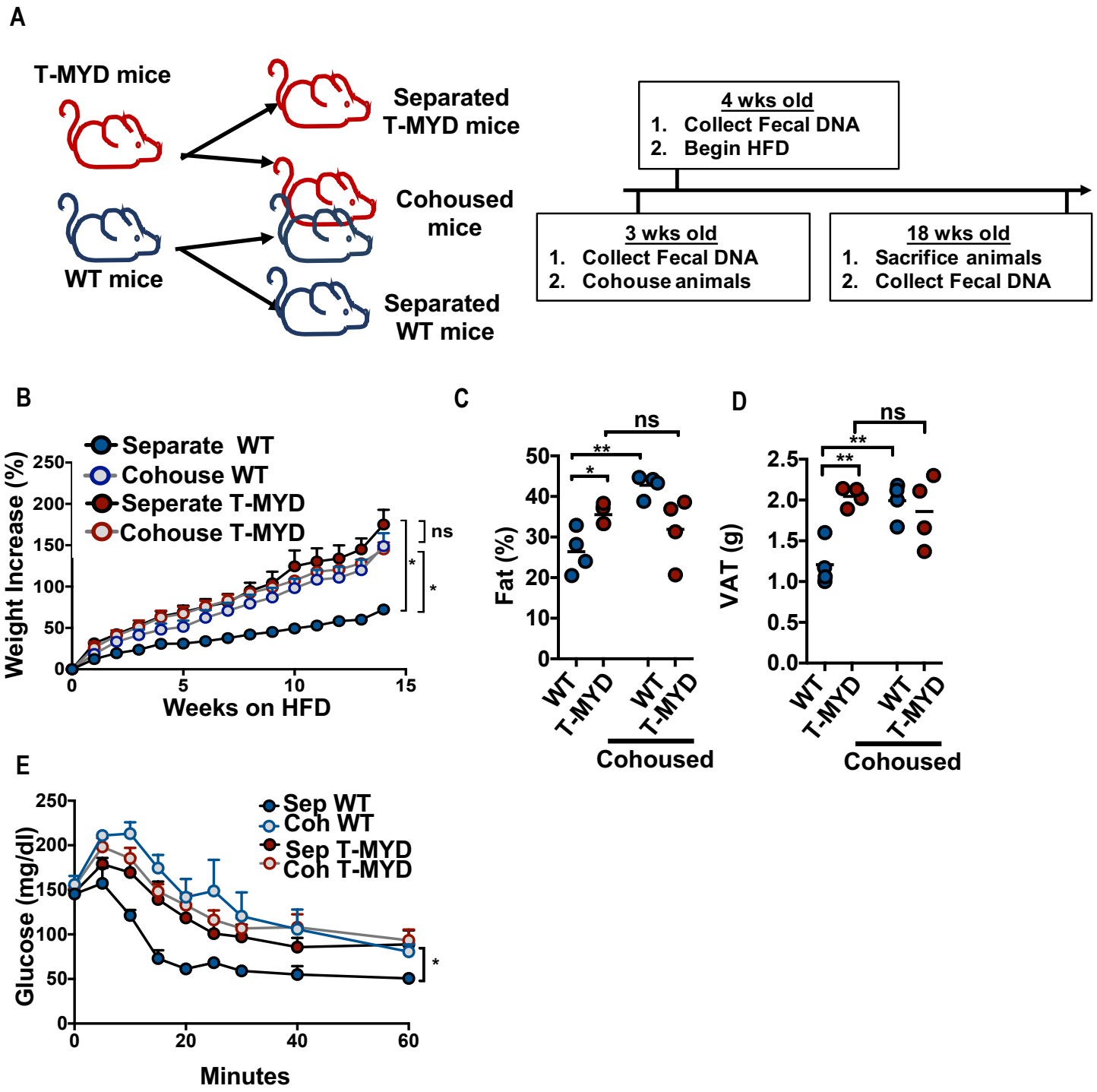


Fig. S5. Dysbiosis within T-Myd88$^{-/-}$ mice transfers obesity to WT animals during co-housing. (**A**) Schematic of cohousing experiment and schematic of timeline for cohousing experiment. (**B**) Percent weight increase, (**C**) percent fat, and (**D**) grams of VAT in separated or cohoused WT and T-Myd88$^{-/-}$ mice fed a HFD (n=4 per cohort). Representative of two independent experiments. (**E**) Blood levels of glucose (mg/dL) measured over time following i.p. glucose (1 mg/g) injection during glucose tolerance test of separated or cohoused WT and T-Myd88$^{-/-}$ mice fed a HFD (n=4 per cohort). Statistics: p-value<0.05 (*); p-value<0.01 (**); p-value<0.001 (***) repeated measures ANOVA (B,E), two-tailed, unpaired *t* test (C,D). Error bars indicate SD.

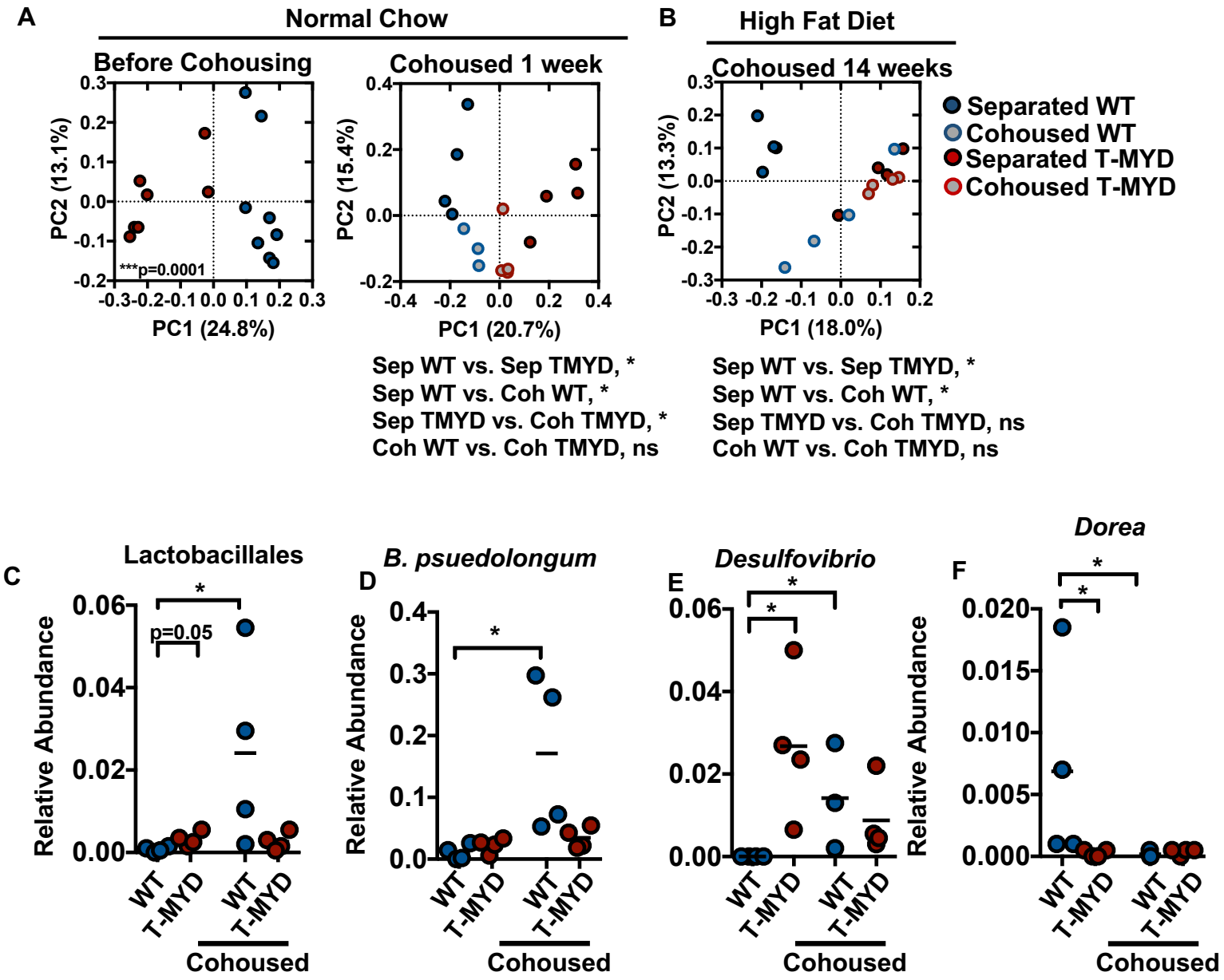


Fig. S6. Determination of transmissible organisms during co-housing. (A and **B)** Beta diversity measured by unweighted Unifrac analysis of separated or cohoused WT and T-Myd88$^{-/-}$ mice fed a normal chow both prior to cohousing and one week following cohousing (A) and then after 14 weeks of HFD (B). (**C** and **D**) Relative abundance of indicated organisms within fecal 16S sequencing samples from separated or cohoused WT and T-Myd88$^{-/-}$ mice at the final time point (n=4 per cohort). (**E**) Relative abundance of *Desulfovibrio* within fecal samples from indicated animals just one week after co-housing. (**F**) Relative abundance of *Dorea* in indicated animals after 12 weeks of cohousing. Statistics: p-value<0.05 (*); p-value<0.01 (**); p-value<0.001 (***) permanova (A,B) and a Mann-Whitney *U* test (C-F).

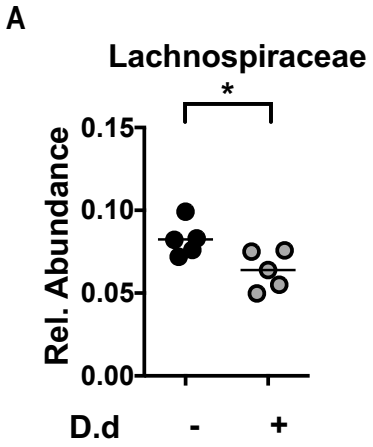


Fig. S7. Expansion of *Desulfovibrio* leads to loss of Clostridia. (A) Relative abundance of Lachnospiraceae within fecal 16S sequencing samples from mice colonized with or without *D. desulfuricans* and fed a HFD (n=5 per cohort). Statistics: p-value<0.05 (*); p-value<0.01 (**); p-value<0.001 (***) Mann-Whitney *U* test (A).

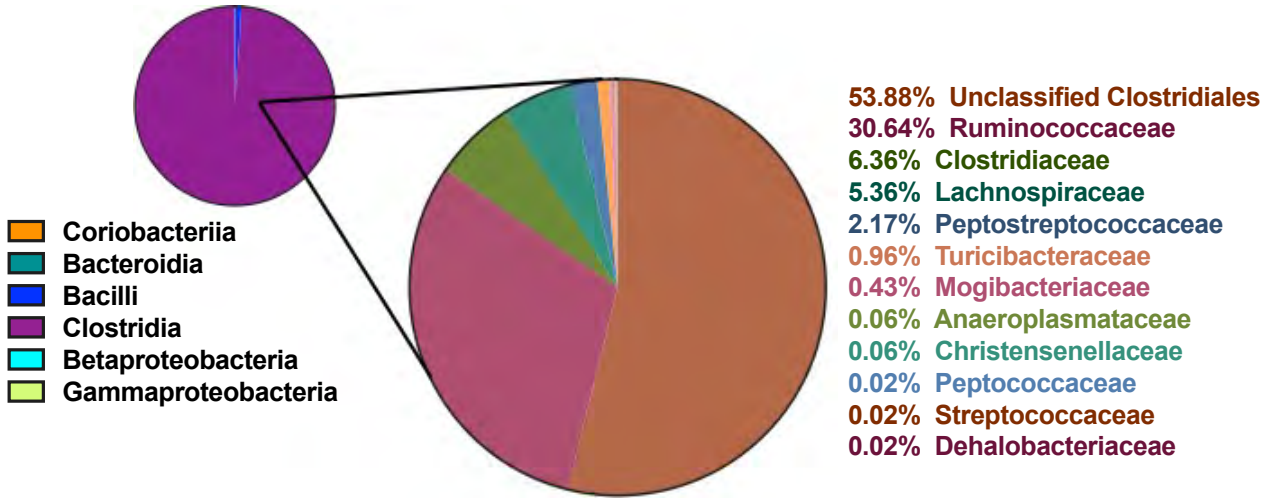


Fig. S8. Microbiota composition from germfree mice colonized with spore-forming microbes. Parts of whole graph from 16s sequencing of fecal microbiota of germfree mice colonized with spore-forming clostridia consortium.

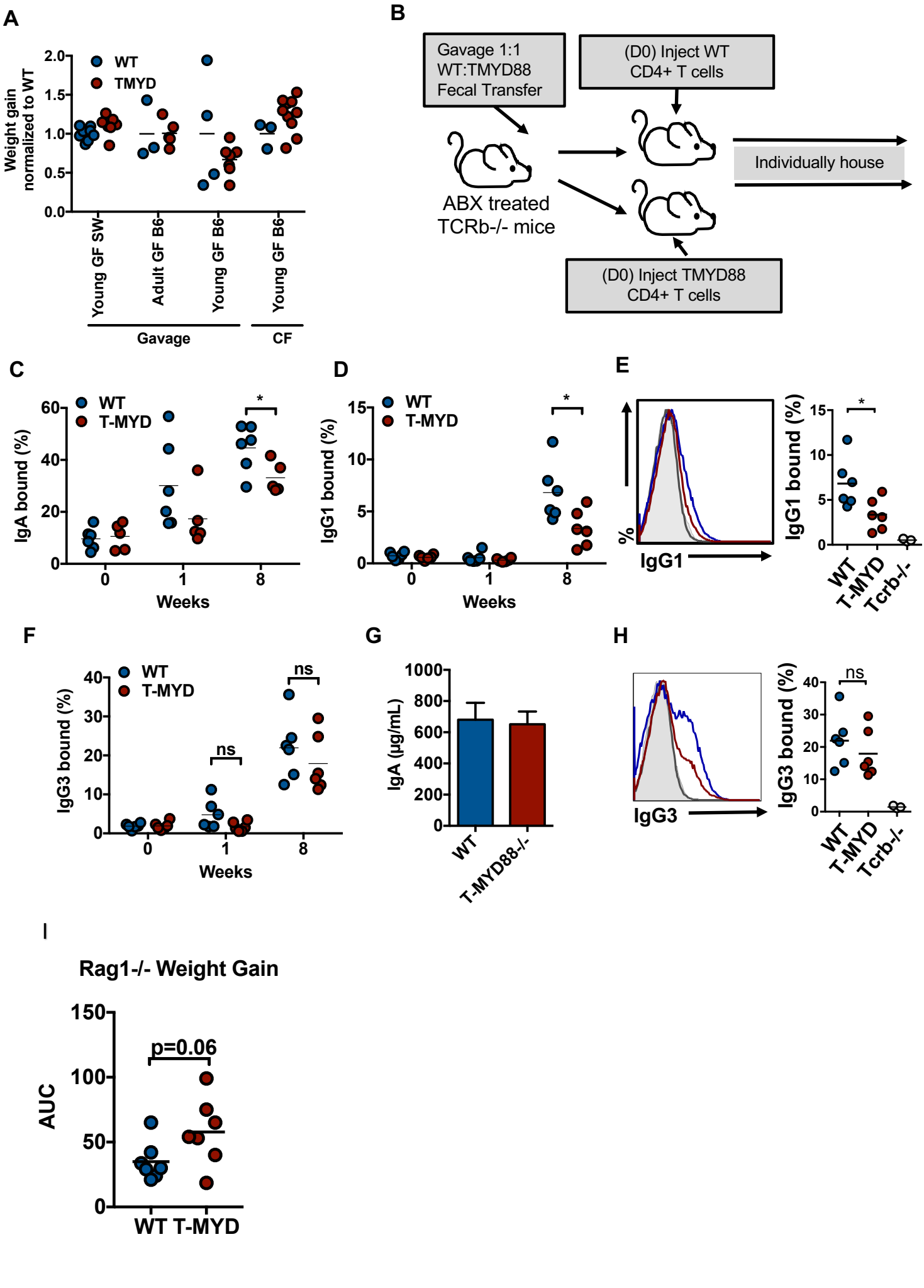

A
Weight gain normalized to WT
WT
TMYD
Young GF SW
Adult GF B6
Young GF B6
Young GF B6
Gavage
CF
B
Gavage 1:1 WT:TMYD88 Fecal Transfer
(D0) Inject WT CD4+ T cells
ABX treated TCRb-/- mice
Individually house
(D0) Inject TMYD88 CD4+ T cells
C
IgA bound (%)
WT
T-MYD
Weeks
D
IgG1 bound (%)
WT
T-MYD
Weeks
E
%
IgG1
IgG1 bound (%)
WT
T-MYD
Tcrb-/-
F
IgG3 bound (%)
WT
T-MYD
ns
Weeks
G
IgA (µg/mL)
WT
T-MYD88-/-
H
IgG3
IgG3 bound (%)
ns
WT
T-MYD
Tcrb-/-
I
Rag1-/- Weight Gain
AUC
p=0.06
WT T-MYD

Fig. S9. T cell shaping of the microbiota is associated with spontaneous weight gain. (**A**) Weight gained in germfree mice given WT or T-Myd88$^{-/-}$ microbiota through multiple methods of transfer (CF=cross fostered). (**B**) Schematic of experimental strategy. Tcrb$^{-/-}$ animals were depleted of the microbiota by antibiotic treatment and subsequently gavaged with a 1:1 mixture of microbiota from WT or T-Myd88$^{-/-}$ animals. WT or T-Myd88$^{-/-}$ T cells were transplanted into T cell deficient animals. (**C**) Flow cytometry was used to quantify the percentage of IgA bound bacteria within Tcrb$^{-/-}$ mice given WT or T-Myd88$^{-/-}$ cells at Day 0, Week 1, and Week 8 (n=6 per cohort). (**D,E**) Flow cytometry was used to quantify the percentage of IgG1 bound bacteria within Tcrb$^{-/-}$ mice given WT or T-Myd88$^{-/-}$ cells at Day 0, Week 1, and Week 8. (**F**) Flow cytometry was used to quantify the percentage of IgG3 bound bacteria within Tcrb$^{-/-}$ mice given WT or T-Myd88$^{-/-}$ cells at Day 0, Week 1, and Week 8. (**G**) Concentration of luminal IgA (μg/mL) was measured within Tcrb$^{-/-}$ mice given WT or T-Myd88$^{-/-}$cells after 8 weeks using an ELISA. Error bars indicate SD. (**H**) Representative flow cytometry plot was previously gaited on SyBR Green^{+} cells in order to quantify the percentage of IgG3 bound bacteria within Tcrb$^{-/-}$ mice given WT or T-Myd88$^{-/-}$ cells after 8 weeks. (**I**) AUC of weight gained of Rag1 $^{-/-}$ mice colonized with WT or T-Myd88$^{-/-}$ fecal microbiota (n= 7 per cohort). Statistics: p-value<0.05 (*); p-value<0.01 (**); p-value<0.001 (***) two-tailed, unpaired *t* test (A, C-I).

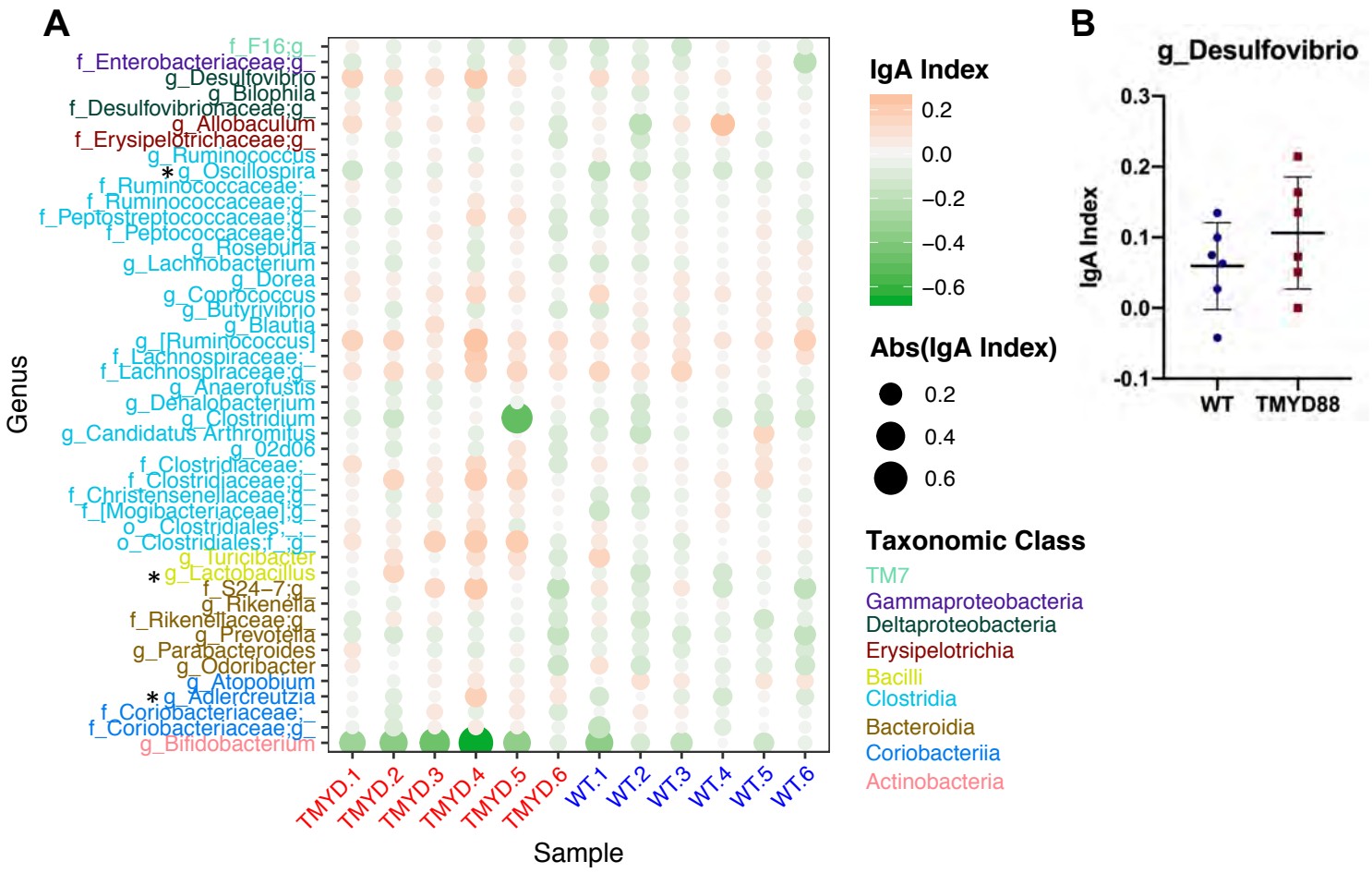


Fig. S10. IgA targeting of bacterial communities (**A**) IgA bound and unbound bacteria were analyzed from cecal contents of Tcrb$^{-/-}$ given either WT or T-Myd88$^{-/-}$ T cells. The IgA index was calculated for each genus in each animal (columns). Bubbles are colored by enrichment in the bound or unbound fraction and sized by the magnitude of enrichment (the absolute value of the IgA index). Genus taxa strings are colored according to their taxonomic class. Significantly differentially bound genera between genotypes are indicated (*, $p<0.05$; Wilcoxon rank sum test)(**B**) *Desulfovibrio* IgA targeting in this dataset. Error bars indicate SD.

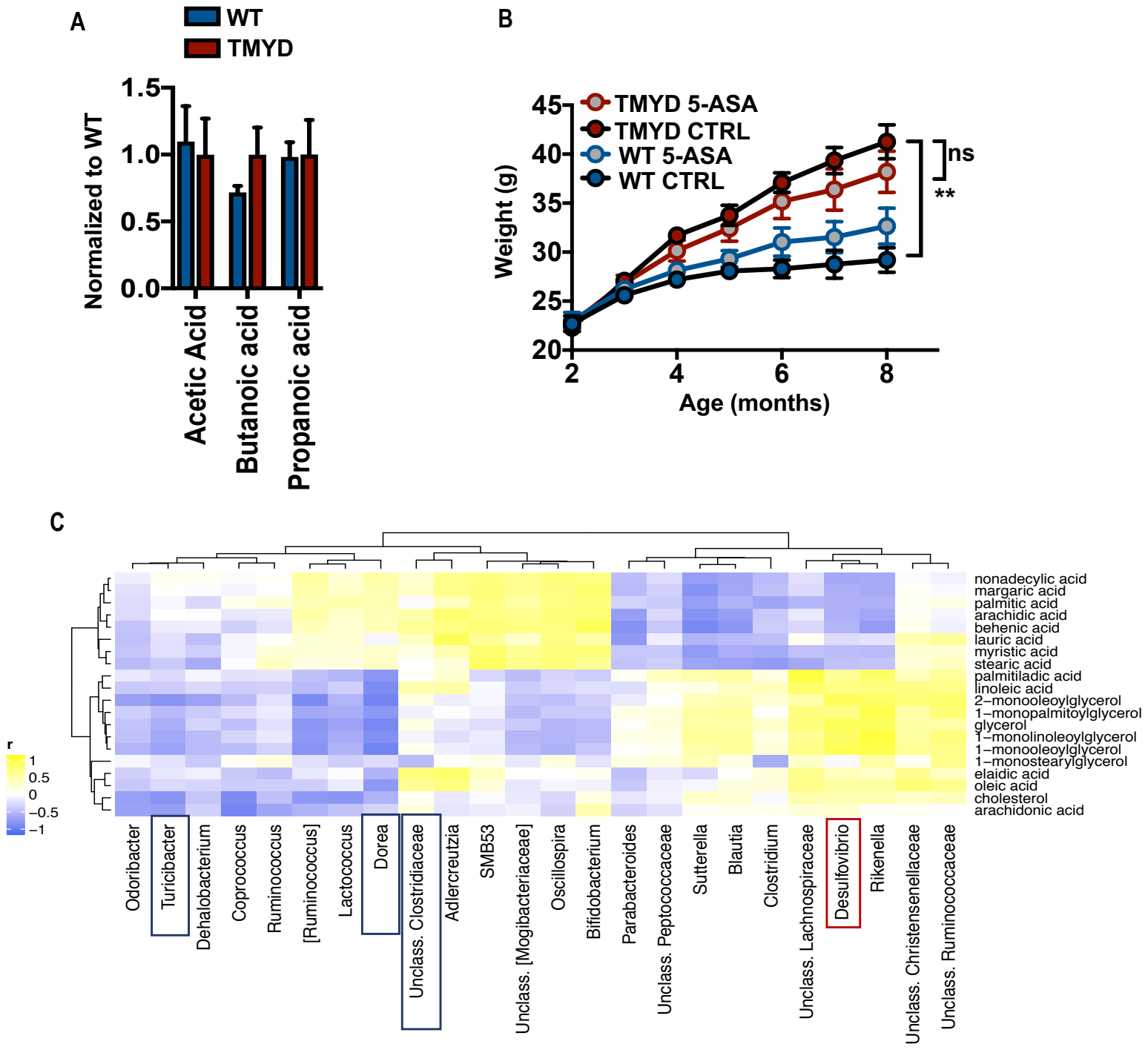


Fig. S11. Gut metabolites are associated with weight gain (**A**) GC– MS detected SCFAs of cecal contents of WT and T-Myd88$^{-/-}$ mice (WT, n=3; T-Myd88$^{-/-}$ n=5). (**B**) Grams of weight gained by WT and T-Myd88$^{-/-}$ mice fed control diet or 5-ASA diet, starting at 2 months of age (WT CTRL, n=3; WT 5-ASA, n=4; T-MYD CTRL, n=3; TMYD 5-ASA, n=4). Error bars indicate SD. (**C**) Spearman rank order correlation between relative abundances of Clostridia and fatty acid and monoacylglycerol metabolites (n=12). Statistics: p-value<0.05 (*); p-value<0.01 (**); p-value<0.001 (***) two-tailed, unpaired *t* test (A), and repeated measures ANOVA (B).