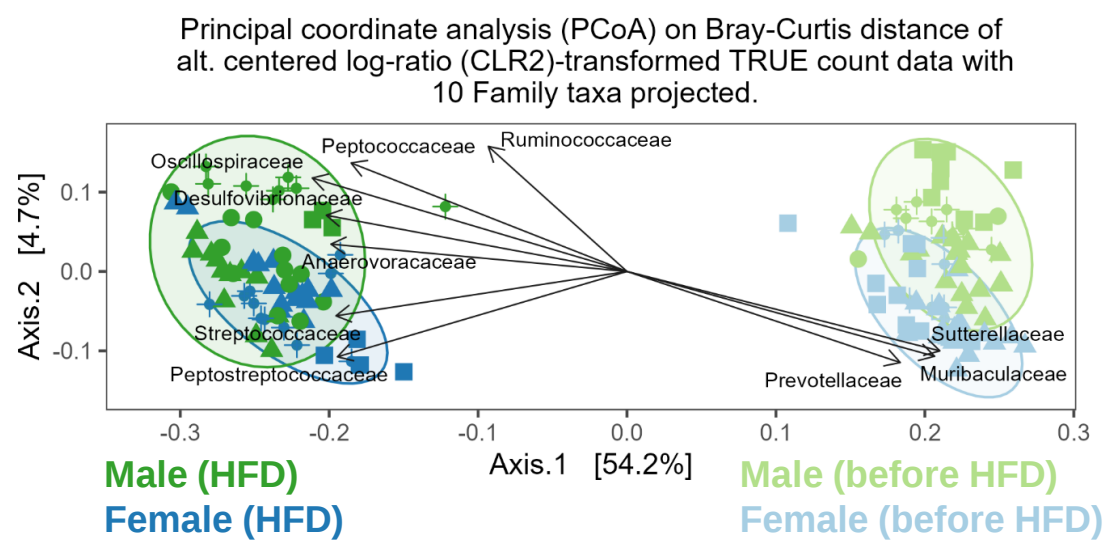
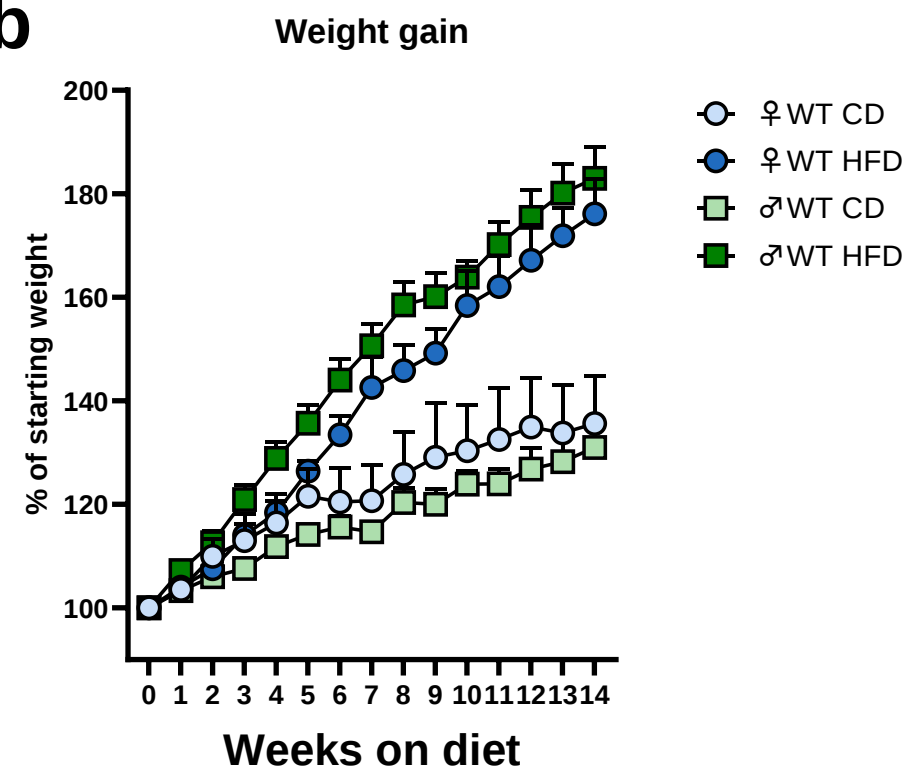


Supplemental Figure 1

a

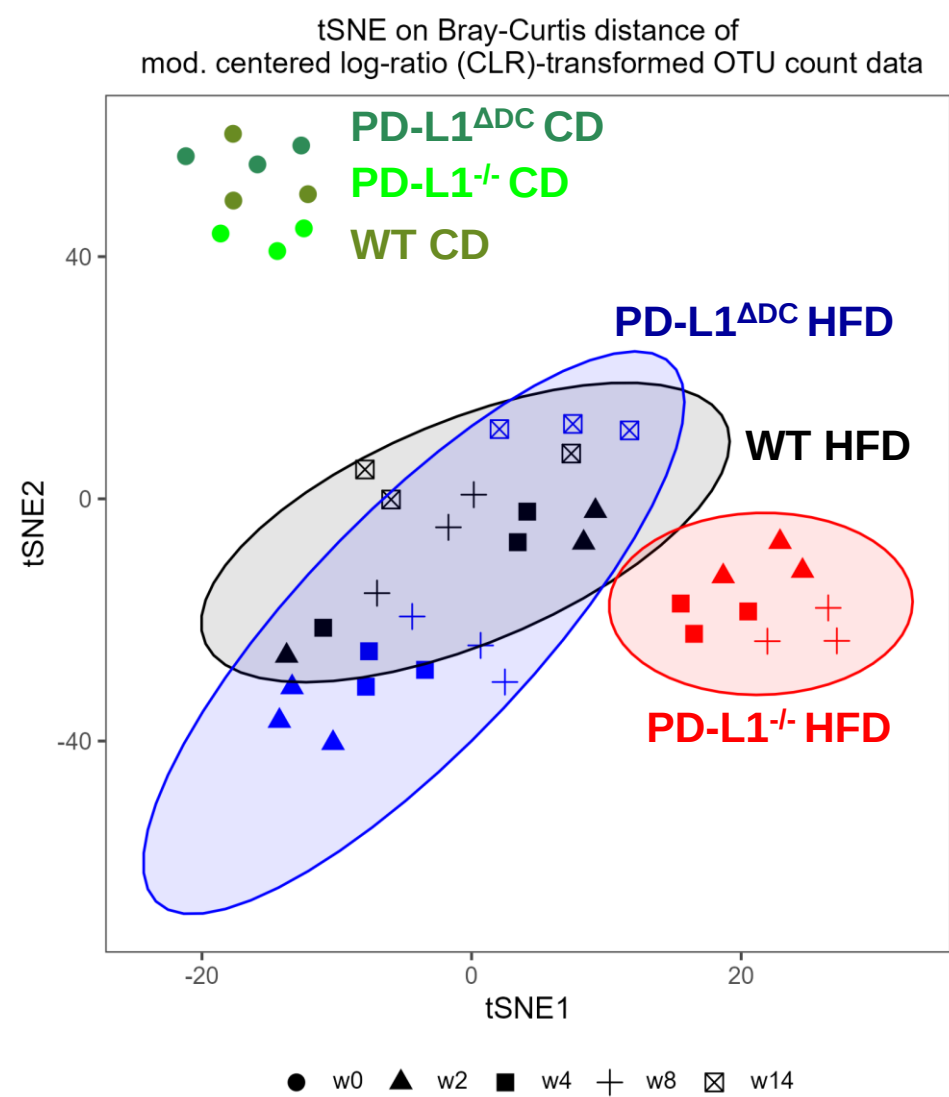


b



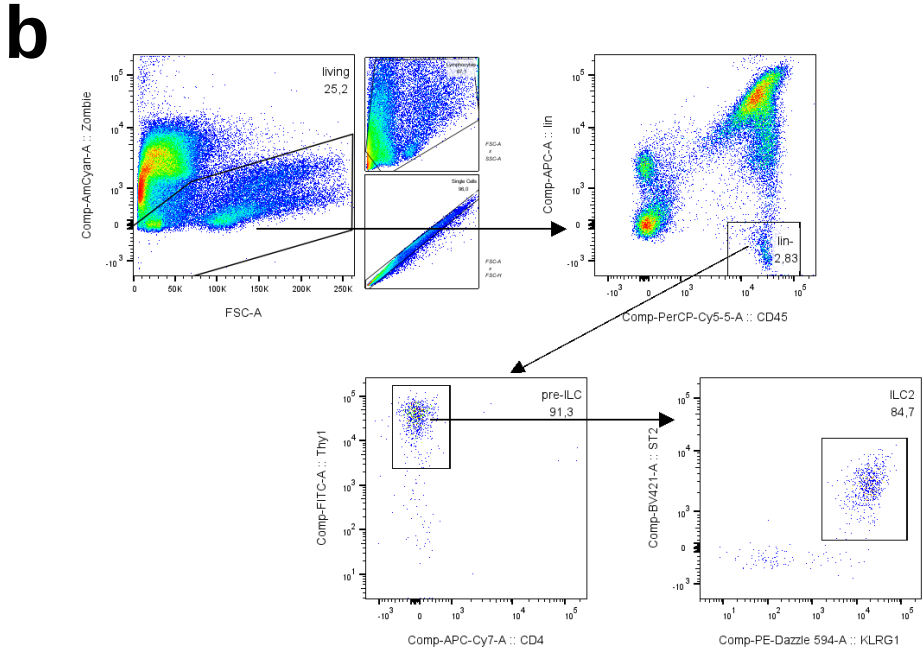
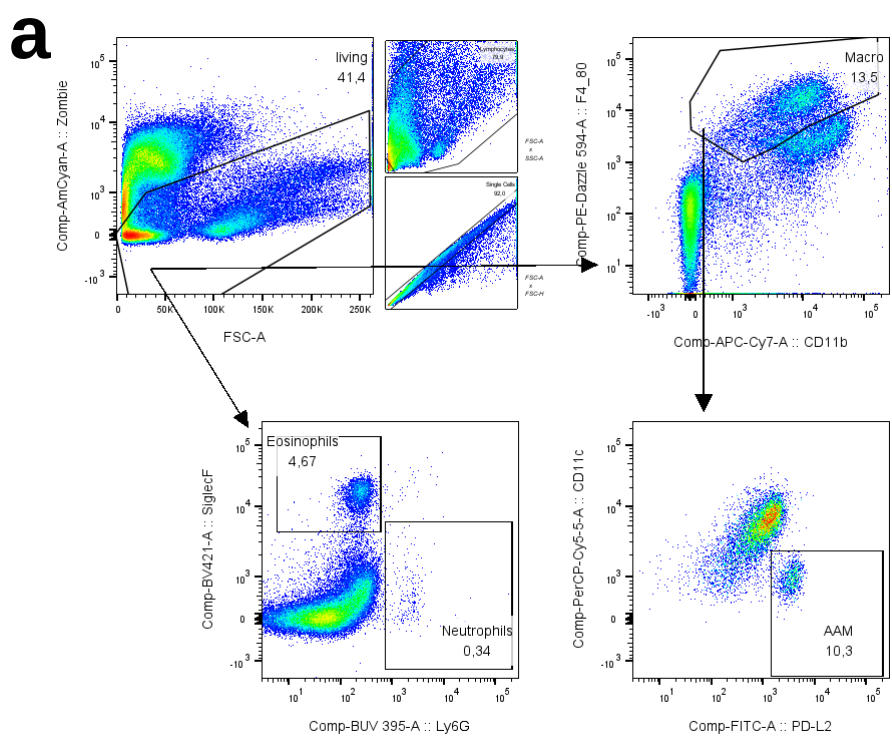
Supplemental Figure 1. a) Principal coordinate analysis of the microbiota of male and female mice before and on HFD. The ten family taxa with the highest differential abundance are indicated. b) Weight gain of male and female mice kept on CD or HFD. Data show the mean + SEM of 6 mice per group from two independent experiments.

Supplemental Figure 2



Supplemental Figure 2. tSNE plot on Bray-Curtis distance of CLR-transformed OTU count data. Depicted are the longitudinal data of WT, PD-L1^{-/-} and PD-L1^{ADC} mice before HFD diet feeding (closed circles, w0) and 2 (triangles), 4 (squares), 8 (crosshairs) and 14 weeks (crossed squares) on HFD. Representative data shown (n=3 per group) from one out of two independent experiments.

Supplemental Figure 3



Supplemental Figure 3. Representative gating strategy for flow cytometry data. a) Gating strategy for eosinophils (Siglec-F⁺Ly6G⁻), neutrophils (Siglec-F⁺Ly6G⁺) and alternatively activated macrophages (AAM; F4/80⁺CD11b⁺CD11c⁻PD-L2⁺) in white adipose tissue (WAT). b) Gating of WAT ILC2 (lineage⁻Thy1⁺ST2⁺KLRG1⁺).

Supplemental Table 1

Supplemental Table 1. Description of the clusters depicted in the unsupervised clustering heatmap in Figure 3b.

#	Taxon	Tax. level
Lean cluster (L)		
1	<i>Eubacterium nodatum</i> group	Genus
2	<i>Clostridioides</i>	Genus
3	ASF356	Genus
4	<i>Fusimonas</i>	Genus
5	<i>Amedibacillus</i>	Genus
6	<i>Parasutterella</i>	Genus
7	<i>Paramuribaculum</i>	Genus
8	<i>Anaerotignum</i>	Genus
9	<i>Otoolea</i>	Genus
10	<i>Muribaculaceae</i>	Family
11	<i>Alistipes</i>	Genus
12	<i>Kineothrix</i>	Genus
13	<i>Ruminococcus</i>	Genus
14	RF39	Order
15	<i>Sangeribacter</i>	Genus
16	<i>Lepagella</i>	Genus
17	<i>Limosilactobacillus</i>	Genus
18	<i>Lactobacillus</i>	Genus
19	<i>Turicimonas</i>	Genus
20	<i>Duncaniella</i>	Genus
21	<i>Muribaculum</i>	Genus
22	<i>Agathobaculum</i>	Genus
23	<i>Candidatus Stoquefichus</i>	Genus
24	<i>Gastranaerophilales</i>	Order
25	<i>Rhodospirillales</i>	Order
26	<i>Clostridia</i> UCG 014	Order
27	<i>Xylanibacter</i>	Genus
28	<i>Anaerostipes</i>	Genus
29	A2	Genus
30	UBA1819	Genus
31	<i>Lawsonibacter</i>	Genus
32	<i>Mordavella</i>	Genus
33	<i>Turicibacter</i>	Genus
34	<i>Butyricicoccus</i>	Genus
35	<i>Clostridia</i>	Class
36	<i>Lachnospiraceae</i> UCG 001	Genus
37	<i>Tyzzarella</i>	Genus
38	<i>Anaerobium</i>	Genus
39	<i>Lachnospiraceae</i> NK4A136 group	Genus

#	Taxon	Tax. level
Obesity cluster 1 (O1; "Adaptation")		
1	<i>Granulimonas</i>	Genus
2	<i>Thomasclavelia</i>	Genus
3	<i>Faecalibaculum</i>	Family
4	<i>Bacteroides</i>	Genus
5	<i>Romboutsia</i>	Genus
6	<i>Rikenellaceae</i> RC9 gut group	Genus
7	<i>Eisenbergiella</i>	Genus
8	GCA-900066575	Genus
9	<i>Hungatella</i>	Genus
10	<i>Coprobacillus</i>	Genus
11	<i>Erysipelatoclostridaceae</i>	Family
12	<i>Dubosiella</i>	Genus
13	<i>Parabacteroides</i>	Genus
14	<i>Alloprevotella</i>	Genus
15	<i>Desulfovibrio</i>	Genus
16	<i>Helicobacter</i>	Genus
17	<i>Mucispirillum</i>	Genus
18	<i>Mycoplasma</i>	Genus
19	<i>Absiella</i>	Genus

#	Taxon	Tax. level
Obesity cluster 2 (O2; "Obesity")		
1	<i>Akkermansia</i>	Genus
2	<i>Clostridia</i> vadinBB60 group	Order
3	UCG-010	Family
4	<i>Sporofaciens</i>	Genus
5	<i>Christensenellaceae</i>	Family
6	<i>Intestinimonas</i>	Genus
7	<i>Candidatus Sacharimonas</i>	Genus
8	<i>Anaerovorax</i>	Genus
9	<i>Streptococcus</i>	Genus
10	<i>Acetivibrio</i>	Genus
11	<i>Anaerotruncus</i>	Genus
12	<i>Eubacterium coprostanoligenes</i> gr.	Family
13	<i>Roseburia</i>	Genus
14	<i>Incertae Sedis</i>	Genus
15	<i>Lachnoclostridium</i>	Genus
16	<i>Enterorhabdus</i>	Genus
17	<i>Schaedlerella</i>	Genus
18	<i>Lachnospiraceae</i> FCS020 group	Genus
19	<i>Neglectibacter</i>	Genus
20	<i>Oscillospiraceae</i>	Family
21	<i>Peptococcaceae</i>	Genus
22	UCG-009	Genus
23	<i>Lachnospiraceae</i>	Family
24	<i>Mailhella</i>	Genus
25	<i>Flintibacter</i>	Genus
26	<i>Ruminococcaceae</i>	Family
27	<i>Oscillibacter</i>	Genus
28	<i>Negativibacillus</i>	Genus
29	<i>Bilophila</i>	Genus
30	<i>Peptococcus</i>	Genus
31	<i>Desulfovibrionaceae</i>	Family
32	<i>Pseudoflavonifractor</i>	Genus
33	<i>Eubacterium xylanophilum</i> group	Genus
34	<i>Lachnospiraceae</i> UCG-006	Genus
35	<i>Eubacterium brachy</i> group	Genus
36	NK4A214 group	Genus
37	<i>Odoribacter</i>	Genus
38	<i>Colidextribacter</i>	Genus
39	UCG-003	Genus
40	<i>Rikenella</i>	Genus
41	<i>Robinsoniella</i>	Genus
42	<i>Ligilactobacillus</i>	Genus
43	<i>Firmicutes</i>	Phylum
44	<i>Lactobacillaceae</i>	Family
45	<i>Clostridium</i>	Genus
46	<i>Hominisplanchenecus</i>	Genus
47	<i>Enterococcus</i>	Genus
48	<i>Acetatifactor</i>	Genus
49	<i>Murimonas</i>	Genus
50	<i>Culturomica</i>	Genus
51	<i>Erysipelotrichaceae</i>	Family
52	<i>Blautia</i>	Genus

Supplemental Table 2

Supplemental Table 2. Comparison of microbiome changes in PD-L1-/- mice and anti-PD-L1-treated WT mice under HFD. Orange-highlighted rows indicate concordant PD-L1-dependent changes (key overlap). Arrows indicate direction of change (↑ increased, ↓ decreased).

Taxon	Cluster	PD-L1 ^{-/-} vs. WT (HFD)	anti-PD-L1 vs. isotype (HFD)	Overlap
Lean-associated taxa (lost under HFD)				
<i>Lachnospiraceae</i> (UCG-001, NK4A136)	Lean	↓ under HFD	↓ under HFD	Concordant ↓
<i>Muribaculaceae</i>	Lean	↓ under HFD	↓ under HFD	Concordant ↓
<i>Parasutterella</i>	Lean	↓ under HFD	↓ under HFD	Concordant ↓
<i>Bifidobacterium</i>	Lean	↓ under HFD	↓ under HFD	Concordant ↓
<i>RF39/Gastranaerophilales</i>	Lean	↓ under HFD	↓ under HFD	Concordant ↓
PD-L1-dependent divergence under HFD				
<i>Christensenellaceae</i>	Adaptation	↑ vs. WT-HFD	↑ vs. isotype	Concordant ↑
<i>Bacteroidales</i>	Adaptation	↑ vs. WT-HFD	↑ vs. isotype	Concordant ↑
<i>Akkermansia</i>	Adaptation	↑ vs. WT-HFD	↑ vs. isotype	Concordant ↑
<i>Erysipelotrichaceae</i>	Adaptation	↑ vs. WT-HFD	↑ vs. isotype	Concordant ↑
<i>Parabacteroides</i>	Adaptation	↑ vs. WT-HFD	↑ vs. isotype	Concordant ↑
<i>Rikenellaceae</i>	Adaptation	differential	↑ vs. isotype	Partial overlap
<i>Faecalibaculum</i>	Adaptation	differential	↑ vs. isotype	Partial overlap
<i>Odoribacter</i>	Obesity	↓ vs. WT-HFD	↓ vs. isotype	Concordant ↓
<i>Escherichia/Shigella</i>	Obesity	↓ vs. WT-HFD	↓ vs. isotype	Concordant ↓
<i>Streptococcus</i>	Obesity	↓ vs. WT-HFD	↓ vs. isotype	Concordant ↓
Classic obesity-associated taxa (<i>Oscillospiraceae</i> -dominated)				
<i>Oscillospiraceae</i>	Obesity	↑ but < WT	↑ but < isotype	Concordant (attenuated ↑)
<i>Peptostreptococcaceae</i>	Obesity	↑	↑	Concordant ↑
<i>Romboutsia</i>	Obesity	↑	↑	Concordant ↑
<i>Bilophila</i>	Obesity	↑	↑	Concordant ↑
HFD-sensitive, PD-L1-independent				
<i>Mucispirillum</i>	Other	↓ under HFD	↓ under HFD	Not PD-L1-dependent
<i>Tyzzereella</i>	Other	↓ under HFD	↓ under HFD	Not PD-L1-dependent
<i>Lachnoclostridium</i>	Other	↓ under HFD	↓ under HFD	Not PD-L1-dependent