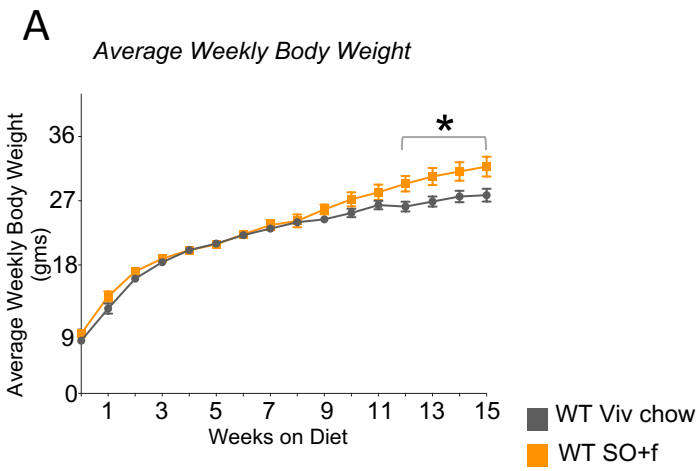
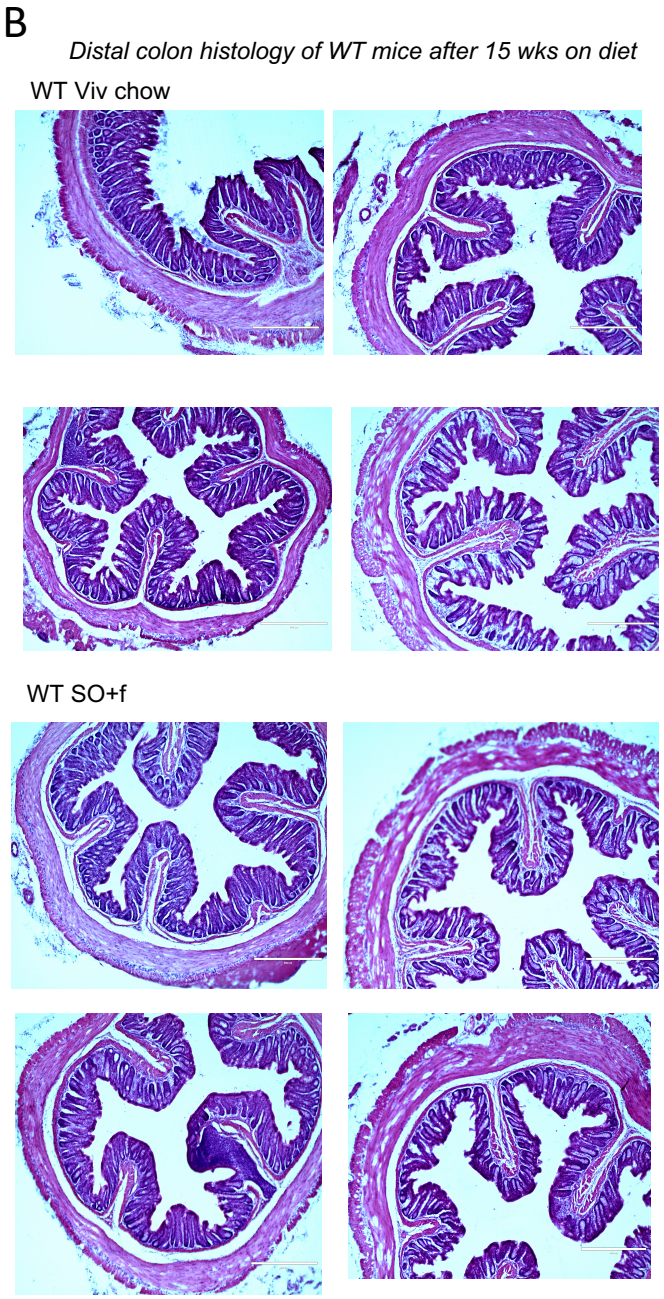
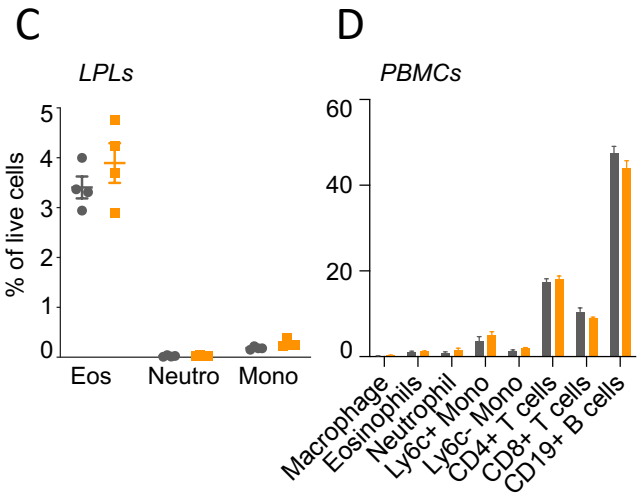
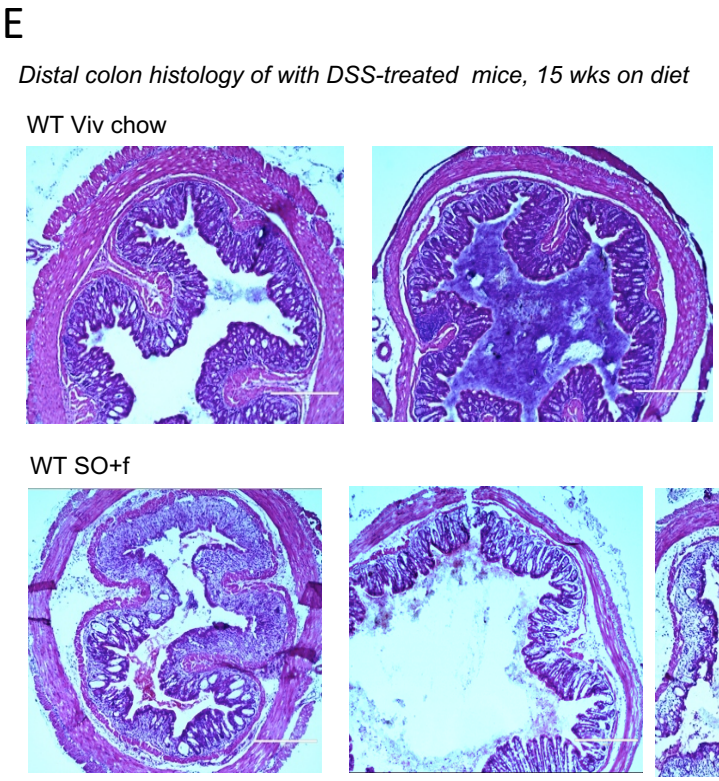


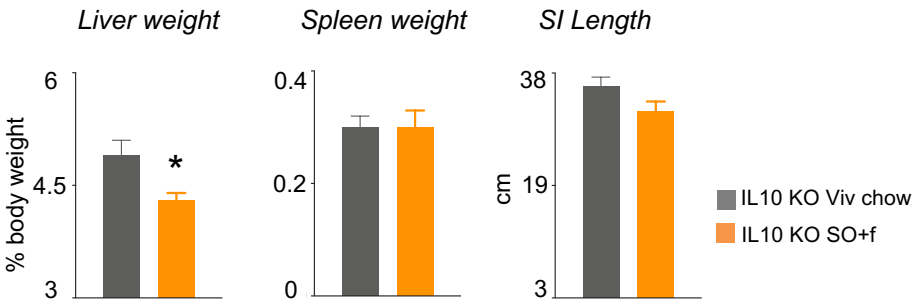






Supplementary Figure 1. Effect of soybean oil diet on DSS-induced colitis in WT male mice. Weekly body weights (**A**), colonic histology (**B**), immune cell analysis of lamina propria lymphocytes (LPLs, **C**) and PBMCs (**D**) in WT mice after 15 weeks on Viv chow or SO+f diet. **P* < 0.05, T-test. N=3-8 per group Colonic histology (**E**) in WT mice after 15 weeks on diet followed by 6-day DSS treatment. Scale bar for is 100 μm, images taken at 10x magnification (**C**,**E**).

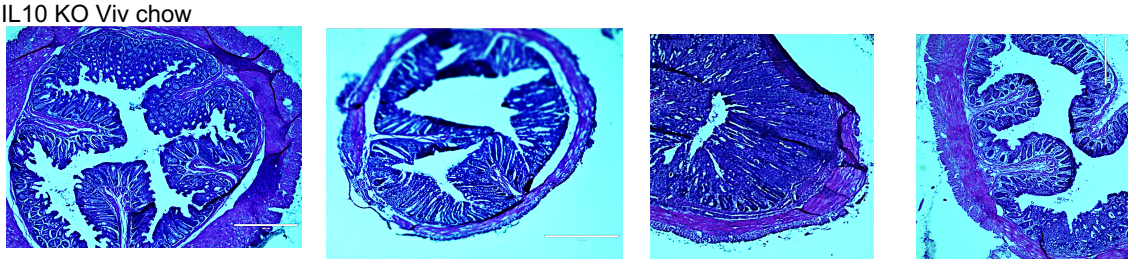
A



B

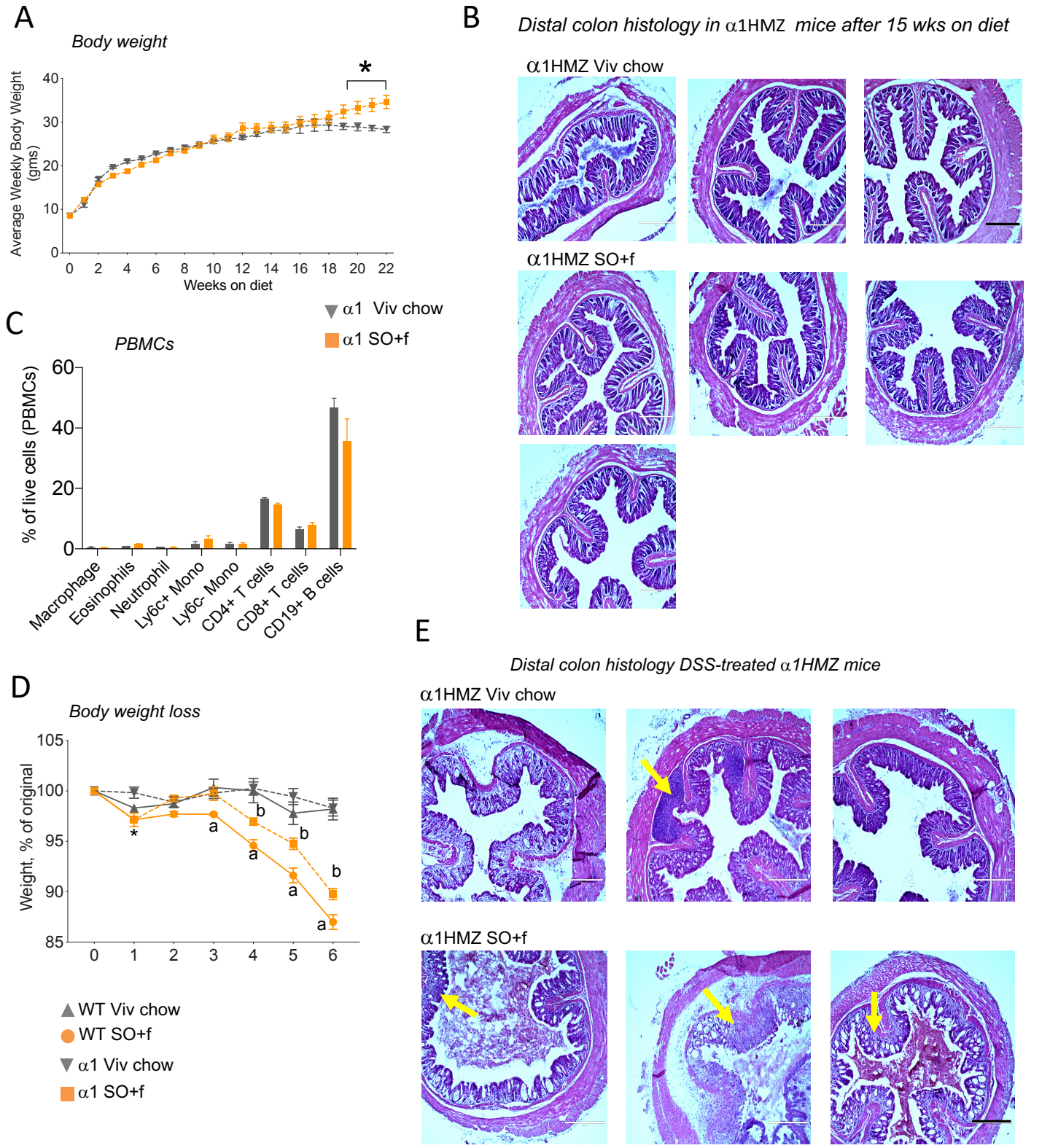
Distal colon histology

IL10 KO Viv chow

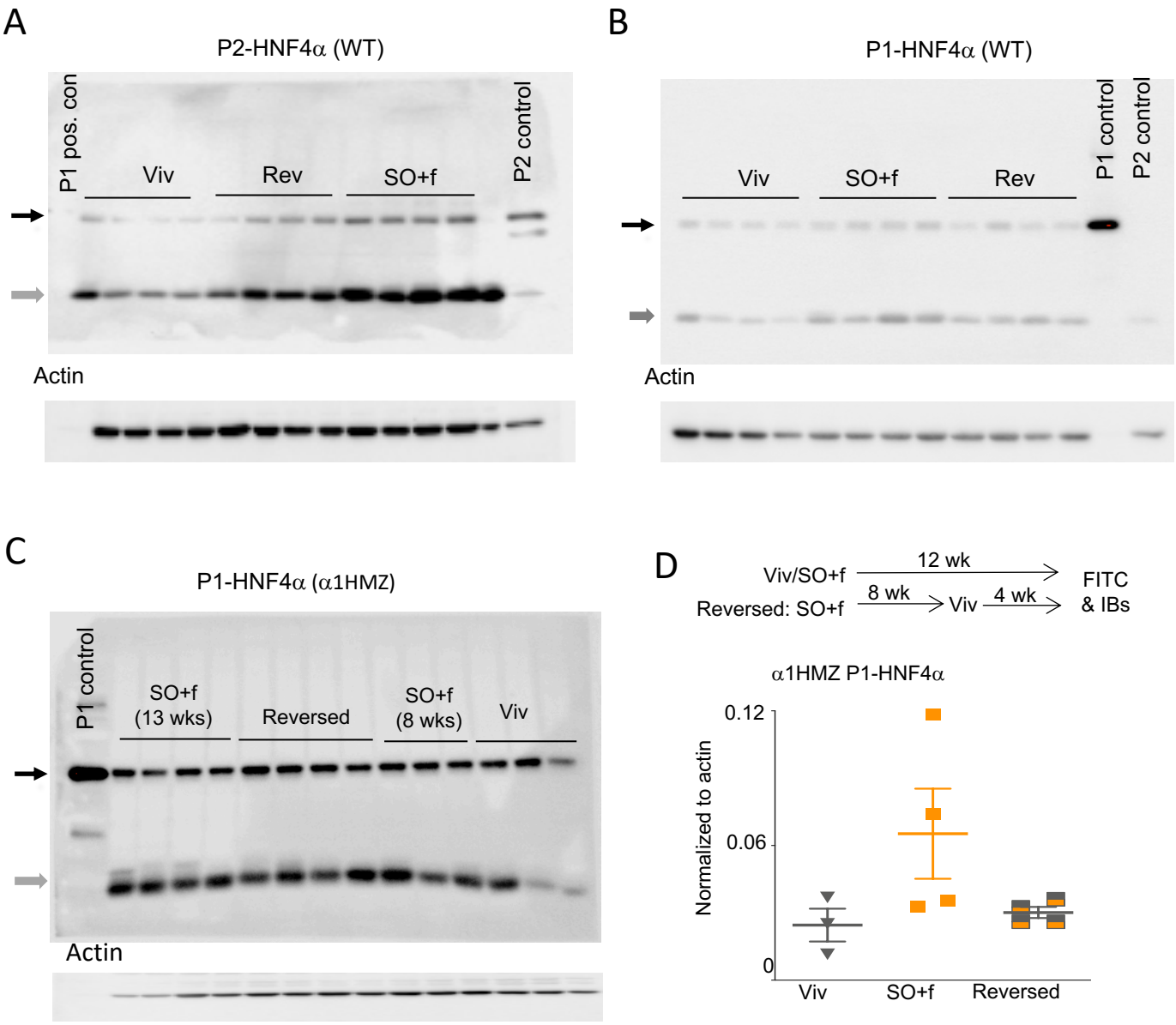


IL10 KO SO+f

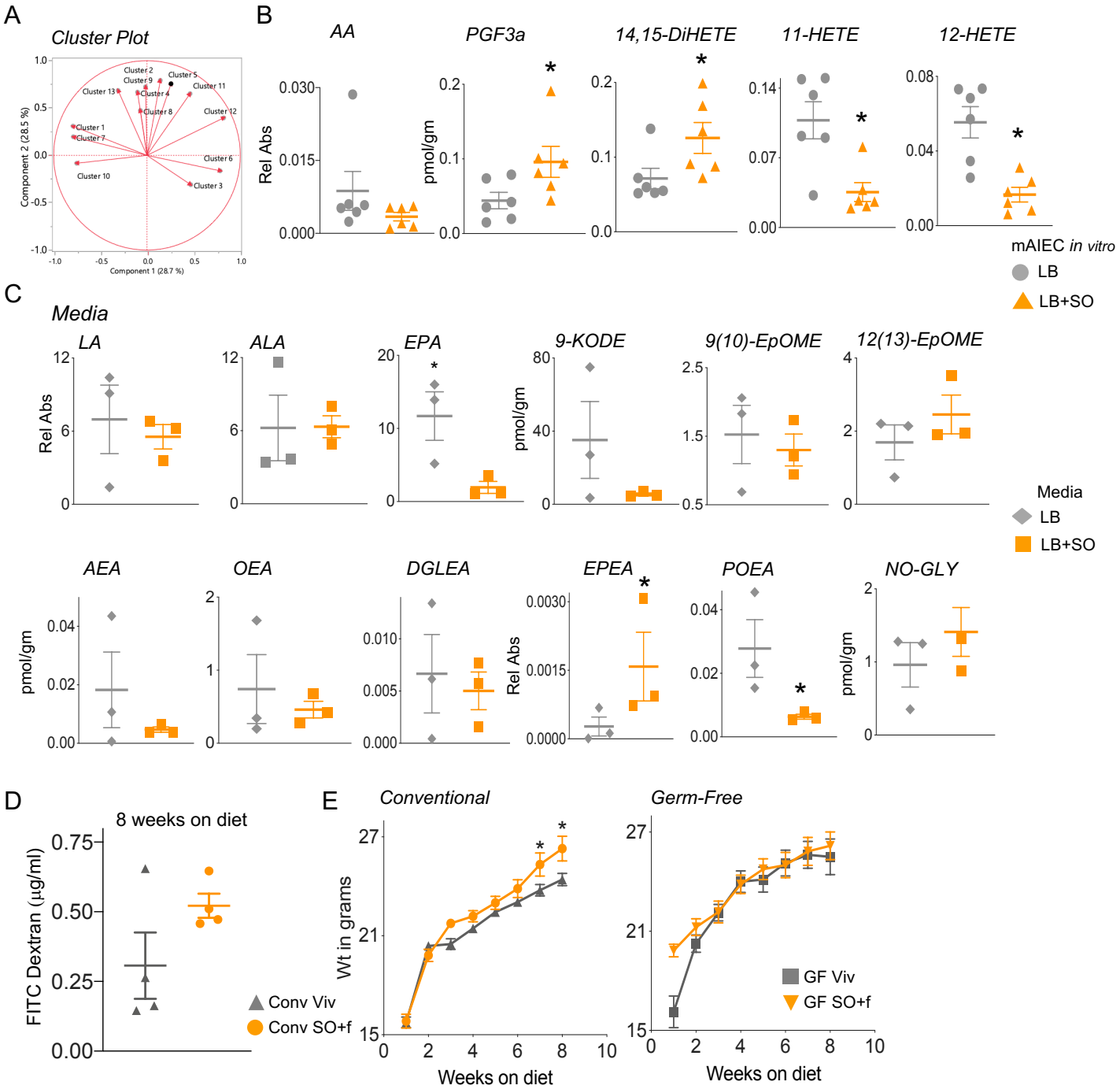
Supplementary Figure 2. Effect of soybean oil diet on IL10 deficient male mice.
Liver and spleen weights as percent of body weight and small intestinal length (**A**) and colonic histology (**B**) in IL10 KO mice after 10 weeks on Viv chow and SO+f diet. Scale bar for is 100 μm, images taken at 10x magnification. * $P < 0.05$ vs other diet, T-test. N=5-12 per group.



Supplementary Figure 3. Effect of soybean oil diet on DSS-induced colitis in α1HMZ male mice.
Weekly body weights up to 22 weeks on diet (**A**), colonic histology (**B**) and immune analysis in peripheral blood mononuclear cells (PBMCs) after 15 weeks on diet in α1HMZ mice (**C**). **D)** Comparison of % body weight loss between WT and α1HMZ mice on Viv chow or SO+f for 15 weeks, treated with 2.5% DSS in drinking water for 6 days (same data as in Fig. 1A and 2A). * α1HMZ SO+f vs α1HMZ Viv, ^{a} WT SO+f vs WT Viv, ^{b} α1HMZ SO+f vs WT SO+f: $P < 0.05$ vs other diet, repeated measures 2-way ANOVA, Tukey's post-hoc. N=3-4 per group **E)** Colonic histology in α1HMZ mice after 15 weeks on diet followed by 6-day DSS treatment. Arrow: immune cell infiltrate.



Supplementary Figure 4. Effect of soybean oil diet on HNF4α isoform balance in the colon. A-C) HNF4α immunoblots (quantification shown in Figure 2F)**.** P1 control-nuclear extract from HCT116 cells expressing P1-HNF4α ; P2 control-nuclear extract from α7HMZ mouse. Black arrow: HNF4α; Gray arrow: non-specific band. **D)** Quantification of the P1-HNF4α signal normalized to total protein, as determined by actin staining of the same blot. N=3-4 per group.



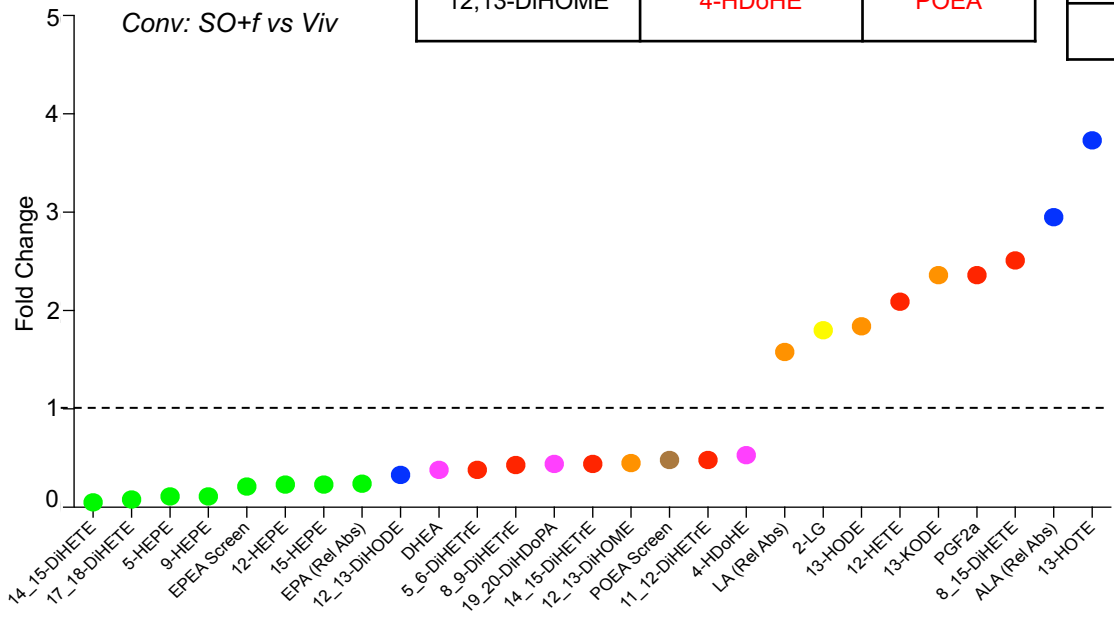
Supplementary Figure 5. Effect of soybean oil on metabolome of of mAIEC grown *in vitro* and barrier function, body weight and metabolome of germ-free vs conventional mice.
Cluster plot for Principal Components Analysis (PCA) shown in Figure 4A (**A**) and absolute levels of fatty acids, oxylipin and endocannabinoid metabolites in mAIEC grown with or without soybean oil in media (**B**) and the media (Luria Broth, with or without added SO) (**C**). **D)** Epithelial permeability in conventionally raised WT mice after 8 weeks on indicated diet. **E)** Weekly body weights in indicated groups of mice. * $P < 0.05$, T-test. N=6-8 per group. **F)** Cluster plot for PCA shown in Figure 5B of oxylipin and endocannabinoid metabolites in IECs from conventional or germ-free WT mice on SO+f or Viv diets for 8 wks. N=6 per group.

Dysregulated Metabolites in SO+f vs Viv chow in Conv mice only
13-HODE
13-HOTE
13-KODE
PGF2a
8,9-DiHETrE
11,12-DiHETrE

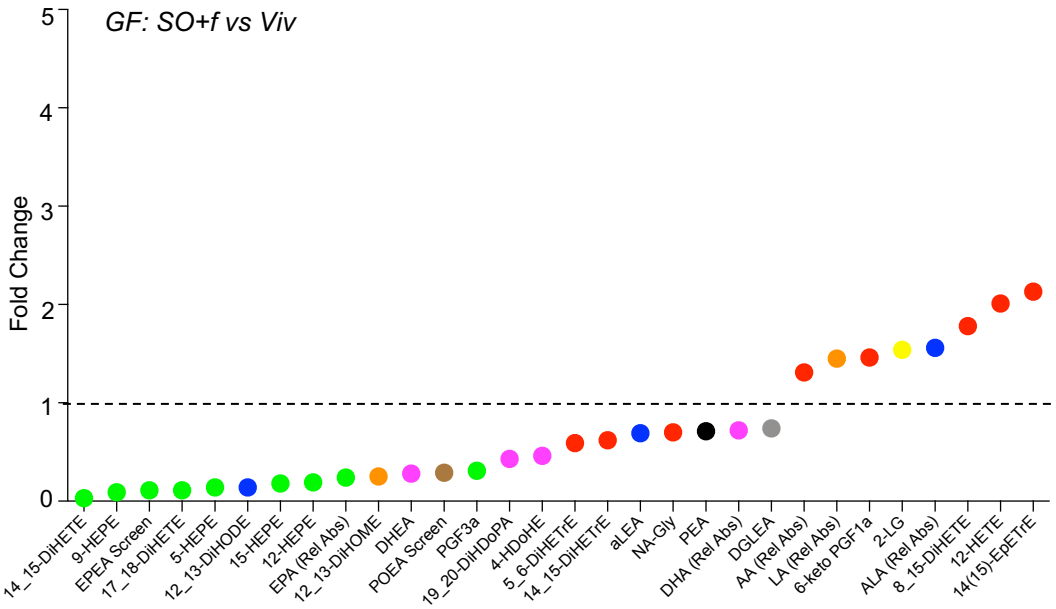
Dysregulated Metabolites in SO+f vs Viv chow in Conv and GF mice		
12-HETE	12-HEPE	5, 6-DiHETrE
2-LG	14,15-DiHETE	5-HEPE
8,15-DiHETE	14,15-DiHETrE	9-HEPE
ALA	15-HEPE	DHEA
LA	17,18-DiHETE	EPA
12,13-DiHODE	19,20-DiHDoPA	EPEA
12,13-DiHOME	4-HDoHE	POEA

Dysregulated Metabolites in SO+f vs Viv chow in GF mice only
14(15)-EpETrE
6-keto PGF1a
AA
aLEA
DGLEA
DHA
NA-Gly
PEA
PGF3a

* Red font- down in Viv chow fed mice



- ALA- alpha linoleic acid
- EPA- eicosapentenoic acid
- LA- linoleic acid
- AA- arachidonic acid
- POA- palmitoleic acid
- DHA- docosahexenoic acid
- OA- oleic acid
- LG- linoleoyl glycerol
- PA- palmitic acid
- DGLA- Dihomo-γ-linolenic acid

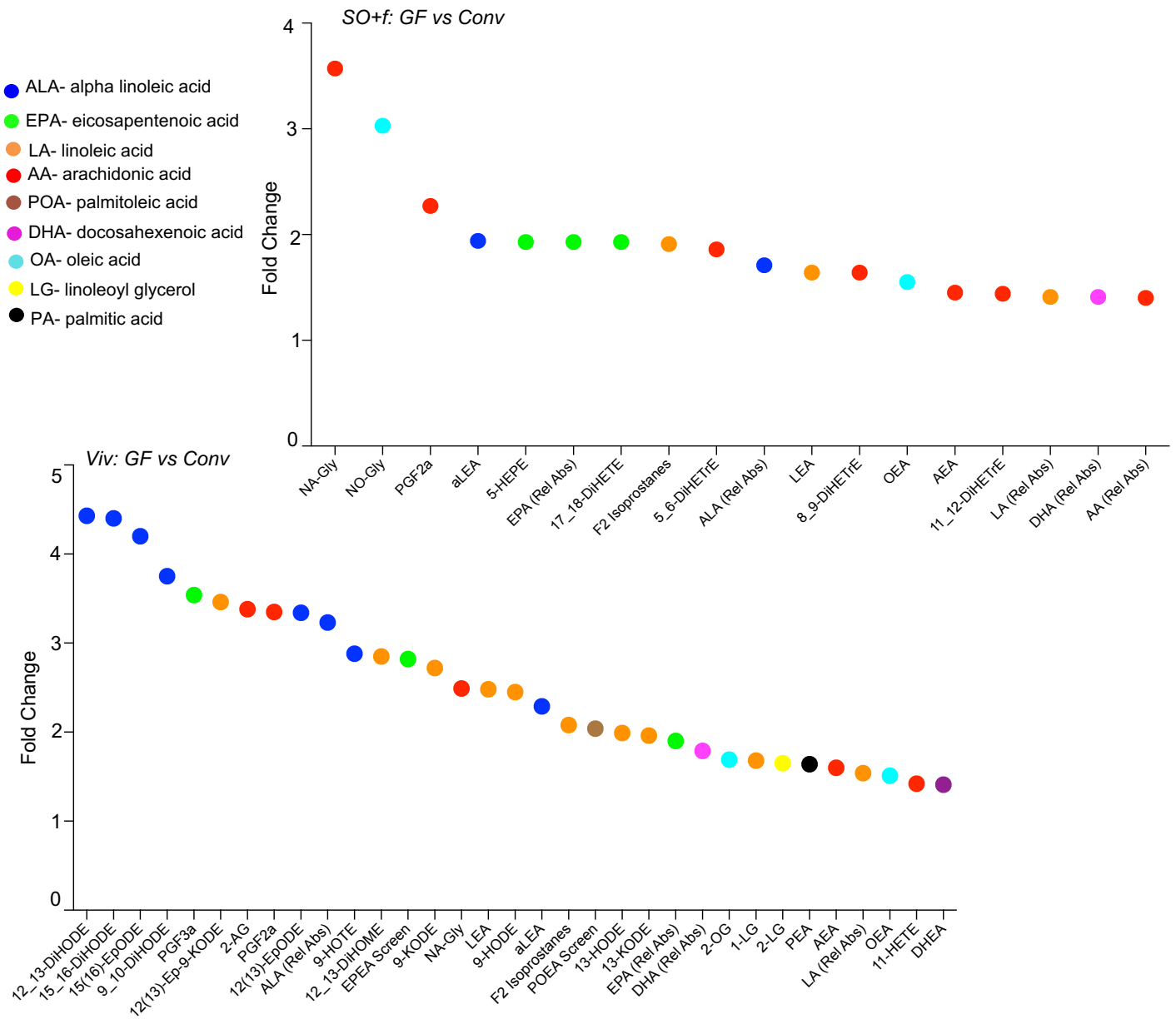


Supplementary Figure 6. Comparison of effect of diet on metabolite levels in IECs of conventional and germ-free mice.

Dysregulated Metabolites in GF vs Conv in Viv chow only		
1-LG	15, 16-DiHODE	9-KODE
11-HETE	15(16)-EpODE	DHEA
12,13-DiHODE	2-AG	EPEA
12, 13-DiHOME	2-LG	PEA
12(13)-Ep-9-KODE	2-OG	PGF3a
12(13)-EpODE	9, 10-DiHODE	POEA
13-HODE	9-HODE	
13-KODE	9-HOTE	

Dysregulated Metabolites in GF vs Conv in Viv and SO+f	
AEA	LA
ALA	LEA
aLEA	NA-Gly
DHA	OEA
EPA	PGF2a
F2 Isoprostanes	

Dysregulated Metabolites in GF vs Conv in SO+f only
11, 12-DiHETrE
17, 18-DiHETE
5, 6-DiHETrE
5-HEPE
8, 9-DiHETrE
AA
NO-Gly



Supplementary Figure 7. Comparison of effect of microbiome on metabolite levels in IECs of conventional versus germ-free mice.