

Supplementary Materials

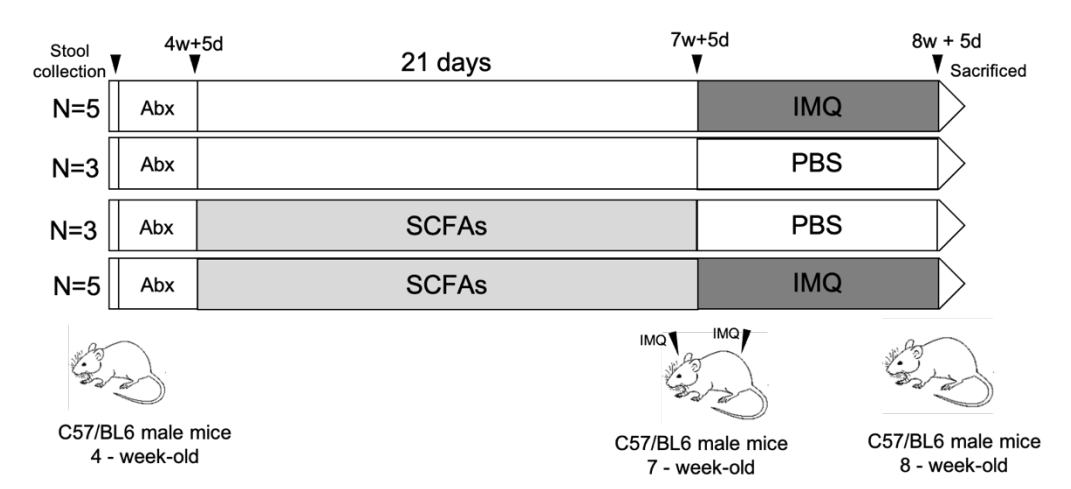
Supplementary Figure 1. Schematic of the experimental protocol for evaluating the impact of short-chain fatty acids (SCFAs) and anti-IL17 treatment in IMQ-induced inflammation in mice. (A) Initial experiments assessed the effects of topical IMQ application on mice, with and without SCFAs. (B) Further experiments examined the influence of anti-IL17 on the response of mice pre-treated with SCFAs. After 3 days of acclimatization, mice aged 4 weeks were treated with antibiotics for 2 days, followed by 21 days of SCFAs in drinking water. At 7 weeks of age, mice received topical IMQ and concurrent anti-IL17 (or isotype control) injections for 7 days. Mice were sacrificed at 8 weeks of age for analyses. Stool samples were collected for microbiome analysis before and after SCFAs and IMQ treatments. Anti-IL17A and IgG-isotype controls were administered twice a week. IMQ, imiquimod; SCFAs, short-chain fatty acids.

Supplementary Figure 2: Skin changes in mice ears Following Various Treatments. (A, B, C) Treatment with Short-Chain Fatty Acids (SCFAs) and IL-17 antagonists resulted in a significant reduction of imiquimod (IMQ)-induced skin thickening in the right ear (treated) as compared to the IMQ-IgG-isotype control group. * p value <0.05, ** p value <0.01. (D) Immunohistochemical staining and subsequent analysis with Image J software revealed a reduction in epidermis thickness gain in the treated right ear among mice receiving SCFAs and anti-IL17 treatment. * p value <0.05. (E) SCFAs and anti-IL17 significantly reduced IMQ-induced skin erythema/scaling and (F) splenic weight in IMQ mice. The comparison of organ weight changes of (G) spleen, (H) liver, and (I) fat tissue on various experimental groups. IMQ, imiquimod; SCFAs, short-chain fatty acids; PBS, phosphate buffered saline.

Supplementary Figure 3. The alpha-diversity of fecal microbiome before and after IMQ treatment, between different treatment groups of mice, such as (A) SCFAs+IMQ+IgG-isotype vs. SCFAs+IMQ+anti-IL17, (B) SCFAs + IMQ vs. SCFAs + PBS, and (C) IMQ + IgG-isotype vs. SCFAs +IMQ + IgG-isotype. ST3 is the time point before IMQ; ST is the time point after IMQ. IMQ, imiquimod; SCFAs, short-chain fatty acids; PBS, phosphate buffered saline.

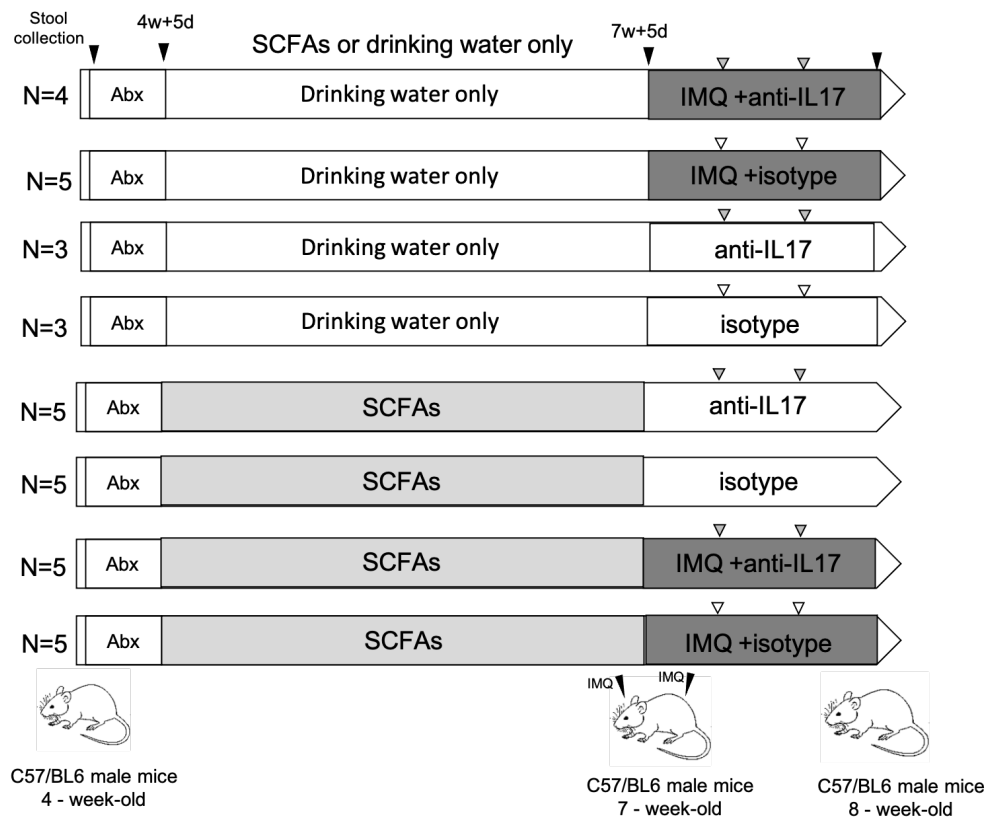
Supplementary Figure 4. Immunohistochemical (IHC) analysis for epithelial tight junction proteins of different treatment groups. (A) Nuclear Claudin-3 expression was not significantly lost in the ear skin, (B) ileum, and (C) colon epithelium. The expression pattern of Claudin-2 was similar, not presented here. IMQ, imiquimod; PBS, phosphate buffered saline; SCFAs, short-chain fatty acids.

Supplementary Figure 1A.

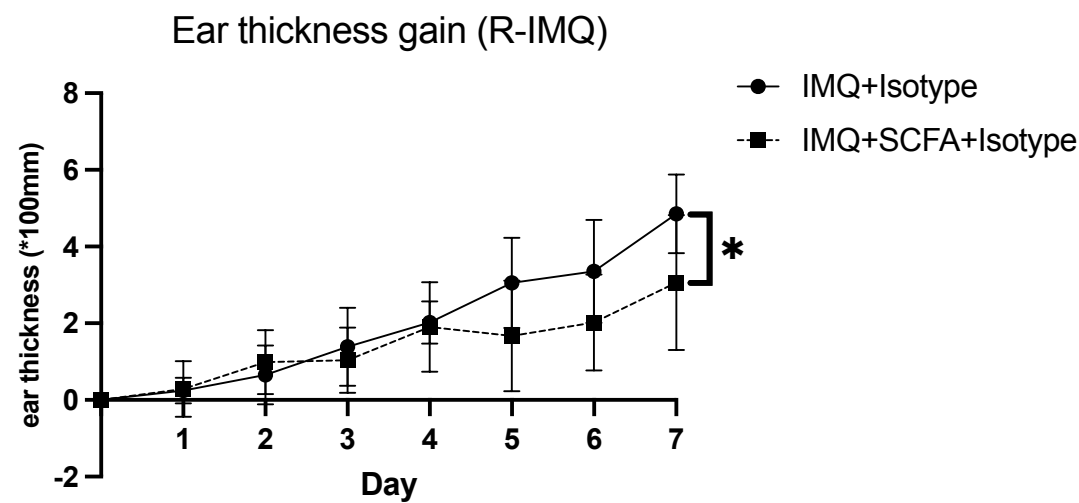


IMQ, imiquimod. SCFAs, short-chain fatty acids.

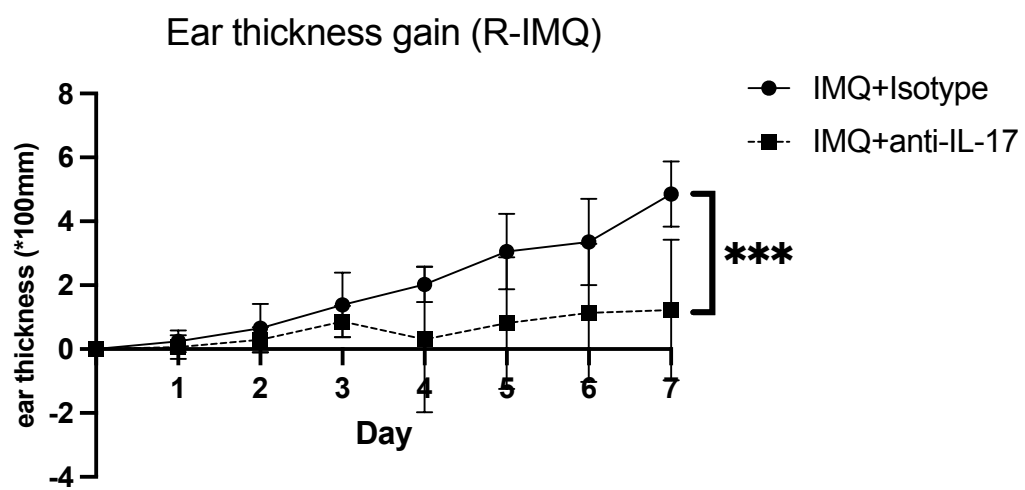
Supplementary Figure 1B.



Supplementary Figure 2A.

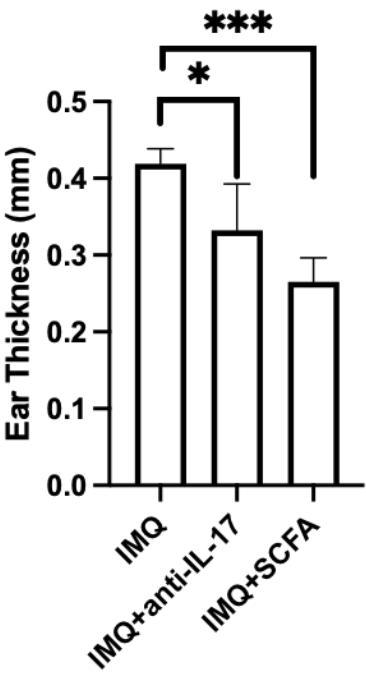


* p value < 0.05 , ** p value < 0.01 , *** p value < 0.001

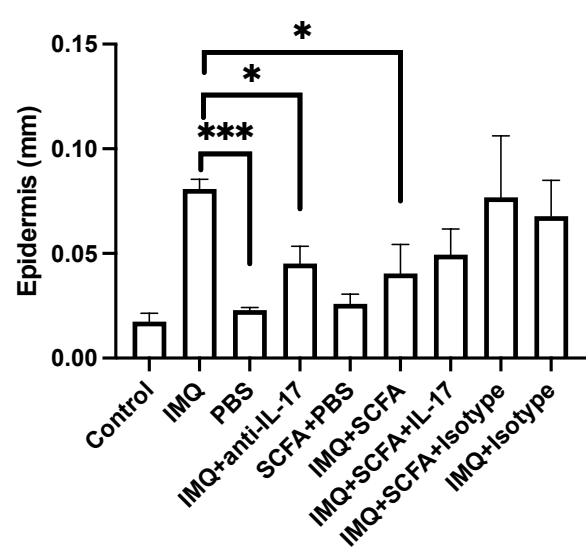


* p value < 0.05 , ** p value < 0.01 , *** p value < 0.001

Supplementary Figure 2C.

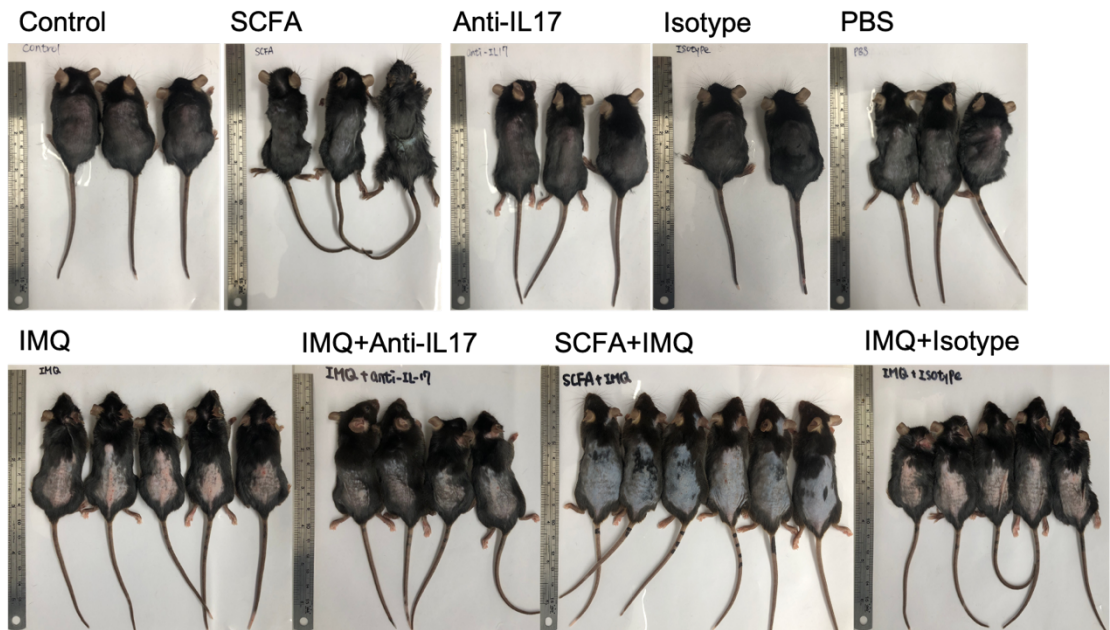


Supplementary Figure 2D.

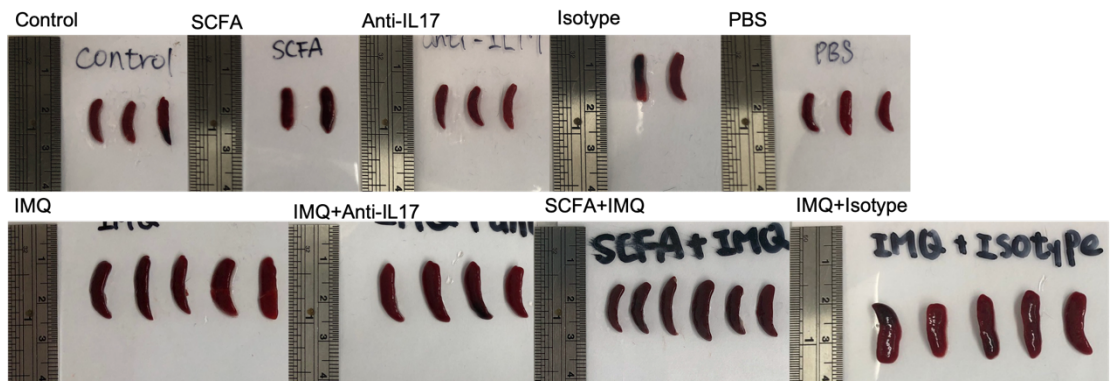


* p value < 0.05, ** p value < 0.01, *** p value < 0.001.

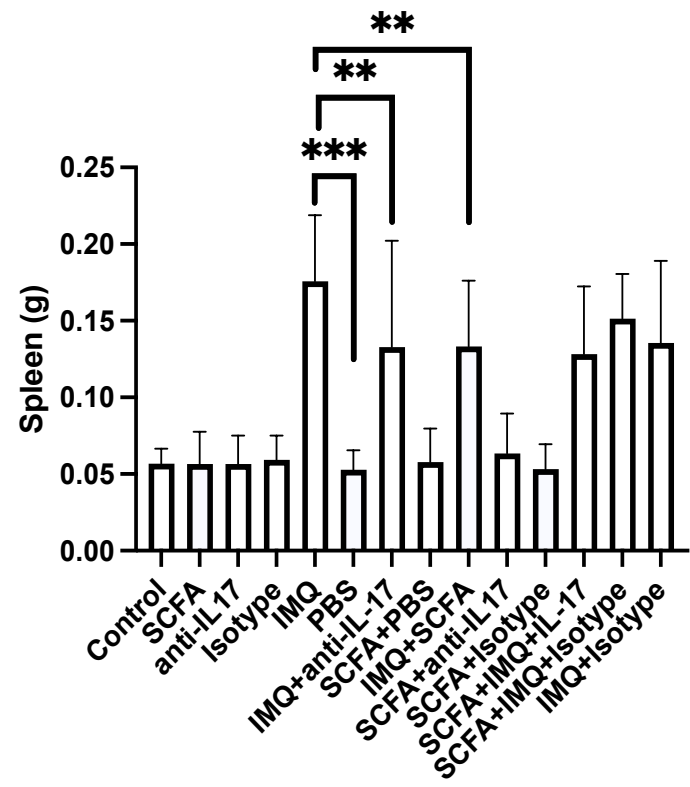
Supplementary Figure 2E.



Supplementary Figure 2F.

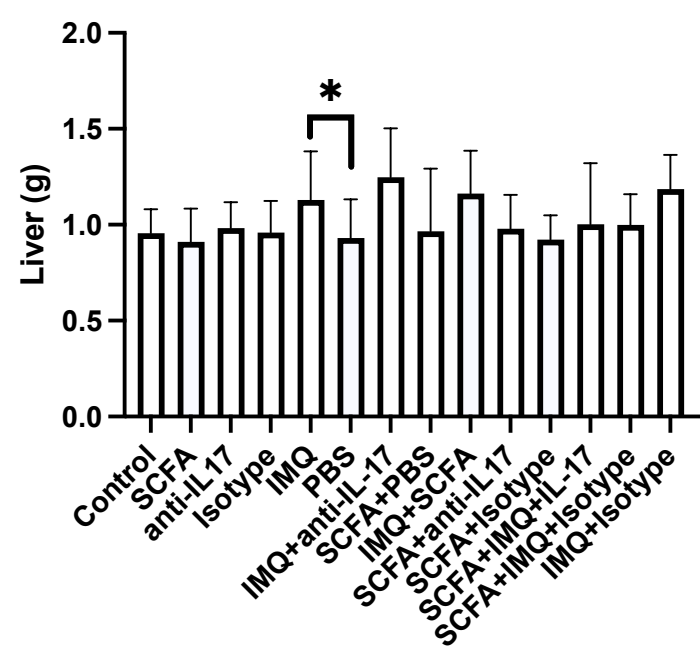


Supplementary Figure 2G.



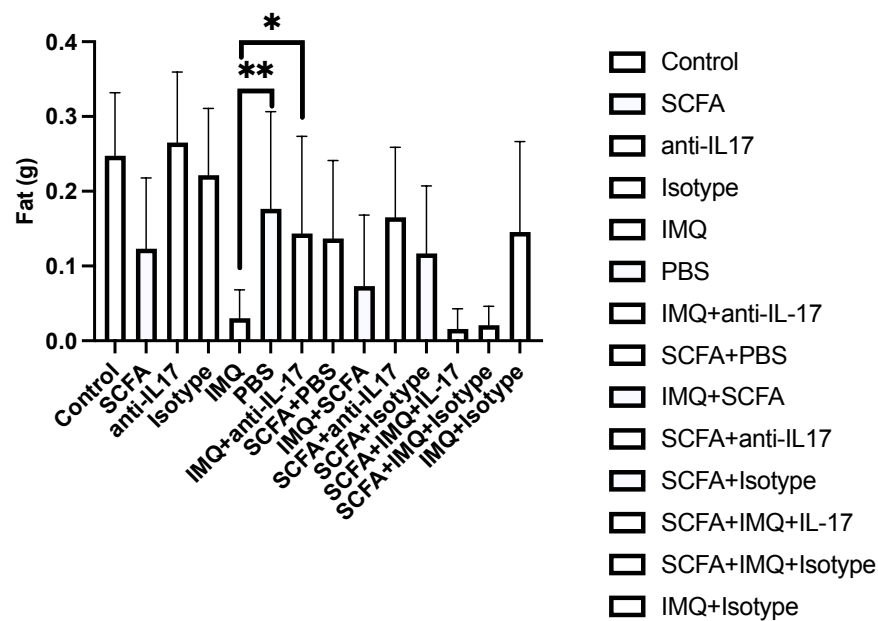
* p value < 0.05, ** p value < 0.01, *** p value < 0.001

Supplementary Figure 2H



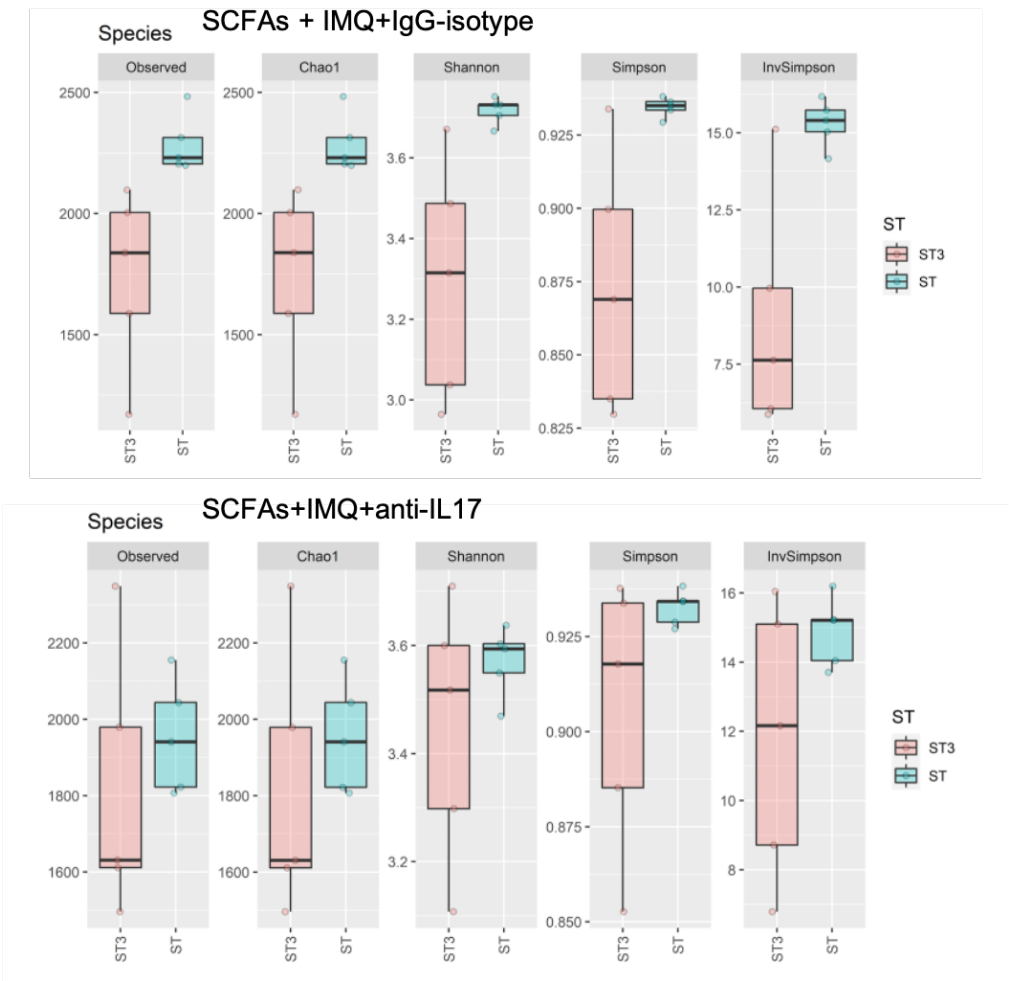
* p value < 0.05, ** p value < 0.01, *** p value < 0.001

Supplementary Figure 2I.

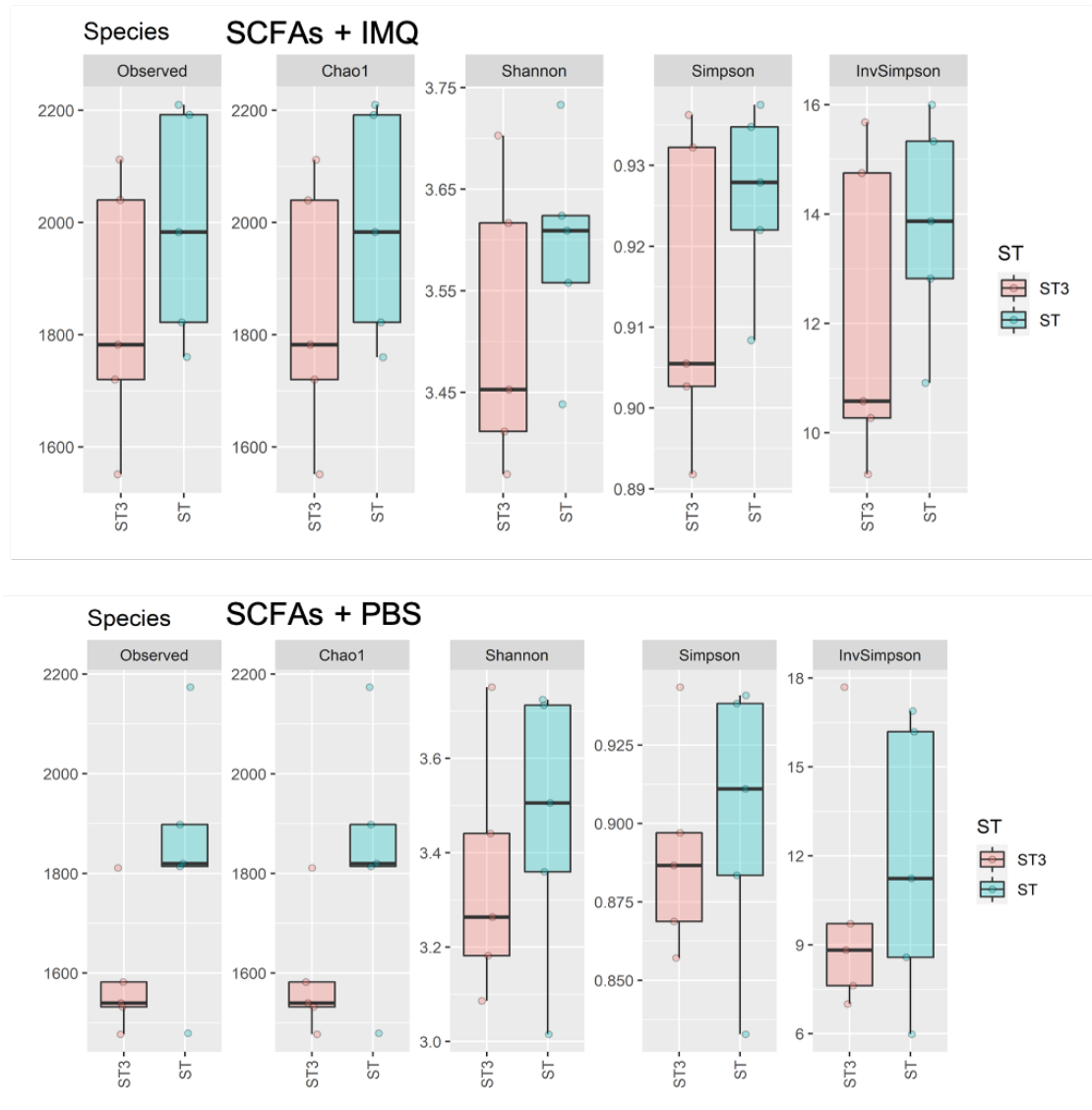


* p value < 0.05, ** p value < 0.01, *** p value < 0.001

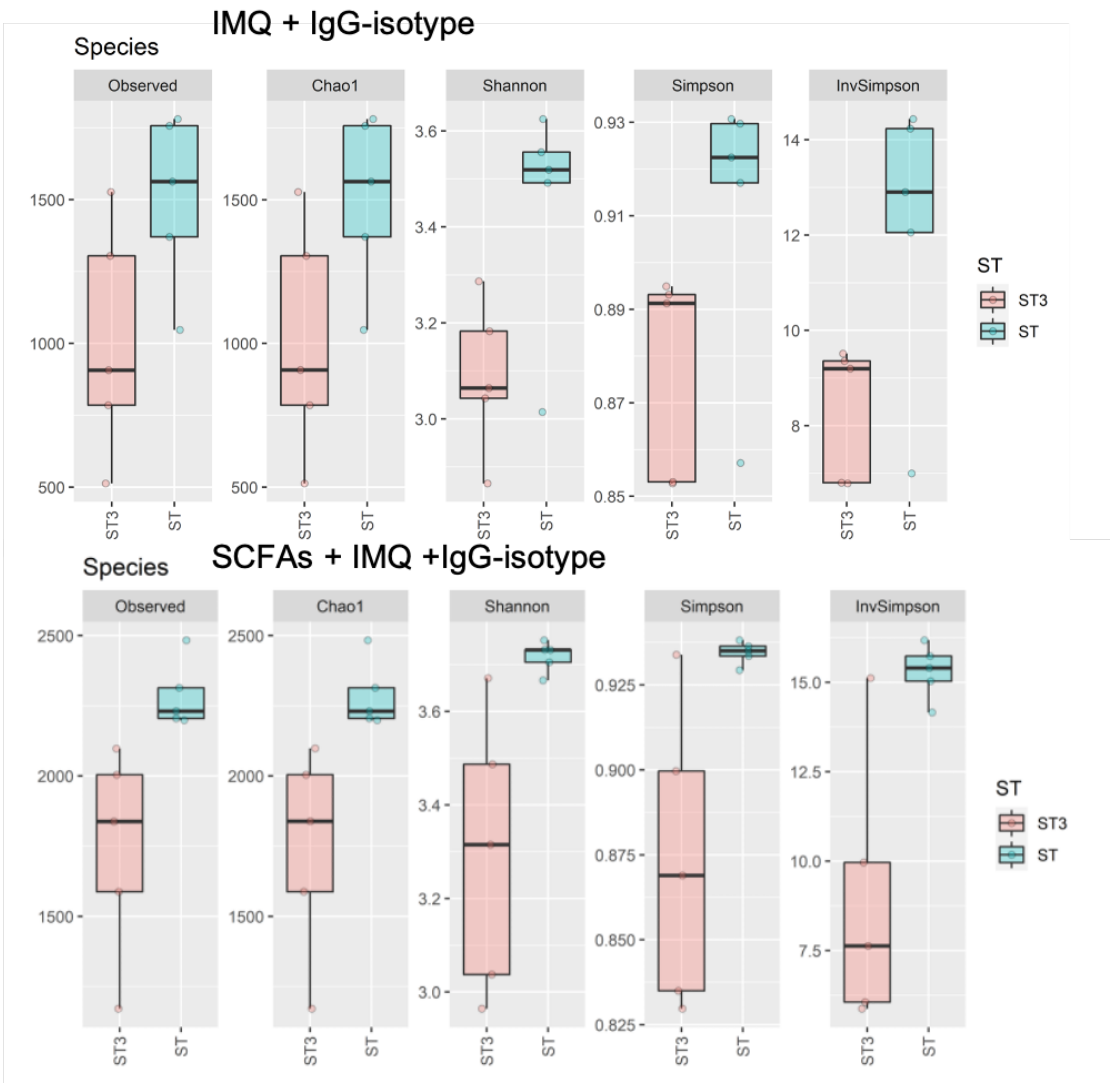
Supplementary Figure 3A.



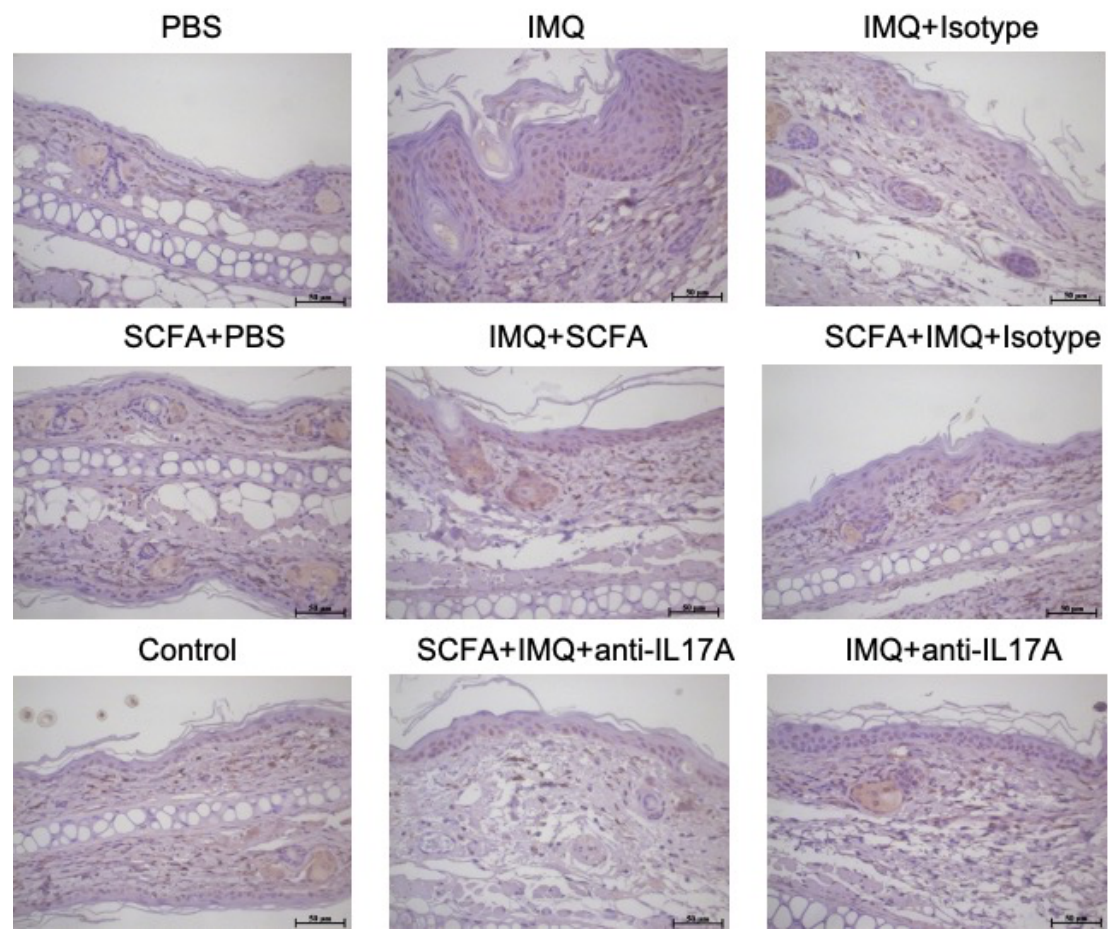
Supplementary Figure 3B.



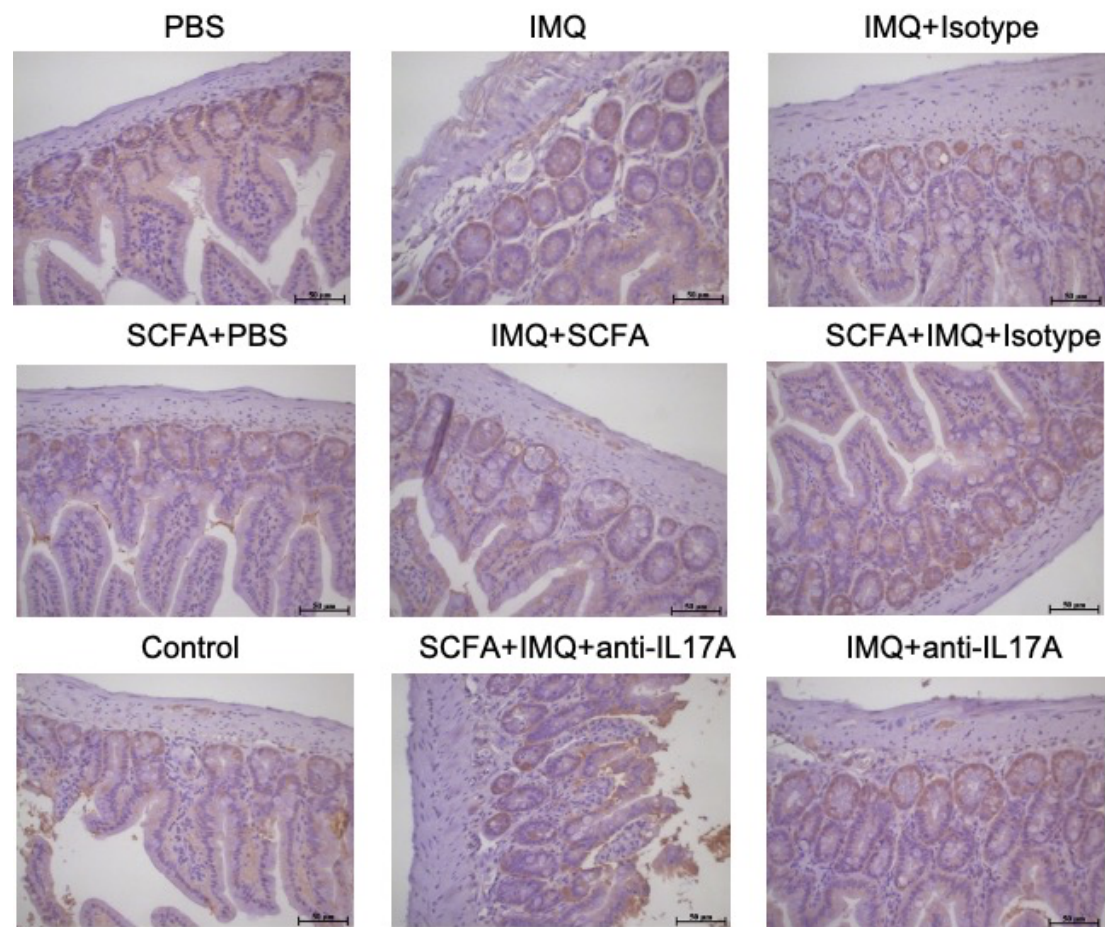
Supplementary Figure 3C.



Supplementary figure 4A.



Supplementary figure 4B.



Supplementary figure 4C.

