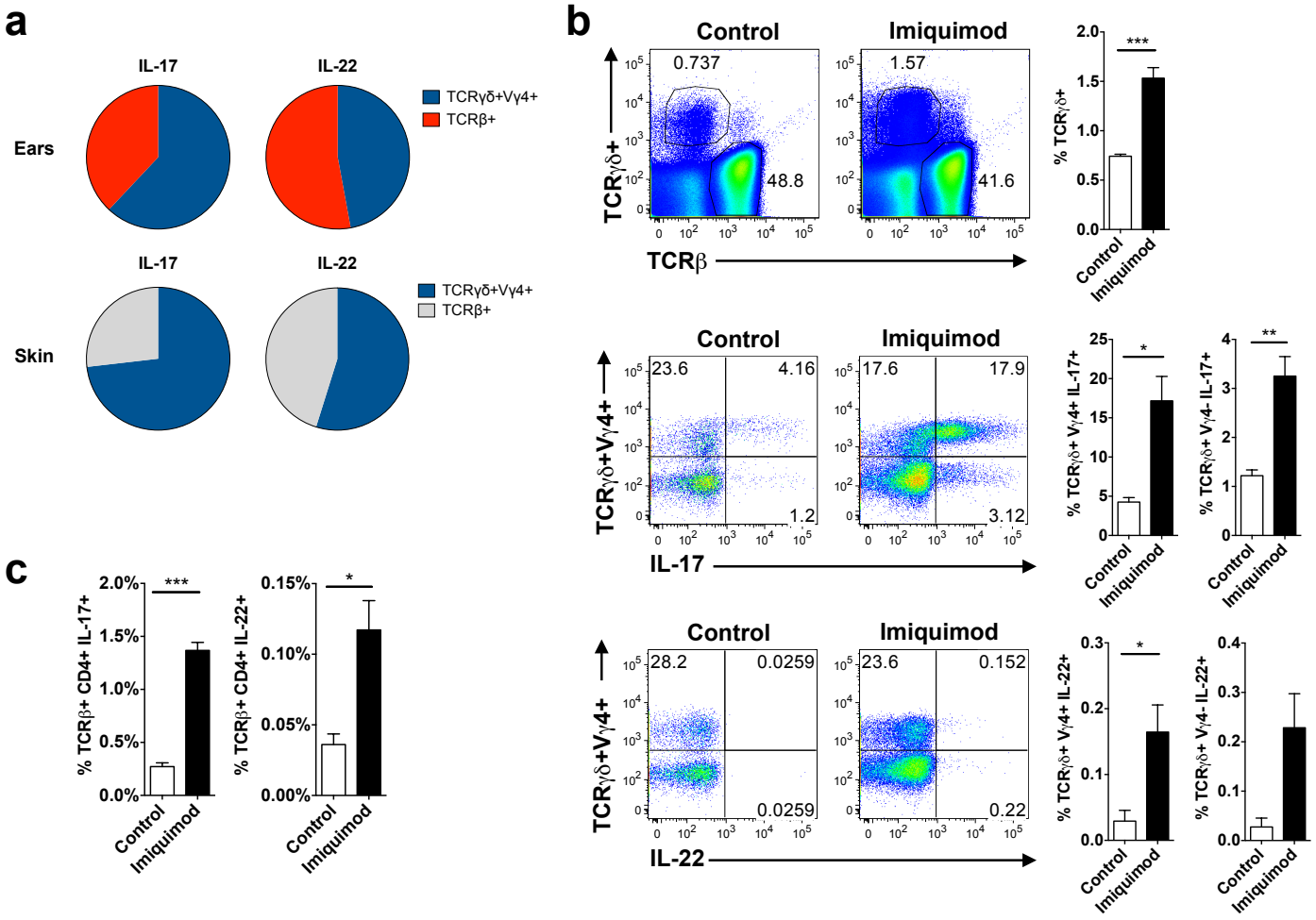
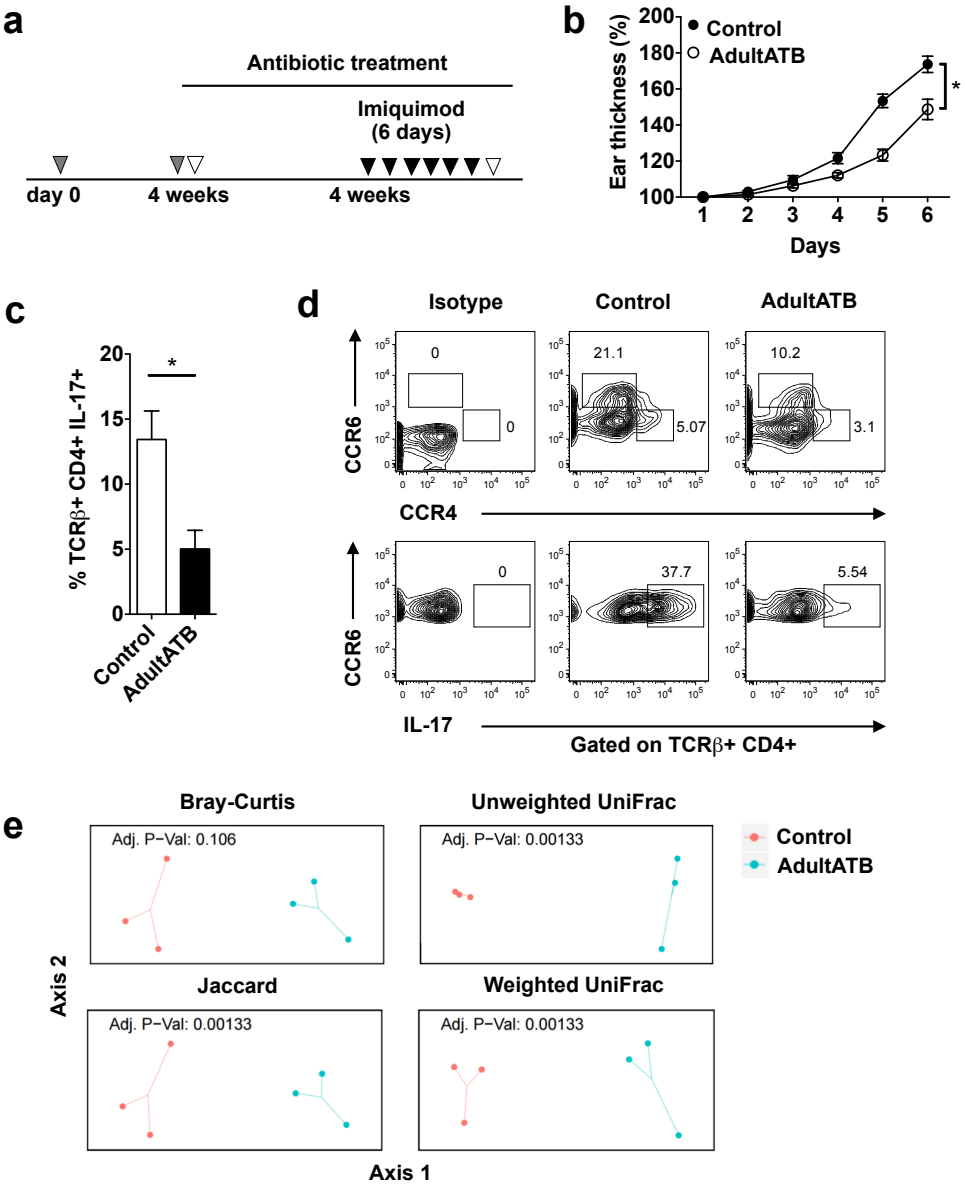


Supplementary Figure 1

Increase of local and systemic inflammation after Imiquimod treatment

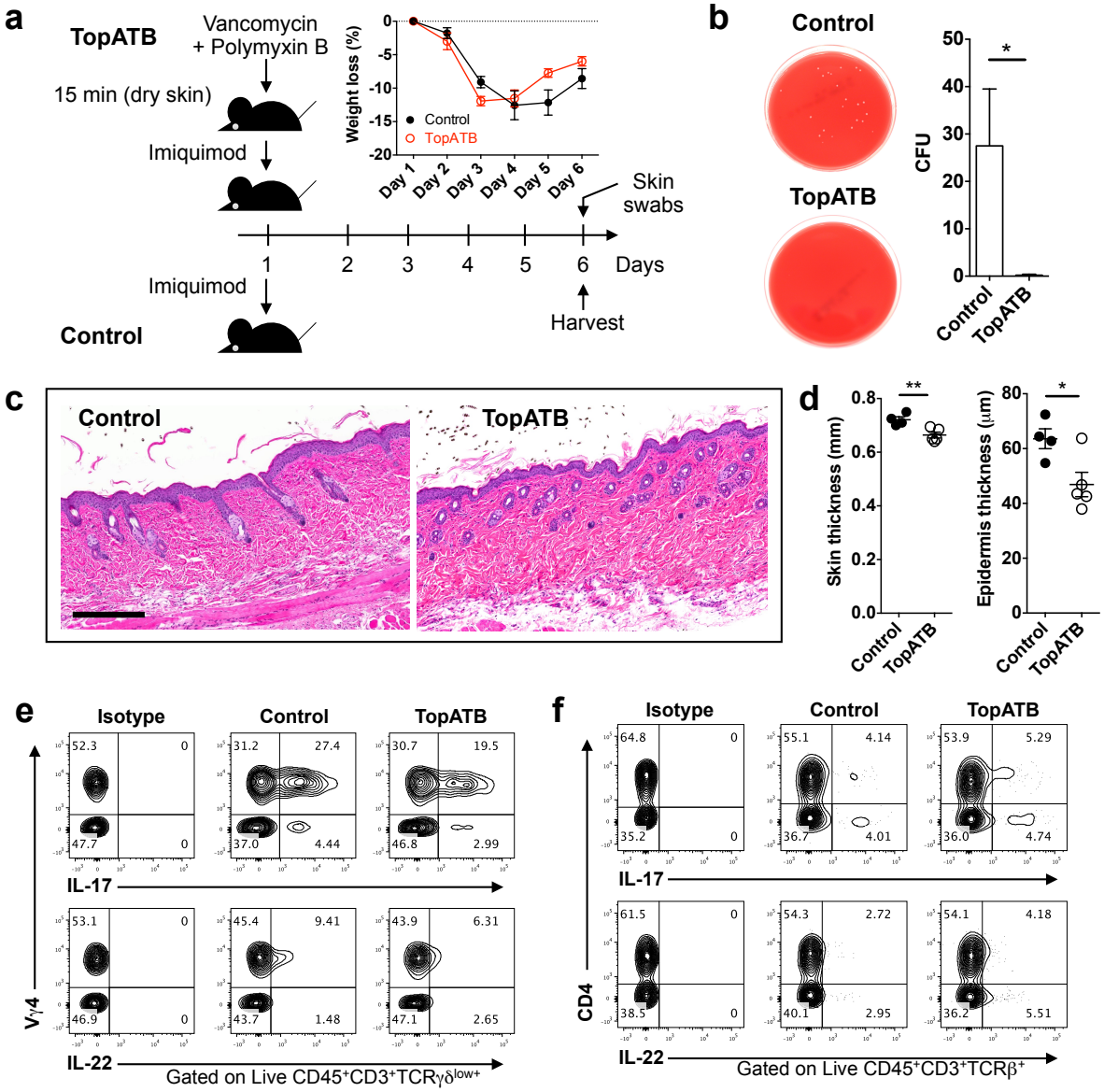
a) Total number of IL-17$^+$ and IL-22$^+$ dermal TCR$\gamma\delta^+$Vγ4$^+$ or TCRβ^+ cells in back skin and ears of the Imiquimod treated mice. **b)** Representative FACS plot of TCR$\gamma\delta^+$Vγ4$^+$IL-17$^+$ or TCR$\gamma\delta^+$Vγ4$^+$IL-22$^+$ cells in skin draining lymph nodes after Imiquimod treatment. Control (n=3), Imiquimod (n=4). **c)** Increased frequency of TCRβ^+CD4$^+$IL-17$^+$ and TCRβ^+CD4$^+$IL-22$^+$ cells in spleen after Imiquimod treatment. Control (n=3), Imiquimod (n=4). Data representative of 3 experiments. Results are shown as mean ± S.E.M., significance was determined by unpaired two-tailed student's *t*-test (**P* < 0.05, ***P* < 0.01, ****P* < 0.001).



Supplementary Figure 2

Antibiotic treatment in adult mice ameliorates severity of psoriasis induced by Imiquimod

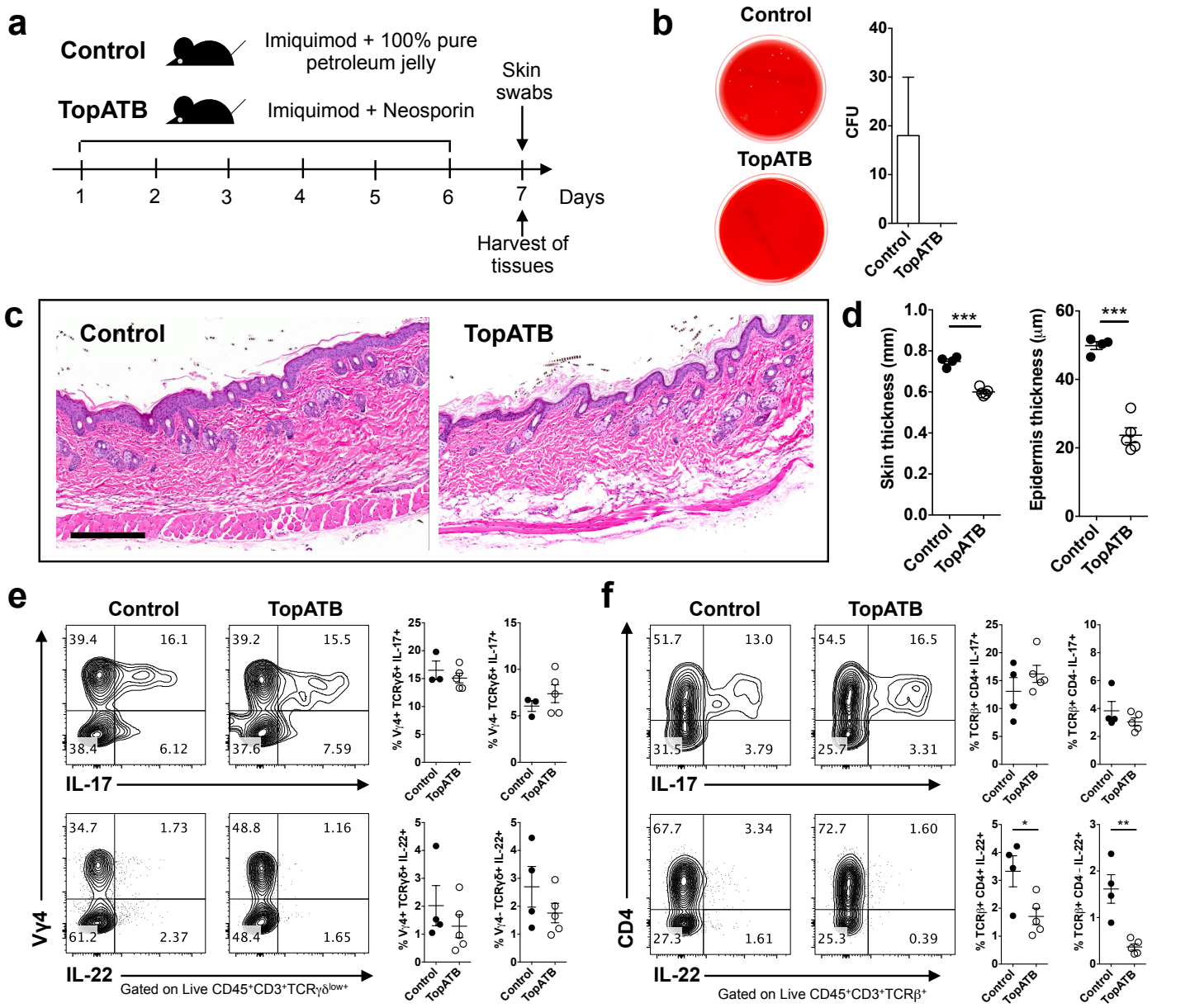
a) Scheme of immunization. **b)** Ear thickness time-course in AdultATB and Control mice during 6-days Imiquimod treatment. **c)** Frequency of TCRβ$^+$CD4$^+$IL-17$^+$ cells in lamina propria lymphocytes (LPL) in small intestine (SI) in AdultATB and Control mice after antibiotic and Imiquimod treatment. Data are representative of 3 experiments. **d)** Effect of antibiotic treatment on the expression of chemokine receptors CCR6 and CCR4 in the LPL-SI after antibiotic treatment. Upper panel: Representative FACS plots of CCR6 vs. CCR4 within CD45$^+$/Live CD4$^+$TCRβ$^+$ cells in the LPL-SI. Lower panel: Frequencies of CCR6$^+$IL-17$^+$ cells within TCRβ$^+$CD4$^+$ T cells in LPL-SI. **e)** Beta diversity (PCoA) was used to compare distance measure (Unweighted and Weighted Unifrac), diversity (Jaccard) or dissimilarity (Bray-Curtis) between AdultATB and Control mice. Results are shown as mean ± S.E.M., significance was determined by unpaired two-tailed student's *t*-test (*P < 0.05).



Supplementary Figure 3

Topical antibiotic treatment ameliorates the development of psoriasis induced by Imiquimod with decreased IL-17$^+$ and IL-22$^+$ skin resident γδ T cells.

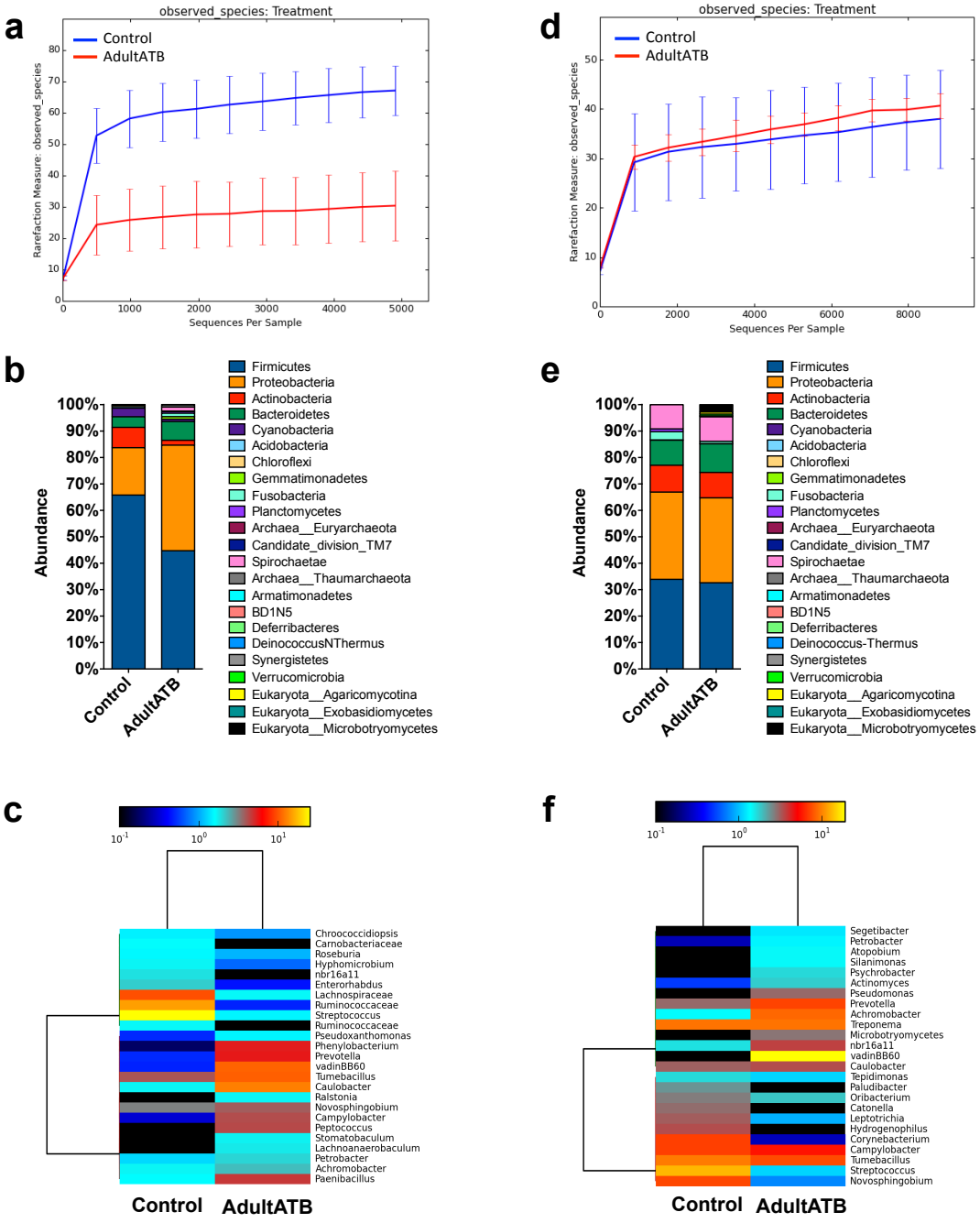
a) C57BL6 mice (7-weeks old) were treated by topical application of antibiotic water (Vancomycin+Polymyxin B, TopATB, n=5 mice) and after ~15 min the mice were treated on the dry skin with Imiquimod daily for 5 consecutive days. Control mice (n=4) were treated daily only with Imiquimod for 5 consecutive days. Mice were monitored daily; skin tissues were harvested at day 6 (see scheme on A). **b)** Skin swabs were collected at day 6 after treatment and were soaked in PBS. An aliquot of eluted skin bacteria was spread on 5% sheep blood agar plates and cultured overnight at 37ºC. 16h later, the number of Colony Forming Units (CFU) was calculated. Controls n=4, TopATB n=5. **c)** H&E analysis of skin sections of Control and TopATB mice. Scale bar = 300μm. **d)** Thickness of skin measured by Digimatic Caliper at day 6 in Control and Imiquimod treated mice. Data are shown as mean ± S.E.M. of the skin thickness of individual mice. Epidermal thickness was measured using ImageScope Software. **e)** Representative FACS plots of Vγ4$^+$TCRγδ$^+$IL-17$^+$ or Vγ4$^+$TCRγδ$^+$IL-22$^+$ cells in the skin of Control or TopATB mice. **f)** Representative FACS plots of TCRβ$^+$CD4$^+$17$^+$ or TCRβ$^+$CD4$^+$IL-22$^+$ cells in the skin of Control or TopATB mice. Results are shown as mean ± S.E.M., significance was determined by unpaired two-tailed student's *t*-test (*P < 0.05, **P < 0.01).



Supplementary Figure 4

Topical treatment with an antibiotic ointment ameliorates development of Imiquimod-induced psoriasis

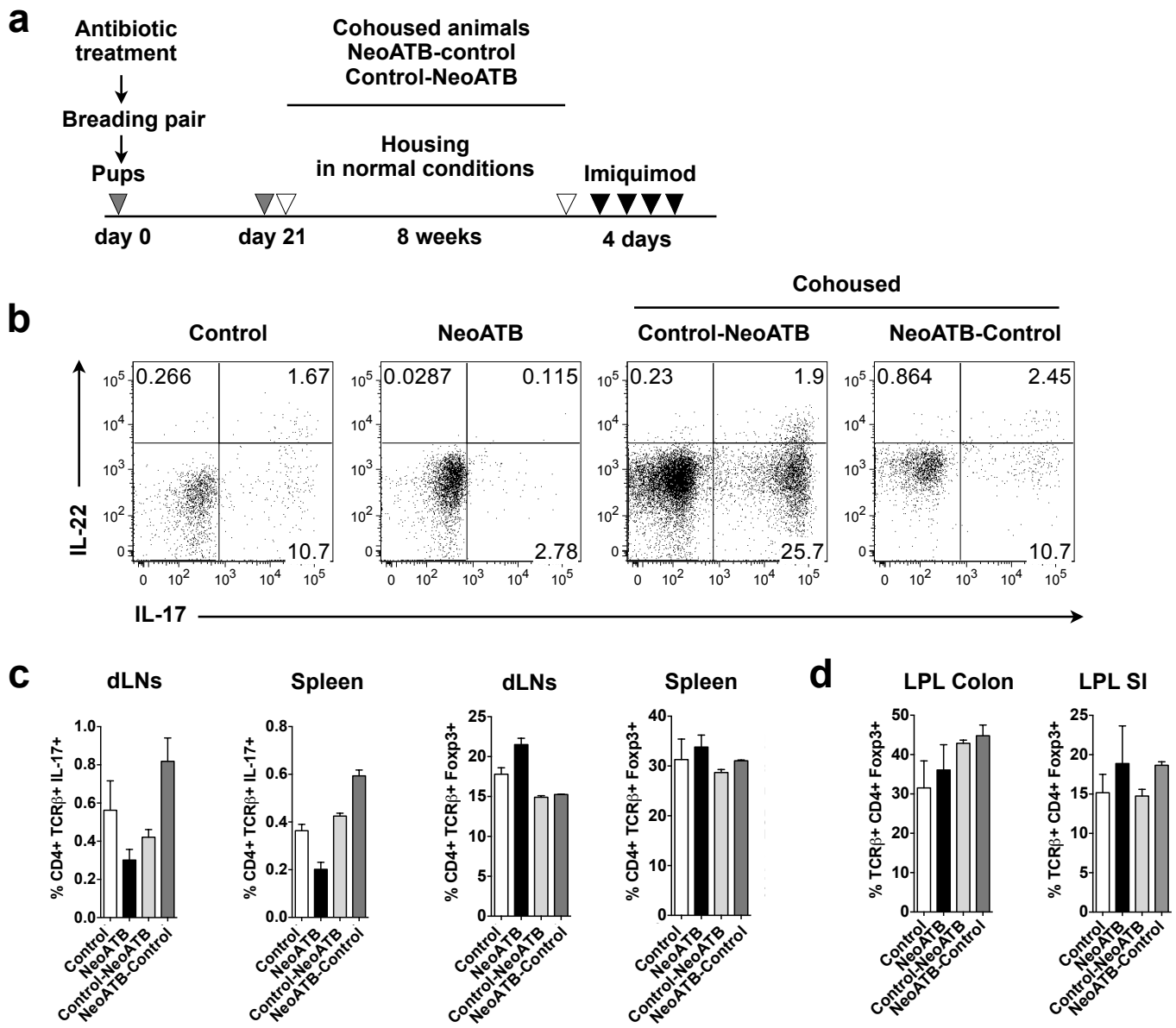
Immunization scheme. Mice were treated daily by either topical application of Imiquimod or 100% pure petroleum jelly (Control, n=4), or with a combination of Imiquimod and antibiotic ointment - Neosporin (TopATB, n=5) for 6 consecutive days. **b)** Skin swabs were collected at day 7 after treatment and were soaked in PBS. An aliquot of eluted skin bacteria was spread on 5% sheep blood agar plates and cultured overnight at 37ºC. 16h later, the number of Colony Forming Units (CFU) was calculated. Control n=4, TopATB n=5. **c)** Representative H&E staining of skin samples collected at day 7. Scale bar = 300μm. Thickness of skin was measured using Digimatic Caliper at day 7 in Control and TopATB treated mice. Data are shown as mean ±S.E.M. of the skin thickness of individual mice. Epidermal thickness was measured using ImageScope Software. **d)** Representative FACS plots of $V\gamma4^+IL\text{-}17^+$ (upper panel) or $V\gamma4^+IL\text{-}22^+$ cells (lower panel) in skin of Control (n=3-4) or TopATB mice (n=5). **e)** Representative FACS plots of $TCR\beta^+CD4{+}IL\text{-}17^+$ (upper panel) or $TCR\beta^+CD4^+IL\text{-}22^+$ cells (lower panel) in skin of Control (n=4) or TopATB mice (n=5). Results are shown as mean ± S.E.M., significance was determined using an unpaired two-tailed student's *t*-test (*$P < 0.05$; **$P < 0.01$).



Supplementary Figure 5

16S rRNA analysis of skin microflora before and after Imiquimod treatment in mice exposed to antibiotics at adult age

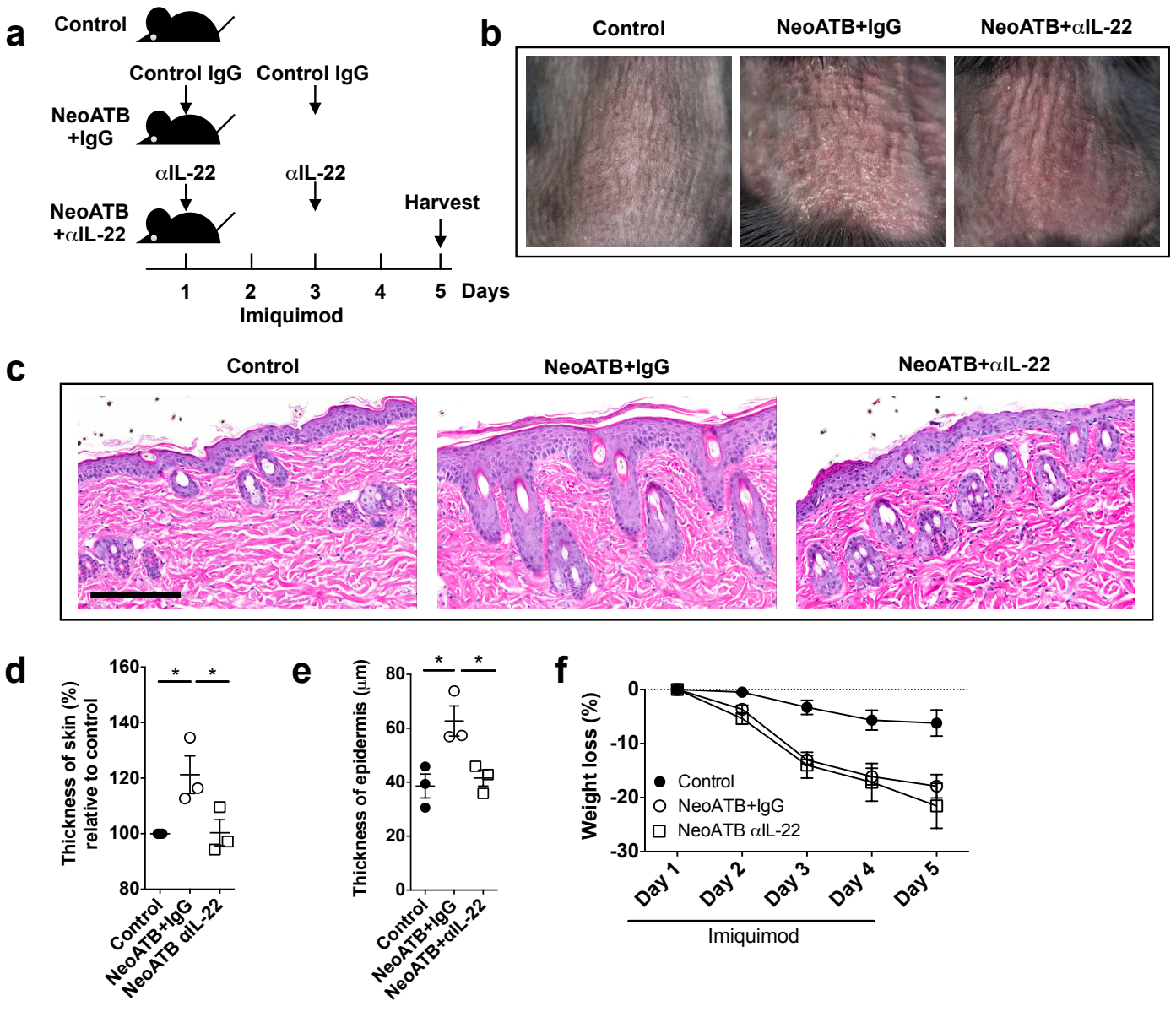
Skin swabs from the shaved back skin of AdultATB or Control mice were collected (n=3) and analyzed using 16S rRNA sequencing of region V4. **a)** Diversity of the skin microflora (Observed Species) in AdultATB treated mice compared to Controls before Imiquimod treatment in adult age. **b)** Skin microflora analysis at the phylum level between AdultATB and Control mice before Imiquimod treatment in adult age. Summarizing data showing average from 3 mice **c)** Heat map analysis showing top 25 different skin taxa in the skin of AdultATB and Control mice before Imiquimod treatment. **d)** Diversity of the skin microflora (Observed Species) in AdultATB treated mice compared to Controls after Imiquimod treatment in adult age. **e)** Skin microflora analysis at the phylum level between AdultATB and Control mice after Imiquimod treatment in adult age. Summarizing data showing average from 3 mice. **f)** Heat map analysis showing top 25 different skin taxa in the skin of AdultATB and Control mice after Imiquimod treatment.



Supplementary Figure 6

Neonatal antibiotic treatment increases severity of psoriasiform dermatitis induced by Imiquimod treatment in adult age

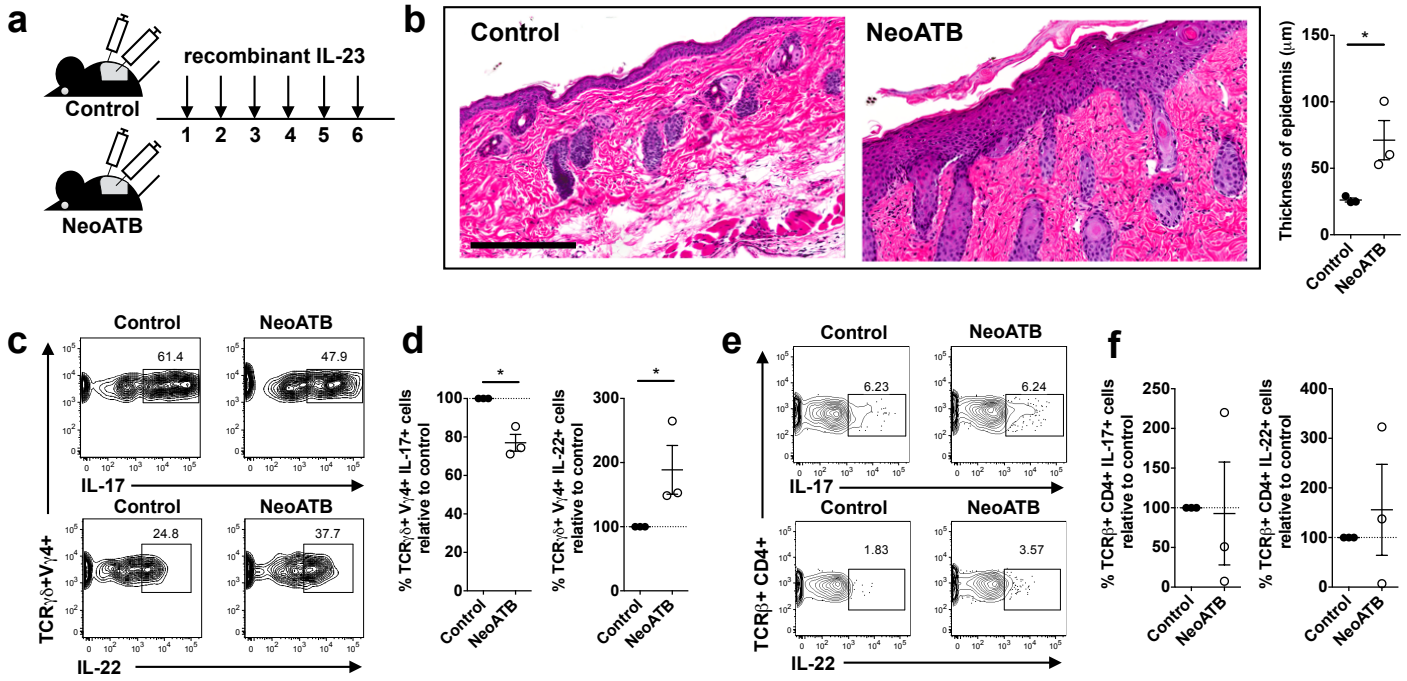
a) Immunization scheme **b)** Representative FACS plots of frequencies of Th17 cells within lamina propria lymphocytes in small intestines of Control, NeoATB, and co-housed (Control-NeoATB and NeoATB-Control) mice after Imiquimod treatment. Cells were gated on $CD45^+TCR\beta^+CD4^+$ cells. Data are representative of 3 experiments. **c)** Frequency of $TCR\beta^+CD4^+IL\text{-}17^+$ and $TCR\beta^+CD4^+Foxp3^+$ cells in the skin draining lymph nodes (dLN) and spleen after Imiquimod treatment in NeoATB, Control, Control-NeoATB and NeoATB-Control groups. Results are shown as mean ± S.E.M. **d)** Frequency of $TCRb^+CD4^+Foxp3^+$ cells in the lamina propria lymphocytes (LPL) of colon or small intestine (SI) after Imiquimod treatment in NeoATB, Control, Control-NeoATB and NeoATB-Control groups. Results are shown as mean ± S.E.M.



Supplementary Figure 7

Intradermal injection of anti-IL-22 antibody in NeoATB mice ameliorates severity of disease induced by Imiquimod

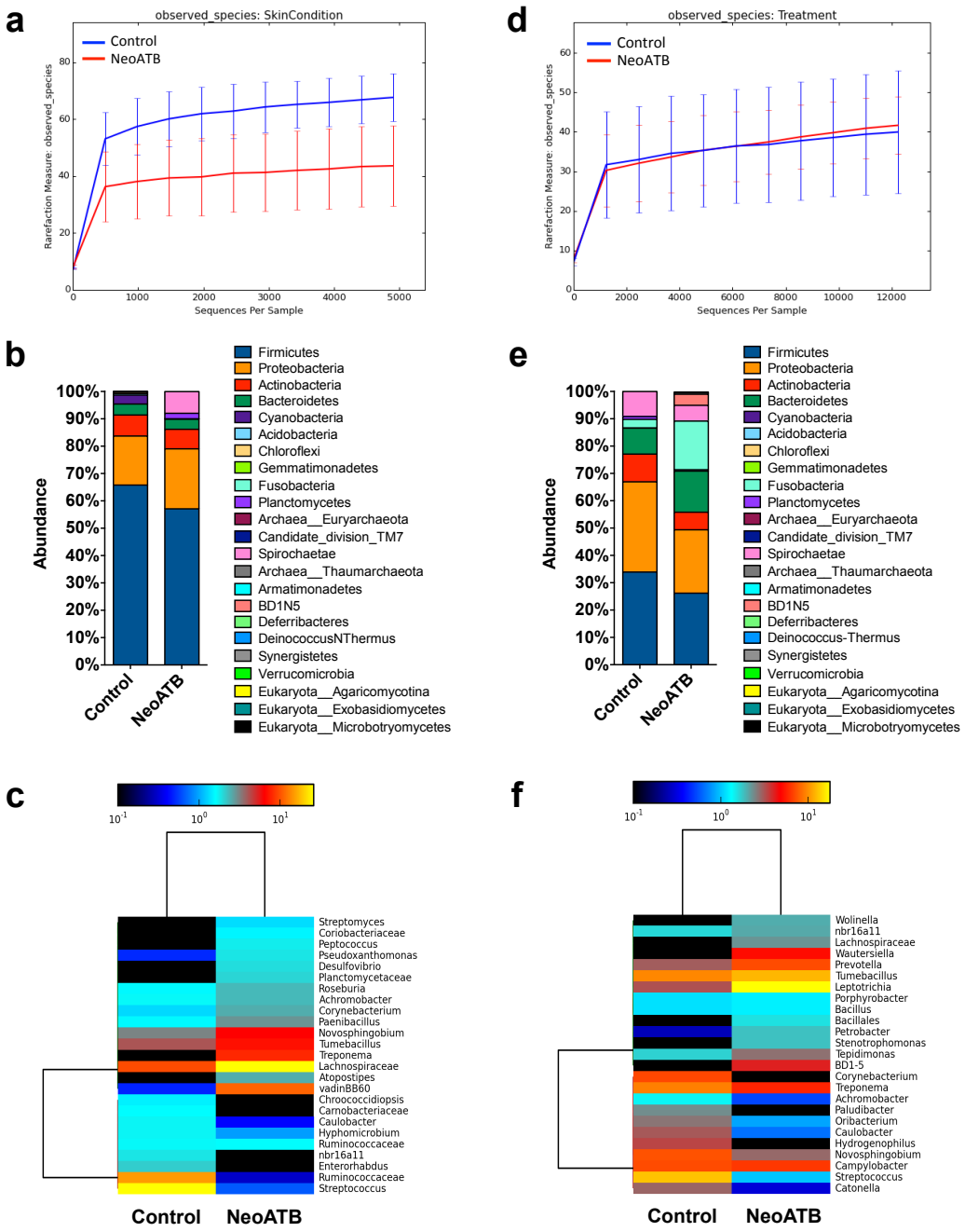
a) Experimental scheme. NeoATB mice (n=3) were intradermally injected at day 1 (50 μg) and day 3 (15 μg) of control IgG (NeoATB+IgG) or neutralizing anti-IL-22 (NeoATB+aIL-22) antibodies during 4 days of Imiquimod treatment. Mice without neonatal antibiotics treatment (Control, n=3) were treated only with Imiquimod for 4 days. **b)** Representative photographs of back skin in Control, NeoATB+IgG and NeoATB+aIL-22 injected mice 4 days after Imiquimod treatment. **c)** Representative H&E staining of skin samples of Control, NeoATB+IgG and NeoATB+aIL-22 injected mice collected at day 5. Scale bar = 200μm. **d)** Skin thickness of Control, NeoATB+IgG or NeoATB+aIL-22 treated mice measured at day 5. Skin thickness was measured by digimatic caliper at least by two measurements and data are shown as mean ± S.E.M. of the measurements of individual mice. **e)** Epidermal thickness was measured using ImageScope Software. **f)** Weight loss of Control, NeoATB+IgG or NeoATB+aIL-22 injected mice during Imiquimod treatment monitored daily. Results are shown as mean ± S.E.M., significance was determined using one-way ANOVA followed by Tukey's posttest (*$P < 0.05$).



Supplementary Figure 8

Neonatal antibiotic treated mice developed an exacerbated form of psoriasis after recombinant IL-23 injection at adult age

a) Immunization scheme. Control or NeoATB mice were intradermally injected with recombinant IL-23 (1 μg/day) in two locations (0.5 μg to each) on either side of shaved back skin for 6 consecutive days **b)** Haematoxylin and eosin (H&E) staining of back skin at day 6 after daily injection of recombinant IL-23, Scale bar = 200μm. The bar graph indicates the measurements of thickness of epidermis. Thickness of epidermis was determined using ImageScope software along different areas of epidermal layer. **c)** Flow cytometry of TCRγδ$^+$Vγ4$^+$IL-17$^+$ (upper panel) and TCRγδ$^+$Vγ4$^+$IL-22$^+$ (lower panel) cells in the skin of control and NeoATB treated mice after 6 consecutive IL-23 intradermal injections. **d)** Relative frequencies of TCRγδ$^+$Vγ4$^+$IL-17$^+$ and TCRγδ$^+$Vγ4$^+$IL-22$^+$ cells normalized to frequencies in control mice (*P < 0.05). **e)** Flow cytometry of TCRβ$^+$CD4$^+$IL-17$^+$ (upper panel) and TCRβ$^+$CD4$^+$IL-22$^+$ cells in the skin of control and NeoATB treated mice after 6 consecutive IL-23 intradermal injections. **f)** Relative frequencies of TCRβ$^+$CD4$^+$IL-17$^+$ and TCRβ$^+$CD4$^+$IL-22$^+$ cells normalized to frequencies in control mice. Data represents summary of 2 independent experiments. Data were analyzed using unpaired student *t*-test (*P < 0.05).



Supplementary Figure 9

16S rRNA analysis of skin microflora before and after Imiquimod treatment in mice exposed to antibiotics at neonatal age

Skin swabs from the shaved back skin of NeoATB or Control mice were collected (n=3) and analyzed using 16S rRNA sequencing of region V4. **a)** Diversity of the skin microflora (Observed Species) in NeoATB treated mice compared to Controls before Imiquimod treatment in adult age. **b)** Skin microflora analysis at the phylum level between NeoATB and Control mice before Imiquimod treatment in adult age. Summarizing data showing average of 3 mice **c)** Heat map analysis showing top 25 different skin taxa in the skin of NeoATB and Control mice before Imiquimod treatment. **d)** Diversity of the skin microflora (Observed Species) in NeoATB treated mice compared to Controls after Imiquimod treatment in adult age. **e)** Skin microflora analysis at the phylum level between NeoATB and Control mice after Imiquimod treatment in adult age. Summarizing data showing average of 3 mice **f)** Heat map analysis showing top 25 different skin taxa in the skin of NeoATB and Control mice after Imiquimod treatment.