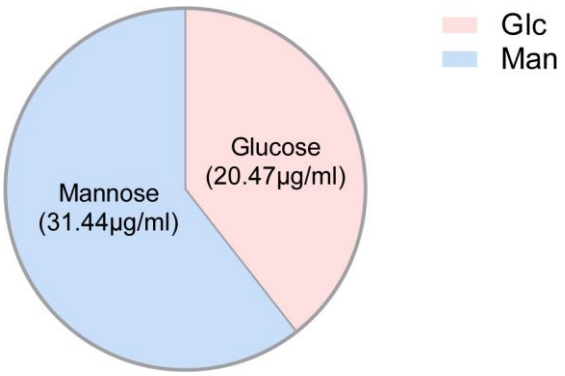


Figure S1. Monosaccharide composition of BEVs.

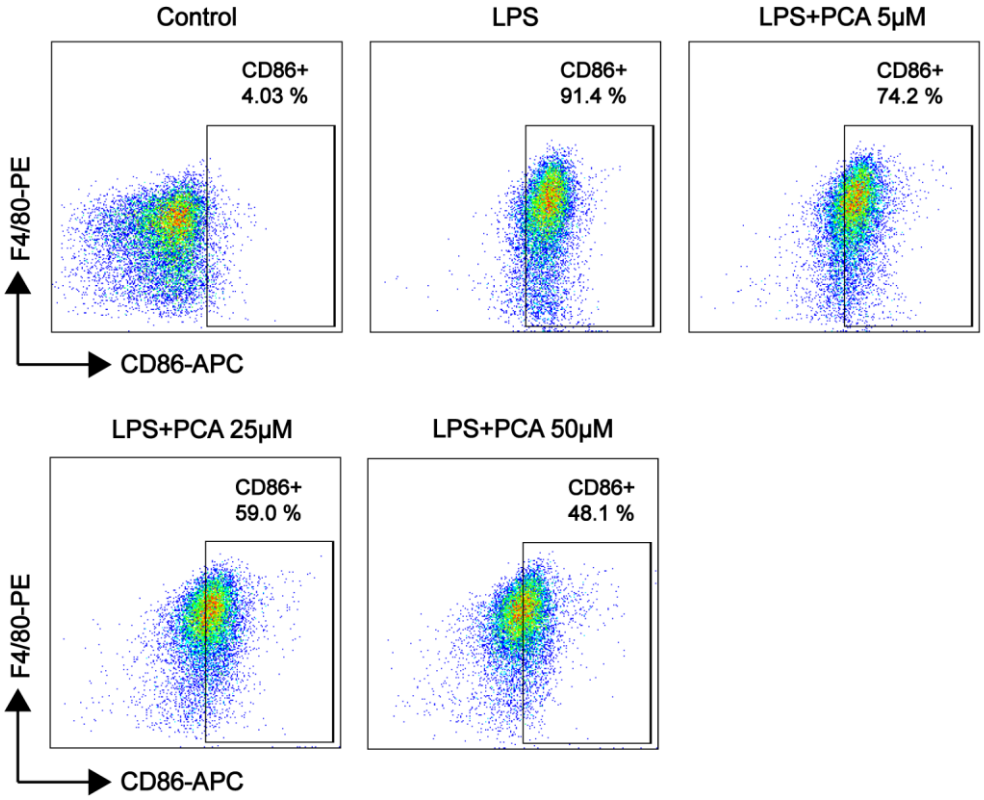


Figure S2. Flow cytometry analyses of M1 marker CD86 of LPS-treated RAW264.7 cells stimulated by protocatechualdehyde. Data are presented as means ± SD. Statistical analysis was performed using One-way ANOVA analysis followed by Tukey's HSD multiple comparison.

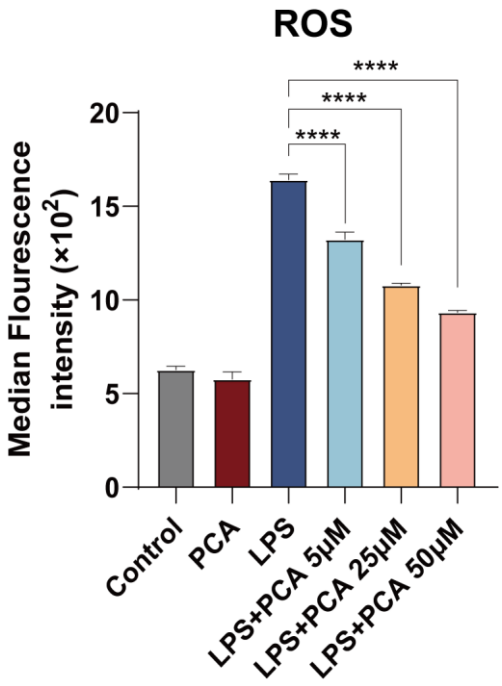
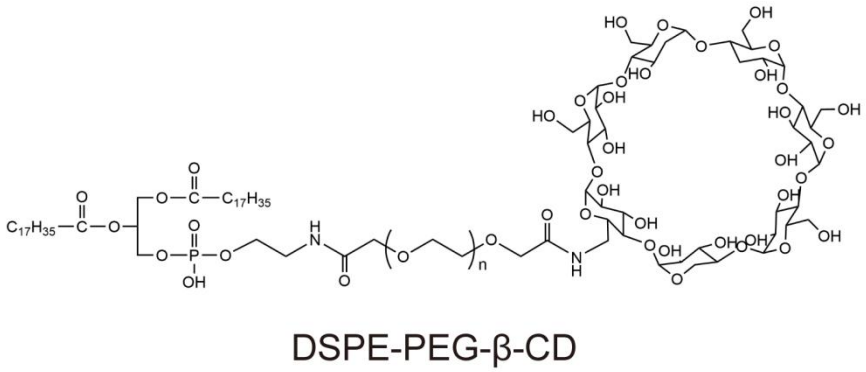
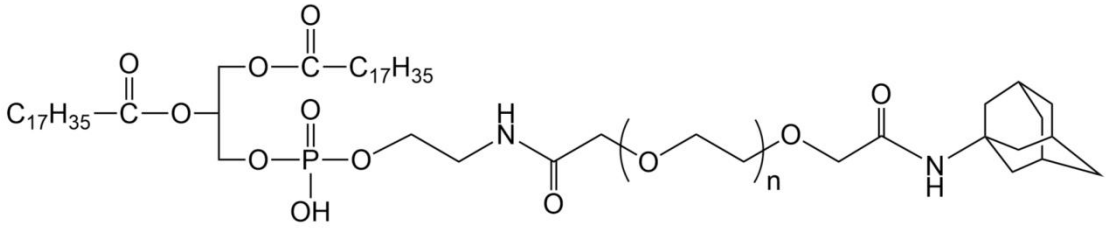


Figure S3. Flow cytometric histograms of RAW 264.7 macrophages treated with BEVs showing intracellular ROS (DCFH-DA) signals. Data are presented as means ± SD. Statistical analysis was performed using One-way ANOVA analysis followed by Tukey's HSD multiple comparison. ****$p < 0.0001$.



DSPE-PEG-β-CD



DSPE-PEG-ADA

Figure S4. The chemical structure of DSPE-PEG-β-CD and DSPE-PEG-ADA

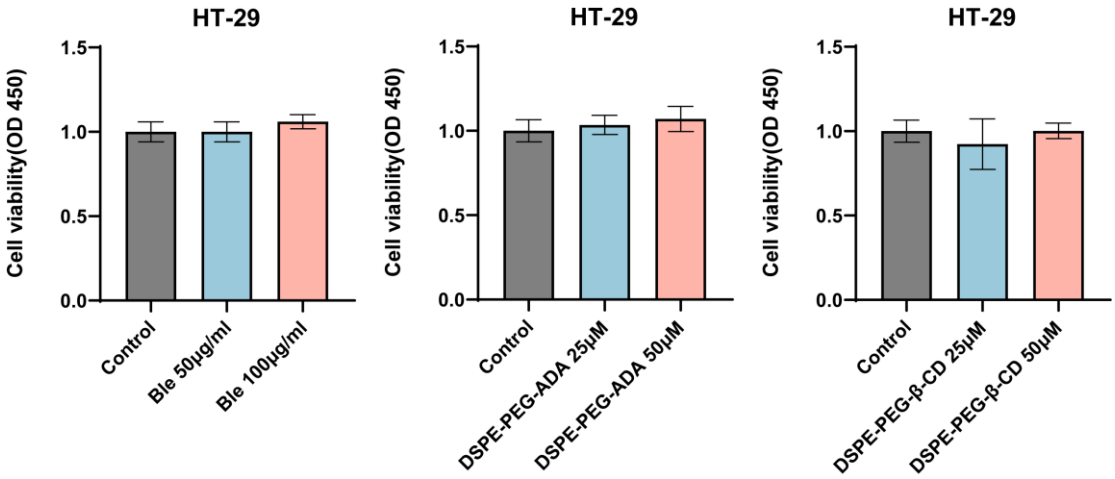


Figure S5. Cell viability of HT-29 against BEVs, DSPE-PEG-β-CD and DSPE-PEG-ADA. Cell viability was detected by CCK-8 assay by the absorbance at 450 nm measured after co-incubation for 24 hours. The concentrations of BEVs were 50μg/mL and 100μg/mL. The concentrations of DSPE-PEG-β-CD and DSPE-PEG-ADA were 25μM and 50μM.

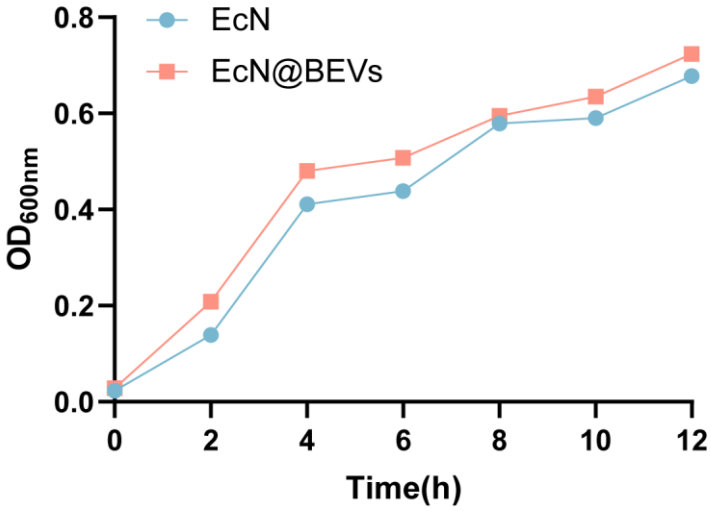


Figure S6. The growth curves of native EcN and EcN@BEVs. Bacteria were cultured in LB medium at 37 °C, and the value of OD600 was recorded in 2h intervals by a microplate reader.

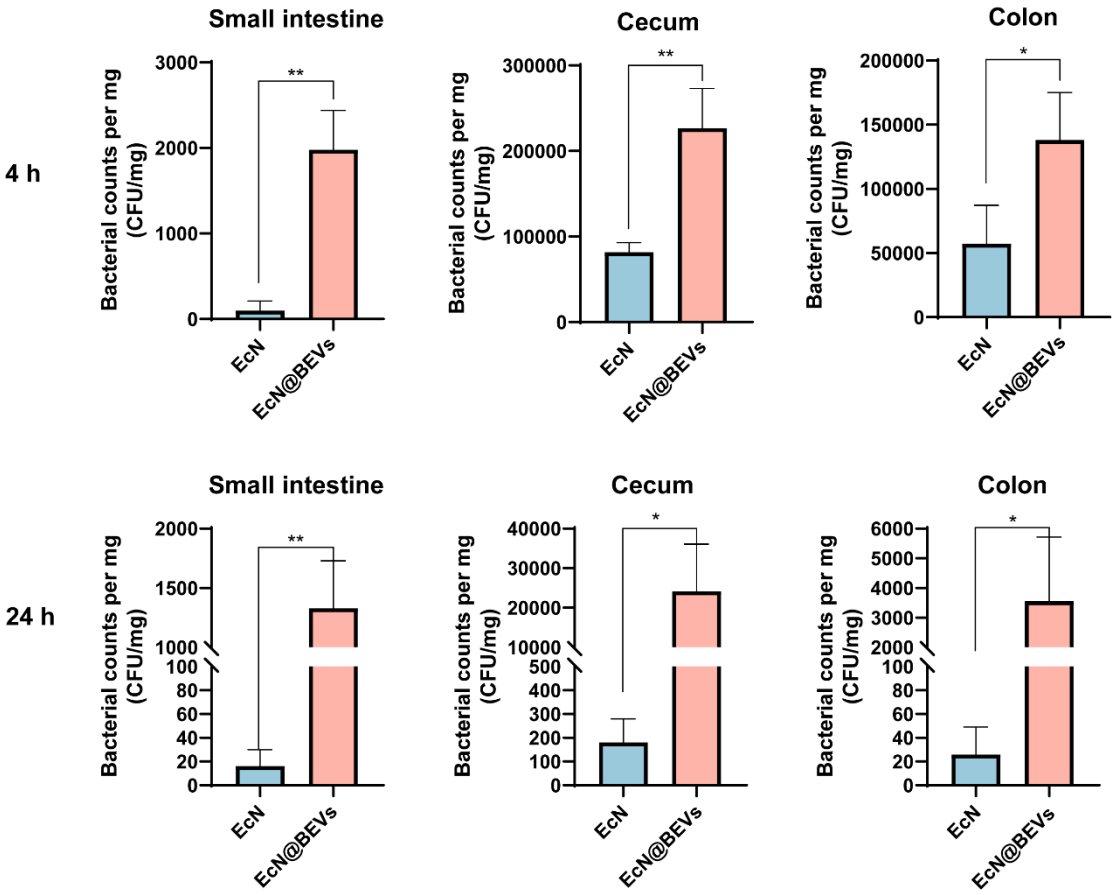


Figure S7. Bacterial counts of native EcN and EcN@BEVs colonizing at the small intestine, caecum and colon after oral gavage for 4h and 24h. CFU represented as colony-forming units. Data are presented as means ± SD (n = 3). Statistical analysis was performed using Student's t test. *$p < 0.05$, **$p < 0.01$.

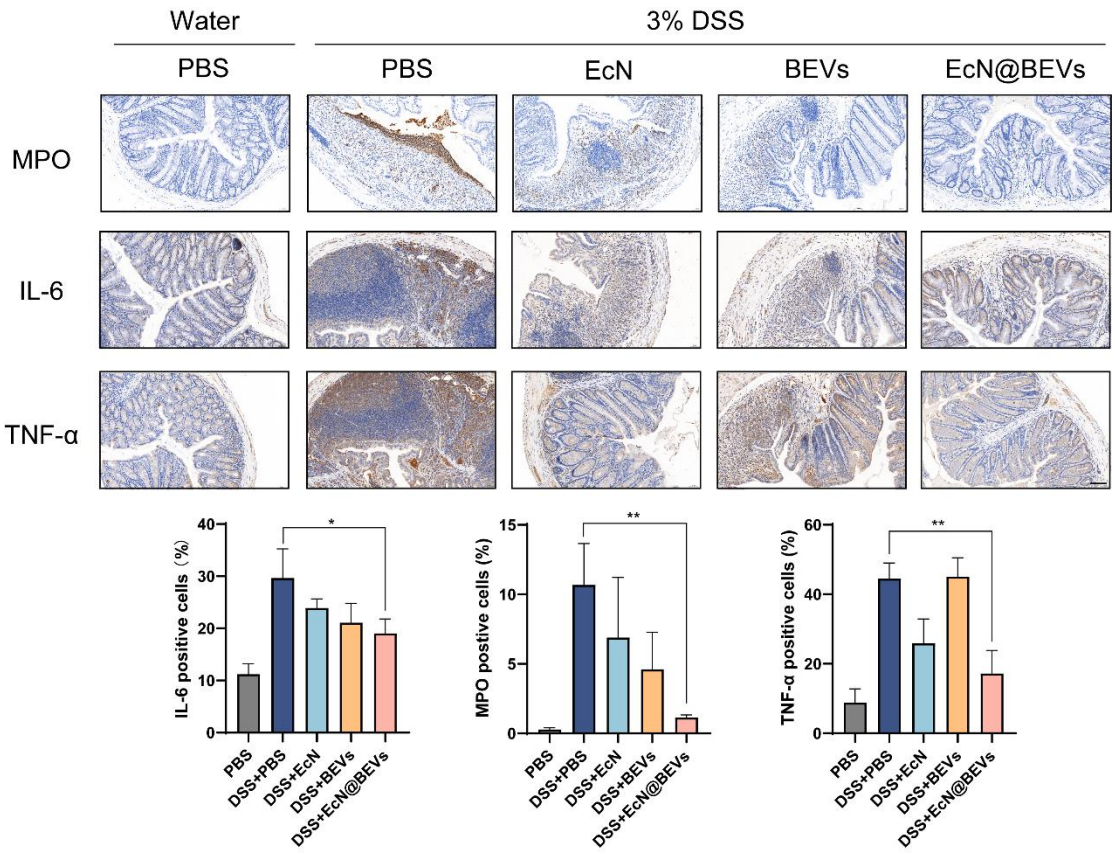


Figure S8. EcN@BEVs alleviated DSS-triggered immune activation. Immunohistochemical staining revealing a significant reduction in the number of IL-6, TNF-α, and MPO-positive cells following EcN@BEVs administration. Scale bar: 50 μm. Data are presented as means ± SD. Statistical analysis was performed using One-way ANOVA analysis followed by Tukey's HSD multiple comparison. *$p < 0.05$, **$p < 0.01$.

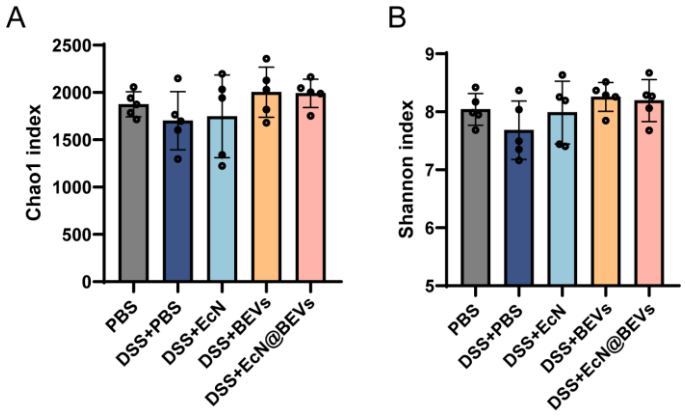


Figure S9. The α diversity of the gut microbiota was increased with the treatment of EcN@BEVs. Comparison of alpha diversity assessed by (A) Chao1 index, (B) Shannon index.

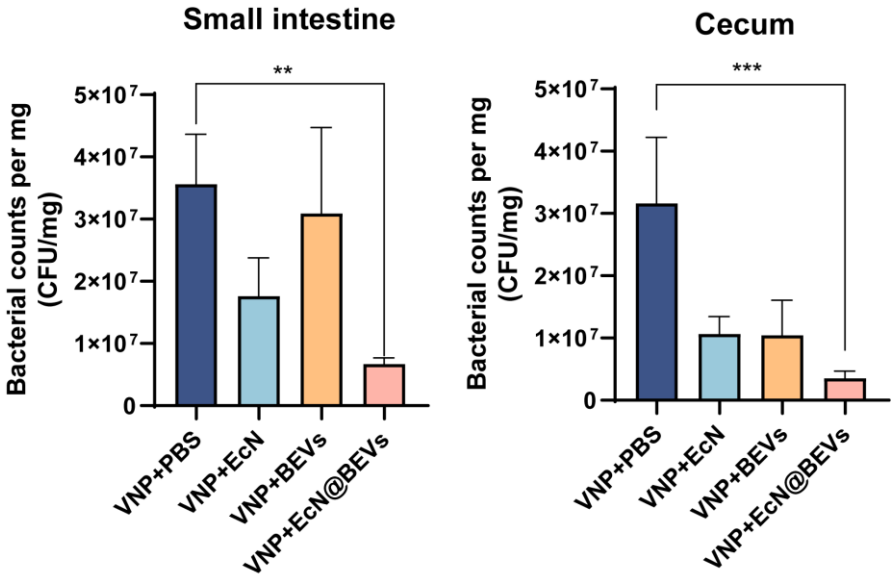


Figure S10. Quantification of bacterial populations in the small intestine and cecum across treatment groups. Data are presented as means ± SD. Statistical analysis was performed using One-way ANOVA analysis followed by Tukey's HSD multiple comparison. $^{**}p < 0.01$, $^{***}p < 0.001$.

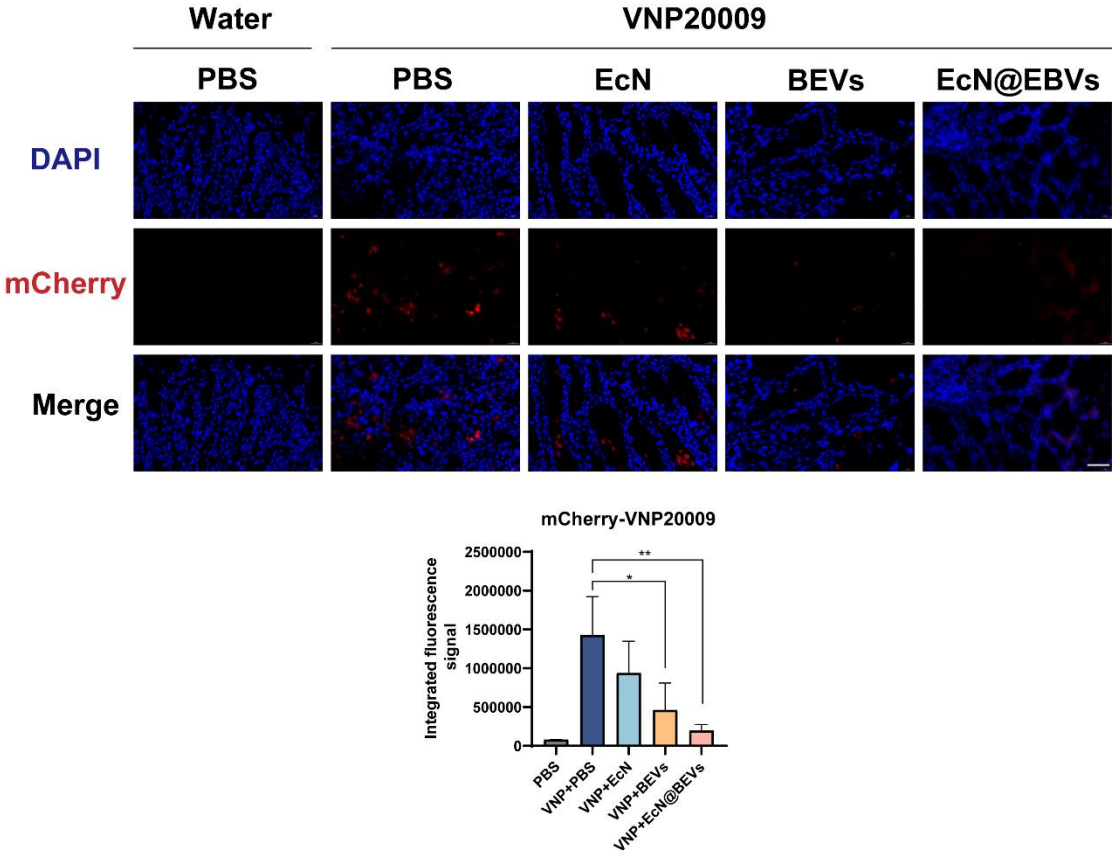


Figure S11. Representative immunofluorescence images showing VNP20009 with intrinsic red fluorescence in the colon. Scale bar: 40 μm. Data are presented as means ± SD. Statistical analysis was performed using One-way ANOVA analysis followed by Tukey's HSD multiple comparison. $^{*}p < 0.05$, $^{**}p < 0.01$.

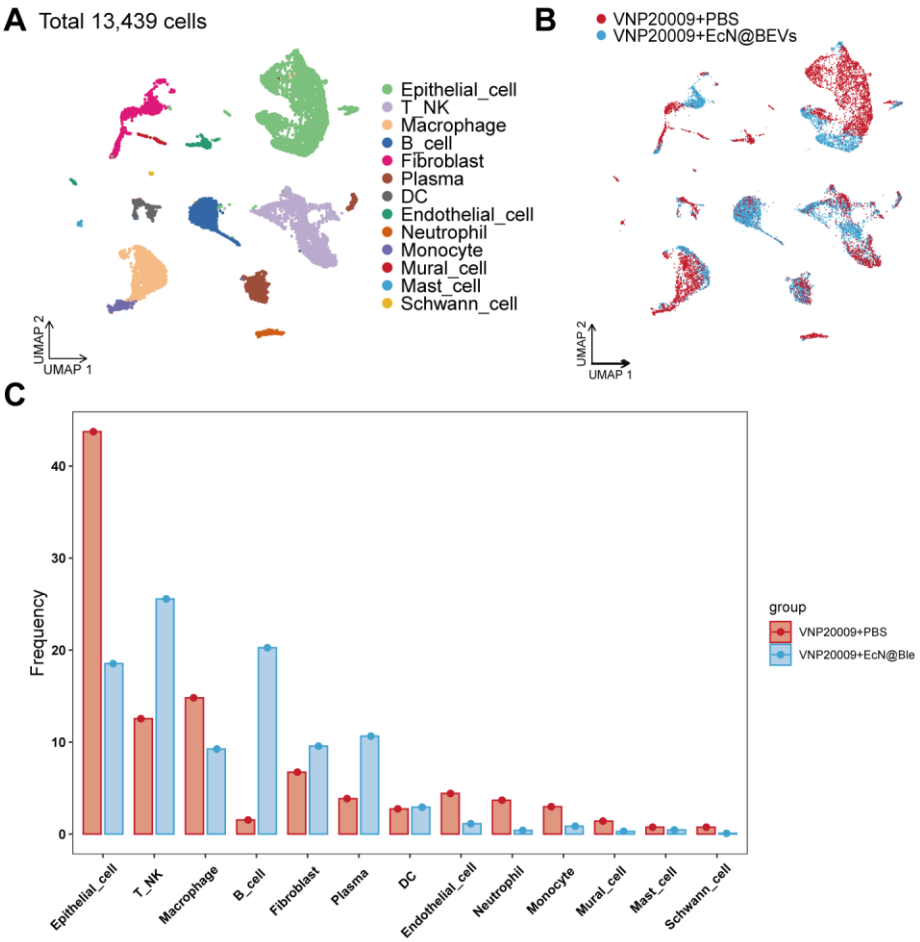


Figure S12. scRNA-seq analysis of colonic cells from VNP20009-infected mouse and EcN@BEVs-treated mouse (with 13439 total cells from 2 mice). (A) UMAP plot showing cell compositions of the colons. (B) UMAP plot showing cell populations across two samples. (C) Column plots of different cell subpopulations in two samples.

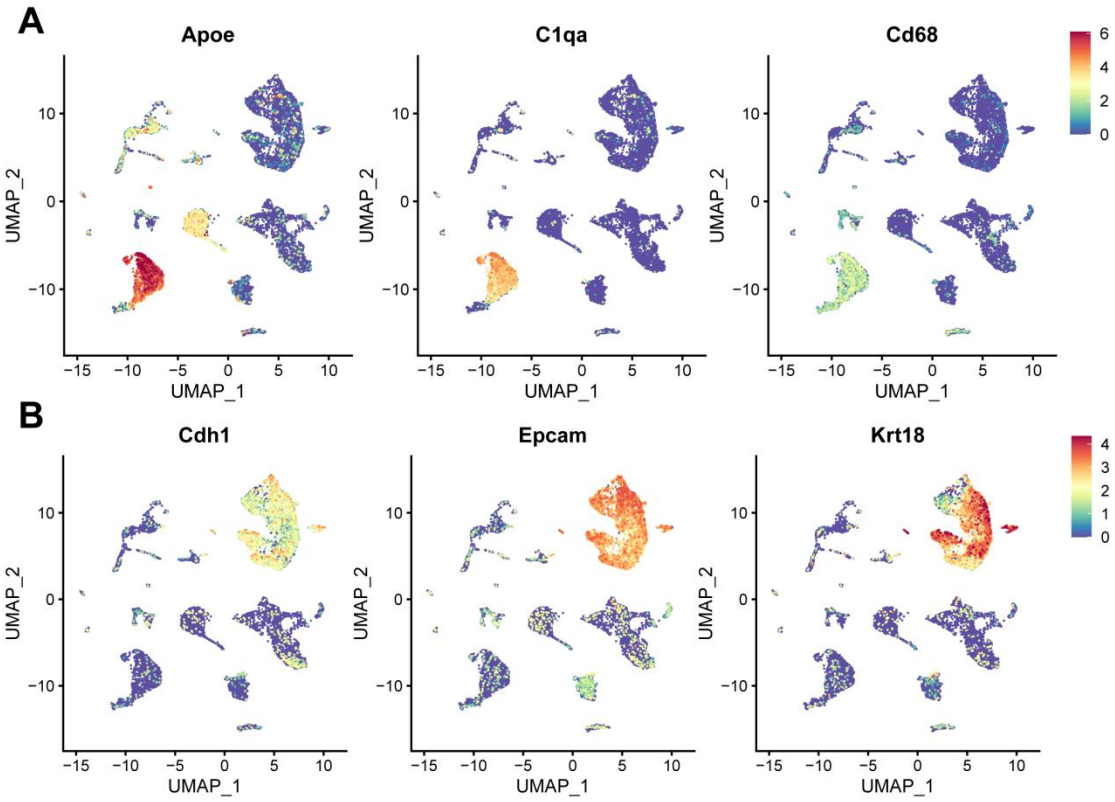


Figure S13. UMAP plot showing the macrophage markers and the epithelial cell markers. (A) The macrophage markers. (B) The epithelial cell markers.