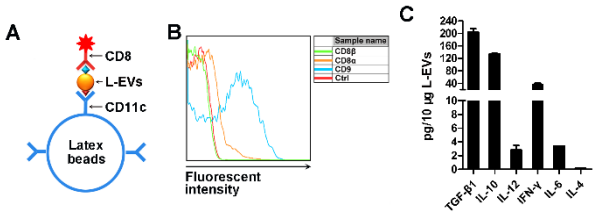
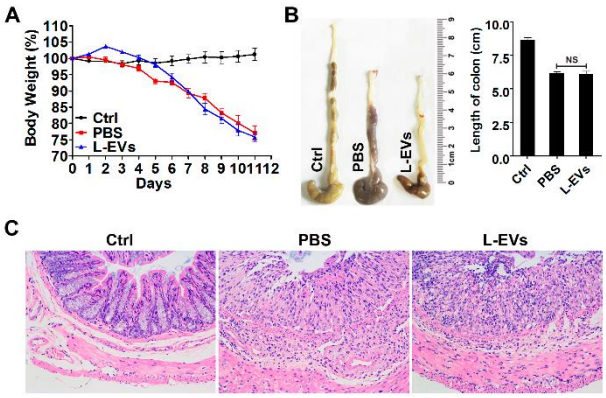
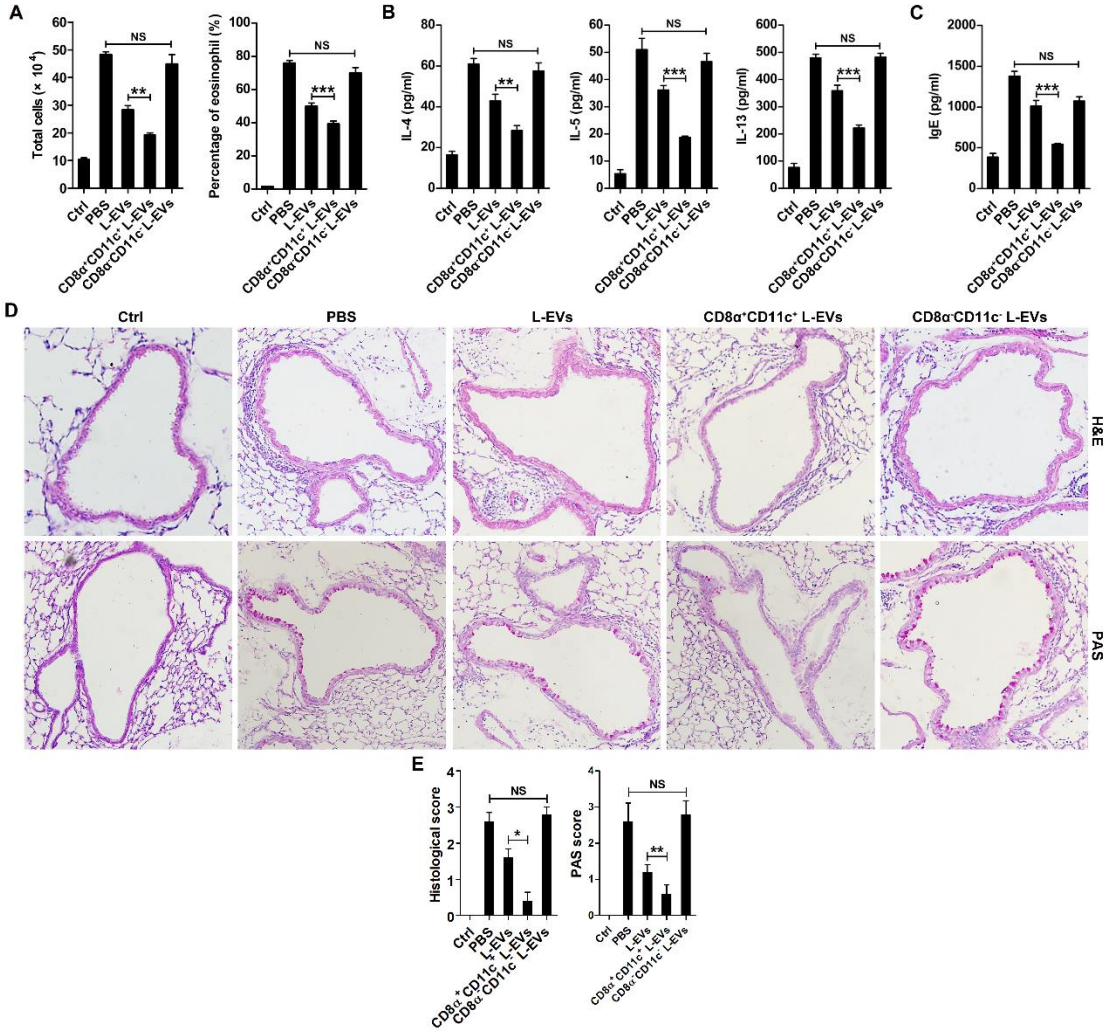



**Supplemental Figure 1**. L-EVs consisted of $CD8\alpha^{+}CD11c^{+}$ EVs. (**A**) Scheme for detection of $CD8\alpha^{+}CD11c^{+}$ EVs using flow cytometry. (**B**) EVs were captured with anti-CD11c antibody-coated latex beads, and the bound EVs were detected with anti-CD8α and anti-CD9 antibody. (**C**) After three freeze-thaw cycles, the indicated cytokines in the $CD8\alpha^{+}CD11c^{+}$ L-EVs were detected by ELISA (n = 3). The data are representative of three independent experiments.

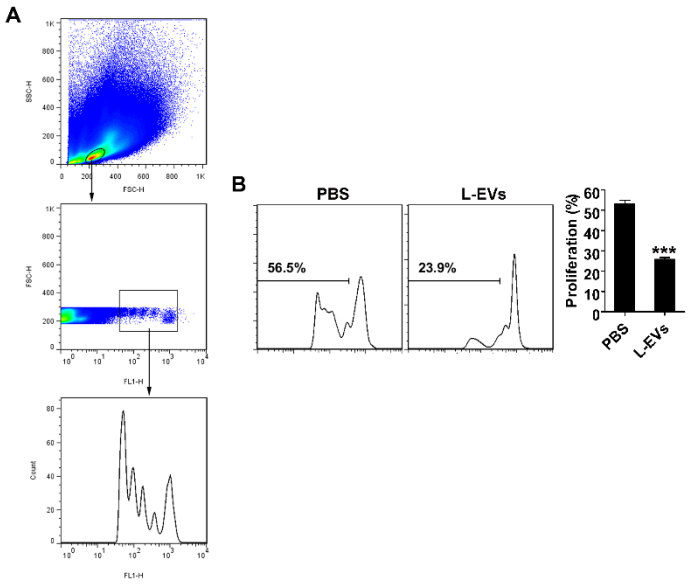



**Supplemental Figure 2.** L-EVs could not alleviate murine IBD. (**A-C**) Mice (n = 5 mice/group) were given drinking water containing 2% DSS on day 0. On days -2 and 2, the mice were intravenously treated with 200 μl of PBS or L-EVs (50 μg/200 μl PBS). The body weights were measured daily (A). Appearance (left) and statistical analysis (right) of colonic length on day 11 (B). Histological appearance on day 11. Representative colonic sections stained with H&E (C). (**A, B**) The data are shown as the mean ± SEM pooled from three independent experiments. (**C**) Representative photomicrographs of three independent experiments are shown. *P* values were generated by one-way ANOVA, followed by TukeyKramer multiple comparisons test; NS: not significant.




**Supplemental Figure 3.** CD8α$^+$CD11c$^+$ L-EVs were responsible for the protective effects of L-EVs in murine asthma. (**A-D**) Mice (n = 5 mice/group) were subjected to asthmatic induction on day 0. On days 24, 25 and 26, mice were intravenously injected with 200 μl of PBS or the indicated L-EVs (50 μg/200 μl PBS). Then, the mice were euthanized 24 h later, and BALF and serum were collected. Total cells and eosinophils in BALF were counted (A). The levels of IL-4, IL-5 and IL-13 in BALF were measured by ELISA (B). The level of IgE in the serum was measured by ELISA (C). Representative photomicrographs of H&E and PAS staining of lung sections are shown. Magnification: × 200 (D). (**E**) Quantitative analysis of lung inflammation and mucus production. (**A-C, E**) The data are shown as the mean ± SEM pooled from three

independent experiments. (**D**) Representative photomicrographs from three independent experiments are shown. *P* values were generated by one-way ANOVA, followed by TukeyKramer multiple comparisons test; ** $p < 0.01$, and *** $p < 0.001$; NS: not significant.




**Supplemental Figure 4.** L-EVs inhibited antigen-specific $CD4^+$ T cell proliferation in hLNs. (**A**) Gating strategy for Fig. 5E and this figure. Living lymphocytes were first gated and then the CFSE positive cells. The proliferation of CFSE positive cells were analyzed in flow histogram. (**B**) Mice were treated as described in Fig. 5D. Lymphocytes in hLNs were isolated 3 days later, and the proliferation of $CFSE^+$ cells was detected by flow cytometry (left) and statistically analyzed (right) (n = 3). The data are shown as the mean ± SEM pooled from three independent experiments. *P* values were generated by paired two-tail Student's *t* test; *** $p < 0.001$.