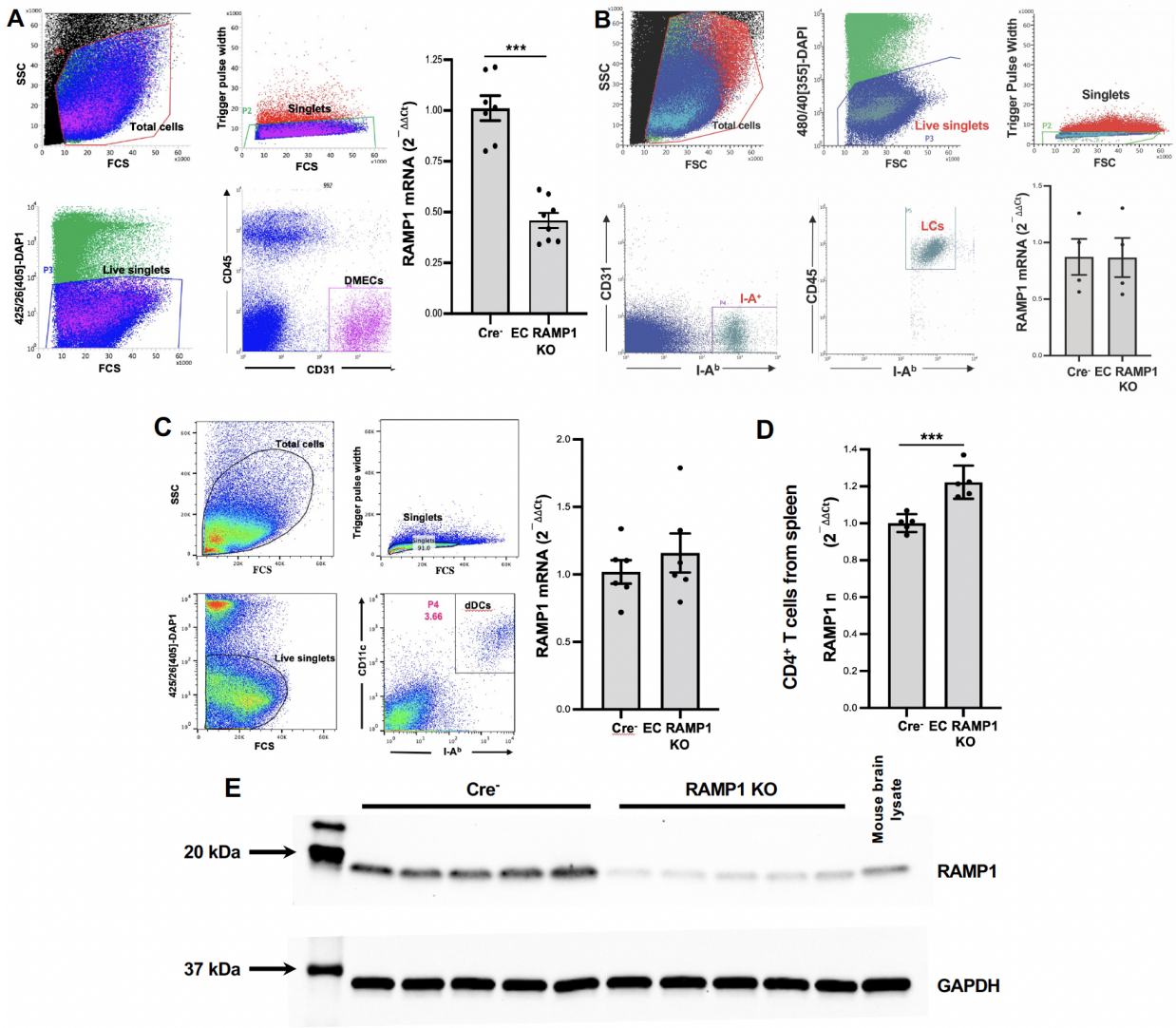
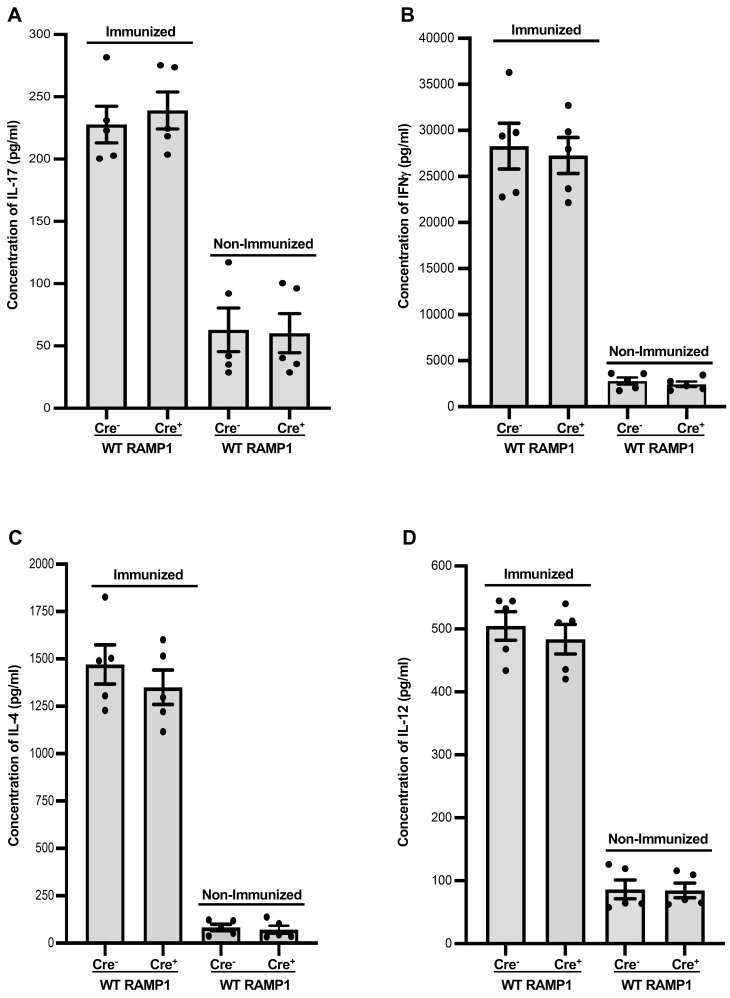
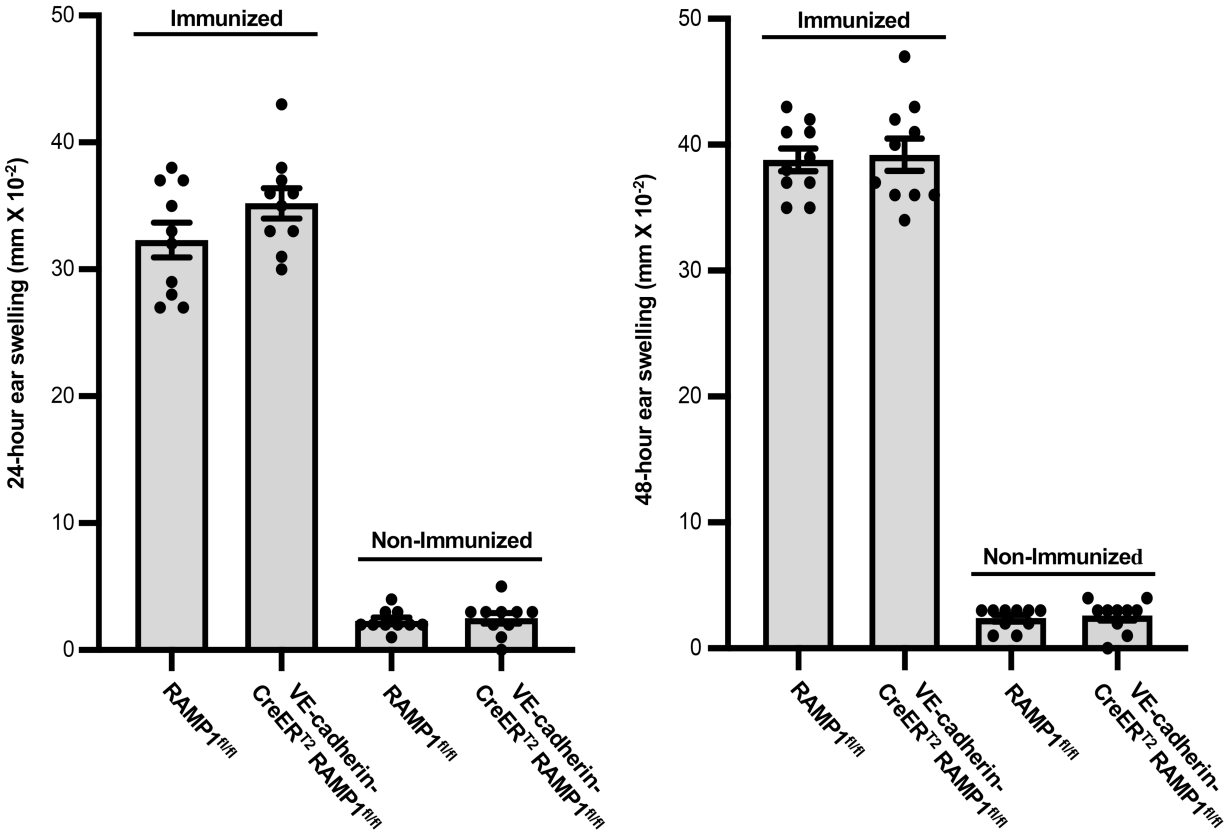



**Supplemental Fig. 1.** RAMP1 expression in DMECs from EC RAMP1 KO mice is deficient while it is not reduced in epidermal LCs, DDCs or $CD4^+$ T cells. Total RNA was extracted and qRT-PCR performed for RAMP1 for each group of cells described below. (**A**) DMECs were isolated from RAMP1 KO mice and $Cre^-$ mice. RAMP1 expression was greatly reduced in DMECs from EC RAMP1 KO mice vs. ECs from $Cre^-$ mice. N=7/group. (**B**) LCs were isolated from EC RAMP1 KO and $Cre^-$mice. No difference in RAMP1 expression was observed between these 2 groups. N=4/group. (**C**) $CD11c^+$ DDCs were isolated from EC RAMP1 KO and $Cre^-$ mice. No difference in RAMP1 expression was observed between these 2 groups. N=6/group. (**D**) $CD4^+$ T cells were isolated from the spleens of EC RAMP1 KO and $Cre^-$ mice. RAMP1 expression was consistently slightly higher in $CD4^+$ T cells from EC RAMP1 KO mice vs. $CD4^+$ T cells from $Cre^-$ mice. N=5/group. Bars represent mean +/- SEM for all groups. ***p<0.001. FACS strategy for **A-C**: Total cells; then singlets; then live singlets; then sorting of $CD31^+$, $CD45^-$ cells (**A**), $CD31^-$, $CD45^+$, $I\text{-}A^+$ cells (**B**) or $I\text{-}A^+$, $CD11c^+$ cells (**C**). For **(D),** $CD4^+$ T cells isolated from spleens by magnetic antibody techniques. Dots represent individual mouse values. (**E**) RAMP1 protein expression is greatly decreased in DMECs from EC RAMP1 KO mice compared to $Cre^-$ controls by Western blotting.




**Supplemental Fig. 2**. Mice expressing the wild-type RAMP1 alleles with VE-cadherin-CreER$^{T2}$ had no change in draining lymph node CD4$^{+}$ T cell production of cytokines after immunization. Mice expressing the wild-type RAMP-1 allele (Tm1c) without VE-cadherin-CreER$^{T2}$ and mice expressing the wild-type RAMP1 alleles with VE-cadherin-CreERT2 were immunized to DNFB or mock-immunized on the shaved dorsa. Three days later, mice were euthanized and draining lymph nodes harvested. A single-cell suspension of CD4$^{+}$ T cells from the draining lymph nodes was prepared and cells were placed in culture and stimulated with anti-CD3 and anti-CD28 monoclonal antibodies. Supernatants were harvested after 72-hours and assayed by ELISA for cytokine content. As shown, no difference in production of (**A**) IL-17A, (**B**) IFN-γ**,** (**C**) IL-4 or (**D**) IL-22 was seen between Cre$^{-}$ and Cre$^{+}$ immunized mice. N=10/group, dots represent individual mouse values.




**Supplemental Fig. 3.** VE-cadherin-CreER$^{T2}$ RAMP1$^{fl/fl}$ mice treated with vehicle alone instead of Tx and immunized to DNFB showed no change in the CHS response compared to RAMP1$^{fl/fl}$ without Cre control mice also treated with vehicle alone. Groups of RAMP1$^{fl/fl}$ without Cre and VE-cadherin-CreER$^{T2}$ RAMP1$^{fl/fl}$ mice were treated with vehicle alone instead of Tx at age 2 and 3 weeks. After aging for several weeks, mice were immunized to DNFB by application of DNFB to the shaved dorsum or mock-immunized as described in Materials and Methods. Seven days later, mice were challenged by application of DNFB to the ears and the CHS response quantified by measurement of 24- and 48-hour ear swelling. As shown, there was no significant difference between the CHS response of immunized RAMP1$^{fl/fl}$ without Cre and VE-cadherin-CreER$^{T2}$ RAMP1$^{fl/fl}$ mice. Bars represent mean +/- SEM. N=5/group, dots represent individual mouse values.

**Supplemental Table 1.** Data set of blinded semi-quantitative evaluation of inflammatory infiltrate of histologic sections of ears challenged for contact hypersensitivity. *N=15; each slide rated on a 0 to 6 scale as described in the Materials and Methods for total infiltrate, neutrophil infiltrate and lymphocyte infiltrate.*

| | Overall Infiltrate | | | | Neutrophils | | | | Lymphocytes | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Immun EC RAMP1 KO | Immun Cre- | Non-Immun EC RAMP1 KO | Non-Immun Cre- | Immun EC RAMP1 KO | Immun Cre- | Non-Immun EC RAMP1 KO | Non-Immun Cre- | Immun EC RAMP1 KO | Immun Cre- | Non-Immun EC RAMP1 KO | Non-Immun Cre- |
| | 4 | 6 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 5 | 6 | 1 | 1 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 |
| | 4 | 6 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 |
| | 5 | 6 | 1 | 1 | 0 | 0 | 0 | 0 | 2 | 2 | 2 | 0 |
| | 5 | 6 | 1 | 1 | 0 | 3 | 0 | 0 | 2 | 3 | 0 | 0 |
| | 2 | 3 | 1 | 2 | 2 | 4 | 0 | 0 | 3 | 3 | 1 | 1 |
| | 3 | 4 | 1 | 1 | 1 | 4 | 0 | 0 | 3 | 3 | 1 | 0 |
| | 2 | 4 | 1 | 1 | 2 | 4 | 0 | 1 | 3 | 2 | 0 | 1 |
| | 3 | 4 | 3 | 1 | 4 | 4 | 0 | 0 | 3 | 2 | 0 | 0 |
| | 3 | 4 | 1 | 1 | 2 | 4 | 0 | 0 | 3 | 3 | 0 | 0 |
| | 3 | 5 | 1 | 1 | 0 | 2 | 0 | 0 | 2 | 3 | 0 | 0 |
| | 3 | 5 | 2 | 3 | 2 | 2 | 0 | 0 | 2 | 3 | 1 | 1 |
| | 3 | 5 | 2 | 2 | 0 | 0 | 0 | 0 | 2 | 2 | 1 | 1 |
| | 3 | 5 | 2 | 2 | 0 | 3 | 0 | 0 | 1 | 3 | 1 | 1 |
| | 3 | 5 | 1 | 1 | 0 | 1 | 0 | 0 | 3 | 3 | 0 | 0 |
| **Mean:** | **3.40** | **4.93** | **1.33** | **1.40** | **0.87** | **2.20** | **0.00** | **0.07** | **1.93** | **2.53** | **0.47** | **0.33** |
| **Std Dev:** | **0.99** | **0.96** | **0.62** | **0.63** | **1.25** | **1.66** | **0.00** | **0.26** | **1.16** | **0.64** | **0.64** | **0.49** |
| | **$p<0.0002$; Immun EC RAMP1 KO *vs* Immun $Cre^-$** | | | | **$p<0.02$; Immun EC RAMP1 KO *vs* Immun $Cre^-$** | | | | **$p=0.091$; Immun EC RAMP1 KO *vs* Immun $Cre^-$** | | | |