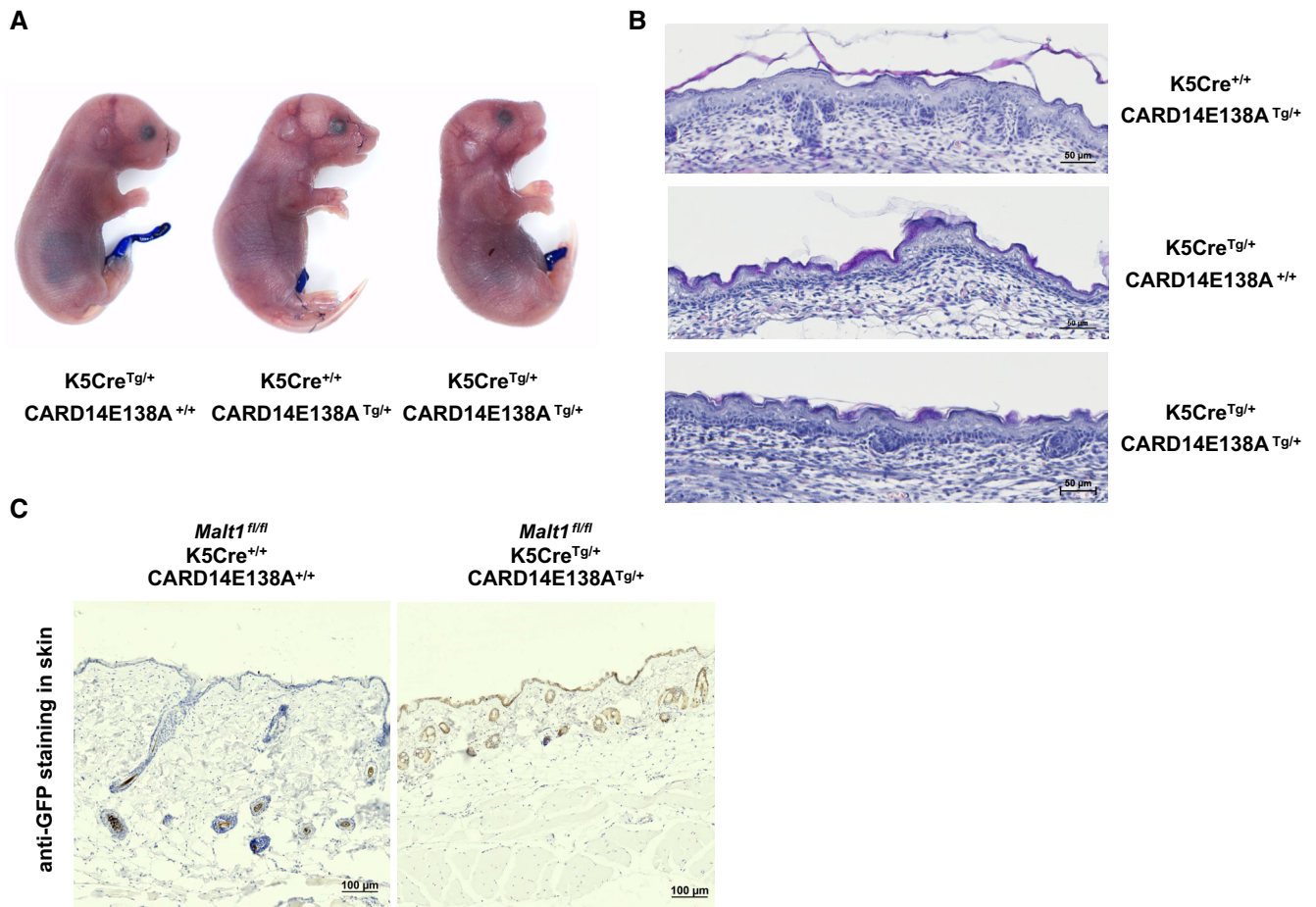


## Expanded View Figures

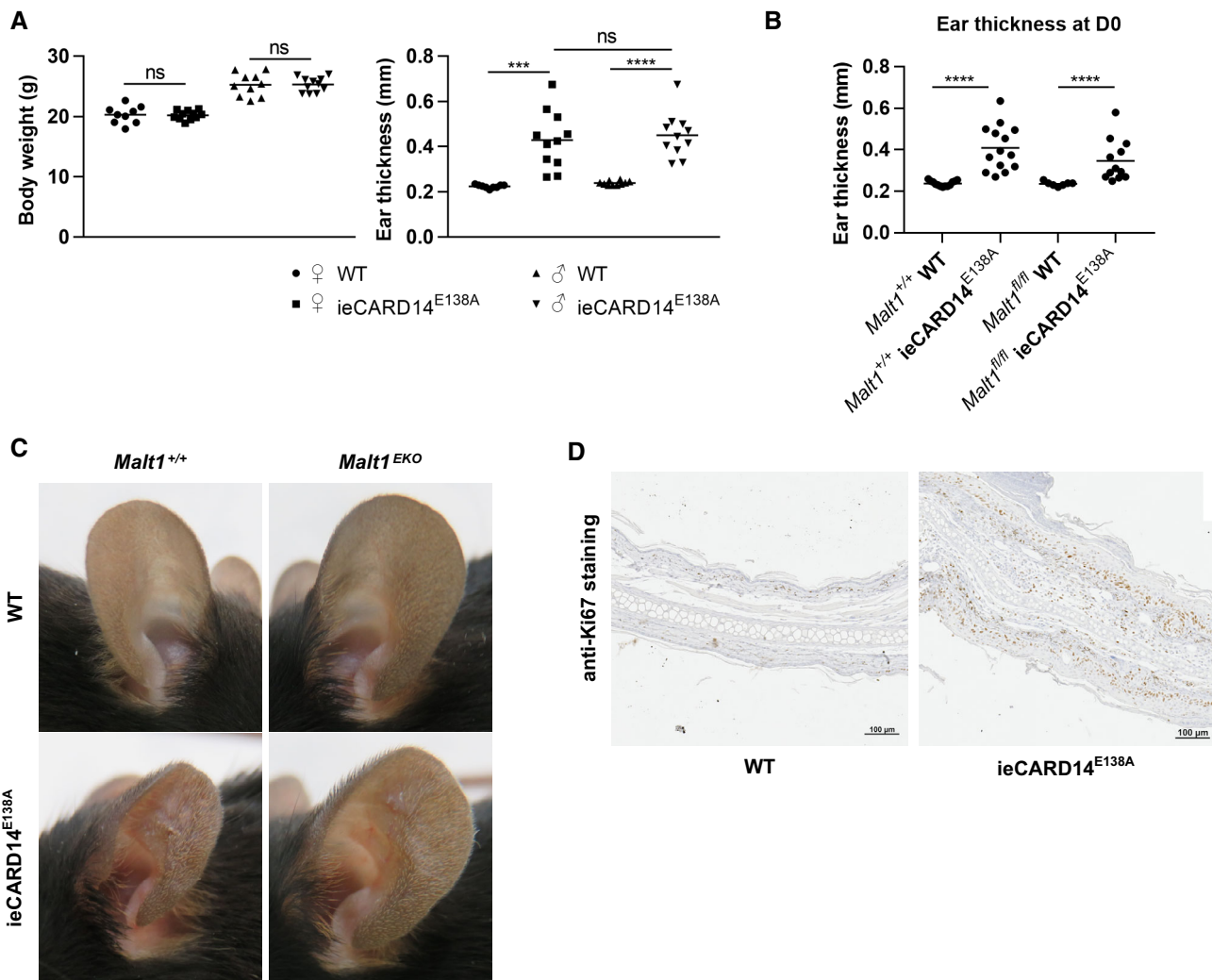


**Figure EV1. Effect of constitutive skin epidermal CARD14<sup>E138A</sup> expression on skin barrier function and structure.**

A Toluidine blue staining of K5Cre<sup>Tg/+</sup> CARD14E138A<sup>+/+</sup>, K5Cre<sup>+/+</sup> CARD14E138A<sup>Tg/+</sup>, and K5Cre<sup>Tg/+</sup> CARD14E138A<sup>Tg/+</sup> E18.5 pups.

B Histological sections of skin tissue of K5Cre<sup>+/+</sup> CARD14E138A<sup>Tg/+</sup>, K5Cre<sup>Tg/+</sup> CARD14E138A<sup>+/+</sup>, and K5Cre<sup>Tg/+</sup> CARD14E138A<sup>Tg/+</sup> pups at E18.5 stained with hematoxylin and eosin (scale bar represents 50 μm). CARD14E138A<sup>+/+</sup> = Rosa26<sup>+/+</sup>, CARD14E138A<sup>Tg/+</sup> = Rosa26<sup>LSL-CARD14-E138A/+</sup>.

C Immunohistochemical staining of GFP in sections of skin tissue from Malt1<sup>fl/fl</sup> K5Cre<sup>+/+</sup> CARD14E138A<sup>+/+</sup> and Malt1<sup>fl/fl</sup> K5Cre<sup>Tg/+</sup> CARD14E138A<sup>Tg/+</sup> mice of 5 months old (scale bar represents 100 μm).



**Figure EV2. Psoriasis-like symptoms upon leaky and tamoxifen-induced CARD14<sup>E138A</sup> expression in the ears of ieCARD14<sup>E138A</sup> mice.**

- A** Body weight and ear thickness of untreated 8-week-old WT and ieCARD14<sup>E138A</sup> males and females. Each symbol represents one mouse; the line represents the mean value ( $n \geq 9$  mice per group). WT = K14creER<sup>Tg/+</sup> Rosa26<sup>+/+</sup>, ieCARD14<sup>E138A</sup> = K14creER<sup>Tg/+</sup> Rosa26<sup>LSL-CARD14-E138A/+</sup>. Statistical difference between WT and ieCARD14<sup>E138A</sup> groups was determined using an unpaired t-test (normality of data was tested with a D'Agostino-Pearson normality test) (\*\*\* $P < 0.001$ , \*\*\*\* $P < 0.0001$ ).
- B** Ear thickness of untreated 8-week-old Malt1<sup>+/+</sup> WT, Malt1<sup>+/+</sup> ieCARD14<sup>E138A</sup>, Malt1<sup>fl/fl</sup> WT, and Malt1<sup>fl/fl</sup> ieCARD14<sup>E138A</sup> mice. Each symbol represents one mouse; the line represents the mean value ( $n \geq 7$ ). Statistical difference between two groups was determined using a Mann–Whitney U-test (\*\*\*\* $P < 0.0001$ ).
- C** Representative images from Malt1<sup>+/+</sup> WT, Malt1<sup>+/+</sup> ieCARD14<sup>E138A</sup>, Malt1<sup>fl/fl</sup> WT, and Malt1<sup>fl/fl</sup> ieCARD14<sup>E138A</sup> mice 4 days after tamoxifen treatment.
- D** Immunohistochemical staining of the proliferation marker Ki67 in sections of ear tissue from WT and ieCARD14<sup>E138A</sup> mice 4 days after tamoxifen treatment (scale bare represents 100 μm).

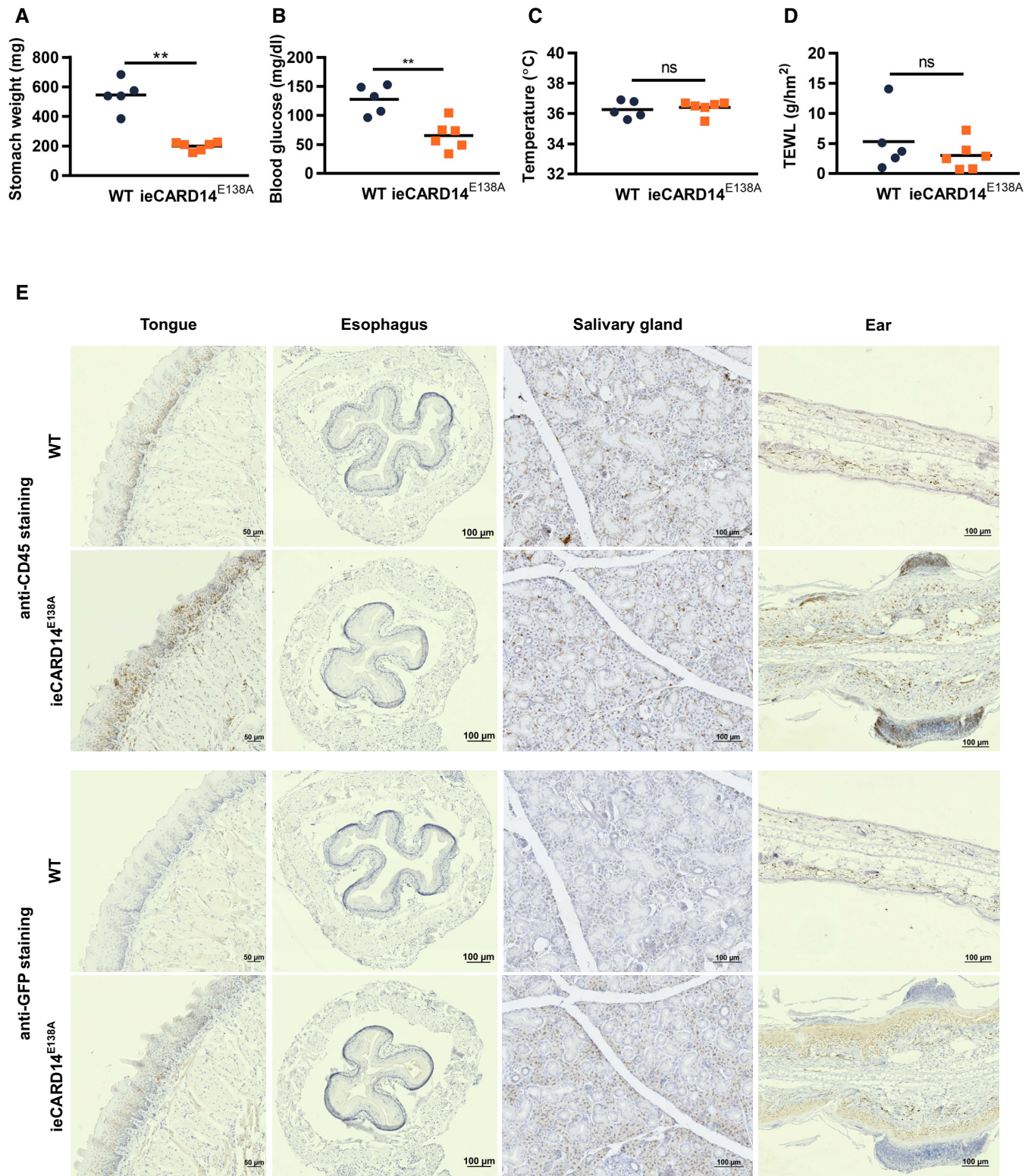
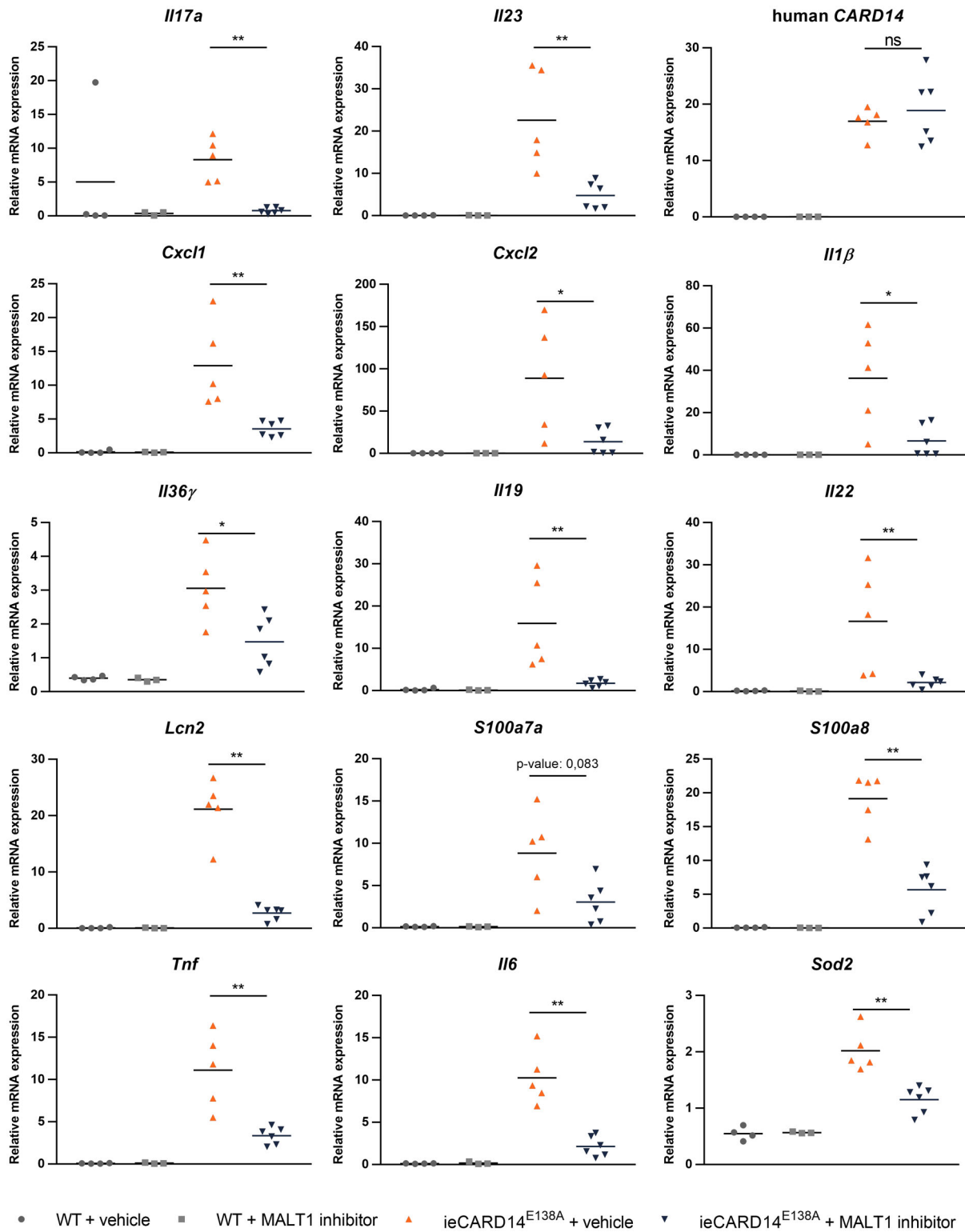


Figure EV3.

**Figure EV3. Tamoxifen-induced K14Cre-driven CARD14<sup>E138A</sup> expression in the tongue and salivary glands induces oral inflammation and decreased food uptake.**

- A–D Stomach weight (A), blood glucose levels (B), body temperature (C), and transepidermal water loss (TEWL) (D) of WT and ieCARD14<sup>E138A</sup> mice three (C) or four (A, B and D) days after tamoxifen treatment. WT = K14creER<sup>Tg/+</sup> Rosa26<sup>+/+</sup>, ieCARD14<sup>E138A</sup> = K14creER<sup>Tg/+</sup> Rosa26<sup>LSL-CARD14-E138A/+</sup>. Each symbol represents one mouse; the line represents the mean value ( $n \geq 4$  mice per group). Statistical difference between WT and ieCARD14<sup>E138A</sup> groups was determined using a Mann–Whitney *U*-test (ns:  $P > 0.05$ ,  $**P < 0.01$ ).
- E Representative images of immunohistochemical staining of CD45 and GFP in sections of tongue, esophagus, salivary gland, and ear tissue from WT and ieCARD14<sup>E138A</sup> mice 4 days after tamoxifen treatment (CD45- and GFP-stained sections of each organ are derived from the same WT and ieCARD14<sup>E138A</sup> mouse; scale bar represents 50  $\mu\text{m}$  in sections of tongue tissue and 100  $\mu\text{m}$  in sections of esophagus, salivary gland, and ear tissue).



**Figure EV4. MALT1 inhibition reduces proinflammatory gene expression in ears of ieCARD14<sup>E138A</sup> mice.**

mRNA expression levels of the indicated genes in ears relative to reference genes (*Hprt1* and *Tbp*). Each symbol represents one mouse; the line represents the mean value ( $n \geq 3$ ). Statistics: Differences between ieCARD14<sup>E138A</sup> + vehicle and ieCARD14<sup>E138A</sup> + MALT1 inhibitor groups were determined using a Mann-Whitney *U*-test (\* $P < 0.05$ , \*\* $P < 0.01$ ). WT = K14creER<sup>Tg/+</sup> Rosa26<sup>c+/+</sup>, ieCARD14<sup>E138A</sup> = K14creER<sup>Tg/+</sup> Rosa26<sup>LSL-CARD14-E138A/+</sup>.