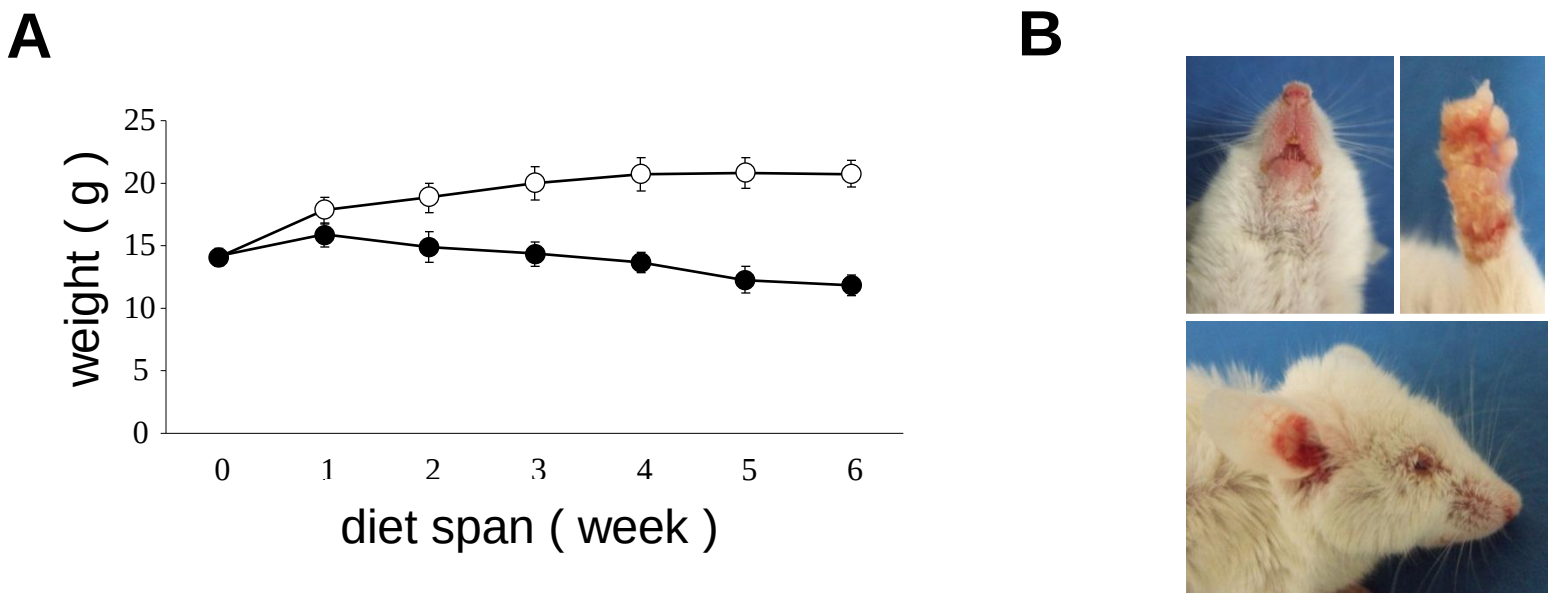
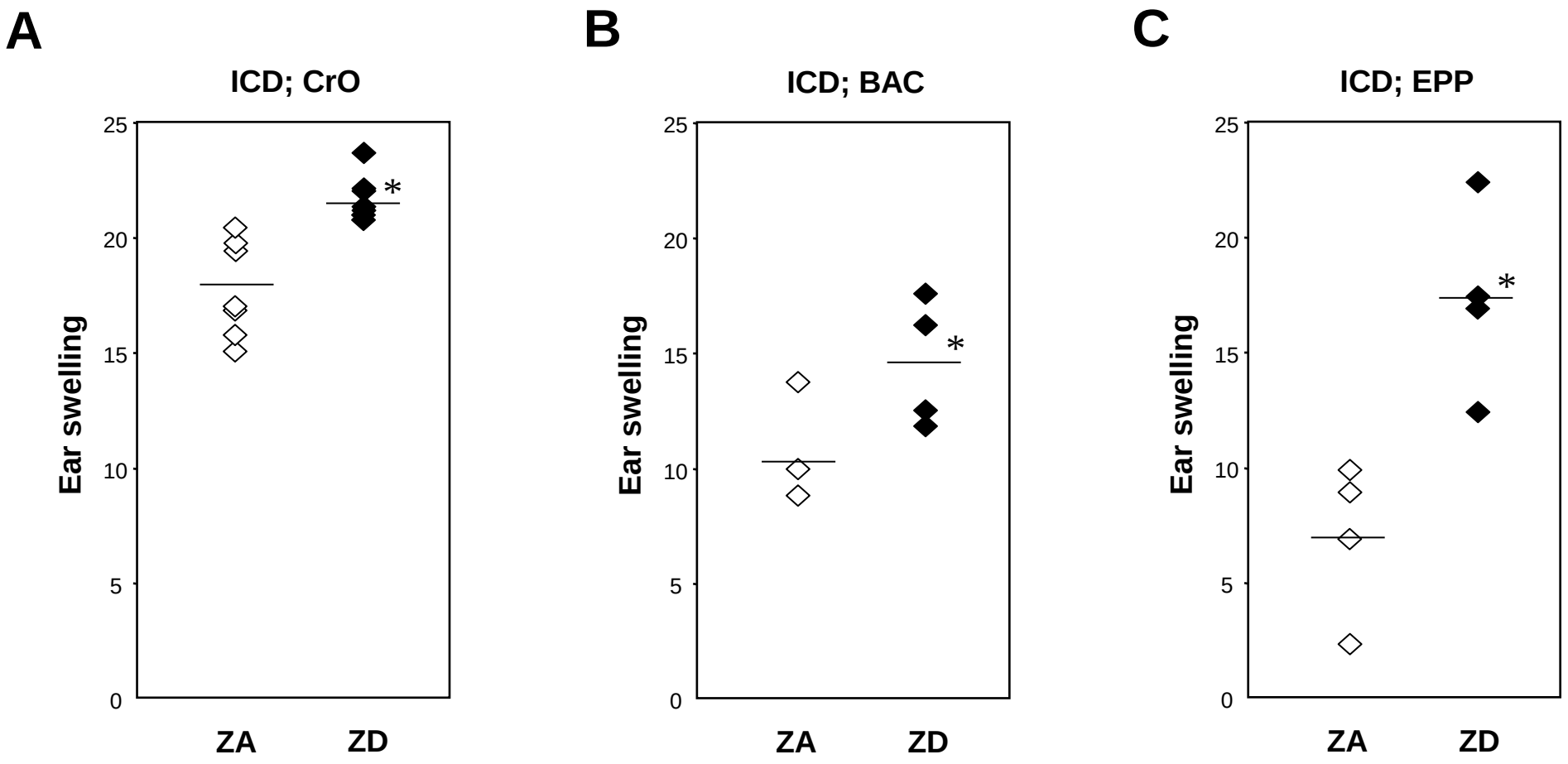
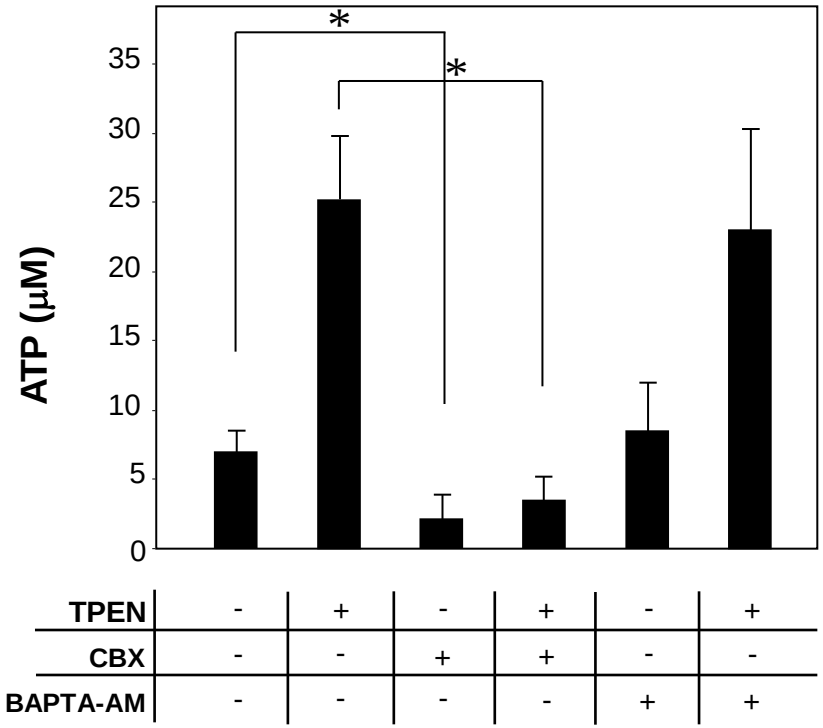


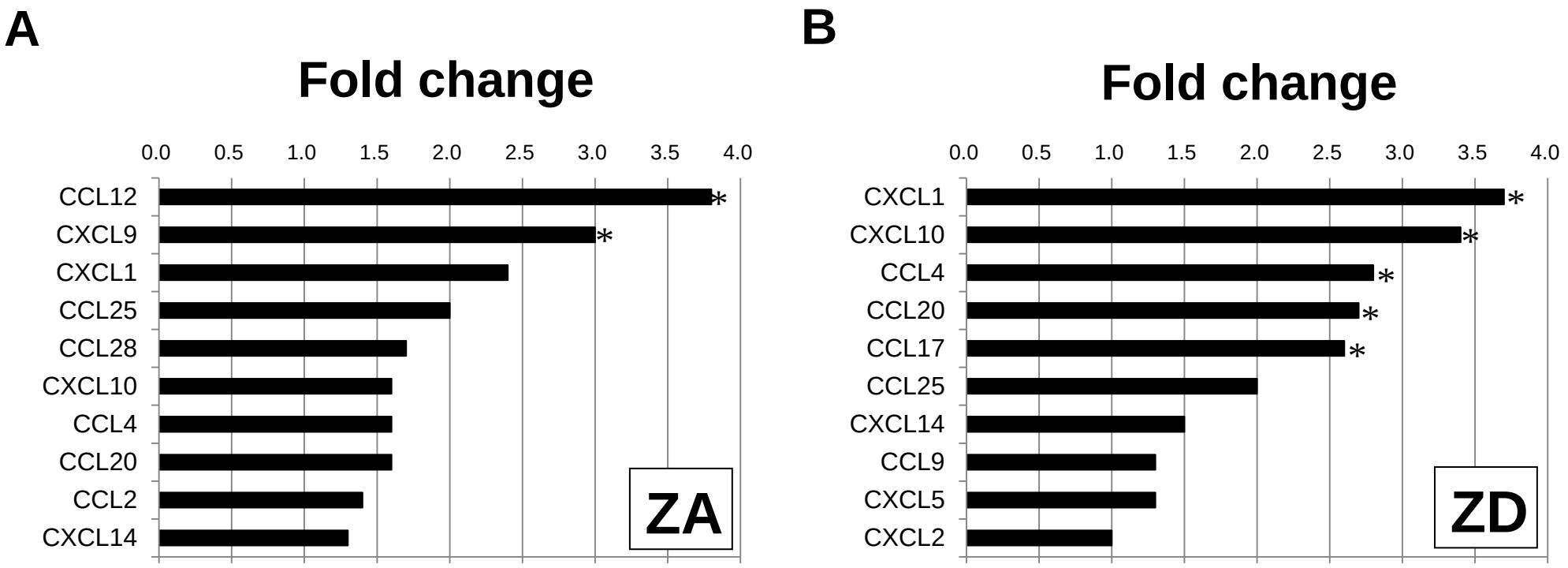
Supplemental Figure 1. Body weight and cutaneous symptoms in Zn deficient mouse. Five-week-old Balb/c mice were fed by Zn deficient or Zn adequate diet for 6 weeks. (A) Time-course changes of body weight of ZA (○) or ZD (●) mouse. (B) A mild periorbital alopecia and a slight acral and perioral parakeratosis observed in ZD mouse.



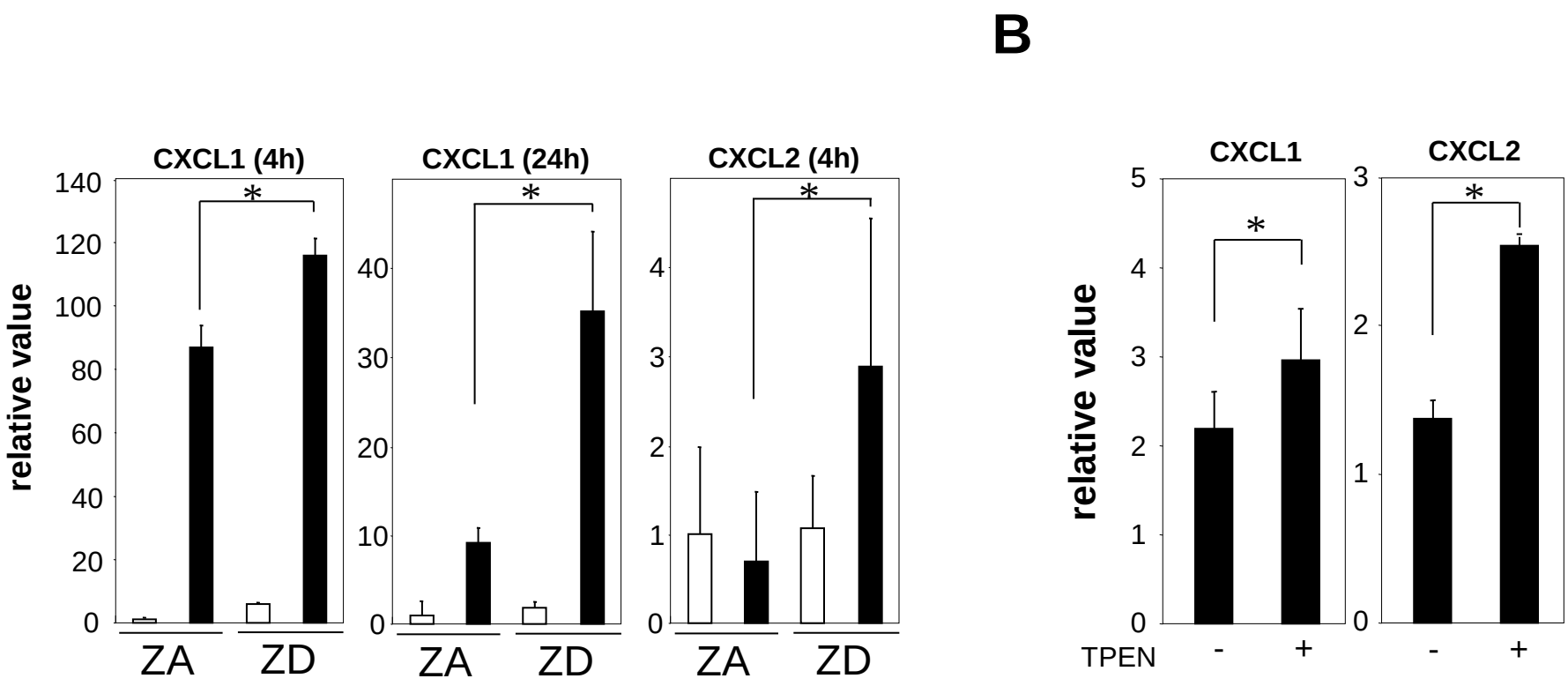
Supplemental Figure 2. Zn deficient mice demonstrate severe irritant contact dermatitis. ICD to CrO (A), BAC (B) or EPP (C) was induced in ZA (◇) and ZD (◆) mice as described in Methods (n=5). Ear thickness was evaluated at 24 hrs after irritants application. (A-C) Summary of the mean swelling responses from individual experiments in seven (CrO), four (BAC) and four (EPP) separate experiments. Mean values in each group are shown as horizontal marks. *, $P < 0.05$ compared with ZA mice.



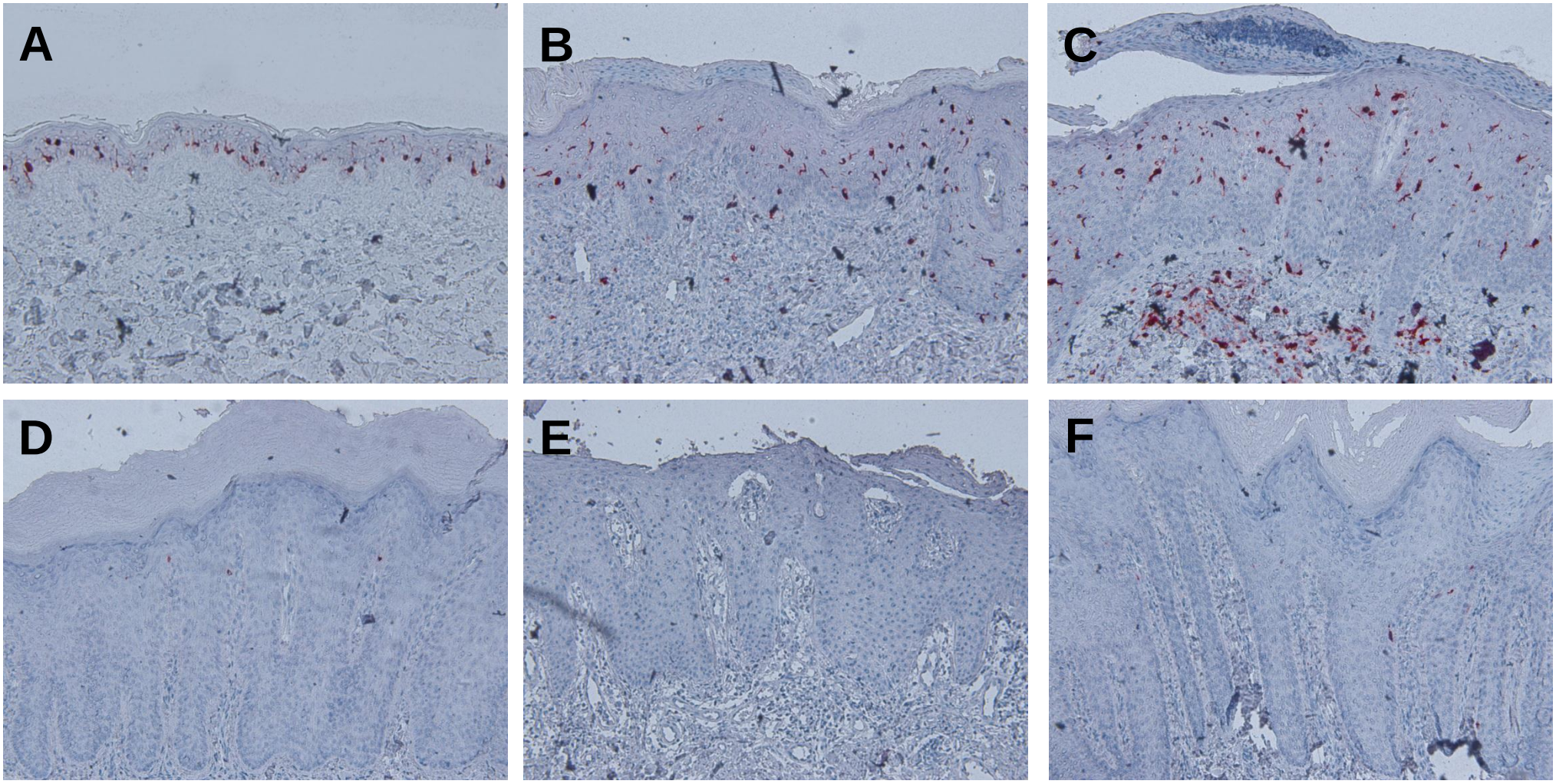
Supplemental Figure 3. The release of ATP from keratinocytes treated with CrO is mediated by membrane channels. Pam-212 keratinocytes were pre-treated with or without 2 μM TPEN, cultured in the presence or absence of CBX (30 μM) or BAPTA-AM (2 μM) for 10 min., and then stimulated with CrO. ATP in the culture supernatants was quantified 10 min. after CrO stimulation. *$P < 0.05$, indicates a statistically significant difference. Data are representative of three independent experiments.



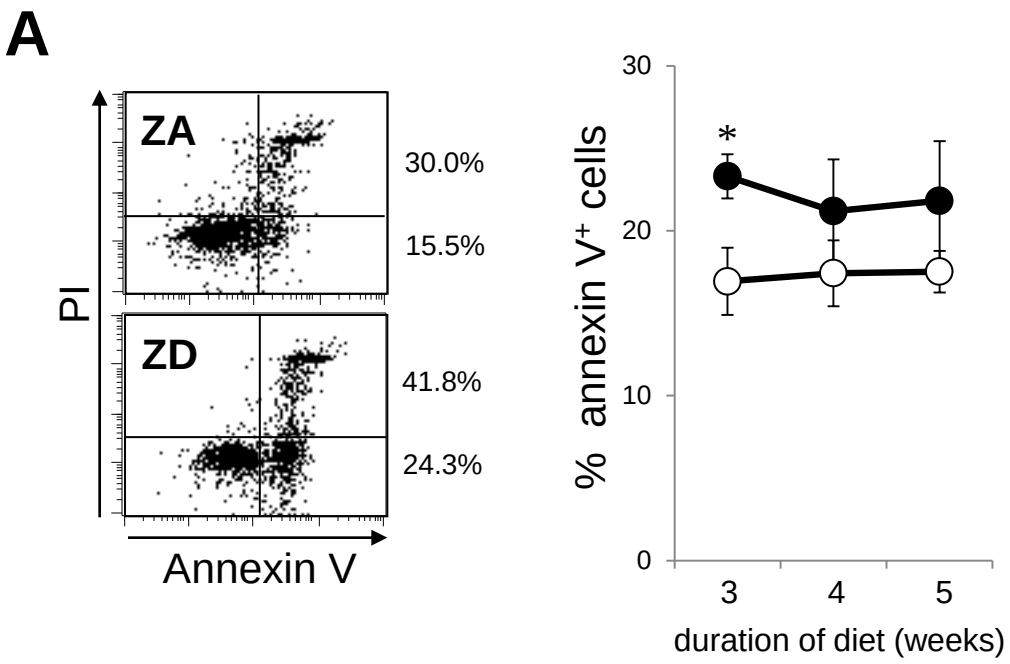
Supplemental Figure 4. Chemokine genes in epidermal sheets up-regulated by croton oil application. mRNA expression profiles for 44 chemokines in epidermal sheets obtained from ZA and ZD mice 24 hrs after vehicle or CrO application *in vivo* were quantified by DNA microarray analysis. (A, B) Summary of the 10 most up-regulated chemokines. Fold change was demonstrated as the ratio of each chemokine gene expression in croton oil-applied epidermis to that in vehicle-applied epidermis. *, P <0.05



Supplemental Figure 5. Zn deficiency increases CXCR1 and CXCR2 gene expression in keratinocytes following treatment with BAC. (A) 10% BAC (black bars) or vehicle alone (white bars) was painted on the ears of ZA and ZD mice (n = 5). Epithelial sheets were obtained from the ears at 4 hrs or 24 hrs, and total RNA was extracted. (B) Pam212 keratinocytes were cultured in the presence or absence of 2 μM TPEN. Total RNA was extracted 4 hrs after 0.01% BAC exposure. Quantitative real-time RT-PCR analysis of CXCL1 and CXCL2 was performed for each (A, B). mRNA expression was normalized to GAPDH. The fold induction was calculated from the normalized mRNA expression by BAC-stimulated keratinocytes relative to non-stimulated zinc-adequate keratinocytes. *, $P < 0.05$ compared with zinc-adequate controls. Data are representative of two independent experiments.



Supplemental Figure 6. Loss of epidermal LCs in AE patients. Immunohistochemical staining for langerin (red) in normal skin (A) and the erythematous lesions in atopic dermatitis (B), psoriasis vulgaris (C) or three AE (D-F) patients. Original magnification: 200x.



Supplemental Figure 7. Zn deficiency induces apoptosis in LCs. (A) Cell suspensions of epidermis from mice fed ZA (○) or ZD (●) diets for the indicated time were stained for annexin V, PI and I-A antigen. A representative FACS analysis of I-A+-gated cell suspensions from mice fed ZA or ZD diets for 3 weeks. (B) Cell suspensions of epidermis from ZA mice or (C) human monocyte-derived LCs were cultured in the presence or absence of TPEN for 48 hrs, and stained for annexin V, PI and I-A or human langerin antigen, respectively. (A-C) The percentages of annexin V positive and PI negative cells were assessed within each I-A+- or langerin+-gated cell population. Results are the mean ± SD (n = 3). *, P <0.05 compared with zinc-adequate controls. Data are representative of three independent experiments.