The role of ASIC3 ion channel in pathogenesis of psoriasis

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RESULTS
In the study we induced psoriasis-like skin inflammation in model animals and investigated whether the phenotypes are different with or without ASIC3. After IMQ application for 7 days (Figure 1.A, B), we observed spleenaxa in model animals, which can be the result of inflammation. Also we found that spleenaxa in ASIC3 KO mice is less significant than that in WT mice(Figure 1.C, D). In a reference it is reported that nociceptive sensory neurons drive IL-23 mediated psoriasis-like skin inflammation (3). Based on another reference (4), we used different methods to achieve peripheral denervation and compare spleen weight in these groups(Figure 1.E, F). Our results show that ASIC in TRPV1+ neurons may be a key molecular in driving inflammation.

At morphological level we found that ASIC3 knock out or knock down results in thinner psoriasis skin and less ki-67 staining intensity, which represent the keratinocyte proliferation in skin tissue. Also ASIC3 KO can reverse the “anti-psoriasis” effect of peripheral denervation (Figure 2).

IL-23, IL-17, and IL-22 are key cytokine in the process of psoriasis. IL-23 can be released by dendritic cells in dermal tissue and activates γδT7 lymphocytes to release IL-17 and IL-22. IL-17 recruits neutrophils and IL-22 induces keratinocyte proliferation. Consistently, by ELISA we found that the level of these cytokines are lower in ASIC3 KO model animals (Figure 3), which further support our hypothesis that ASIC3 is involved in the process of psoriasis.

CONCLUSIONS
Our experiment results provide basic evidence that ASIC3 in peripheral sensory neurons contributes to the process of psoriasis. Although the underlying mechanism is still not delineated, it is reasonable to suppose that ASIC3 channel can sense the change in affected tissue (as its major function) and interact with immune cells, thus influence the level of certain cytokines.

FUTURE PLAN
To further investigate the mechanism of how ASIC3 channel contribute to process of psoriasis, we plan to do transcriptome analysis of dorsal root ganglion (DRG) of model animals to find out the changes of mRNA before and after psoriasis modeling, and in WT and ASIC3 KO model animals, to screen out potential molecular intermediate (neurotransmitter, etc.) between nervous and immune system. Electrophysiological analysis of DRG can help study whether DRG response to signaling molecular from immune cells. Flow-cytometry is also necessary for understanding which subset of immune cells are regulated by ASIC3 channel. These data will help fulfill the working model of our hypothesis.