Involvement of sensory neurons in the pathophysiology of atopic dermatitis

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Both the nervous and immune systems have evolved to detect and protect the organism from danger, including to noxious/tissue-damaging stimuli, pathogen invasion and exposure to environmental antigens. The innate and adaptive immune system within the skin has a major role in this, to the extent that the skin is sometimes considered an immunologic organ. Historically, the sensory nervous and immune systems have been considered separate entities, where now we realize that they can work together to support host defense and resolution of tissue damage. These systems interact through cell surface G protein-coupled receptors, receptor tyrosine kinases, cytokines, growth factors, and neuropeptides. While this crosstalk is adaptive in many settings, such as during injury, it can also become dysfunctional and contribute to disease (as described in Foster, Seehus et al., 2017). Although allergic/atopic skin disorders are considered to be largely immune-mediated, and treatment for skin allergy/atopic dermatitis and psoriasis is currently targeted only at the immune system, we hypothesize that sensory neurons contribute in an important way to the pathophysiology of immune reactions in the skin and this provides an opportunity for a new therapeutic approach, one that would involve targeting the neurons rather than just immune cells. Here, we use targeted sensory neuronal ablation by Cre-driven diphtheria toxin as well as the temporary pharmacological silencing of nociceptors by sodium channel blockade to test the effects of sensory neuron ablation/silencing on a model of atopic dermatitis. We find that not only do nociceptors contribute extensively to the pathophysiology of atopic dermatitis, but by specifically activating nociceptors using optogenetics, we can induce an immunological response in the skin, thus providing novel insights into the neurocircuitry of the neuroimmune response.

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