Rodent Model of Atopic Dermatitis Associated with Itch Sensitization

Atopic dermatitis (AD) patients suffer from chronic itch that affects their social interactions. These patients exhibit an increased incidence of suicidal ideation, anxiety, and depression, resulting in a significant reduction in their quality of life. Additionally, chronic itch often triggers a vicious itch- scratch cycle that results in intractable skin inflammation. The incidence of AD in children worldwide has been estimated at up to 20%, with a large majority experiencing moderate to severe itch. Antihistamines are largely ineffective against the chronic itch of AD, and there are few additional treatment options. There is therefore a large demand to develop novel treatments for this condition.

In conditions of chronic itch such as AD, it is hypothesized that peripheral and/or central itch- signaling neurons become sensitized to provide a stronger itch signal to the central nervous system. This sensitivity results in symptoms of spontaneously occurring itch, itch in response to non-itchy light touch (“alloknesis”), and increased itch in response to a normally itchy stimulus such as an insect bite (“hyperknesis”). However, the cellular and molecular mechanisms that underlie this process are currently unknown. In the present study, we developed behavioral tools to assess itch sensitization in an animal model of AD.

At the level of the spinal cord, molecular receptors for the neuropeptides gastrin-releasing peptide and substance P play an important role in sending itch signals to the brain. Using our animal model of AD, we found that the molecular receptor for substance P plays an important role in the sensitization of itch, while the molecular receptor for gastrin-releasing peptide is partially involved. Our model will help to identify targets for the development of anti-itch strategies. For example, the molecular receptor for substance P in the spinal cord is a potential target to treat chronic itch.