Title: Upregulated Natriuretic Peptide B Expression as a Hallmark of Chronic Itch

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Abstract: Chronic itch can arise via multiple etiologies from dermatological conditions, such as eczema and psoriasis, to systemic diseases including liver disease and kidney failure. However, it is unclear whether there are common molecular characteristics for chronic itch and whether these may be selective for chronic itch compared to chronic pain. To identify candidate common peripherally expressed molecular features specific for chronic itch, we examined transcriptomic data of sensory neurons that were collected from three models of chronic itch in mouse and a monkey model of contact dermatitis and compared them to data from three models of pain in mouse, and clinical data from patients with neuropathic pain. Our analyses revealed the upregulation of *Nppb* expression in sensory neurons is consistently associated with models of itch, but not models of pain. Further our cellular characterization showed that increased expression of *Nppb* arises by increased cell-autonomous expression rather than recruitment of expression of *Nppb* in other classes of sensory neurons. Since *Nppb* is a well-established itch neurotransmitter, our findings suggest that the increased expression of *Nppb* in sensory neurons may contribute to chronic itch. Additionally, based on our findings, we propose that *Nppb* is a conserved biomarker of chronic itch.

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