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**“Basophils and neuromedin B: unexpected regulators of
helminth-induced inflammation”**

by
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ABSTRACT

Type 2 cytokine responses, characterized by the production of interleukin (IL)-4, 5, and 13; promote anti-helminth immunity and initiate tissue repair, but can result in chronic immunopathologies when not properly restricted. Basophilia is recognized as a common feature of helminth infections, however, the roles basophils play in regulating these responses remain unknown. A growing body of evidence suggests that cross-talk between specialized immune cell populations direct the intensity of type 2 cytokine responses. For example, it has been proposed that basophils provide important signals to group 2 innate lymphoid cells (ILC2s) and CD4⁺ T helper type 2 (T_H2) cells thereby promoting their secretion of type 2 cytokines. Additionally, recent studies have also revealed that the coordinated actions of innate immune cells and the nervous system initiate anti-helminth immunity. However, whether the immune and nervous systems also communicate in order to limit type 2 inflammation and promote tissue integrity remains poorly defined.

Here, we demonstrate that helminth-induced ILC2 responses are exaggerated in the absence of basophils, resulting in increased lung inflammation and diminished pulmonary function. Further, we show that ILC2s from basophil-depleted mice express reduced amounts of the receptor for the neuropeptide, neuromedin B (NMB). Importantly, co-culture with basophils or basophil-associated molecules was sufficient to enhance NMB receptor (NMBR) expression on ILC2s. Moreover, NMB stimulation inhibited ILC2 cytokine responses from control but not basophil-depleted mice, suggesting that basophils prime ILC2s to respond to NMB-mediated inhibitory signals. Similar to ILC2s, T_H2 cells from basophil-depleted mice also exhibit reduced levels of NMBR, which was associated with their persistent activation that resulted in chronic tissue remodeling. Collectively, these data suggest that basophils operate as a transition switch on ILC2s and T_H2 cells needed for them to respond to NMB-derived inhibition in a manner that properly regulates helminth-induced inflammation.