Mast cell interleukin-5 is critical to homeostasis of regulatory B cells in hypersensitive immune responses

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Mast cells (MCs) are the culprit cells in immediate hypersensitivity (also known as type I hypersensitivity) through the activation of IgE-bound high affinity receptor FcεRI. When MCs are activated by an allergen, preformed granule associated mediators, including histamines, eicosanoids, and pro-inflammatory cytokines are secreted from mast cells to cause allergic diseases such as atopic dermatitis, allergic rhinitis, asthma, and anaphylaxis. However, we recently discovered a beneficial role of mast cells that we had not expected at all. Peripheral immune tolerance plays a role in the maintenance of body homeostasis against acute and chronic inflammatory responses at local disease tissue. Our studies suggest that new types of regulatory immune cells play an important role in maintaining the immune tolerance. Regulatory B cells (Bregs), also referred to as Interleukin-10 (IL-10)-producing B subsets, are known to suppress various immune responses. However, the evidence of its development and maintenance mechanism is still insufficient. In contact hypersensitivity (CHS), we found that Bregs control the activation of IL-13-producing type 2 innate lymphoid cells (ILC2s) in IL-10-dependent manner and its regulatory effect is mainly appeared in lymph nodes. Very surprisingly in the further study, IL-5 produced from lymphoid tissue MCs increased the population of IL-10-producing B-1a lineage Breg subsets and played an important role in suppressing CHS. Overall, these results uncover a previously unknown function of MCs in Breg-mediated regulatory mechanisms in CHS.