TSLP and Allergic Inflammation

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Allergic inflammatory responses are believed to be inappropriate responses to innocuous environmental antigens that lead to chronic Th2-type responses. While the role of Th2 cytokines, especially IL-4 and IL-13, are well-documented in this response, the initial triggering factor remains to be determined. Our data suggests that the cytokine thymic stromal lymphopoietin (TSLP) is involved in both initiating and perpetuating allergic inflammatory responses. TSLP is expressed by epithelial cells at barrier surfaces, and its expression is elevated in the lesional skin of atopic dermatitis patients, and in the lungs of asthmatics. In the mouse, TSLP is elevated in antigen-driven models of airway inflammation, and transgenic expression in the skin or lung leads to the spontaneous development of inflammatory disease at the site of transgene expression. Finally, mice that cannot respond to TSLP fail to develop antigen-driven airway inflammation, showing that TSLP is both necessary and sufficient for this disease. We have used a variety of techniques to identify downstream mediators of TSLP-mediated disease, and show that dendritic cell responses to TSLP are critical to disease development. In addition, IL-4 and IL-13 are important mediators of TSLP signals, and functional blockade of these cytokines can reverse disease pathology. We have also extended the functional characterization of TSLP and disease to include contact hypersensitive responses to haptens, and have shown that antigens that require Th2-responses for disease development also require intact TSLP signaling, while those that use Th1-type cytokine responses do not. Taken as a whole, these data demonstrate the importance of TSLP to Th2-type immunity, and suggest that TSLP blockade may be an efficacious means of controlling allergic inflammatory responses.

References

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