Allergic Inflammation – The Enemy Within

Allergic inflammation is often seen as an adequate part of host response to helminthic infestation. However, when dysregulated in chronic allergic diseases, it presents suffering for the individual and a challenge for the health care provider. In this issue, the *Journal of Innate Immunity* publishes several articles that define key roles played by the cellular network (i.e. mast cells, eosinophils and dendritic cells) in steering pro-allergic immune responses. In a timely review article, Akuthota et al. [1], discuss the emerging appreciation that eosinophils are multi-functional cells providing immune defensive as well as pro-allergic functions – particularly in the context of allergic airway disease. Similarly, it is now recognized that mast cells too are crucial players in microbial immune surveillance as well as in allergic immunity. McAlpine et al. [2] discuss their elaborate expression of pattern-recognition receptors, broad tissue distribution, combined with their key effector roles in allergic inflammation, suggesting that they are capable of mediating microbial-induced exacerbations of allergic diseases [2]. In a related study, Enoksson et al [3] show that mast cells are endowed with intracellular pattern-recognition receptors such as Nod1 that on activation by exogenous danger signals like M-TriDAP (a degradation product of bacterial peptidoglycan) induce release of pro-inflammatory mediators, further supporting a role for mast cells in host immune defense against bacteria [3]. While the pulmonary system [4, 5] is susceptible to allergic airways disease on activation by such diverse challenges as ambient air pollutants [4] and indoor allergens such as German cockroach frass [5], the innate immune system fulfills an important role in the pathogenesis of allergic atopic dermatitis [6]. In complementary studies, Bezemer et al [4] and Page et al [5] show that ambient airborne pollutants and German cockroach frass respectively, can promote a rapid onset of allergic inflammation via activation of stimulatory myeloid dendritic cells [4, 5]. Conceptual frameworks that advanced our understanding of how the pulmonary innate immune system is modulated by ambient pollutants, xenobiotics and respirable areoallergens have also been previously discussed [6, 7]. Interestingly, the dendritic cell appears to be the crucial link for sensing “environmental danger” in the lung and bridging the innate arm of immunity with the adaptive pro-allergic response [8, 9]. Sensing of so-called “dangerous environmental signals” by dendritic cells appears to require functional transmembrane expression of the mucin-like molecule Muc1 that is capable of fine-tuning Toll-like receptor signaling and regulating the inflammatory response [9]. In the final article, Maintz and Novak [10] discuss dysregulation of innate immunity in the pathogenesis of atopic dermatitis, a disease frequently promoted by microbial super-infection. They propose a revised paradigm where a disturbed innate immune system is constituted by genetic susceptibility, disturbed barrier functions, dampened anti-microbial defense and interplay between NK cells and plasmacytoid dendritic cells. Together, this permits entry of infectious microorganisms that exacerbates an ongoing pernicious cycle of Th2-driven allergic inflammation in the skin [10]. Continued research will further elucidate the complex network of

cells and signaling pathways that result in allergic inflammation. Recently discovered mechanisms, as described in the articles of this issue, can serve as models for development of novel therapeutic strategies.

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