Th2/Innate Immune Responses in the Pathogenesis of Occupational Asthma

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Previous studies suggested that various immunologic/non-immunological mechanisms are involved in the pathogenic mechanism of occupational asthma (OA), moreover they could be much different according to kinds/molecular weights of causative agents. Prevalence causes of OA in Korea are known to be isocyanates (the representing agent of low molecular agent) and wheat flour/grant dusts (the representing agent of high molecular agent). This review summarized recent studies demonstrating active involvement of innate immune responses as well as Th2 responses caused by these agents.

Regarding isocyante-induced OA, it is known that the prevalence of serum specific IgE to isocyanate-human albumin conjugate was lower (30%-40%) than that of allergic asthma. There have been several reports to demonstrate neutrophil activation interacting with epithelial cells in its pathogenic mechanism, in which decreased levels of progranlin/clusterin with increased levels of periostin/TGFB1 were noted in OA patients compared to asymptomatic exposed workers and non-exposed controls. Increased expressions of epithelial cell-derived autoantigens such as CK19 and TG2 triggered by neutrophils were noted. These findings indicate that ROS-mediated epithelial cell activation could induce/enhance innate immune responses as well as Th2 responses in isocyanate-induced OA. Regarding baker's asthma, although several studies have suggested IgE-mediated responses as the major pathogenic mechanism to develop work-related respiratory symptoms (WRS) and baker' s asthma. However, considering that LPS and fungi are contained in wheat flours, innate immune mechanisms are suggested to be major mechanisms to induce airway inflammation and develop WRS. Our recent studies demonstrated neutrophil activation interacting with TLR4 polymorphisms and activated epithelial cells (higher level of S100A89/A9). In addition, lowered TGFB1 (having immunoregulatory effect released from epithelial cells) may enhance type-2 airway inflammation to develop WRS in exposed workers. In conclusion, epithelial cells have key roles to induce/augment Th2/innate immune responses and airway remodeling in patients with OA. Further interventions

are needed to understand the role of innate immune responses and therapeutic interventions to improve the clinical outcome of OA.

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