Der p 38 is a bidirectional regulator of eosinophils and neutrophils in allergy

Min Hwa Hong[1], Ayesha Kashif[2], Geunyeong Kim[2], Beom Seok Park[3], Na Rae Lee[1], Eun Ju Yang[4], Ji Young Mun[5], Hyosun Choi[2], Sang-Hoon Kim[1], Hyun Jik Kim[6], Soo Jin Lee[2], Ji-Sook Lee[7], Yujin Hong[2], and In Sik Kim[2]

[1]Eulji University College of Medicine
[2]Eulji University School of Medicine
[3]Eulji University
[4]Daegu Haany University
[5]Korea Brain Research Institute
[6]Seoul National University College of Medicine
[7]Wonkwang Health Science University

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Abstract

Background: The house dust mite (HDM) is the most common cause of allergic diseases, and TLR4 acts as an overarching receptor for allergic responses. This study aimed to identify novel allergen binding to TLR4 in HDMs and unveil its unique role in allergic responses. Methods: Der p 38 was purified and characterized by LC-MS/MS-based peptide mapping. Biolayer interferometry and structure modeling unveiled TLR4-binding activity and the structure of recombinant Der p 38. The allergenicity of Der p 38 was confirmed by a skin prick test, and basophil activation and dot blot assays. Results: The skin prick test identified 24 out of 45 allergic subjects (53.3%) as Der p 38-positive subjects. Der p 38-augmented CD203c expression was noted in the basophils of Der p 38-positive allergic subjects. In animal experiments, Der p 38 administration induced the infiltration of neutrophils as well as eosinophils and exhibited clinical features similar to asthma via TLR4 activation. Persistent Der p 38 administration induced severe neutrophil inflammation. Der p 38 enhanced cytokine production in human bronchial epithelial cells, which inhibited apoptosis in neutrophils and eosinophils. The mechanisms involved LYN, PI3K, AKT, ERK, and NF-κB. Conclusions: These findings showed that Der p 38 is a bridge allergen between eosinophilic and neutrophilic inflammation, and contribute to understanding the TLR4-mediated complex pathogenesis of allergic diseases.

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