Airway G-CSF identifies neutrophilic inflammation and contributes to asthma progression

Young-Min Kim1, Hyekang Kim2,6, Seungwon Lee2,6, Sora Kim2, Jong-Uk Lee3, Youngwoo Choi4, Han Wook Park1, Gihoon You2, Hansol Kang1, Seyoung Lee1, Jong-Sook Park5, Yunji Park2, Hae-Sim Park4, Choon-Sik Park2, and Seung-Woo Lee1,2

Affiliations: 1Dept of Life Sciences, Pohang University of Science and Technology, Pohang, Republic of Korea. 2Division of Integrative Biosciences and Biotechnology, Pohang University of Science and Technology, Pohang, Republic of Korea. 3Dept of Interdisciplinary Program in Biomedical Science Major, Soochunhyang Graduate School, Bucheon, Republic of Korea. 4Dept of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Republic of Korea. 5Division of Allergy and Respiratory Disease, Soochunhyang University Bucheon Hospital, Bucheon, Republic of Korea. 6These authors contributed equally to this work.

Correspondence: Seung-Woo Lee, Division of Integrative Biosciences and Biotechnology, Dept of Life Sciences, Pohang University of Science and Technology (POSTECH), 77 Cheongam-Ro, Nam-Gu, Pohang, Gyeongbuk 37673, Republic of Korea. E-mail: sw_lee@postech.ac.kr

ABSTRACT Stratification of asthmatic patients based on relevant biomarkers enables the prediction of responsiveness against immune-targeted therapies in patients with asthma. Individualised therapy in patients with eosinophilic asthma has yielded improved clinical outcomes; similar approaches in patients with neutrophilic asthma have yet to be developed. We determined whether colony-stimulating factors (CSFs) in the airway reflect the inflammatory phenotypes of asthma and contribute to disease progression of neutrophilic asthma.

We analysed three different mouse models of asthma and assessed cytokine profiles in sputum from human patients with asthma stratified according to inflammatory phenotype. In addition, we evaluated the therapeutic efficacy of various cytokine blockades in a mouse model of neutrophilic asthma.

Among the CSFs, airway granulocyte CSF (G-CSF) contributes to airway neutrophilia by promoting neutrophil development in bone marrow and thereby distinguishes neutrophilic inflammation from eosinophilic inflammation in mouse models of asthma. G-CSF is produced by concurrent stimulation of the lung epithelium with interleukin (IL)-17A and tumour necrosis factor (TNF)-α; therefore, dual blockade of upstream stimuli using monoclonal antibodies or genetic deficiency of the cytokines in IL-17A×TNF-α double-knockout mice reduced the serum level of G-CSF, leading to alleviation of neutrophilic inflammation in the airway. In humans, the sputum level of G-CSF can be used to stratify patients with asthma with neutrophil-dominated inflammation.

Our results indicated that myelopoiesis-promoting G-CSF and cytokines as the upstream inducing factors are potential diagnostic and therapeutic targets in patients with neutrophilic asthma.

Copyright ©ERS 2020