Allergy Asthma Immunol Res. 2022 Jan;14(1):5-7
https://doi.org/10.4168/aair.2022.14.1.5
pISSN 2092-7355·eISSN 2092-7363

Allergy, Asthma & Immunology Research AAIR

Editorial

Interleukin-17 Can Be the Target of Novel Treatment Strategies for Particulate Matter–Induced Allergic Diseases

Byeong-Gon Kim [1,2] **Moo Kyun Park** [1,2*]

[1]Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University College of Medicine, Seoul, Korea
[2]Sensory Organ Research Institute, Seoul National University Medical Research Center, Seoul, Korea

▸ See the article "Particulate Matter Exposure Aggravates IL-17-Induced Eye and Nose Inflammation in an OVA/Poly(I:C) Mouse Model" in volume 14 on page 59.

Received: Dec 15, 2021
Accepted: Dec 16, 2021
Published online: Dec 29, 2021

Correspondence to
Moo Kyun Park, MD, PhD
Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University College of Medicine, 101, Daehak-ro, Jongno-gu, Seoul 03080, Korea.
Tel: +82-2-2072-2447
Fax: +82-2-745-2387
Email: aseptic@snu.ac.kr
entpmk@gmail.com

ORCID iDs
Byeong-Gon Kim
https://orcid.org/0000-0002-9056-455X
Moo Kyun Park
https://orcid.org/0000-0002-8635-797X

Disclosure
There are no financial or other issues that might lead to conflict of interest.

Air pollution is the single most significant environmental health risk.[1] Data from the World Health Organization (WHO) show that more than 90% of people worldwide breathe polluted air.[2] Particulate matter (PM), one of the most important components of air pollution, has a significant impact on human health and well-being. PM contributes to the onset and aggravation of asthma and allergic diseases.[3] The Europe 2021 report shows that most urban dwellers were exposed to concentrations of fine PM ($PM_{2.5}$; 97% of the dwellers) and coarse PM (PM_{10}; 81%) above WHO recommendations.[4] Numerous epidemiological studies have demonstrated the link between allergic diseases and PM.[3,5] PM induces excessive reactive oxygen species production and induces mitochondrial damage and autophagy in bronchial epithelial cells through AMP-activated protein kinase.[6] PM can change the epigenetics and microbiota in the airways.[7] $PM_{2.5}$ is more harmful than PM_{10} in terms of respiratory and allergic diseases and can reach the terminal part of the lung and systemic circulation.[8]

PM has electrostatic properties and can adhere to airborne allergens.[3] PM can interact with aeroallergens and promote airway sensitization by modulating the allergenicity of airborne allergens.[3] Several studies have reported the molecular mechanism of PM-induced allergic diseases.[9] It has been suggested that granulocyte-macrophage colony-stimulating factor, tumor necrosis factor (TNF)-α, interleukin (IL)-1α, IL-1β, IL-4, IL-6, IL-8, IL-17, IL-23 and macrophage inflammatory protein-2 play a role in the development of PM-induced allergic and immunologic diseases.[10] Although there are reports on strategies to prevent PM-induced allergic diseases such as avoidance behavior or reduction of PM production, a few studies are available on the treatment.[9,10] However, the development of treatment strategies is important because avoidance behavior may have a limited effect depending on the environmental situation and reduction of PM production will take a long time, especially in underdeveloped countries.

In the current issue, Bae *et al.*[11] propose that IL-17 is an essential mediator of PM-induced allergic conjunctivitis and allergic rhinitis. They also suggest an interesting treatment target for PM-induced allergic diseases using IL-17 pathways. Bae *et al.*[11] exposed OVA/Poly(I:C) mouse models, whose Th-17-associated inflammatory response is greater than that of the conventional OVA/alum model, to micro-and nano-sized titanium dioxide (TiO_2). Symptoms of allergic rhino-conjunctivitis and inflammatory parameters including IL-4, IL-17, and interferon-γ levels were analyzed. In particular, the role of IL-17 was investigated with IL-17-

neuralizing antibody (IL-17Ab). They found that treatment with IL-17Ab significantly improved the tear break-up time in the eyes and the symptom score of sneezing and nasal rubbing. Immunohistochemical staining demonstrated that IL-17Ab decreased the levels of IL-17 and neutrophils in the eyes and the nose of the OVA/Poly(I:C) model. Histological staining showed that the levels of TNF-α and IL-1β in conjunctiva were decreased after IL-17Ab treatment.

IL-17 is secreted by Th17 cells and is a cytokine related to T-cell and neutrophil activation. IL-17 affects tissue cells and IL-17 receptors are expressed in all epithelial cells.[12] IL-17 has related allergic responses and is elevated mainly in acute and severe forms of allergic diseases.[10,12] The IL-17 family consists of 6 members (IL17A to IL-17F). The IL-17 receptors, IL-17RA, IL-17RB/IL-25R, IL-17RC, IL-17RD/SEF, and IL-17RE, play a role in the development and exacerbation of allergic diseases.[12,14] Anti-IL-17 therapy has been proposed to be promising for asthma patients.[15] IL-17 increases the levels of proinflammatory and profibrotic cytokines. Interestingly, IL-17 decreases the effect of glucocorticoid in the airway epithelium by inducing epigenetic changes and inflammatory cytokine production. In this regard, anti-IL-17 therapy may be important in severe and steroid-resistant bronchial asthma.[15] Allergic rhinitis patients have a higher serum level of IL-17 than healthy controls.[10] IL-17 is considered a new biological treatment target in inflammatory autoimmune or immune-mediated diseases.[16] However, there is still controversy on the role of IL-17 in atopic dermatitis.[17]

Understanding the IL-17 pathway may provide a new strategy for the treatment of PM-induced allergic diseases. Further translational studies and clinical trials using anti-IL-17 therapy in the eyes and the ears are needed. Topical applications have fewer side effects and a higher therapeutic dosage than systemic applications in the eyes and the nose. Further studies about targeting IL-17 or another molecular target for PM-induced allergic diseases are expected.

REFERENCES

1. Brunekreef B, Holgate ST. Air pollution and health. Lancet 2002;360:1233-42.
PUBMED | CROSSREF
2. World Health Organization. 9 out of 10 people worldwide breathe polluted air, but more countries are taking action [Internet]. Geneva: World Health Organization; 2018 [cited 2018 May 2]. Available from: https://www.who.int/news/item/02-05-2018-9-out-of-10-people-worldwide-breathe-polluted-air-but-more-countries-are-taking-action.
3. Baldacci S, Maio S, Cerrai S, Sarno G, Baïz N, Simoni M, et al. Allergy and asthma: effects of the exposure to particulate matter and biological allergens. Respir Med 2015;109:1089-104.
PUBMED | CROSSREF
4. European Environment Agency. Europe's air quality status 2021-update [Internet]. Copenhagen: European Environment Agency; 2021 [cited 2021 Dec 7]. Available from: https://www.eea.europa.eu/publications/air-quality-in-europe-2021/air-quality-status-briefing-2021.
5. Sompornrattanaphan M, Thongngarm T, Ratanawatkul P, Wongsa C, Swigris JJ. The contribution of particulate matter to respiratory allergy. Asian Pac J Allergy Immunol 2020;38:19-28.
PUBMED
6. Sachdeva K, Do DC, Zhang Y, Hu X, Chen J, Gao P. Environmental exposures and asthma development: autophagy, mitophagy, and cellular senescence. Front Immunol 2019;10:2787.
PUBMED | CROSSREF
7. Kish L, Hotte N, Kaplan GG, Vincent R, Tso R, Gänzle M, et al. Environmental particulate matter induces murine intestinal inflammatory responses and alters the gut microbiome. PLoS One 2013;8:e62220.
PUBMED | CROSSREF
8. Genc S, Zadeoglulari Z, Fuss SH, Genc K. The adverse effects of air pollution on the nervous system. J Toxicol 2012;2012:782462.
PUBMED | CROSSREF

9. Leikauf GD, Kim SH, Jang AS. Mechanisms of ultrafine particle-induced respiratory health effects. Exp Mol Med 2020;52:329-37.
PUBMED | CROSSREF
10. Bae JS, Kim JH, Kim EH, Mo JH. The role of IL-17 in a lipopolysaccharide-induced rhinitis model. Allergy Asthma Immunol Res 2017;9:169-76.
PUBMED | CROSSREF
11. Bae JS, Oh SB, Kim J, Kim H, Kim JH, Kim EH, et al. Particulate matter exposure aggravates IL-17-induced eye and nose inflammation in an OVA/Poly(I:C) mouse model. Allergy Asthma Immunol Res 2022;14:59-72.
CROSSREF
12. Chung SH, Ye XQ, Iwakura Y. Interleukin-17 family members in health and disease. Int Immunol 2021;33:723-9.
PUBMED | CROSSREF
13. Hofmann MA, Fluhr JW, Ruwwe-Glösenkamp C, Stevanovic K, Bergmann KC, Zuberbier T. Role of IL-17 in atopy-a systematic review. Clin Transl Allergy 2021;11:e12047.
PUBMED | CROSSREF
14. Kirkham BW, Kavanaugh A, Reich K. Interleukin-17A: a unique pathway in immune-mediated diseases: psoriasis, psoriatic arthritis and rheumatoid arthritis. Immunology 2014;141:133-42.
PUBMED | CROSSREF
15. Chesné J, Braza F, Mahay G, Brouard S, Aronica M, Magnan A. IL-17 in severe asthma. Where do we stand? Am J Respir Crit Care Med 2014;190:1094-101.
PUBMED | CROSSREF
16. Amin K, Issa SM, Ali KM, Aziz MI, Hama Amieen HM, Bystrom J, et al. Evidence for eosinophil and IL-17 mediated inflammation in allergic rhinitis. Clin Mol Allergy 2020;18:6.
PUBMED | CROSSREF
17. Sugaya M. The role of Th17-related cytokines in atopic dermatitis. Int J Mol Sci 2020;21:1314.
PUBMED | CROSSREF