

Correspondence

Reply

To the Editor:

To describe the cytokines induced by diesel exhaust particle (DEP) exposure (IL-1 β , IL-6, TNF- α), we used the term proinflammatory, which has historically been associated with these cytokines. We agree with Inoue et al.¹ that the role of IL-6 in allergic inflammation remains controversial because experiments using IL-6-deficient mice suggest a protective role in a murine asthma model whereas in a similar OVA model anti-IL6R antibody treatment decreased bronchoalveolar lavage fluid T_H2 cytokines and airway hyperresponsiveness.² The role of IL-6 in asthma has been recently reviewed elsewhere.³ In light of the importance of IL-6 in T_H17 differentiation and the association between IL-17A and severe asthma, a reassessment of the role of IL-6 (and IL-1 β) in asthma, especially severe asthma, is warranted.

We characterized the T_H17 cells in the lungs following exposure to DEP,⁴ and we fully expect these T_H17 cells to be ROR γ t positive. We have started to assess the ability of DEP-pulsed bone marrow-derived dendritic cells to induce T_H17 differentiation of highly purified naive CD4⁺CD62L⁺CD44⁻ cells and found that by itself DEP did not enable bone marrow-derived dendritic cells to promote T_H17 differentiation of naive CD4⁺ T cells (data not shown). We are actively pursuing experiments to understand the mechanism by which *in vivo* DEP exposure results in T_H17 accumulation in the lung.

In our study, we confirmed that co-exposure of DEP and an allergen (in our case, house dust mite) markedly increased airway resistance, bronchoalveolar lavage fluid eosinophilia, T_H2 cytokines, and allergen sensitization.⁴ Similar findings were made by numerous groups, including by Inoue et al, using different allergens, particles, and mouse strains, underscoring the important contribution of pollution-associated particles to experimental asthma exacerbation.⁵ We have recently confirmed our findings in young 3- to 6-week-old BALB/c mice using 2 different doses of DEP.⁶

Estimates of DEP exposure were derived from a previously developed land-use regression model.⁷ The modeled pollutant, elemental carbon attributable to traffic, was initially derived at ambient monitoring stations in the Cincinnati airshed using detailed receptor model analyses and is a surrogate marker of

traffic-related air pollution primarily derived from diesel exhaust.⁸ Thus, concentrations of elemental carbon attributable to traffic are not analogous to particulate matter less than 2.5 μ m in diameter but, rather, represent the estimated DEP fraction of particulate matter less than 2.5 μ m in diameter.

Eric B. Brandt, PhD^a

Patrick H. Ryan, PhD^b

Gurjit K. Khurana Hershey, MD, PhD^a

From ^athe Division of Asthma Research; and ^bthe Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio. E-mail: eric_dominique_brandt@yahoo.com.

Disclosure of potential conflict of interest: E. B. Brandt and G. K. Khurana Hershey have received research support from the National Institutes of Health. P. H. Ryan declares that he has no relevant conflicts of interest.

REFERENCES

1. Inoue K-i, Tanaka M, Takano H. DEP-induced T_H17 response in asthmatic subjects. *J Allergy Clin Immunol* 2014 XXX: XXX-XXX.
2. Doganci A, Eigenbrod T, Krug N, De Sanctis GT, Hausding M, Erpenbeck VJ, et al. The IL-6R α chain controls lung CD4⁺CD25⁺ Treg development and function during allergic airway inflammation *in vivo*. *J Clin Invest* 2005;115: 313-25.
3. Rincon M, Irvin CG. Role of IL-6 in asthma and other inflammatory pulmonary diseases. *Int J Biol Sci* 2012;8:1281-90.
4. Brandt EB, Kovacic MB, Lee GB, Gibson AM, Acciani TH, Le Cras TD, et al. Diesel exhaust particle induction of IL-17A contributes to severe asthma. *J Allergy Clin Immunol* 2013;132:1194-204.
5. Maes T, Provoost S, Lanckacker EA, Cataldo DD, Vanoirbeek JA, Nemery B, et al. Mouse models to unravel the role of inhaled pollutants on allergic sensitization and airway inflammation. *Respir Res* 2010;11:7.
6. Acciani TH, Brandt EB, Khurana Hershey GK, Le Cras TD. Diesel exhaust particle exposure increases severity of allergic asthma in young mice. *Clin Exp Allergy* 2013;43:1406-18.
7. Ryan PH, Lemasters GK, Levin L, Burkle J, Biswas P, Hu S, et al. A land-use regression model for estimating microenvironmental diesel exposure given multiple addresses from birth through childhood. *Sci Total Environ* 2008;404: 139-47.
8. Sahu M, Hu S, Ryan PH, Le Masters G, Grinshpun SA, Chow JC, et al. Chemical compositions and source identification of PM_{2.5} aerosols for estimation of a diesel source surrogate. *Sci Total Environ* 2011;409:2642-51.

<http://dx.doi.org/10.1016/j.jaci.2013.12.1097>