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Letter to the Editor

The Impact of Diesel Exhaust Particles on Tight Junctional Proteins on Nose and Lung in a Mouse Model

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To the Editor,

Air pollutants penetrate deeply into the airways, reaching the bronchioles and alveoli, and then entering the bloodstream to trigger organ inflammation, dysfunction, and toxicity. Especially, diesel exhaust particles (DEP) induce airway hyperresponsiveness (AHR) and affect airway epithelial cells and regulatory T cells of the innate immunity.[1] Recent studies showed that allergic rhinitis (AR) and asthma are considered part of the one airway disease linked epidemiologically and pathophysiologically.[2,3] The upper and lower airways are describe as a single functional unit, so the impairment of nose function in rhinosinusitis may be responsible in part for bronchial pathology.[4] The mechanisms in AR and asthma are naso-bronchial reflex, postnasal drip of inflammatory cells and/or mediators from the nose into the lower airways, and absorption of them into the systemic circulation and finally the lung.[5,6] This study was to evaluate the effect of DEP on the nose and lung in a mouse model. DEP inhalation methods in mice were conducted as previously described.[7] AHR was more prevalent in the DEP exposure group than in the sham group, as well as was higher in the 8-week (8w) DEP group than in the 4-week (4w) DEP group (**Figure A**). The DEP exposure group had a significantly large number of inflammatory cells in bronchoalveolar lavage fluid (BALF) (**Figure B**) and nasal lavage fluid (NLF) (**Figure C**) compared with the sham group, as well as in the 8w DEP group than in the 4w DEP group.

Barrier dysfunction in the lung allows allergens to activate the epithelium and produce cytokines that are permissive for the induction and development of T helper type 2 responses.[8] Tight junctions (TJs) act as a semipermeable barrier to the paracellular transport of ions, solutes, and cells.[9] Claudins (CLDNs) are the structural molecules of TJs. There are 27 known CLDNs, and expression of different CLDNs is responsible for changes in electrolyte and solute permeability in cell layers.[10] However, there is no report on expression change in CLDNs in DEP exposed cells and mice. We evaluated the effect of DEP on CLDNs in the nose and lung. Lung and nasal level of CLDN-4, -5, and -17 by western blotting increased in the 4w DEP group compared to the sham group (**Figure D**). On histological examination, the DEP exposure group had a heavy infiltration of inflammatory cells and exudative changes in the bronchi and nasal tissue by H&E staining (**Figure E**). Lung and nasal levels of TJ protein CLDN-4 and -5 expression by IHC increased in the 4 and 8w DEP group compared to the sham group (**Figure E**). This was expected, since TJs comprise the major barrier to

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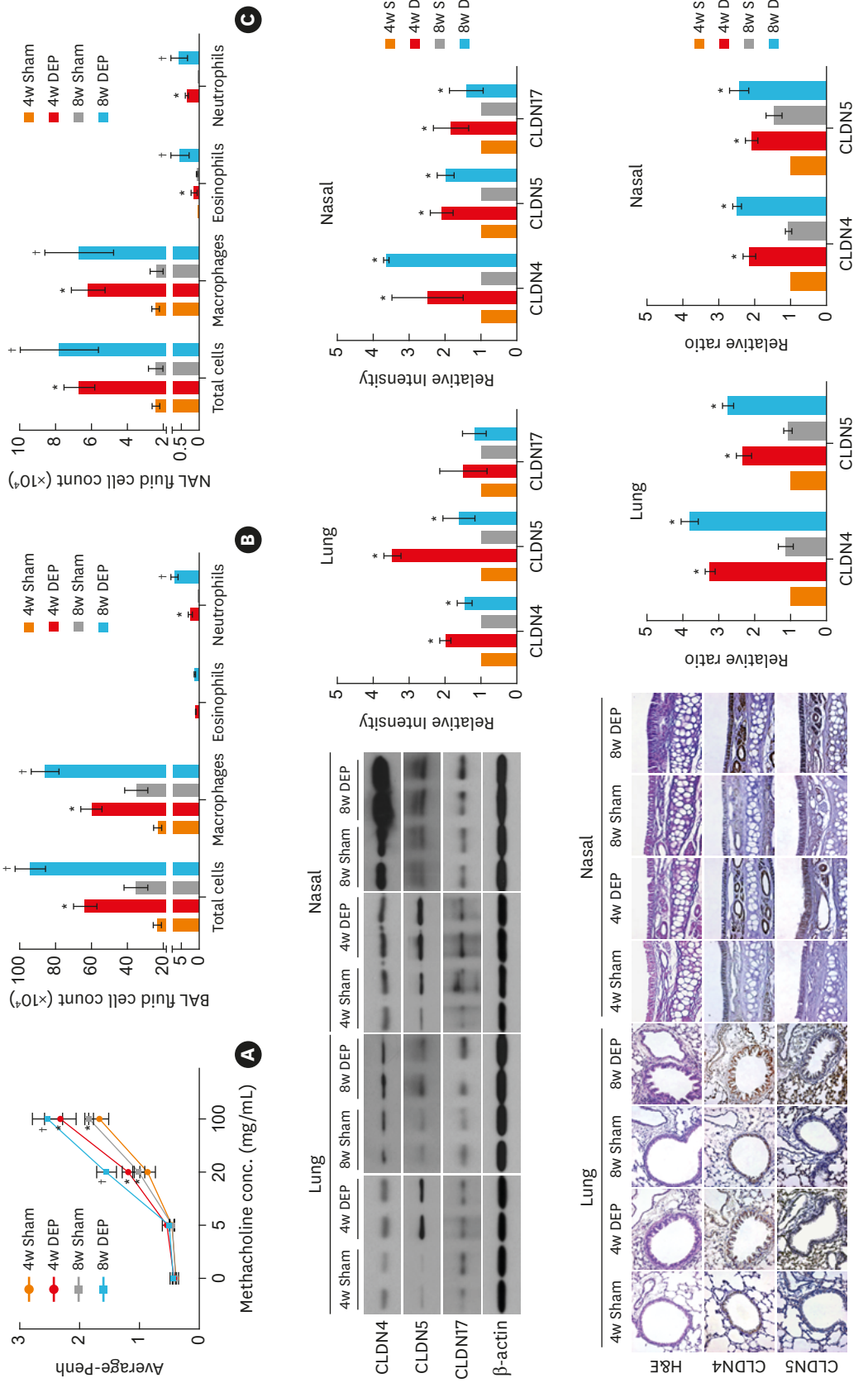

Figure. (A) DEP exposure increased airway hyperresponsiveness in mice model. DEP exposure changed cell differentials in BALF (B) and NLF (C) in mice. (D) CLDNs expression by western blotting in both nose and lungs of mice exposed to DEP for 4w and 8w. (E) CLDNs expression by immunohistochemical stain in both nose and lungs of mice exposed to DEP for 4w and 8w. Each data represents the means ± SEM of eight mice per group.
DEP, diesel exhaust particles; BALF, bronchoalveolar lavage fluid; NLF, nasal lavage fluid; CLDNs, claudins; 4w, 4-week; 8w, 8-week; SEM, standard error of mean.
*$P < 0.05$, DEP group vs. Sham group †$P < 0.05$, 4w DEP group vs. 8w DEP group, respectively.

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paracellular transit pathways in epithelium and endothelium in the nose and lung, suggesting that TJ integrity can be preserved in the nose and lung of mice exposed to DEP.

In this study the expression of CLDN-4, -5 and -17 were different in both the nose and lung of mice exposed to DEP, suggesting that cell barrier integrity has similar changes between the upper and lower airways. These findings thus raise the possibility that modulation of cell barrier in the nose and lung can be a useful alternative treatment to airway disease.

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