

Correspondence

Pin1 blockade in asthma by naphthoquinone?

To the Editor:

Esnault et al¹ reported an important role of Pin1 in rat allergic asthma. In the study they conducted pharmacologic blockade of Pin1 with its inhibitor, juglone (5-hydroxy-1, 4-naphthoquinone). However, they did not refer to the possibility of proallergic effects of naphthoquinone but implicated the clinical utility of Pin1 inhibition. Quinones are ubiquitously distributed in nature and represent a class of toxicologic intermediates that can induce a variety of hazardous effects *in vivo*, such as acute cytotoxicity, immunotoxicity, and carcinogenesis.² Their unique nature contains (1) generation of free radicals through redox activation and (2) possession of a highly reactive electrophilic site that reacts readily with thiolate anions in proteins to yield thioether adducts.²⁻⁴ To date, we have focused on the adverse effects of one of the naphthoquinones, 1, 2-naphthoquinone (1, 2-NQ), which is involved in diesel exhaust particles and atmospheric particulate matter 2.5 from the view of environmental pollution. As for its abrogating effects on airway biology, 1, 2-NQ induces tracheal contraction in a dose-dependent manner *ex vivo*, at least in part through the activation of vanilloid receptor 1.⁵ The underlying mechanisms involve phosphorylation of protein tyrosine kinases, such as epidermal growth factor receptor (EGFR).⁵ Furthermore, our recent study has shown that 1, 2-NQ inactivates protein tyrosine phosphatases, negative regulators of EGFR, and consequently prolongs transactivation of EGFR with its downstream signaling pathways *in vitro*.⁴

We have also examined the effects of 1, 2-NQ on murine allergic asthma. Pulmonary exposure to NQ dose-dependently aggravated allergic airway inflammation characterized by infiltration of eosinophils and lymphocytes around the airways and an increase in goblet cells in the bronchial epithelium.⁶ In addition, 1, 2-NQ plus allergen enhanced airway hyperresponsiveness⁷ and the local expression of IL-4, IL-5, eotaxin, macrophage chemoattractant protein 1, and keratinocyte chemoattractant⁶ compared with allergen alone. Impressively, moreover, 1, 2-NQ exhibited an interesting effect on allergen-specific immunoglobulin isotype (subclass) switching.⁶ In brief, 1, 2-NQ almost dose-dependently increased allergen-specific IgG_{2a} and IgE; in

contrast, the allergen-specific IgG₁ titer was highest in animals treated with the lowest dose of 1, 2-NQ (unpublished observation).⁶ Thus the unbalanced T_H1/T_H2 polarization induced by 1, 2-NQ found in our *in vivo* experiment⁶ could partly explain the unexpected data of Esnault et al¹ (ie, transcript levels of IL-4 and IFN- γ in bronchoalveolar lavage fluid cells).

In conclusion, although we agree with the possibility that Pin1 participates in the pathogenesis of allergic asthma, care should be taken in the use of naphthoquinones as potential therapeutic options for allergic diseases because of their complicated effects.

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