

Environmental Immunoamplifiers for Allergy

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The prevalence of allergic disorders has rapidly increased throughout the world [1,2]. Alternation in environmental factors such as allergen load, infectious disease profile, vaccination, and the environmental adjuvants and so on, rather than genetic factors such as polymorphism, is likely to be regarded as the cause of this increase [3]. In relation to this, developed countries in which dramatic environmental change exist reportedly possess more populations of allergies than rural ones [3], although general allergens including insects and pollens are more abundant in urban areas. As for considering the moderate complex, it is implicated that environmental risk factors for immunotoxicity on allergy are epidemiologically, at least in part, attributable to environmental pollutants mainly produced/released from industries including endocrine disruptors like environmental estrogens (or xenoestrogens) as well as other factors as mentioned above. Nonetheless, there are few to scientifically prove the link between environmental chemicals and promotion/exacerbation of allergy.

Air-existing gaseous pollutants such as sulfur and nitrogen dioxide and ozone reportedly have potential to worsen allergic asthma [4,5]. In addition to gaseous pollutants, it has been generally recognized that Diesel exhaust particles (DEP), derived from diesel engine-powered automobiles and major constituents of atmospheric particulate matters, have an adverse health impact in the context of immunotoxic potential, e.g. allergic asthma and systemic lupus erythematosus [6,7]. Especially, with their potent adjuvant effects, DEP synergistically worsen allergic asthma pathophysiology [6]. As well, thanks to multifaceted basic researches for decades, their immunotoxicity has been solved at both cellular and molecular levels [8]. Since DEP have vast numbers of chemicals including xenoestrogens, it can be imagined that some of these chemicals are responsible for the immunotoxicity; however, it awaits further investigation to clarify the issue.

Phthalic acid ester plasticizers are widely used in flexible polyvinyl chloride products including vinyl flooring and wall covering, food containers, and infant toys, which is detected in house dust. Previously, causal relationship between phthalate exposure and induction, increase, and/or exacerbation of allergic diseases including asthma, dermatitis, and eczema has been implicated, in particular in children [9,10]. On the other hand, our group has reported that di-(2-ethylhexyl) phthalate (DEHP), widely used [1.8 million metric tons/year] among phthalates, potentiates atopic dermatitis-like skin lesions in allergen-stimulated NC/Nga mice [10]. Nevertheless, there are still much environmental chemicals to determine its immunotoxicological potential on allergy, maybe developing alternative "allergy/atopy test models" consisting in vitro, in vivo, and patient compartments. Furthermore, achieving goals, not only toxicologists but also clinicians (respirologists, dermatologists, allergologists, and pediatricians) will be expected to collaborate comprehensively.

In conclusion, since if any, there are still few comprehensive researches linking environmental pollutants and allergy promotion, accumulation of scientific evidence involving (in silico) in vitro, in vivo, and translational human studies are requested potentially. Also, significantly, low dose immunoamplifying effects of environmental chemicals should be elucidated from the point of No Observed Adverse

Effect Level. Finally, biologically, it might be important/interesting and should be clarified in the future that the immunomodulating impacts are via activation of some intra/extracellular receptors such as peroxisome proliferative activated receptors as alternative "xenoestrogens" rather than endocrine and reproductive disruptors.

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