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Letter to the Editor

No increase in the serum periostin level is detected in elementary school-age children with allergic diseases

Dear Editor

Periostin is a secreted extracellular matrix protein that has been shown to play an important role in the pathogenesis of allergic diseases, including both Th2 inflammation and tissue remodeling.[1,2] Originally, the periostin gene was reported to be a "Th2 signature" gene that is upregulated in IL-13-stimulated bronchial epithelial cells.[3,4] In addition to blood eosinophilia and the exhaled nitric oxide level, the serum periostin level is thought to be a good biomarker of airway eosinophilic inflammation and airway remodeling in adult asthmatics[5,6] and may be useful for predicting the effects of therapies targeting mediators of Th2 inflammation, such as anti-IL-13 antibodies[7] or anti-IgE antibodies,[8] in patients with bronchial asthma. The serum periostin levels are also increased in adult patients with atopic dermatitis[9] and are believed to reflect the status of chronic skin inflammation. Taken together, the serum periostin level is a promising biomarker of allergic diseases in adults. However, little is known about the usefulness of this parameter as a biomarker for allergic diseases in childhood.

We recruited 304 elementary school-age children from an elementary school attached to Chiba University. The study protocol was approved by the Committee on Human Research of Chiba University. Informed consent was obtained from each of the study subjects and their guardians. The diagnosis of current bronchial asthma was made according to the ISSAC (International Study of Asthma and Allergies in Childhood) questionnaire. Concurrent physician-diagnosed atopic dermatitis, allergic rhinitis and food allergies were assessed. Of the 156 children with any type of allergic disease, 27.6% had multiple allergic diseases. Children without any allergic diseases and those not exhibiting serum specific IgE to house dust mites, cedar pollen or egg whites were defined as "healthy children." We recruited 204 adult volunteers without any allergic diseases as healthy adults. The characteristics of the subjects are shown in Supplementary Table 1.

The serum periostin levels were measured using a sandwich enzyme-linked immunosorbent assay, as previously described.[6] Differences in the serum periostin levels between the study groups were determined using the Kruskal–Wallis test followed by Dunn's multiple comparisons test. The relationships between the serum levels of periostin and the age, IgE or eosinophil counts were assessed by an analysis of variance and Spearman's rank correlation.

Unexpectedly, we did not detect any increase in the serum periostin level in children with allergic diseases in comparison to healthy children (Fig. 1). In addition, compared to that observed in the healthy adult controls, the serum periostin levels were significantly higher in the elementary school-age children, regardless of the presence or absence of allergic diseases (Fig. 1). To clarify whether our non-significant results were due to a lack of statistical power, we conducted post hoc power analyses using the G*Power 3.1[10] software program. The post hoc power of ANOVA (calculated effect size 0.80, α error 0.05, total sample size 84, number of groups 6) was 1.00, thus suggesting that our negative finding may not be attributed to the fact that we utilized a limited sample size. We did not detect any correlations between the serum periostin level and the blood eosinophil count or serum total IgE level, suggesting that the serum level of periostin is not associated with an atopic status in elementary school-age children (Supplementary Fig. 1).

To clarify the normal ranges of serum periostin at different ages, we plotted the serum levels of periostin for both healthy children and healthy adults. The serum levels of periostin appeared to slightly increase in an age-dependent manner in childhood, although the correlation coefficient was low (r 0.35, $p < 0.05$) (Fig. 2A). On the other hand, the serum levels of periostin in adulthood appeared to be lower than those in childhood, and to slightly decrease during adulthood (r 0.17, $p < 0.05$) (Fig. 2B). As periostin is

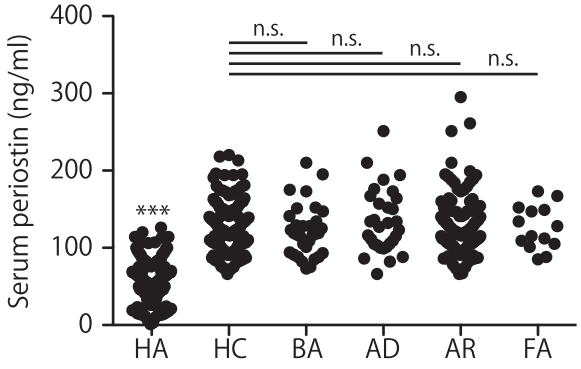

Fig. 1. No differences in the serum levels of periostin were seen between the children with and without allergic diseases. The serum levels of periostin in the children with allergic diseases were not significantly different from those without allergic diseases. The serum levels of periostin in the children were significantly higher than those observed in the healthy adults, regardless of the presence or absence of allergic diseases (***$p < 0.001$, compared to each group of children). Abbreviations: HA, Healthy adults; HC, Healthy children; BA, Bronchial asthma; AD, Atopic dermatitis; AR, Allergic rhinitis; FA, Food allergies; n. s., not significant.

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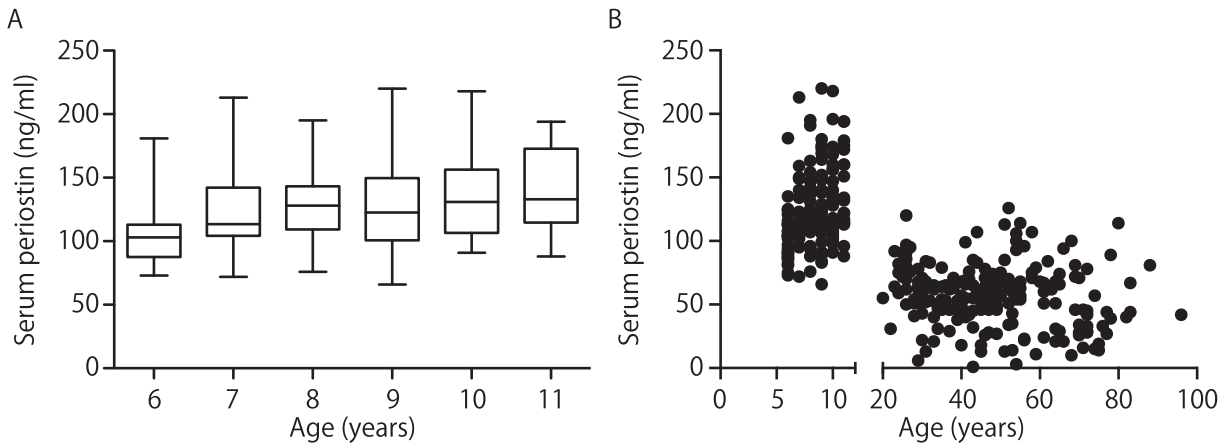

Fig. 2. The serum periostin levels in the subjects without allergic diseases. A) The serum periostin levels in the elementary school-age children without allergic diseases. Bottom of the box, 25th percentile; Line in the middle of box, median; Top of the box, 75th percentile; Whiskers, to the smallest value and to the largest value. B) The serum periostin levels in the subjects without allergic diseases in both elementary school-age children and adults.

produced by osteocytes and periosteal osteoblasts,[11] the serum level of periostin may thus be largely influenced by the rate of bone metabolism in childhood.[11] Therefore, the high baseline level of serum periostin may mask any increase in the serum periostin level due to allergic diseases in childhood.

In conclusion, no increase in the serum periostin level was detected in elementary school-age children with allergic diseases, likely due to the high rate of bone turnover in this group. Further studies are needed to clarify the normal ranges of serum periostin at other ages (infancy and adolescence) and for which age groups the serum periostin level is a useful biomarker.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.alit.2015.04.001.

Conflict of interest

JO is an employee of Shino-Test Corporation. The rest of the authors have no conflict of interest.

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