



Letter to the Editor

Periostin in the bronchial lavage fluid of asthma patients



Dear Editor

Serum periostin has recently emerged as a novel and useful biomarker for bronchial asthma.¹ Serum periostin is a surrogate biomarker reflecting type 2 immune responses because periostin is a downstream molecule of interleukin-4 (IL-4) or IL-13, the signature cytokines of type 2 immune responses. This characteristic of periostin can potentially be applied to predict the efficacy of antagonists such as anti-IL-13 or anti-IgE antibodies against type 2 immune responses. Furthermore, we have recently found that since periostin reflects tissue remodeling or fibrosis in bronchial asthma, it can predict hypo-responsiveness to inhaled corticosteroids in asthma patients, particularly in those who are late-onset and eosinophil-dominant.^{2,3}

In spite of the usefulness of periostin as a biomarker for bronchial asthma, serum periostin can be affected by periostin produced in sites other than lung tissues, particularly bones. Therefore, it would be of great benefit in caring for and treating asthma patients if periostin in lung tissues could be specifically detected. However, it remains obscure how periostin is secreted from the cells and circulated in asthma patients. No study has yet been performed to investigate whether periostin is secreted in the bronchial lumens of asthma patients. Bronchial resident cells—epithelial cells, fibroblasts, and endothelial cells—are assumed to be sources of periostin in lung tissues.^{4–6} It has been demonstrated *in vitro* that periostin can be secreted from the basal side, but not from the apical side, in bronchial epithelial cells.⁴ These results negate the notion that periostin is secreted in the bronchial lumens in asthma patients. In contrast, it has been reported that periostin is highly detected in nasal lavage fluid in chronic rhinosinusitis patients, which may nevertheless support this notion.⁷ Therefore, in this study, we examined periostin in the bronchial lavage fluid (BLF) of asthma patients to explore whether it can be a more specific biomarker for bronchial asthma.

Ten asthma patients and ten healthy donors were recruited from the Iwate Medical University Hospital. Bronchial asthma was diagnosed according to the criteria by Global Initiative for Asthma, Global Strategy for Asthma Management and Prevention, updated 2010. Spirometry was performed and airway methacholine responsiveness was measured using an Astograph (Jupiter 21, CHEST, Tokyo, Japan). The asthma patients had no other

medical disorders and were not current smokers; the ten healthy subjects were nonallergic and nonsmokers. This study was approved by the Iwate Medical University Hospital Ethics Committee. The details of the asthma patients are described in Table 1. All the asthma patients were well controlled with inhaled corticosteroids.

Bronchial lavage was performed by inserting a flexible fiberoptic bronchoscope (Olympus; Olympus Optical Co Ltd, Tokyo, Japan) under local anesthesia, as previously described.⁸ BLF was extracted from one of the subsegmental bronchi of the left lingular division by injection of 20 mL aliquots of sterile saline pre-warmed to 36.5 °C twice and gently aspirated back into polypropylene tubes kept on ice. We obtained 20–25 mL of BLF from each asthma patient. Immediately after lavage, mucus was removed from the fluid by filtration through gauze, and the fluid was then centrifuged at 200 × g for 10 min at 4 °C. The supernatant was decanted and stored at –80 °C. Ten mL of BLF supernatant was concentrated to 1.0 mL (ten-fold) by centrifugation using Centrifugal Filter Devices (Amicon Ultra-0.5, Merck Millipore, Darmstadt, Germany). Periostin in BLF was detected as previously described with a slight modification, using the biotin-streptavidin system to increase the sensitivity.^{2,9,10}

The BLF from seven asthma patients showed no detectable periostin (data not shown). Although periostin was detectable in the BLF of the remaining three asthma patients, the periostin levels were less than 200 pg/mL. To quantify the tiny amounts of periostin in BLF, we concentrated proteins in BLF by ten-fold. The original periostin concentrations were estimated to be 7–511 pg/mL in eight asthma patients by the ten-fold enriched BLF, and the remaining two showed no detectable periostin (Table 1). When we concentrated 100–150 mL of bronchoalveolar lavage fluid (BALF) from 10 normal donors by ten-fold, periostin concentrations were estimated to be 78–648 pg/mL in nine normal donors and one normal donor showed no detectable periostin (data not shown). We were sure of these values because the detection limit of our high-sensitivity periostin ELISA kit was as much as 3 pg/mL. The value of the periostin concentration in BLF was significantly lower than the serum periostin concentrations, not only in asthma patients ($n = 734$, median: 74.0 ng/mL, average: 82.1 ng/mL, SEM: 1.48, range: 14–440 ng/mL), but also in the normal donors ($n = 302$, median: 54.4 ng/mL, average: 53.9 ng/mL, SEM: 1.49, range: 1–130 ng/mL).^{2,9,10} These results suggest that secretion of periostin into the bronchial lumens of asthma patients does not occur or is negligible. Secretion or production manner of periostin in the lumens may be different among the sites, because periostin is

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Table 1

Clinical backgrounds and periostin concentration in BLF in bronchial asthma patients.

Patient	Age (yr)	Sex	Duration of asthma (yr)	Allergic rhinitis	Treatment	Blood eosinophils (/μL)	FEV1, % of predicted value	FeNO (ppb)	Periostin (pg/mL)
1	48	M	11	–	FP 400 μg MON 10 mg	390	72.6	25	7
2	41	M	38	–	FP 400 μg	296	63.0	34	148
3	72	M	65	–	FP 200 μg SLM 100 μg PRN 450 mg	251	48.1	39	310
4	43	M	40	+	FP 500 μg SLM 100 μg	658	96.8	52	21
5	40	F	39	–	BUD 200 μg	341	78.5	30	N. D.
6	40	F	38	–	BUD 400 μg	179	59.1	46	N. D.
7	68	M	9	–	FP 200 μg	32	98	44	111
8	39	M	1	+	FP 100 μg	293	119.3	62	342
9	48	M	41	–	FP 200 μg	280	93.4	34	511
10	44	M	43	+	FP 500 μg SLM 100 μg	285	71.1	134	41

FEV1, forced expiratory volume in 1 s; FeNO, fractional exhaled nitric oxide; FP, fluticasone propionate; MON, montelukast sodium; SLM, salmeterol; PRN, pranlukast hydrate; BUD, budesonide; N. D., not detected.

highly detected in nasal lavage fluid in chronic rhinosinusitis patients.

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Conflict of interest

JO is an employee of Shino-Test Corporation. KI received a consultant's fee from Chugai Pharmaceutical and a research grant from Shino-Test. The rest of the authors have no conflict of interest.

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