Periostin: A Potential Biomarker and Therapeutic Target in Pulmonary Diseases

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ABSTRACT -- Periostin is a matricellular, nonstructural protein belonging to the fasciclin family and is encoded by the POSTN gene in humans. Periostin plays an important role in maintaining a normal tissue matrix in the lungs. Despite the vital role as a structural mediator in tissue growth and repair, periostin is involved in the pathogenic mechanism during tissue remodeling and fibrosis. Periostin is a chemoattractant mediator, promotes eosinophil recruitment and adhesion on the airways sub-epithelial membrane of asthmatic patients. POSTN gene was identified as one of the highly expressed genes induced by interleukins IL-13, IL-5 and IL-4 - the key cytokines of Th2 immune responses in the bronchial tissues of asthmatic patients. This review highlights the potential role of periostin as a validated biomarker in respiratory disease progression and its candidacy to predict the response to treatments targeting Th-2 cytokines in bronchial asthma. In addition, its potential role in COPD, IPF, lung cancer and lung infection, is also speculated.

INTRODUCTION

Periostin is a protein found in the extracellular matrix and also known as osteoblast-specific factor 2 (OSF2). Initially recognized in the periodontal ligament and was first isolated in 1993 from the osteoblast cells of mouse. It has a complex protein structure of 93.3 kDa and contains 811 amino acids (1). Periostinzz belongs to the fasciclin family, a nonstructural protein encoded by the POSTN gene in humans. Periostin is believed to have a role in the development and remodeling of many tissues, such as bone, heart, skin, lungs, and thyroid tissues (2,3) as well as wound repair (4). Despite its vital role as a structural mediator in tissue growth and repair, periostin is involved in the pathogenic mechanism during tissue remodeling and fibrosis. Periostin is highly expressed after mechanical stress at the site of injury or inflammation, and it contributes to tumor genesis pathway of various types of solid tumors (5). Also, it is involved in various allergic disorders like atopic dermatitis and rhino sinusitis. Periostin was highly expressed in the dermal–epidermal junction and accelerated wound healing through enhancing proliferation and migration of dermal fibroblasts compared to periostin-deficient mice (6). Over expression of periostin is substantially associated with tissue remodeling, higher collagen deposition, and cell necrosis in response to injury. Increased urinary periostin levels were positively associated with high blood creatinine and proteinuria in patients with chronic kidney disease, suggesting its potential role in early diagnosis of kidney disease (7). Transforming growth factor-beta (TGF-β), a pro-inflammatory cytokine, induced significant expression of periostin in cardiomyocytes causing myocardial remodeling (8). An increasing number of studies have shown that periostin plays a key role in exacerbating the Th2 inflammatory pathway, eosinophil recruitment, bronchial smooth muscle hypertrophy, and lung function decline (9,10). POSTN gene was identified as one of the highly expressed genes induced by interleukins IL-13, IL-5 and IL-4, the key cytokines of Th2 immune responses, in the bronchial tissues of asthmatic patients (11). The serum level of periostin is considered a good predictor of response to lebrikizumab (anti-IL-13 antibody) and inhaled corticosteroids (ICS) therapy in severe asthmatic individuals (12). The aim of this review is to highlight the emerging and promising functions of periostin in respiratory disorders as a novel diagnostic biomarker with evidence from already published experimental and clinical data. This may also emphasize the possible role of periostin as a therapeutic target for airway inflammation and

airway remodeling and a predictive marker to ascertain the efficacy of therapy.

IMPLICATION OF PERIOSTIN IN VARIOUS PATHOLOGICAL CONDITIONS

Periostin plays a significant role in cellular functions and regulation of extracellular matrix (ECM) integrity. Over expression of periostin has been observed in a wide range of inflammatory and fibrotic disorders, including airway inflammation, skin inflammation, cardiac remodeling, and atherosclerotic plaques (2). Periostin and other ECM components are highly expressed in collagen-rich connective tissues when subjected to continuous tissue damage, such as tendons, skin, heart valves, and periodontal ligaments. Generally, growth factors such as TGF-β, mechanical stress and various cytokines are involved in up-regulation and pathophysiological processes associated with periostin (13). Besides, periostin is highly expressed and has an active pathogenic role in many metastasizing and solid tumors, such as breast cancer, lung cancer, liver carcinoma, etc. (5).

Periostin plays a substantial role in inflammatory bowel diseases through mediating NF-κB signaling. In experimental model of ulcerative colitis (UC), POSTN-deficient mice displayed a low level of pro-inflammatory cytokines in the intestinal epithelial cells (14). Moreover, higher levels of serum periostin have been observed after unilateral ureteral obstruction in wild-type mice, and inhibition POSTN gene could protect kidney injury and interstitial fibrosis (15,16).

Periostin is also expressed in vascular smooth muscle endothelial cells to facilitate cell proliferation, migration, and differentiation. High levels of serum periostin were associated with vascular lesions, angiogenesis, and atherosclerotic plaques in young patients (17). Periostin knockout in mice could reduce the levels of pro-fibrotic markers and protect against liver fibrosis induced by carbon tetrachloride by modulating its interaction with Integrin alpha receptors (α_v) (18). A significant correlation has been observed between elevated liver enzymes and serum periostin in both acute and chronic hepatitis patients as well (19,20).

Recent findings from a cross-sectional study showed that increased serum periostin levels were significantly associated with higher lipid profile, anthropometric measures, and inflammatory biomarkers among patients with acute coronary syndrome (ACS) and obese T2DM patients (21).

PERIOSTIN IN RESPIRATORY DISORDERS

Various studies have been established the essential role of periostin in healthy and pathological conditions of the respiratory tract. Periostin can directly interact with tissue collagen cross-linking, as well as being an essential protein for ECM integrity. Periostin and collagen-1 are matricellular components, which are highly expressed in the bronchial epithelium as a response to lung insults.

Infectious diseases of the lung

Idiopathic interstitial pneumonias (IIPs) are acute or chronic lung disorders of unknown etiology characterized by variable degrees of fibrosis and interstitial or intra-alveolar inflammation. IIPs are classified in different categories based on their histopathologic characteristics, including usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP), and cryptogenic organizing pneumonia (COP). Periostin might have an important role in secondary interstitial pneumonia, such as collagen tissue disease-associated ILD. The serum levels of periostin in RA-ILD patients (interstitial lung disease associated with rheumatoid arthritis) were significantly increased when compared with control subjects. Several biomarkers, such as KL-6, surfactant protein (SP)-A and SP-D, are elevated in serum of IIP patients, thus providing potential biomarkers for the diagnosis of IIPs. Periostin is distinct from KL-6 in that IPF/UIP can be distinguished from COP by measurement of serum levels of periostin but not KL-6. The distribution of periostin in immune-histochemical studies suggests that it is expressed in areas of fibroblast proliferation. Thus, periostin might be a potential novel component to distinguish IIPs with fibrosis (22).

Tuberculosis (TB) remains a leading global cause of death, even in the era of established anti-TB treatments. A recent systematic review found that more than 10% of cases of community-acquired pneumonia in Asia was caused by Mycobacterium tuberculosis. The clinical manifestations of Pulmpnary TB (PTB) and non-tuberculous pneumonia (non-PTB) are typically indistinguishable, thus prompt diagnosis of PTB as the cause of pneumonia may be delayed. In view of this, serum IFN-γ, and matrix metalloproteinases like MMP-1, MMP-9, and periostin levels could be useful markers for distinguishing between PTB and non-PTB. The matrix metalloproteinases (MMPs)

are responsible for turnover, degradation, and catabolism of the extracellular matrix, and MMP-1 and MMP-9 are reportedly associated with formation and cavitation of TB granuloma. Also, Periostin is a relevant ECM protein, which has been proven to drive Th2 inflammation in asthma and lung and idiopathic pulmonary fibrosis (IPF). Periostin is produced by fibroblasts and alveolar epithelial cells, which are known to play an active role in formation of TB granuloma. Periostin levels are higher in patients with PTB as well. So, the serum markers that differentiate between tuberculous and non-tuberculous pneumonia could be clinically relevant. A recent clinical data revealed that both PTB and non-PTB patients had higher levels of serum interferon gamma (IFN-γ), matrix MMP-1, MMP-9, and periostin (23).

Up-regulation of periostin expression was observed in nasal mucosa during allergic rhinitis and chronic rhinosinusitis (CRS), so it could be involved in the growth of nasal polyps (24), edema and mucus hypersecretion in nasal tissues. Patients with eosinophilic esophagitis were shown to have significant levels of periostin (25). Kanemitsu et al investigated the sputum of CRS patients who underwent endoscopic sinus surgery with and without comorbid asthma. The study findings showed that the increased levels of periostin, eosinophils and fractional exhaled nitric oxide (FeNO) were associated with olfactory dysfunction and eosinophilic nasal polyps. High serum periostin level is also associated with sub-epithelial fibrosis in allergic eosinophilic inflammation such as otitis media (26). Specimens from the middle ear of patients with eosinophilic otitis media (EOM) have been examined and the results showed that accumulation and immunoreactivity of periostinin the basement membrane enhanced eosinophil infiltration and mucosal thickness (27). Periostin is one of the most highly expressed genes involved in the pathogenesis and epithelial repair of CRS, and it has been found to play an active role in enhancing mucosal inflammation and eosinophilic recruitment. Ninomiya et al. performed RNA-sequencing and quantitative real-time PCR to identify gene expression in chronic rhinosinusitis with nasal polyps (CRSwNP) patients. Expression of POSTN gene was found to be the highest among the up-regulated genes (28). In addition, there is a significant correlation between serum periostin, blood eosinophils, serum IgE levels, and the comorbidity of sinusitis (29). Aspirin can exacerbate asthma, and one of the plausible mechanisms is the up-regulated periostin levels in respiratory mucosa (30). Table 1 depicts the potential role of periostin in the pathogenesis of various respiratory conditions.

Bronchial asthma

Bronchial asthma is a heterogeneous respiratory syndrome, characterized by persistent airway inflammation, mucus hypersecretion, mucosal thickening, and eventually airway remodeling and respiratory failure. Mechanical or physiological damage to the respiratory epithelium is attributed to exposure to multiple factors, such as environmental allergens and airborne pathogens, which can induce the expression of fibrotic factors such as periostin, TGF-β2, and vascular endothelial growth factor (31). House dust mites(HDM) sensitization could induce maximal T-cell hyper responsiveness in the airways epithelium of POSTN $^{+/+}$ compared to periostin-null mice (32). The pathogenic mechanisms of periostin in type 2 inflammation and bronchial airways remodeling include the following: (i) increasing periostin production in respiratory eosinophils and fibroblasts which is stimulated by IL-4, IL-13, and TGF-β; (ii) periostin binding to the integrin receptors triggers eosinophil trafficking and recruitment into the airway epithelium; and finally, (iii) periostin induces collagen production, mucus secretion, and airway remodeling and obstruction (33), as shown in Figure 1. The contribution of periostin in hypoalveolarization and interstitial fibrosis is explored in hyperoxic broncho pulmonary dysplasia (BPD) in neonatal mice. The study shows that hyperoxia could induce periostin accumulation in the alveolar walls compared to periostin knockout mice. Periostin expression in the lung mesenchymal stromal cells of human infants with BPD is also investigated in the same study, where BPD is significantly associated with increased level of periostin in the lung tissues (34).

In contrast, two studies provided evidence that the immunization and challenge of periostin-deficient mice with OVA or *Aspergillus fumigatus* resulted in increased peripheral Th2 responses and airway hyper responsiveness in mice, suggesting that periostin could have a potential protective effect on IgE-mediated allergy and airway hyper responsiveness (35,36). A recent study on adult Egyptian patients with asthma evaluated periostin levels in sputum samples. The findings suggest that higher periostin levels were significantly correlated

Table 1: Potential role of periostin in the pathogenesis of various respiratory conditions depicted in various animal and clinical studies.

Disease	Population	Specimen	Study findings
Asthma	Mice C57BL/6	Lung tissue, BALF	Reduced IL-4, IL-25, and periostin mRNA expression in POSTN-deficient mice compare with POSTN$^{+/+}$ mice treated with HDM (32).
	Mice, human infants	Lung tissue	Periostin knockdown limited hypoalveolarization and myofibroblast differentiation in neonatal mice. High periostin expression in the lung tissues of human infants with hyperoxic BPD (34).
	Patients with allergy and/or asthma	Blood	Periostin activated eosinophil recruitment and adhesion in the airway epithelium (41).
Idiopathic pulmonary fibrosis (IPF)	C57BL/6 mice	Lung tissue	Periostin-deficiency prevented the development of pulmonary fibrosis after bleomycin injury in mice (56).
	Human patients with IPF (aged 36-79 years)	Lung biopsy	Up-regulation of periostin expression in fibrotic lung parenchyma was triggered by fibrogenic cytokines such as TGF-β and IL-1 (58).
Lung cancer	Non-small-cell lung cancer A549 cells	Cell culture medium	Up-regulation of periostin in non-small-cell lung cancer A549 cells in response to hypoxia, which in turn promoted the survival of A549 lung cancer cells (65).
	Lung cancer patients	BALF	Proteomic analysis and ELISA assay of BALF showed increasing in periostin expression in all subtypes of lung cancers (67).
Other respiratory illness	TDI-OA patients	Serum	Periostin was involved in the progressive airway inflammation and decline in the lung function in TDI-OA (44).
	Infants < 36 months	Serum	Periostin and squamous cell carcinoma antigen were highly expressed during the pathogenesis of RSV-induced acute bronchitis (76).
	Mice, PH patients	Lung tissue	Periostin knockdown attenuated the development of PH in chronic hypoxia-induced PH mouse models. increased POSTN expression in the lung homogenates of PH patients (68).
	OSA Patient (aged 20-80 years)	Serum	Consistent increases in serum periostin in patients with severe obstructive sleep apnea (OSA) with albuminuria (77).

BALF, bronchoalveolar lavage fluid; IL, interleukin; HDM, house dust mite; BPD, bronchopulmonary dysplasia; TGF-β, transforming growth factor-beta; TDI-OA, toluene diisocyanate induced occupational asthma; RSV, respiratory syncytial virus. PH, pulmonary hypertension; OSA, obstructive sleep apnea.

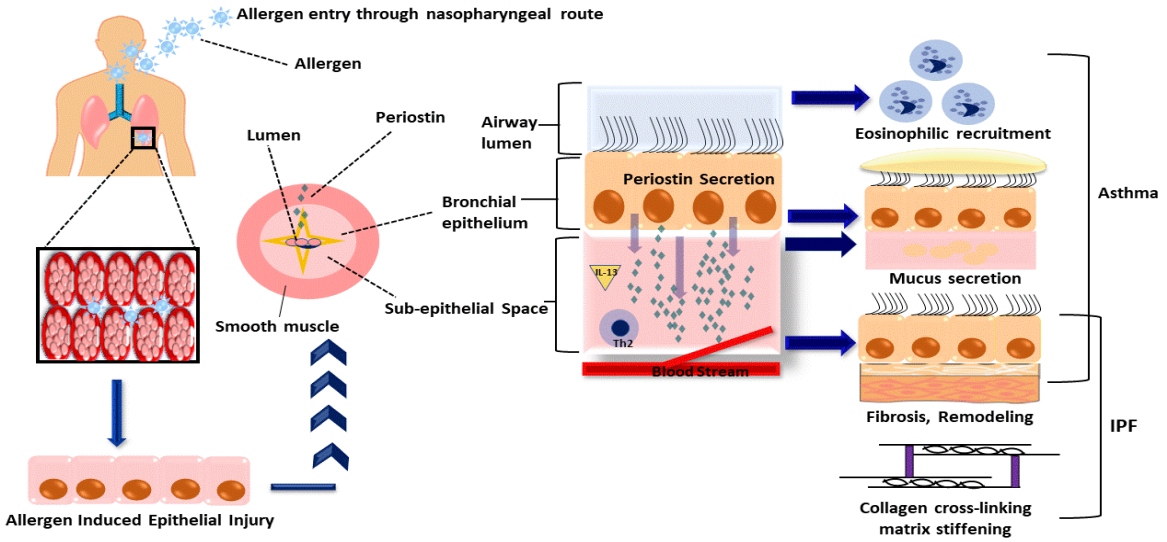

Figure 1: Pathogenesis of allergic asthma and idiopathic pulmonary fibrosis (IPF) in response to allergen-induced epithelial damage and the role of periostin.

with eosinophilic asthma and persistent airflow limitation (37). Similarly, another study demonstrated a mutual relation between sputum periostin, sputum eosinophils and persistent airflow limitations despite treatment with high-dose of inhaled corticosteroids compared to normal individuals (38). Moreover, higher serum periostin levels have been reported in patients with chronic cough and airway hyper-responsiveness than those suffering from chronic cough without airway hyper responsiveness(39). IL-4 and IL-13 play an active role in inducing periostin expression, and they share the same receptor and signal transduction pathways (40). Periostin is a chemoattractant mediator, promotes eosinophil recruitment and adhesion on the airway sub-epithelia membrane in asthmatic patients (41). A significant increase in serum periostin was discovered in patients with eosinophilic asthma(42). Therefore, periostin might be a potential biomarker to distinct eosinophilic asthma subtypes. A recent study evaluated the mutual correlation between the serum level of periostin and exercise-induced bronchoconstriction in asthmatic children. The study results demonstrated that the serum levels of periostin were significantly higher in asthmatic children with both positive exercise and positive mannitol bronchial provocation test (BPT) than in those with both negative mannitol BPT and controls. High periostin level was also associated with a maximum decrease

in forced expiratory volume (FEV1) (43). Periostin could play an essential role in the activation and recruitment of neutrophils and macrophages in a murine model of bleomycin-induced lung fibrosis (33). Chronic exposure to Toluene Di-isocyanate (TDI) can induce airway inflammation (Occupational asthma, OA). Individuals with TDI-OA have experienced a significant increase of serum periostin level, progressive airway inflammation, and a decline in lung functions (44). Fractional exhaled nitric oxide (FeNO), along with serum periostin, is a valuable non-invasive indicator for predicting lung function decline in individuals with severe asthma (45). In another study, serum periostin, blood eosinophils, and FeNO levels were higher in children with asthma than in control subjects (46). Furthermore, biopsy samples from asthmatic patients have been examined, and the histopathology reports showed that a higher periostin level in the lung tissues was positively associated with lung function decline (47). Both children and adult patients with exacerbated asthma had higher levels of serum periostin than those with stable asthma and healthy controls (48,49). In contrast, the results of a cross-sectional study (ACTRN12614000122651) on asthmatic Chinese population showed that the serum periostin could not differentiate between asthmatics and non- asthmatics (50). Moreover, studies have shown that there is no correlation between serum periostin level and allergic diseases, so periostin has limited usefulness as a predictor of allergic asthma (51,52). Based on these findings, periostin is considered as an active mediator that can hasten Th2 inflammation and trigger airways remodeling in acute exacerbation of asthma. Therefore, much attention should be given to this field of research.

Idiopathic pulmonary fibrosis

Fibrosis is a pathological wound healing after chronic inflammation or tissue injury. It is characterized by excessive deposition of collagen and fibronectin (53). IPF is a progressive lung disease of unknown cause that has a three- to five-year life expectancy (54). As it turns out, periostin plays a key role as a fibrotic and growth factor. Hence, it is involved in the cellular mechanisms of abnormal alveolar repair and sub-epithelial fibrosis in bronchial asthma. It has been reported that POSTN gene is highly expressed in the thickened airway epithelium of IPF patients (55). An *in vivo* study evaluated the pathological mechanism of periostin in lung fibrosis model in mice. The study findings revealed that a genetic deficiency of periostin protected mice from pulmonary fibrosis after bleomycin administration, which was attributed to impaired production of cytokines by periostin-deficient fibrocytes(56). TGF-β, a fibrotic factor, upregulates POSTN gene, which in turn induces the production of type I collagen in the lung fibroblasts and reduces airway distensibility (57). Periostin plays a pivotal role in the production of chemokines in pulmonary fibroblasts, and its serum level could predict early progression of IPF at 48 weeks (53). An *in-vitro* study demonstrated that periostin knockdown could inhibit the production of chemokines in the lung fibroblast in response to TNF-α administration compared to control cells. Additionally, periostin deficiency in mice could inhibit neutrophils and macrophages recruitment and decreased periostin expression after bleomycin administration (33). Fibrogenic cytokines, such as TGF-β and IL-13, may contribute to enhance periostin expression in the fibrotic lung parenchyma (58). In a clinical study, serum periostin level was

found to be a reliable predictive biomarker of shortened overall survival (OS) and time to event (TTE) in IPF patients after long-term follow-up (59). Bacterial infection or changes in the pulmonary microbiome can promote periostin release in the alveolar wall. A cell line study evaluated the immunomodulatory and anti-fibrotic effects of clarithromycin through down-regulation of periostin expression induced by IL-13 in human lung fibroblasts (60). Ohta and colleagues have developed a new diagnostic kit to detect monomeric serum periostin, which is more specific to IPF. They found that the efficacy of monomeric periostin in diagnosing IPF and predicting its short-term progression was superior to oligomeric (total) periostin and conventional biomarkers such as KL-6, SP-D, and LDH (61). periostin gene knockdown of the lung fibroblasts significantly reduced the expression of transcription factors and cell cycle regulators, such as cyclin and cyclin-dependent kinase (CDK) (62).

Periostin is one of the reliable biomarkers that properly define the clinical stage of pulmonary sarcoidosis. Higher plasma periostin levels have been observed in patients with sarcoidosis compared to healthy subjects(63).

Lung cancer

Periostin is over expressed in many epithelial malignant cancers, including lung cancer. Periostin is being studied as a biomarker and therapeutic target in lung cancer. POSTN gene was recognized as one of the divergent genes that promote metastatic tumors(64). It has been shown that periostin, TGF-β, and basic fibroblast growth factor (bFGF) have increased the survival of A549 cells, and they were highly expressed in non-small cell lung cancer (NSCLC) as a response to hypoxia (65). The mean serum periostin level was higher in NSCLC patients than in healthy participants (66). This molecular pathway might open a window and be a target for lung cancer treatment. A clinical trial conducted by Nakamura et al (UMIN000012339) demonstrated that periostin and squamous cell carcinoma antigen were highly expressed during the pathogenesis of acute bronchitis caused by respiratory syncytial virus (RSV), and they were associated with the subsequent development of asthma. In a recent study, proteomic analysis, and ELISA assay of periostin in BAL fluid of lung cancer patients showed increasing periostin levels in all subtypes of lung cancer (67).

Pulmonary hypertension

Vascular remodeling is one of the histopathological features of the small pulmonary arteries leading to pulmonary hypertension (PH). Significant increases in periostin levels in the pulmonary arterioles and vascular endothelium have been reported in hypoxic patients with PH. Knockdown of periostin attenuated the development of PH induced by chronic hypoxia in mice via improvement the hemodynamic and cardiac responses and reducing the release of ET (endothelin)-1, hypoxia-inducible factor (HIF-1α), and vascular endothelial growth factor (VEGF) in the pulmonary artery smooth muscle cells (68).

Chronic Obstructive Pulmonary Disease (COPD)

Type 2 - driven eosinophilic inflammation is more common in asthma, but COPD is suspected to have different pathogenic mechanisms and characterized by Th1 inflammatory response. Data from a clinical study demonstrated that COPD smokers and former-COPD smokers had greater serum periostin than normal smokers. Higher periostin levels have been observed in both tobacco smoke- as well as bio-mass cooking-induced COPD compared to healthy controls. But no association was observed between periostin levels, inflammatory cell counts and lung function (69). Periostin level in asthmatic patients was found to be higher than in those with COPD (70). While little information exists about the implication of periostin in COPD, it's potential as a surrogate biomarker in this population is still questionable.

PERIOSTIN AS A PREDICTIVE BIOMARKER IN RESPONSE TO ASTHMA THERAPY

Accumulating evidence acknowledged the potential role of periostin as a validated biomarker predicting the response to the treatments targeting type 2 cytokines in asthma. A study has shown that periostin level had the best variable predictive in identifying the patients who got maximum benefit after lebrikizumab treatment when compared to other inflammatory markers(71). Researchers analyzed the serum level of periostin, FeNO, and peripheral blood eosinophil count as potential markers during Th2 inflammation and predictors for response to omalizumab treatment in allergic asthma patients. The results revealed that periostin-high subgroup (serum periostin level >50 ng/ml) experienced a

decreased rate of severe exacerbations compared with periostin-low group(72). Another clinical study investigated the association between serum periostin level and progressive lung function decline in asthmatic patients using ICS therapy. The study findings showed that increased serum periostin was associated with greater airflow limitation, confirming the potential role of serum periostin as a reliable biomarker for the progressive decline in the lung functions in patients with corticosteroid-resistant asthma (73).

Several studies have shown that increased serum periostin is correlated with high blood and sputum eosinophilia and high FeNO in severe asthma attacks and ICS-resistant asthma patients, suggesting its great potential not only as an ideal marker, but also for categorizing asthma patients as well as predicting the effect of corticosteroid therapy in asthma (74).

CONCLUSION AND PERSPECTIVES

Periostin is an essential component of the ECM and maintains the normal tissue matrix in the lungs. Abnormalities in periostin expression can contribute significantly to the pathogenesis of several chronic respiratory diseases. Periostin expression in the respiratory epithelium is substantially regulated by the Th2 cytokines IL-4 and IL-13. POSTN gene expression in the airway epithelial cells is associated with increasing serum IgE, systemic and bronchial eosinophilia, and increasing the thickness of the reticular basement membrane (25,36). Periostin level is considered a useful diagnostic tool for discriminating the different asthma endotypes and predicting the progression of the disease. Current and ongoing clinical studies continue to explore the role of periostin as a potential biomarker of therapeutic responses in asthmatic patients. Periostin drives several pathophysiological features of IPF, including myofibroblast differentiation, type 1 collagen production, and cross-linking of fibers within the lung matrix. Periostin is present in high concentrations in serum, bronchoalveolar lavage fluid and other biological samples, and can be easily measured by immunoassay (ELISA). Serum periostin is an ideal blood biomarker of Th2 high asthma and had a higher sensitivity and specificity when compared to blood and sputum eosinophils. Thus, periostin could be used in developing asthma therapeutics targeting eosinophilic phenotype of asthma in the future (75).This review highlights the underlying mechanisms and effects of periostin, as well as its potential prognostic and diagnostic function in various respiratory disorders and specifically in bronchial asthma. It has various distinct features that are highly associated with lung tissue remodeling and fibrosis. Further research in this field is ongoing to ascertain the crucial and specific roles of periostin as a therapeutic target and potential biomarker in pulmonary diseases. However, the specificity of periostin as a biomarker for bronchial asthma remains unclear, and though some of the evidence generated through randomized clinical trials looks promising, more quality data needs to be generated. This is probably also the reason that it is still not used in the clinical setting to help in the diagnosis and/or progress of treatment in bronchial asthma. Nevertheless, in view of the increasing interest generated in this protein in recent years, it is anticipated that further clinical and experimental studies in the specific field, may help to redefine the position of periostin as a biomarker in asthma. Further, a single chemical entity/physiological parameter is rarely considered as an absolute biomarker for any specific disease. For example, in obstructive airway diseases like asthma and COPD, pulmonary function test findings are complimented by biomarkers like FeNO, Serum IgE, absolute eosinophil counts, etc. Thus, it is likely that periostin could also play a similar role in bronchial asthma**.**

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