

Bronchial Asthma and Salivary Surfactant Protein D: Review Article

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ABSTRACT

Background: Chronic bronchial inflammation underlies asthma, which is a complex disease with varied and largely reversible blockage of the respiratory route. Asthma is a major public health issue that affects people of all ages around the world. Many countries are seeing an increase in the prevalence of this disease, particularly among children. Among children, asthma is the most frequent long-term condition, accounting for more than half of all missed school days, emergency room consultations, and hospitalizations. Surfactant Protein D, a pattern-recognition molecule, dampens elevated levels of particular antibodies, alveolar macrophage accumulation, eosinophilia, and subepithelial fibrosis and mucous metaplasia, as well as airway hyper-reactivity in allergic asthma in vivo.

Objective: In order to discover the connection between children's bronchial asthma and surfactant protein D.

Conclusion: Salivary SP-D is a simple, low-cost, quick, and noninvasive way to collect saliva from children. Salivary SP-D levels may be linked to asthma exacerbation severity and peripheral airway resistance.

Keywords: Bronchial asthma, Surfactant protein D, Pediatrics.

Bronchial asthma in pediatrics:

Asthma incidence has increased significantly over recent decades, and geographic variation is evident in both the baseline prevalence rate and the extent of the increase. These findings lend credence to the idea that current asthma epidemics may be linked to environmental factors. Studies on asthma risk factors must take into account genetic, environmental, and host factors. Having an asthmatic parent or sibling is not a guarantee that kid will develop asthma ⁽¹⁾.

Salivary Surfactant Protein D:

In the collectin family of C-type lectins, the pattern-recognition molecule surfactant protein D. Surfactant protein A (SP-A) is a human collectin with a tissue distribution and activities that largely coincide with those of surfactant protein D (SP-D). It increases phagocytosis of microorganisms and dying host cells by aggregating and enhancing phagocytosis. Mannan-binding lectin (MBL), another member of the collectin family of proteins that activates complement via the lectin route in association with MBL-associated serine proteases, is another example of a typical member of the collectin family ⁽²⁾.

It has been found that SP-D is found in both pulmonary as well as non-pulmonary tissue. These epithelia and glands have the protein attached to their luminal or outer surfaces in order to function properly. Since most of the places where it is expressed are at the interfaces with blood, tears, cerebrospinal fluid, amniotic fluid, and urine. SP-D participation in pattern recognition would explain this. Non-pulmonary SP-D expression locations may create materials that resemble surfactant, and phospholipid lubrication can be found in a variety of different places throughout the human body. Because it controls the amount of pulmonary surfactant lipids, SP-D has a critical function in the lungs, and although this has not been studied, it has been

hypothesized that SP-D also plays a role in phospholipid homeostasis beyond the lungs ⁽³⁾.

Effects of SP-D:

Researchers have found that SP-D can attach to a wide range of microbes, including bacteria, viruses, fungi, and most recently, helminthic parasites, allowing them to be removed via opsonization and phagocyte recognition ⁽⁴⁾.

Nayak et al. ⁽⁵⁾ conducted a comprehensive assessment of SP-various D's interactions with pathogenic microorganisms.

Other biological or abiotic particles can also be attracted to SP-D, allowing it to aid in their removal from the airways and other possible locations for exposure. There is evidence to support the claim that SP-D can help to clear allergens and apoptotic material from the body, as well as aggregate and remove particle detritus. It has also been shown to impact the intestinal microbiota of mice in several experiments ⁽⁶⁾.

Antimicrobial properties of SP-D include opsonization for phagocytosis as well as aggregation. It is possible that this will increase the effectiveness of neutrophil extracellular traps, neutralization of infectiousness, bacterial and fungal cell membrane destruction, and suppression of innate signals caused by pathogens ⁽⁷⁾. The increased phagocytosis and antibacterial activity of SP-D are advantageous to the host. An increase in the burden of pathogens and the progression of disease may be facilitated by SP-D binding to the pathogen ⁽⁸⁾.

Determinants of SP-D Levels:

Variations in BAL or circulatory SP-D levels are linked to lung disease, according to a number of studies employing disease-selected cohorts ⁽⁹⁾. Furthermore, in a homogenous Caucasian population, factors such as gender, smoking, body mass index, and age were found



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to be key drivers of constitutional levels of circulating SP-D; however, research on age-induced changes in SP-D levels is mixed. Reduced alveolar SP-D levels have been linked to increased oxidative damage in rat studies (10).

SP-D in respiratory illness:

When high amounts of SP-D are present, as well as genetic variations in SFTPD, a variety of lung problems begin, progress, and worsen. The difference in constitutional SP-D levels varies by a factor of 30 or more (11). Because of this, disease-induced serum levels and control levels may be extremely similar. While disease-induced levels in prognosis are important, the link between serum SP-D and mortality in pulmonary illnesses such as COPD and fibrosis is highlighted by acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) (12).

Relation between SP-D and Asthma:

Genetic Association:

Despite the fact that structural SP-D polymorphisms aren't linked to allergic BA, they were linked to less atopy in black people (13).

Association between Phenotypes:

Several investigations have demonstrated that asthmatic patients have systemic SP-D or elevated BAL level that could be attributed to high SP-D production on the airway epithelia (14). As a result, there is a connection between SP-D levels and BAL eosinophils, as well as a connection between the NO content of BAL and oxidized SP-D species in allergic asthma patients' BAL samples. Levels of SP-D may increase further after segmental allergen challenge (15).

In one of the earliest studies of serum SP-D, **Akiki et al.** (16) found no link between asthma and SP-D variation.

Disparities in the prevalence of moderate and severe asthma between studies could account for these findings. For example, pulmonary allergies and allergic rhinitis show an enrichment in serum SP-D and This is viewed as happen in a disease process that is like asthma. SP-D and T helper 2 cell (Th 2)-mediated inflammation are also linked, according to preliminary study (17).

It is possible that discrepancies in clinical observations are because approximately half of all people with steroid naive asthma have a Th 2-high allergic asthma phenotype. **Mackay et al.** (18) research suggests that neutrophilic inflammation or pathogenic load has an effect on this (18).

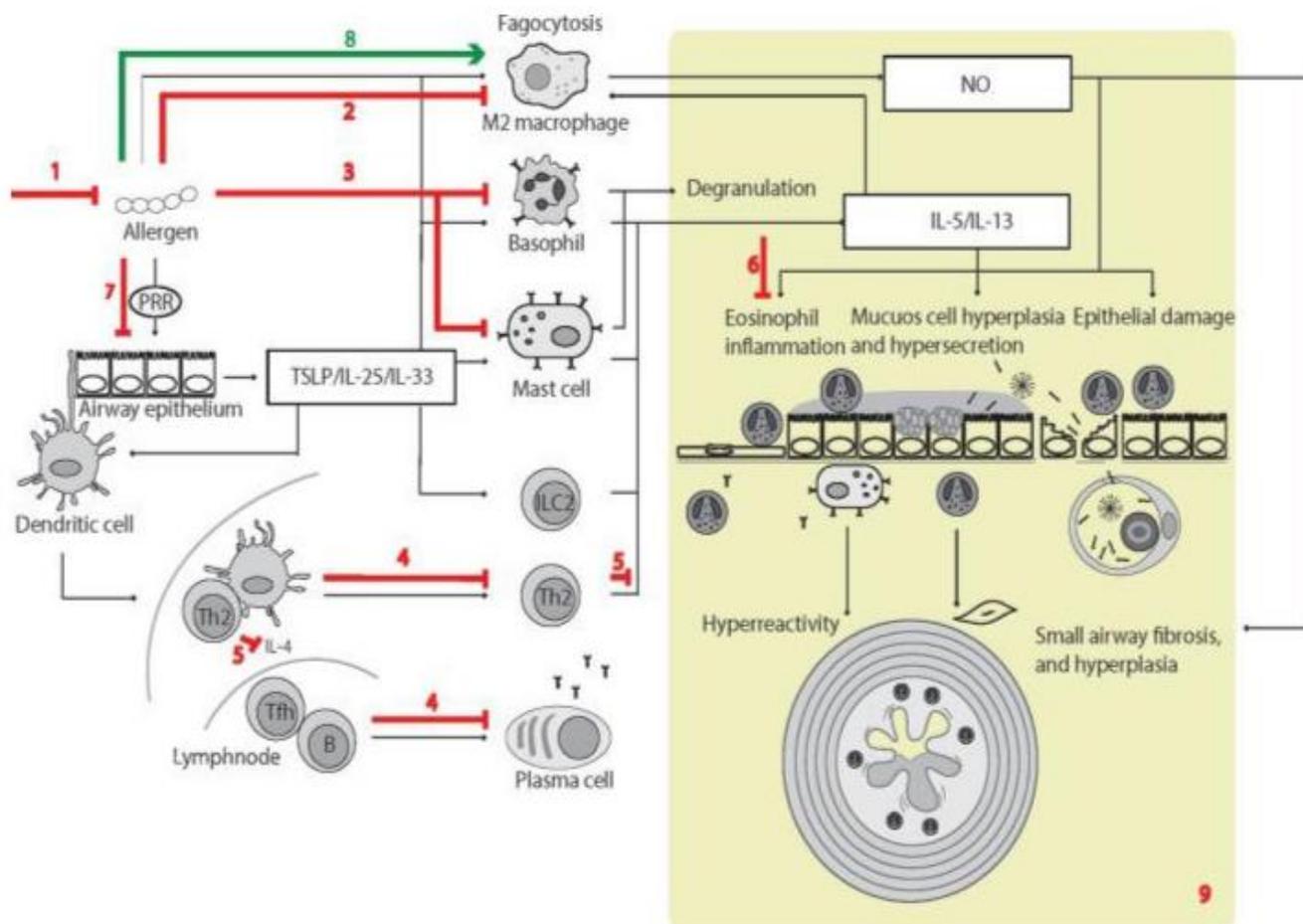


Figure (1): Effects mediated by SP-D in allergic experimental asthma (19).

A few outcomes are still up in the air. In vitro, SP-D can enhance the number of pollen starch granule

(PSG)-positive cells, and in vivo, it can speed up PSG binding and uptake. In contrast, investigations

conducted by **Winkler *et al.*** ⁽²⁰⁾ indicated that it had no effect on the total clearance of PSGs from the mouse lung, nor did it increase T-cell proliferation in response to PSG-positive dendritic cells. Because of this, further examination into the differences in results acquired utilizing human cell cultures or clinically separated cells as compared to those obtained using mice models is required.

Effect of SP-D in Asthma:

The multiple effects of SP-D include reduction of IgE binding to allergens, inhibition of allergen-induced histamine release by basophils and inhibition of allergen-induced mast cell degranulation. Furthermore, allergy elimination via aggregation and alveolar macrophages' binding and absorption of allergens, allergy-induced macrophage reduction of M2 polarization, inhibition of IL-2 release by peripheral blood mononuclear cells, lymphocyte proliferation, and apoptosis induced by CTLA4-dependent T-lymphocytes and reduction of IL-4 and IL-13 production by lymphocytes. However, SP-D dampens epithelial chemotactic signals while increasing allergen contact with the respiratory epithelium, SP-D has dampened eosinophilia, alveolar macrophage buildup, elevated levels of particular antibodies, airway hyper-reactivity, subepithelial fibrosis, and mucous metaplasia in allergic asthma in vivo, among other effects ^(21, 22).

SP-D may play a new role in Th 2 immunity, according to research on the parasite *Nippostrongylus brasiliensis*. There is a correlation between the enhanced SP-D synthesis in Th 2 cells and the production of the interleukin 4 and the interleukin 13 cytokines. When it comes to *N. brasiliensis* infections. However, where SP-D might exert negative feedback control on Th 2 responses, researchers discovered higher type 2 immunity in allergic asthma studies in Sftpd^{-/-} mice. SP-D increases type 2 immunity and serves as a critical regulator of protective anti-*N. brasiliensis* alveolar macrophage and type 2 innate lymphoid cell-mediated IL-13 production, according to the research findings ⁽⁴⁾.

Advantages of salivary SP-D:

Salivary glands, alveolar epithelial cells, and Clara cells without cilia all make SP-D, which is secreted into the bloodstream and circulated throughout the body. Asthmatics' small salivary glands show airway-like inflammation in glandular tissues ⁽⁵⁾.

CONCLUSION

Salivary SP-D is a simple, low-cost, quick, and noninvasive way to collect saliva from children. Salivary SP-D levels may be linked to asthma exacerbation severity and peripheral airway resistance.

Conflict of interest: Nil.

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