

CORRESPONDENCE

Serum IL-23: a surrogate biomarker for asthma?

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Guan and colleagues conducted an experimental study using the murine model to investigate the potential role of an IL-23p40 peptide-based vaccine in reducing skin and airway allergic inflammation [1]. Even though this study is obviously still early for human application, we would like to take advantage for underlining the relevant role of the Th17 pathway in allergic disorders. A very recent Review emphasized the importance of the asthma phenotypes, mainly considering the cytokines profiles involved in the pathogenesis of severe asthma [2]. In this regard, a Th17 phenotype might define patients with severe asthma associated with neutrophilic infiltrate. It is of note that Th17-associated cytokines may be subdivided as inductive (IL-6, TGF- β and IL-23) and effector (IL-17A, IL-17F, IL-21 and IL-22). The last are typically able of inducing neutrophilic infiltrate in airways. However, it has been demonstrated that may induce also chronic inflammatory events.

Recently, a growing list of chronic inflammatory disorders has been linked to Th17 involvement. In this regard, the recent progresses in characterizing the pro-inflammatory IL-17 cytokine family have added an additional layer of complexity on the regulation of allergic inflammation [3]. In addition, IL-17A may play a role in the development of various allergic diseases that have been classically considered to be Th2-mediated disorders [4]. Moreover, IL-17A may be a new biomarker of disease progression and allergy severity, as recently evidenced in patients with allergic rhinitis [5, 6]. In addition, *in vitro* evidence has been provided that allergens are capable of inducing expansion of Th17 cells [7]. Therefore, the Th17 pathway could be considered a relevant player in the allergic inflammatory cascade. Overall, serum IL-17 could be measured as a possible surrogate marker for assessing the degree of inflammation intensity [5].

On the other hand, an adjunctive role might be outlined for IL-23. In fact, IL-23 may be an adjunctive Th17-associate cytokine involved in the worsening of inflammatory phenomena. A possible explanation might be that IL-23 might modulate allergic inflammation influencing Th2 differentiation [8]. Therefore, also the

measurement of IL-23 could be interesting in the management of patients with asthma, mainly assessing the serum levels. In this regard, it has been initially reported that serum IL-23 levels were significantly higher in children with asthma than in healthy well-matched controls [9]. More incisively, a strong and inverse relationship ($r = -0.787$) between serum IL-23 levels and FEV₁ values in the asthma group has been demonstrated. This finding suggested that serum IL-23 could be viewed as a suitable marker of bronchial function impairment in children with allergic asthma. Furthermore, a clinical study with the aim of investigating the possible effect of a 1-month course of inhaled budesonide (200 mcg twice daily) on serum IL-23 levels in a group of 85 children with asthma was designed [10]. The findings showed that corticosteroid was capa-

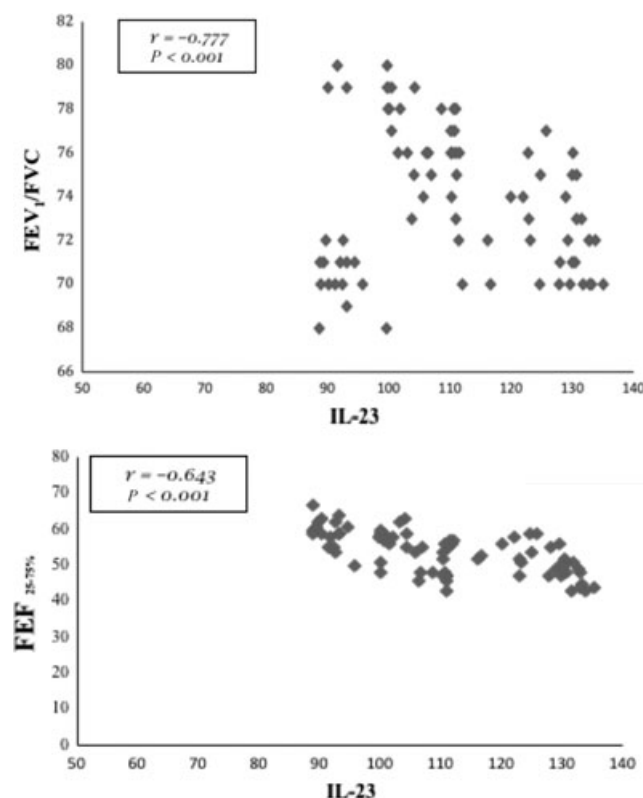


Fig. 1. Relationship between serum IL-23 levels and FEV₁/FVC ratio (upper quadrant) and FEF₂₅₋₇₅ values (lower quadrant) in children with asthma.

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ble of significantly diminishing serum IL-23 levels. In addition, the IL-23 change was significantly associated ($r = -0.583$) with lung function improvement. This study therefore confirmed the relevance of considering the Th17/IL-23 pathway in the management of patients with asthma.

On the other hand, there is consensus that FEV₁ may be within the normal range in persistent asthma, mainly in children, when stable [11]. On the contrary, a more reliable parameter for detecting bronchial airflow limitation could be the FEV₁/FVC ratio. In addition, the forced expiratory flow at 25–75% of the vital capacity (FEF_{25–75}) might be another suitable marker of initial bronchial obstruction [12]. For this reason, we initially investigated whether there is a relationship between serum IL-23 levels and the FEV₁/FVC ratio and FEF_{25–75} values in a group of 80 steroid-naïve children (44 boys,

mean age 9.8 years) with allergic asthma and sensitized only to house dust mites. This preliminary study showed that there were strong and inverse relationships between serum IL-23 levels and FEV₁/FVC ratio, as well as FEF_{25–75} values ($r = -0.776$; and $r = -0.643$ respectively), as shown in the Fig. 1. Therefore, this study confirms the previous report [9] and underlines the clinical relevance of IL-23 measurement. All these findings are consistent with the experimental trial published in this journal [1], highlight the role exerted by the Th17/IL-23 pathway in airway inflammation and airflow obstruction, and shows that corticosteroids are capable of diminishing IL-23 production.

In conclusion, Th17 pathway may be relevant in asthma, and serum IL-23 could be considered an adjunctive surrogate biomarker in assessing asthma severity and airflow obstruction.

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