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EDITORIAL

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Editorial comments on "Multiarray screening identifies plasma proteins associated with Th17 cell differentiation and viral defense in coincident asthma and obesity"

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The clinical associations between asthma and obesity remain poorly understood. The increasing prevalence of both conditions occurring may represent a modern clinical paradox. It is unclear whether reduced physical activity in children with asthma leads to obesity, or if asthma-like symptoms in obese children result directly from the associated excessive abdominal fat, impaired lung function, and heightened Th2 inflammation. Determining the etiology of both diseases and their interconnection is therefore an important research avenue.

A recent study has sought to investigate this through a cross-sectional analysis of Australian children, both with and without asthma, examining their levels of physical activity. Interestingly, the study found no evidence that asthma hindered physical activity.[1] On the other hand, although most studies have shown obesity is linked to a higher risk of asthma, the exact mechanism remains unclear. Many studies refer to obesity as an exacerbation factor for asthma symptoms rather than a direct contributor to the underlying pathophysiological mechanisms of asthma.[2] This highlights the need for continued research to untangle the complex interplay between these two conditions.

In 2019, a study investigating the associations between exposure to endocrine-disrupting chemicals and childhood asthma identified a specific pattern of volatile organic compounds that were significantly linked to the early onset "obese-asthma" phenotype, but not to asthma or obesity independently.[3] This suggests that asthma and obesity may share common risk factors that trigger disease onset of both conditions during early childhood. Supporting this hypothesis, subsequent research has identified 29 genes associated with the obese-asthma phenotypes, including *GBP5* and SOCS, which further highlights the genetic underpinnings of this dual condition.[4]

In this issue, Manell et al. offer valuable insights by investigating novel plasma protein biomarkers specifically associated with the coexistence of asthma and obesity in an adolescent population.[5] The cross-sectional study involved 390 children and adolescents, aged 10 to 19, who were categorized into four groups: healthy controls, individuals with asthma, individuals with obesity, and those with both obesity and asthma (OA).

A proximity extension assay was used to assess the relative plasma concentrations of 113 proteins associated with inflammation and immune response. The study identified five plasma proteins—CCL8, IL-33, IL-17C, FGF-23, and CLEC7A—that were significantly and specifically elevated in the OA group compared to controls. However, after adjusting for age, sex, and sIgE levels, only CCL8 and CLEC7A remained significantly elevated. This suggests that the high levels observed for IL-33, IL-17C, and FGF-23 in the OA group may be partially attributable to atopy.

Drawing on previously published evidence and considering the role of CCL8 in mucosal chemotaxis and Th2 inflammation, Manell et al. propose that viral defense at mucosal barriers may play an important role in obesity-related asthma in children and adolescents.[5] While the exact pathophysiological mechanism behind CCL8 overexpression remains unclear, it is noteworthy that prior studies have confirmed no association between CCL8 and atopy.[6] This, along with the evidence that CCL8 levels are regulated in obese individuals without asthma, strengthens the argument for this chemokine as a promising biomarker for obese-asthma phenotypes.

Additionally, FGF-23, IL-17C, and IL-33, which are linked to mucosal host defense against viral infections and Th17 cell activation, were also regarded as potential biomarkers for concomitant asthma and obesity, though to a lesser extent.[5] Conversely, the elevated levels of CLEC7A in the OA group appear to be additive, reflecting the combined effects of asthma and obese observed separately.

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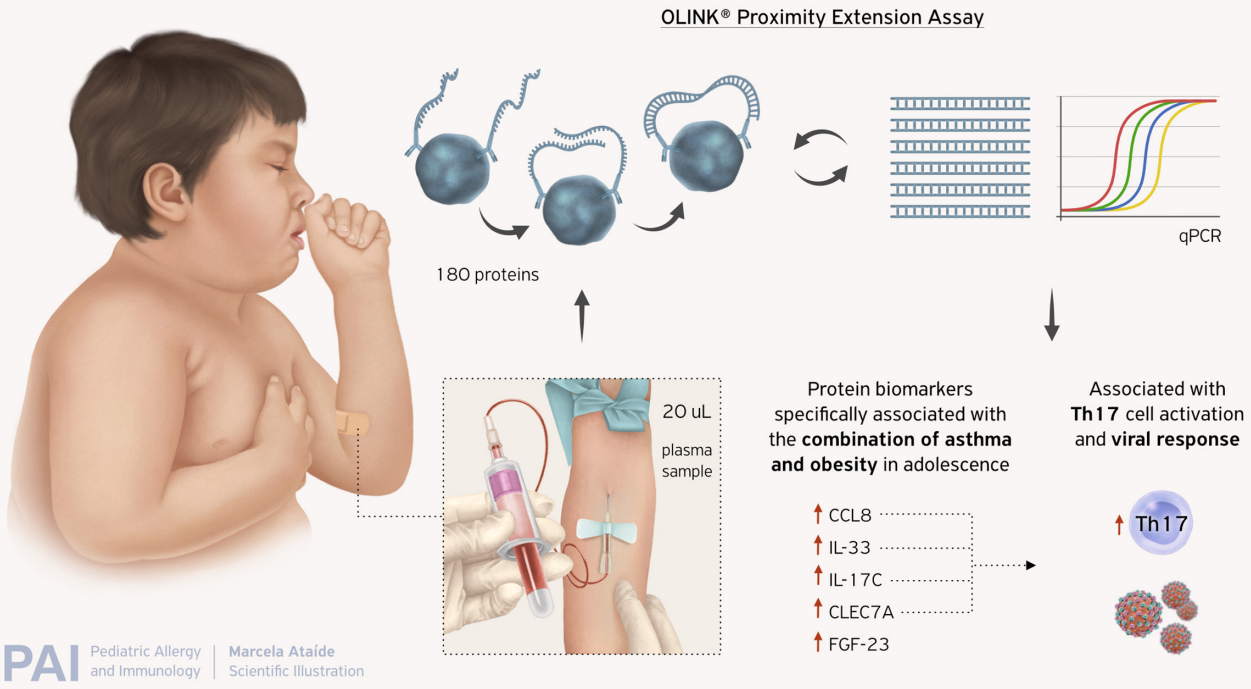
Multiarray screening identifies plasma proteins associated with Th17 cell differentiation and viral defense in coincident asthma and obesity



The work presented by Manell et al. provides a strong foundation for further elucidation into the obesity-asthma relationship and may offer critical insights toward establishing a cohesive pathophysiological explanation for the obese-asthma phenotypes.

AUTHOR CONTRIBUTIONS

João Cavaleiro Rufo: Conceptualization; writing – original draft. **Jitesh Chauhan:** Writing – review and editing. **Ömer Kalayci:** Supervision; writing – review and editing. **Philippe Eigenmann:** Conceptualization; writing – review and editing.

CONFLICT OF INTEREST STATEMENT

None.

PEER REVIEW

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