

Director of the Dermatology STAR Residency at UCLA's David Geffen School of Medicine, for his opinion and suggestions.

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Conflicts of interest: The authors declare they have no conflicts of interest.

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Early life regulation of inflammation in atopic dermatitis by microRNA

DOI: 10.1111/bjd.19475

Linked Article: Nousbeck et al. *Br J Dermatol* 2021; **184**:514–523.

In this issue of the *BJD*, Nousbeck et al. explore the expression of microRNAs (miRNAs) in different blood compartments, and postulate their use as noninvasive biomarkers for paediatric eczema.¹

miRNAs are groups of short (21–24 nucleotides) noncoding RNA molecules, controlling gene expression at the post-transcriptional level.² Even though they are never translated to

protein themselves, miRNAs critically regulate key biological processes, including cell cycle progression and death, differentiation, maturation and activation of immune cells. Importantly, as miRNAs can be detected in different cell-free body fluids, such as serum, plasma, urine, tears, saliva and amniotic fluid, their expression levels have been previously used as diagnostic and prognostic markers in various cancers, tissue injury and inflammation.^{3,4} Aberrant expression of miRNAs has been also reported in inflammatory skin diseases, including psoriasis, systemic sclerosis and lupus.^{4–6}

Investigations into the expression of miRNAs in atopic dermatitis (AD) are timely, as they have been shown to be important regulatory factors in other T-helper (Th) 2-driven inflammatory conditions such as asthma, allergic rhinitis and eosinophilic oesophagitis.⁷ While some reports have examined miRNAs in adult AD, their precise role in the regulation of initiation of AD has yet to be established.

Using HTG-Edge sequencing, Noursbeck et al. report the presence of miRNAs in AD vs. controls. Importantly, the authors identify 10 miRNAs that are expressed differentially in AD, including miRNAs important in the regulation of inflammation (miR-233-3p, miR-126-5p and miR-143-3p). This work uncovers a distinct peripheral blood miRNA signature for paediatric eczema. These differences in expression levels may serve as promising novel biomarkers for the early diagnosis of AD.

These findings corroborate and extend the list of miRNAs dysregulated in AD documented in previous observational studies.^{7–9} Excitingly, the authors found that differential expression of miRNAs in the blood of patients with AD also translates to downstream functional changes in the expression of proinflammatory molecules, corroborating the importance of miRNAs in the development of AD. Previous reports indicate a regulatory role of miRNAs in AD. miR-155, associated with CD4⁺ T cells in patients with AD and increasing after exposure to staphylococcal superantigen, contributes to chronic skin inflammation by increasing the proliferative response of Th cells through the downregulation of cytotoxic T-lymphocyte-associated protein (CTLA)-4.⁸ In contrast, miR-146a is increased in keratinocytes from patients with AD and mediates the anti-inflammatory effect in late AD by controlling nuclear factor kappa B-dependent inflammatory responses in keratinocytes.⁹

Specifically, dysregulation of miR-451a, another negative regulator of inflammation, was identified as a diagnostic biomarker in early life AD. In addition, the authors confirm that targets for miR-451a – PSMD8 (proteasome 26S subunit, non-ATPase 8) and interleukin 6 receptor – were increased in AD and negatively correlated with miR-451a levels.

While the principal limitation of the report by Noursbeck et al. is the small sample size, these findings warrant further investigation. Indeed, that markers of inflammation in the blood correlate with early life diagnosis of AD and may act as diagnostic biomarkers demonstrates the systemic nature of the inflammation in AD. Taken together, this work suggests that targeted therapy to achieve disease modification in AD, and potentially other associated comorbidities such as asthma and

allergy, may need to address miRNA dysregulation at a systemic level.

Acknowledgments: Thanks to Associate Professor Michael Ardern-Jones for critically reviewing this commentary.

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Conflicts of interest: The author declares no conflicts of interest.

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