**Early life regulation of inflammation in AD by microRNA**

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In this issue of BJD Nousbeck and colleagues explore the expression of microRNAs (miRNAs) in different blood compartments, and postulate their use as non-invasive biomarkers for paediatric eczema (1).

MiRNAs are a group of short (21-24 nucleotides) non-coding RNA molecules, controlling gene expression at post-transcriptional level (2). Even though 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 for diagnostic as well as 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 (5) systemic sclerosis (6) and lupus (4).

Investigations into miRNAs expression in AD are indeed very timely, as they have been shown to be important regulatory factors in other Th2 driven inflammatory conditions such as asthma, allergic rhinitis and eosinophilic esophagitis (7). Whilst some reports have examined miRNAs in adult AD, their precise role in the regulation of initiation of atopic dermatitis has yet to be established.

Using HTG-Edge sequencing Nousbeck et al report the presence of miRNAs in AD versus controls. Importantly, the authors identify 10 miRNAs which are expressed differentially in AD including miRNAs important in inflammation regulation (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 a promising novel biomarkers for the early diagnosis of AD.

These findings not only corroborate and extend the list of miRNAs dysregulated in AD documented by previous observational studies (7–9). Excitingly, the authors document that differential expression of miRNAs in blood of AD patients also translates to downstream functional changes in expression of pro-inflammatory molecules, corroborating the importance of miRNAs in development of AD. Previous reports indicate the 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 T(H) cells through the downregulation of CTLA-4 (8). In contrast, miR-146a is increased in keratinocytes from patients with AD and mediates anti-inflammatory effect in late AD 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 and IL6R were increased in AD and negatively correlates with miR-451a levels.

Whilst the principal limitation of Nousbeck’s report is the small sample sizes, 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.

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